IHC and ISH
2010 Product Range
Including Novocastra™ and Bond™ Reagents

Living up to Life
All Novocastra products are listed with their product code and additional information (e.g. clone designation), product type (Kit, Primer Set, etc.), and volume or a guide to the number of tests in one or more of the recommended applications. The first letters of the product code indicate the product type:

- **NCL** Concentrated Primary Antibody, Probe or Miscellaneous Product
- **RTU** Ready-to-use Primary Antibody
- **RE** Manual Detection (Complete System or Individual Component) or Ancillary Reagent
- **PB** Bond ISH Probe
- **AR** Bond Ancillary Reagent
- **DS** Bond Detection System

Bond ready-to-use products include the product code, clone designation (where appropriate) and product size.

- **PA** Bond Ready-to-use Primary Antibody
- **PB** Bond ISH Probe
- **AR** Bond Ancillary Reagent
- **DS** Bond Detection System

Origin products include the product code, number of tests and the clone. All Origin product codes start with “ORG”.

All antibodies, unless otherwise stated, are reactive with their respective human antigens. All monoclonal antibodies are murine and most polyclonal antibodies are of rabbit origin unless otherwise stated.

Species cross-reactivity and more detailed western blotting information that is not indicated in either the product text or datasheet may be obtained at www.leica-microsystems.com or by contacting your local customer support (refer to back page for further details). As a result of customers’ research, the cross-reactivity information is updated regularly, and unless indicated on the datasheet, should be treated only as a guide. Bond and Novocastra products are designed for use in immunohistochemical, microbiological/virological, in situ hybridization, and other techniques.

All antibodies are described as monoclonal or polyclonal, and most are available in a range of formats, e.g., lyophilized (freeze-dried), liquid, and ready-to-use.
Reagent products are designed primarily for immunohistochemical or in situ hybridization use. Other recommended applications may also be indicated. The code letters beside each product provide a key that briefly describes the use of the product.

- **F**: Frozen sections with no pretreatment
- **P**: Paraffin sections with no pretreatment
- **P (HIER)**: Paraffin sections with heat induced epitope retrieval recommended
- **P (Enzyme)**: Paraffin sections with enzyme digestion recommended
- **P (Enzyme+HIER)**: Paraffin sections with enzyme digestion followed by heat induced epitope retrieval recommended
- **P (Enzyme/HIER)**: Paraffin sections with enzyme digestion or heat induced epitope retrieval recommended – optimum pretreatment to be determined by end user
- **W**: Western blotting
- **I**: Immunofluorescence
- **C**: Flow cytometry
- **E**: Electron microscopy
- **O**: Other applications defined in text

Note: There is a quick reference guide to the key symbols located on the bottom of each right-hand page.
The Biosystems Division of Leica Microsystems is a world wide organization with an international sales and support network backed by in-house reagent and automation development. This comprehensive coverage and knowledge makes Leica Microsystems’ Biosystems Division the ideal partner for advanced staining.
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Novocastra Science™ – experience, innovation and support that delivers quality reagents for consistent staining
NEW PRODUCTS

Clinicians and researchers continually strive for better patient outcomes through the discovery of new diagnostic tools. Leica Microsystems aids this important work by continually releasing new, useful antibodies and probes to clinical and research laboratories. This catalog includes 37 new products released in the past 12 months, and with more releases planned for 2010, Leica Microsystems is helping make sure patients receive better care through the latest diagnostic advances.

NOVOCASTRA ANTIBODIES

<table>
<thead>
<tr>
<th>Product Code</th>
<th>Name</th>
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<tr>
<td>NCL-L-AMACR</td>
<td>Alpha-Methylacyl-CoA Racemase (AMACR, p504s)</td>
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<td>NCL-L-CALCITONIN</td>
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<td>NCL-L-CD123</td>
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<td>NCL-L-FRalpha</td>
<td>Folate Receptor Alpha</td>
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<td>NCL-L-FPGS</td>
<td>Folylpolyglutamate Synthetase</td>
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<tr>
<td>NCL-L-Hpylori</td>
<td>Helicobacter pylori</td>
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<tr>
<td>NCL-L-HIG2</td>
<td>Hypoxia Inducible Gene 2 Protein</td>
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<td>NCL-L-IgG</td>
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<td>NCL-L-InhibinA</td>
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<td>NCL-KAP-581</td>
<td>Kappa Light Chain</td>
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<td>NCL-L-LAM-578</td>
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<td>NCL-L-PMS2</td>
<td>Mismatch Repair Protein (PMS2)</td>
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<td>NCL-L-MUM1</td>
<td>Multiple Myeloma Oncogene 1 (MUM-1)</td>
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<td>NCL-MSA-594</td>
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### BOND RTU ANTIBODIES

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<tr>
<td>PA0117</td>
<td>Bcl-2 Oncoprotein</td>
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<td>PA0083</td>
<td>Beta-Catenin</td>
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<tr>
<td>PA0088</td>
<td>CD138 (Syndecan 1)</td>
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<td>Cytokeratin 17</td>
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<td>Luteinizing Hormone</td>
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<td>MLH1 (Mismatch Repair Protein)</td>
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<td>MSH2 (Mismatch Repair Protein)</td>
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<td>PA0491</td>
<td>Myeloperoxidase</td>
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<td>PA0996</td>
<td>Negative Control (Mouse)</td>
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<td>PA0777</td>
<td>Negative Control (Rabbit)</td>
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<td>Neurofilament 200kD</td>
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<td>PA0934</td>
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<tr>
<td>PA0093</td>
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<td>DS9455</td>
<td>Bond Research Detection</td>
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It’s about patients, and everything you need to help them through their journey. Leica Total Histology is all elements of tissue-based pathology brought together – instruments and consumables, history and education, support, and innovation. Now, instruments and consumables form complete systems, each individual step is considered part of a single inclusive process and one partner can support the entire histology workflow. With Total Histology, it’s time to advance workflows, enhance diagnostic clarity and deliver better patient care.
TOTAL HISTOLOGY

Consumables

Specimen Identification

Cryosectioning

Tissue Processing

Embedding

Paraffin Sectioning

Routine Staining

Bond™ Fully Automated IHC and ISH

Novocastra™ Reagents
LEAN CONSULTING

Improve productivity, enhance quality and lower costs with Leica Microsystems’ Lean Histology™ Consulting Service. Leica Microsystems’ Lean Consultants create a roadmap for your laboratory that can improve processes and increase efficiency. Along with an expert, in-person workflow evaluation, Lean Consultants work with you to identify and apply the best combination of people, products, and processes for sustainable improvements that increase performance and aid better patient care through higher quality and faster results.

Please consult your Leica Microsystems representative for availability in your region.
BOND™ READY-TO-USE PRIMARY REAGENTS

With the Bond ready-to-use range, brilliant IHC and ISH have never been easier. Simply load your primary reagent and click “Start”. We’ve done the mixing, dilution and titration; you deliver consistent, high-quality staining.

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BOND-III – DELIVERING WHAT REALLY MATTERS

Quickly finish more high-quality slides with greater productivity. Bond-III helps you deliver what really matters – Lean workflows, rapid turnaround and better patient care.

- Speed – up to 50% faster than previous generation IHC/ISH stainers
- Efficiency – less is more: cut reagent costs and maintenance times
- Quality – superior Novocastra reagents and total tissue care

Also available, Bond-max – lower throughput, same quality and flexibility

BOND™ FULLY AUTOMATED IHC AND ISH
THE WISE THERANOSTIC CHOICE

A fully automated, robust and dependable IHC test for the accurate assessment of HER2 status in breast tissue from patients for whom Herceptin® (trastuzumab) treatment is being considered.

- Fully automated – ready-to-use reagents run on the Bond system, standardizing the staining process and reducing hands-on time, staining variation and repeats
- Consistent – control cell slides with interferometer-verified section thickness and four cell lines (including 2+) provide a consistent, comprehensive control method for assessing assay performance
- Complete – all the reagents required to perform up to 60 tests on the Bond system.

ORACLE™ HER2 BOND™ IHC SYSTEM (TA9145)

Oracle™ HER2 Bond™ IHC System – TA9145
- 60 test slides with HER2 Primary Antibody
- 60 test slides with HER2 Negative Control
- 15 HER2 Control Slides with HER2 Primary Antibody
- 15 positive in-house tissue controls with HER2 Primary Antibody

1. See Herceptin® package insert
2. When used with standard Bond system ancillary reagents
Detection Systems

Bond Polymer Refine Detection

300 Tests (100 μL dispense) or
200 Tests (150 μL dispense) DS9800  P
For In Vitro Diagnostic Use

Components

A state-of-the-art Compact Polymer detection system for use in both immunohistochemistry and chromogenic in situ hybridization. Small multifunctional linkers enhance tissue penetration, producing unsurpassed sensitivity. The system is biotin-free.

Bond Polymer Refine Detection contains a peroxide block, post primary, polymer reagent, DAB chromogen and hematoxylin counterstain. It is supplied ready-to-use for the automated Bond system.

Application

Immunohistochemistry (IHC)

Primary antibody binding to tissue sections can be visualized using Bond Polymer Refine Detection, where it provides intense, high resolution staining. A range of Bond ready-to-use primary antibodies are available, or alternatively, use antibody concentrates diluted with Bond Primary Antibody Diluent (AR9352).

Colon mucosa: immunohistochemical staining with Bond ready-to-use Cytokeratin 8/18 (S3D3) (PA0067) using Bond Polymer Refine Detection.

Chromogenic in Situ Hybridization (ISH)

Bond Polymer Refine Detection produces highly specific, sensitive and reproducible demonstration of nucleic acid sequences through controlled hybridization reactions.

Bond ready-to-use ISH probes (fluorescein/biotin labeled along with Anti-Fluorescein/biotin secondary antibodies) are used in conjunction with Bond Polymer Refine Detection to produce perfectly tuned, optimized ISH staining results on the Bond system.

Hodgkin’s lymphoma: in situ hybridization staining for Epstein-Barr virus (EBV) encoded mRNA with EBER Probe (PB0589) using Bond Polymer Refine Detection.

Bond Polymer Refine Red Detection

100 Tests DS9390  P
For In Vitro Diagnostic Use

Bond Polymer Refine Red Detection is an IVD labeled red detection system for the automated Bond system. Bond Polymer Refine Red Detection is biotin-free, utilizing alkaline phosphatase (AP)-linked compact polymers to provide enhanced tissue penetration and unsurpassed reagent sensitivity. It contains post primary, polymer reagent, Fast Red chromogen, and hematoxylin counterstain and is supplied in a convenient, ready-to-use format.

Human skin stained for melanoma marker HMB45 with NCL-HMB45 using Bond Polymer Refine Red Detection. Note intense cytoplasmic staining of melanocytes in contrast to the brown endogenous melanin.

Bond Intense R Detection

300 Tests (100 μL dispense) or
200 Tests (150 μL dispense) DS9263  P F
For Research Use Only

Components

Bond Intense R Detection is a peroxidase detection system optimized for use on the automated Bond system and is ideal for research applications. It contains a peroxide block, streptavidin/peroxidase conjugate, DAB chromogen and hematoxylin counterstain. Users must supply a biotinylated secondary antibody of their choice.

Application

By allowing a free choice of biotinylated secondary antibody, Bond Intense R Detection is ideal for the detection of primary antibodies from any species. Research applications such as IHC staining of mouse tissues can be accommodated in this manner. The intense deposition of DAB reaction product produces strong immunostaining.

Bond Research Detection

300 Tests (100 μL dispense) or
200 Tests (150 μL dispense) DS9455
For Research Use Only

Components

The Bond research functionality is created together with a research dongle and an “open” Bond Research Detection from Leica Microsystems. This open detection system consists of six standard 30 mL open containers in a reagent tray. The tray is registered on Bond like any other detection system (one barcode only), but each of the containers can be configured with reagent of the user’s choice.

Application

Bond Research Detection offers researchers the ability to tailor applications and fully automate for ease of use.
Ancillary Reagents

Bond Wash Solution 10X Concentrate

1 L AR9590  P
For In Vitro Diagnostic Use

Components
Bond Wash Solution 10X Concentrate is a concentrated buffer solution specifically for use on the automated Bond system. It is available in 1 L quantities, and when diluted will make up 10 L of working solution.

Application
Bond Wash Solution is the only wash buffer that should be used in Bond automated staining procedures. It is formulated for smooth and gentle reagent flow under the Bond Covertile to help ensure that excess reagent is removed from the tissue section before new reagent is added.

Bond Primary Antibody Diluent

500 mL AR9352  P
For In Vitro Diagnostic Use

Components
Bond Primary Antibody Diluent is ready-to-use and available in a quantity of 500 mL.

Application
Bond Primary Antibody Diluent is specifically for diluting concentrated primary antibodies for use on the automated Bond system. It is not intended for the reconstitution of lyophilized reagents.

Bond DAB Enhancer

30 mL AR9432  P
For In Vitro Diagnostic Use

Components
Bond DAB Enhancer is a heavy metal solution for use on the automated Bond system. The no-mix, ready-to-use format simplifies laboratory workflow.

Application
Bond DAB Enhancer changes the color of the DAB reaction deposit from golden to dark brown, providing an increase in contrast between chromogen-specific staining and the slide back drop. This can assist in qualitative identification of antigens.

Bond Dewax Solution

1 L AR9222  P
For In Vitro Diagnostic Use

Components
Bond Dewax Solution is a deparaffinization solution specifically designed for use on the automated Bond system. It is provided ready-to-use in 1 L bottles and can be poured directly into the appropriate bulk reagent container on the instrument.

Application
The use of Bond Dewax Solution allows paraffin wax to be removed from tissue sections before rehydration and staining on Bond. It is specially formulated to be compatible with the automated Bond system, and efficiently removes wax from slides while retaining the integrity of tissue antigens and probe binding sites. Bond Dewax Solution is much less harmful than alternative deparaffinization solutions such as xylene.

Bond Enzyme Pretreatment Kit

1 kit AR9551  P
For In Vitro Diagnostic Use

Components
Bond Enzyme Concentrate, 1 mL
Bond Enzyme Diluent, 200 mL
3 x Bond Open Containers, 7 mL

The enzyme is diluted before use in the Bond Open Containers supplied. The diluted enzyme solution is used for enzymatic digestion on the automated Bond system.

Application

Immunohistochemistry (IHC)
The Bond Enzyme Pretreatment Kit can be used for enzymatic digestion on formalin-fixed, paraffin-embedded tissue sections to assist in epitope exposure. Enzymatic pretreatment improves the staining of some antibodies by exposing epitopes within tissue that have been masked during fixation.

Application
In Situ Hybridization (ISH)
The diluted enzyme solution can also be used for ISH, along with Bond ready-to-use probes. Enzymatic digestion of tissue assists in the penetration of probes and facilitates binding.
Bond Epitope Retrieval Solution 1

1 L AR9961 P
For In Vitro Diagnostic Use

Components
Bond Epitope Retrieval Solution 1 is a 1 L ready-to-use, citrate based pH 6.0 solution. It is specifically for heat-induced epitope retrieval (HIER) on the automated Bond system.

Application
Bond Epitope Retrieval Solution 1 is for use on formalin-fixed, paraffin-embedded tissue sections to expose epitopes within tissue that have been masked during fixation. The solution is gentle on sections as it has a reduced boiling temperature and utilizes Bond’s Covertile technology to prevent reagent evaporation. Some antibodies, such as Bond ready-to-use Thyroid Transcription Factor-1, stain optimally when used with Bond Epitope Retrieval Solution 1. Testing should be carried out to optimize performance.

Alpha Fetoprotein

Clone C3
7 mL Bond ready-to-use PA0963 P
For In Vitro Diagnostic Use

Alpha Fetoprotein (AFP) is an oncofetal antigen of 70 kD found in body fluids, which if detected in high concentrations has clinical implications. AFP is expressed in fetal liver but is not present under normal circumstances in healthy adult tissues. It is reported to be expressed in a proportion of germ cell tumors, with high frequency in yolk sac tumors.

Also available as a Novocastra concentrate, refer to page 56.

Anaplastic Lymphoma Kinase

Clone 5A4
7 mL Bond ready-to-use PA0306 P (HIER)
For In Vitro Diagnostic Use

Anaplastic Large Cell Lymphoma (ALCL) is usually composed of large pleomorphic cells which, are reported to express CD30 antigen and the epithelial membrane antigen (EMA). These tumor cells tend to occur in younger individuals and may be associated with cutaneous and extranodal involvement. A proportion of these cases contain a chromosomal translocation t(2;5) (p23;q35). This results in a hybrid gene encoding part of the nucleophosmin (NPM) gene joined to the cytoplasmic domain of the anaplastic lymphoma kinase (ALK) gene, giving rise to the protein, p80. Large cell lymphomas account for approximately 25 percent of all non-Hodgkin’s lymphomas in children and young adults, of which one third carries the NPM-ALK gene translocation.

Also available as a Novocastra concentrate, refer to page 54.
B Cell Specific Octamer Binding Protein-1 (BOB-1)

**Clone TG14**
7 mL Bond ready-to-use PA0558 P (HIER)
*For In Vitro Diagnostic Use*

B cell specific octamer binding protein-1 (BOB-1), also known as OBF-1 and OCA-B, is a lymphocyte specific transcriptional coactivator protein. It interacts with OCT1 and OCT2 transcription factors and contributes to the transcriptional activity of octamer motifs. BOB-1 has been reported to be detectable in all B cell populations found in reactive lymphoid tissues. The strongest expression is found in germinal center B cells and plasma cells. The expression of BOB-1 in B cell tumors has been reported to be variable. Also available as a Novocastra concentrate, refer to page 59.

Lymphoma: immunohistochemical staining with Bond ready-to-use BOB-1 (TG14) using Bond Polymer Refine Detection.

Bcl-2 Oncoprotein

**bcl-2/100/DS**
7 mL Bond ready-to-use PA0117 P (HIER)
*For In Vitro Diagnostic Use*

Bcl-2 is a member of a family of proteins that are involved in apoptosis. Bcl-2 is an integral inner mitochondrial membrane protein of 25 kD and has a wide tissue distribution. It is considered to act as an inhibitor of apoptosis. For this reason, Bcl-2 expression is inhibited in germinal centers where apoptosis forms part of the B cell production pathway. In 90 percent of follicular lymphomas a translocation occurs which juxtaposes the Bcl-2 gene at 18q21, to an immunoglobulin gene. This t(14;18) translocation can deregulate gene expression and Bcl-2 over-expression can be demonstrated immunohistochemically in the vast majority of follicular lymphomas. Also available as a Novocastra concentrate, refer to page 60.

Tonsil: immunohistochemical staining with Bond ready-to-use Bcl-2 (bcl-2/100/DS) using Bond Polymer Refine Detection.

Bcl-6

**Clone LN22**
7 mL Bond ready-to-use PA0204 P (HIER)
*For In Vitro Diagnostic Use*

Bcl-6 is an oncoprotein that plays a role in the differentiation of normal germinal center B cells. The Bcl-6 antigen is an important marker of follicular, diffuse large B cell and Burkitt’s lymphoma and also nodular, lymphocyte predominant Hodgkin’s disease.

**Product Specific Information**

Bcl-6 (LN22) is recommended as part of a panel of antibodies in the characterization of lymphomas of B cell origin. Also available as a Novocastra concentrate, refer to page 60.

Tonsil: immunohistochemical staining with Bond ready-to-use Bcl-6 (LN22) using Bond Polymer Refine Detection.

Beta-Catenin

**Clone 17C2**
7 mL Bond ready-to-use PA0083 P (HIER)
*For In Vitro Diagnostic Use*

The catenins, (alpha, beta and gamma) are cytoplasmic proteins which bind to the highly conserved tail of the E-cadherin molecule. Beta-catenin is a component of the adherens junction, a multiprotein complex which supports Ca2+ -dependent cell to cell contact which in itself is critical for adhesion, signal transmission and for anchoring the actin cytoskeleton. Beta-catenin’s role is as a transcription effector of the wnt-signalling pathway. Immunohistochemistry is the best way to demonstrate nuclear expression of beta-catenin and wnt-pathway activation. This aberrant expression is observed in human tumorigenesis and especially in colorectal cancer. Also available as a Novocastra concentrate, refer to page 62.

Colon polyp: immunohistochemical staining with Bond ready-to-use Beta-Catenin (17C2) using Bond Polymer Refine Detection.
Bond Products in this catalog are subject to regulatory approval. This catalog is not for use in the USA.

For detailed information on all products please visit our website:
www.leica-microsystems.com

CA19-9 (Sialyl Lewisα)

**Clone C241:5:1:4**
7 mL Bond ready-to-use PA0424 P (HIER)

For In Vitro Diagnostic Use

CA19-9 is an epitope on the sialylated Lewisα carbohydrate structure. Sialylated Lewisα plays a role in cell adhesion by acting as a functional ligand for the inducible adhesion molecule E-selectin. CA19-9 and CA50 (carcinoma associated mucin antigen) are useful serum markers in the diagnosis and follow up of gastrointestinal and pancreatic cancers. In carcinoma of the pancreas, it is reported that the immunohistochemical expression of both CA19-9 and CA50 correlates with tumor differentiation where the strongest staining is observed in well differentiated tumors. These two markers are also reported in a number of benign lesions such as chronic pancreatitis.

**Product Specific Information**

Clone C241:5:1:4 reacts specifically with glycolipids containing Sialyl Lewisα, showing no cross-reaction with Lewisα, Lewisβ, or other structurally related molecules. The epitope recognized by CA19-9 (Sialyl Lewisα) is designated CA19-9 and is similar to CA50 (carcinoma associated mucin antigen).

Also available as a Novocastra concentrate, refer to page 64.

Calcitonin

**Polyclonal**
7 mL Bond ready-to-use PA0406 P (Enzyme)

For In Vitro Diagnostic Use

Calcitonin is a peptide hormone synthesized by the parafollicular cells of the thyroid. It causes reduction in serum calcium, an effect opposite to that of parathyroid hormone (PTH). Calcitonin has been reported to be demonstrated in C cells of normal and hyperplastic thyroid. Staining for calcitonin may be used for the identification of a spectrum of C cell proliferative abnormalities ranging from C cell hyperplasia to invasive tumors.

Also available as a Novocastra concentrate, refer to page 65.

CA125

**Clone Ov185:1**
7 mL Bond ready-to-use PA0539 P (HIER)

For In Vitro Diagnostic Use

CA125 is also known as MUC16. CA125 antigen is usually associated with ovarian epithelial malignancies. Serum assays are widely used to detect this protein in the monitoring of ovarian cancers. CA125 antigen may also be detected by immunohistochemistry and expression has been found in neoplasms such as seminal vesicle carcinoma and anaplastic lymphoma. CA125 antigen is not found exclusively in malignant tumors.

Also available as a Novocastra concentrate, refer to page 64.

Calponin (Basic)

**Clone 26A11**
7 mL Bond ready-to-use PA0416 P (HIER)

For In Vitro Diagnostic Use

Calponin (Basic) is an actin, tropomyosin and calmodulin binding protein thought to be involved in the regulation of smooth muscle contraction. The expression of basic calponin is reported to be restricted to smooth muscle cells and is a marker of the differentiated contractile phenotype of developing smooth muscle. Vascular smooth muscle cells convert to a synthetic dedifferentiated phenotype when this protein is lost and this is a key stage in both atherosclerosis and restenosis of coronary arteries after balloon angioplasty. It is thought that basic calponin exerts its effect via the cortical actin cytoskeleton and therefore influences proliferation, the transformed phenotype and the metastatic potential of tumor cells. Basic calponin mRNA is expressed in smooth muscle of prostate, bowel and aorta whereas neutral and acidic calponin mRNAs are expressed in non-smooth muscle tissues such as heart, placenta, lung, kidney, pancreas, spleen, testis and ovary as well as in smooth muscle-containing tissues.

Also available as a Novocastra concentrate, refer to page 66.
**Calretinin**

**Clone CAL6**
7 mL Bond ready-to-use PA0346 P (HIER)
For In Vitro Diagnostic Use

Calretinin is a calcium-binding protein of 29 kD, reported to be abundantly expressed in neurons. Outside the nervous system, calretinin expression has been demonstrated in a range of cell types including mesothelial cells, steroid producing cells, some neuroendocrine cells, eccrine sweat glands and other cell types. The presence of calretinin is reported to be a useful marker primarily for two purposes: differentiating malignant mesothelioma from carcinomas; and the differential characterization of ovarian stromal tumors. Calretinin-positive cells have also been reported in the convoluted tubules of kidney with some antibodies.

**Product Specific Information**

Bond ready-to-use Calretinin (CAL6) is recommended for use as part of an antibody panel for the identification of mesothelioma.

Also available as a Novocastra concentrate, refer to page 66.

**Carcinoembryonic Antigen**

**Clone II-7**
7 mL Bond ready-to-use PA0004 P (HIER)
For In Vitro Diagnostic Use

Carcinoembryonic antigen (CEA) is a heterogeneous cell surface glycoprotein produced by cells of fetal colon. Low levels are also found on normal mucosal epithelia of the adult colon and a variety of other normal tissues. CEA is encoded by the CEA gene that is located on chromosome 19. It is a member of the CEA gene family, which in turn is a subfamily of the immunoglobulin superfamily. Cell adhesion properties are now well recognized for CEA. It is believed that the expression of this glycoprotein in conjunction with other known adhesion molecules will influence the cell-cell interaction.

Also available as a Novocastra concentrate, refer to page 67.

**CD1a**

**Clone MTB1**
7 mL Bond ready-to-use PA0235 P (HIER)
For In Vitro Diagnostic Use

CD1a is a protein of 43–49 kD expressed on dendritic cells and cortical thymocytes. CD1a expression has been shown to be useful in the differentiation of Langerhans’ cells and interdigitating cells in the skin.

**Product Specific Information**

Bond ready-to-use CD1a (MTB1) is recommended for use in detecting CD1a protein expression in a variety of normal and neoplastic tissues, including Langerhans’ cell histiocytosis and thymomas.

Also available as a Novocastra concentrate, refer to page 70.

**CD2**

**Clone 11F11**
7 mL Bond ready-to-use PA0271 P (HIER)
For In Vitro Diagnostic Use

The CD2 antigen is an accessory molecule, important in mediating the adhesion of activated T cells and thymocytes with antigen-presenting cells and target cells.

**Product Specific Information**

CD2 (11F11) is recommended for use as part of an antibody panel in the characterization of T cell disorders.

Also available as a Novocastra concentrate, refer to page 70.
**CD3**

**Clone LN10**  
7 mL Bond ready-to-use PA0553 P (HIER)  
*For In Vitro Diagnostic Use*

The CD3 antigen is a marker of T cell differentiation. It is first detected in early thymocytes and its appearance is thought to represent one of the earliest signs of commitment to the T cell lineage.  

**Product Specific Information**  
Bond ready-to-use CD3 (LN10) has been specifically designed to supercede Novocastra clone PS1 and produce an unrivaled stain on formalin-fixed, paraffin-embedded tissue.  

CD3 (LN10) can be employed in the characterization of T cell disorders as one component of a panel of antibodies.  

Also available as a Novocastra concentrate, refer to page 70.

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**CD4**

**Clone 4B12**  
7 mL Bond ready-to-use PA0368 P (HIER)  
*For In Vitro Diagnostic Use*

The CD4 molecule (T4) is a single chain transmembrane glycoprotein with a molecular weight of 59 kD. The CD4 antigen is expressed on a T cell subset (helper/inducer) representing 45 percent of peripheral blood lymphocytes and at a lower level on monocytes. Most cases of cutaneous T cell lymphoma, including mycosis fungoides, express the CD4 antigen and HTLV-1 associated adult T cell leukemia/lymphoma is also generally CD4 positive.  

Also available as a Novocastra concentrate, refer to page 71.

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**CD5**

**Clone 4C7**  
7 mL Bond ready-to-use PA0168 P (HIER)  
*For In Vitro Diagnostic Use*

In normal lymphoid tissue CD5 is expressed mainly on T cells. It is reported to be expressed in 95 percent of thymocytes and in a subset of B cells, located primarily in the mantle zones.  

CD5 expression has been described in some T and B lymphomas, however antibodies to CD5 have been found to be useful in antibody panels for the differential diagnosis of small B cell lymphomas.  

Also available as a Novocastra concentrate, refer to page 71.

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**CD7**

**Clone LP15**  
7 mL Bond ready-to-use PA0266 P (HIER)  
*For In Vitro Diagnostic Use*

The CD7 molecule is a membrane-bound glycoprotein of 40 kD and is the earliest T cell specific antigen to be expressed in lymphocytes. CD7 antigen is also the only early marker to persist throughout differentiation. The function and role of the CD7 molecule has not yet been fully identified, although the activation of T cells with gamma/delta receptors has been proposed based on mAb-induced activation. CD7 antigen is reported to be found on the majority of peripheral blood T cells, most natural killer cells and thymocytes.  

Also available as a Novocastra concentrate, refer to page 72.
CD8

Clone 4B11
7 mL Bond ready-to-use PA0183 P (HIER)
For In Vitro Diagnostic Use

The CD8 antigen is found on a sub-set of normal cytotoxic/suppressor cells, which make up 20-30 percent of peripheral blood lymphocytes. It has also been reported on natural killer cells, 80 percent of thymocytes and sub-populations of peripheral blood null cells and bone marrow cells. T cell disorders can be characterized using a panel of antibodies that include CD8 (4B11).

Also available as a Novocastra concentrate, refer to page 72.

Tonsil: immunohistochemical staining with Bond ready-to-use CD8 (4B11) using Bond Polymer Refine Detection.

CD11c

Clone 5D11
7 mL Bond ready-to-use PA0554 P (HIER)
For In Vitro Diagnostic Use

CD11c is a member of the leukocyte integrin family of adhesion proteins expressed in normal cells, with high levels on tissue macrophages and monocytes with weak staining of granulocytes. CD11c antigen has been described on NK cells, activated T cells, lymphoid cell lines including hairy cell leukemia and a proportion of interdigitating dendritic cells.

Product Specific Information

Bond ready-to-use CD11c (5D11) is recommended for use as part of a panel of antibodies in the diagnosis of hematological malignancies and identification of cells of the macrophage/dendritic cell lineage in tissues.

Also available as a Novocastra concentrate, refer to page 73.

Hairy cell leukemia: immunohistochemical staining with Bond ready-to-use CD11c (5D11) using Bond Polymer Refine Detection.

CD10

Clone 56C6
7 mL Bond ready-to-use PA0270 P (HIER)
For In Vitro Diagnostic Use

The CD10 antigen is a metalloendopeptidase which inactivates a number of biologically active peptides. It is expressed on a wide variety of normal and neoplastic tissues of both lymphoid and nonlymphoid origin. CD10 antigen has been identified on cells of lymphoblastic, Burkitt’s and follicular lymphomas and on the cells of patients with chronic myeloid leukemia.

Product Specific Information

CD10 (56C6) is recommended for the differential diagnosis of small B cell lymphoma and the subtyping of lymphoblastic leukemia.

Also available as a Novocastra concentrate, refer to page 73.

Tonsil: immunohistochemical staining with Bond ready-to-use CD10 (56C6) using Bond Polymer Refine Detection.

CD15

Clone Carb-1
7 mL Bond ready-to-use PA0039 P (HIER)
For In Vitro Diagnostic Use

CD15 antigen, also known as X-hapten, is reported to be expressed on 90 percent of circulating human granulocytes, 30 to 60 percent of circulating monocytes and is absent from normal lymphocytes. The CD15 antigen is also expressed on Reed Sternberg cells of Hodgkin’s disease and some leukemias.

Also available as a Novocastra concentrate, refer to page 74.

Hodgkin’s lymphoma: immunohistochemical staining with Bond ready-to-use CD15 (Carb-1) using Bond Polymer Refine Detection.
CD19

**Clone BT51E**
7 mL Bond ready-to-use PA0843 P (HIER)
*For In Vitro Diagnostic Use*

The CD19 molecule is a type I integral membrane glycoprotein with a molecular weight of 90 kDa. This antigen is reported to be expressed by all normal B cells including early B cells. It is also found on follicular dendritic cells, early cells of myelomonocytic lineage and most stabilized B cell lines. The CD19 antigen is not present on T cells or on normal granulocytes.

Also available as a Novocastra concentrate, refer to page 74.

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CD21

**Clone 2G9**
7 mL Bond ready-to-use PA0171 P (HIER)
*For In Vitro Diagnostic Use*

CD21 antigen is a type I integral membrane glycoprotein of molecular weight 140 kDa, which functions as the receptor for the C3d fragment of the third complement component. The CD21 molecule, present on mature B cells, is involved in transmitting growth-promoting signals to the interior of the B cell and acts as a receptor for Epstein-Barr virus. CD21 antigen is reported to be found in B cell chronic lymphocytic leukemias and in a subset of T cell acute lymphoblastic leukemias but is absent on T lymphocytes, monocytes and granulocytes. CD21 antigen is also reported to be expressed in follicular dendritic cells and in follicular and mantle cell lymphomas, mature leukemias and lymphomas.

Also available as a Novocastra concentrate, refer to page 75.

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CD20

**Clone MJ1**
7 mL Bond ready-to-use PA0906 P (HIER)
*For In Vitro Diagnostic Use*

The CD20 antigen is thought to act as a receptor during B cell activation and differentiation. It is expressed on normal and malignant B cells from peripheral blood, lymph node, spleen, tonsil, bone marrow, acute leukemias and chronic lymphocytic leukemias.

**Product Specific Information**

CD20 (MJ1) is recommended for use in the characterization of B cell disorders as one component of a panel of antibodies.

Also available as a Novocastra concentrate, refer to page 75.

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CD22

**Clone FPC1**
7 mL Bond ready-to-use PA0249 P (HIER)
*For In Vitro Diagnostic Use*

The CD22 antigen (BL-CAM) is a type 1 integral membrane glycoprotein with a molecular weight of 130 to 140 kDa. It is a heterodimer of two independently expressed glycoprotein chains present both on the membrane and in the cytoplasm of B lymphocytes. Expression of the CD22 antigen is reported to appear early in B cell lymphocyte differentiation at approximately the same stage as that of the CD19 antigen expression. Surface antigen expression is variable and may be lost upon differentiation. CD22 antigen is also reported to be weakly expressed on myeloid leukemias and non-T cell acute lymphoblastic leukemias and is strongly expressed on hairy cell leukemias. It is absent on peripheral blood T cells, T cell leukemias, granulocytes and monocytes.

Also available as a Novocastra concentrate, refer to page 75.
**CD23**

**Clone 1B12**  
7 mL Bond ready-to-use PA0169 P (HIER)  
*For In Vitro Diagnostic Use*

CD23 antigen, the low affinity IgE receptor, is variably expressed on mantle zone cells and on a sub-population of follicular dendritic cells. Although CD23 is known to be expressed on other cells of hemopoietic origin, expression is absent from a large range of nonlymphoid normal tissues.  

**Product Specific Information**  
CD23 is recommended for use within an antibody panel for the differential diagnosis of small B cell lymphomas where it has been reported to be present in small lymphocytic lymphomas and CLL (chronic lymphocytic leukemias).  

Also available as a Novocastra concentrate, refer to page 76.

![Tonsil: immunohistochemical staining with Bond ready-to-use CD23 (1B12) using Bond Polymer Refine Detection.](image)

**CD25**

**Clone 4C9**  
7 mL Bond ready-to-use PA0305 P (HIER)  
*For In Vitro Diagnostic Use*

CD25 antigen, the alpha subunit of interleukin-2 receptor, is a single-chain glycoprotein with a molecular weight of 55 kD. Following the activation of T cells interleukin-2 (IL-2) is rapidly synthesized and secreted. In response to this a subpopulation of T cells expresses high affinity receptors for IL-2. These cells proliferate, expanding the T cell population which is capable of mediating helper, suppressor and cytotoxic functions. IL-2 receptor is not exclusively found on T cells and is reported to be expressed on HTLV-transformed T and B cells, EBV-transformed B cells, myeloid precursors and oligodendrocytes. It is absent on thymocytes, resting T cells, non-activated B cells and null cells. IL-2 receptor expression is reported to be associated with inflammatory and malignant conditions, lymphoid neoplasia, autoimmune diseases and allograft rejection.  

Also available as a Novocastra concentrate, refer to page 125.

![Tonsil, activated T cells and NK cells: immunohistochemical staining with Bond ready-to-use CD25 (4C9) using Bond Polymer Refine Detection.](image)

**CD30**

**Clone JCM182**  
7 mL Bond ready-to-use PA0790 P (HIER)  
**Clone 1G12**  
7 mL Bond ready-to-use PA0153 P (HIER)  
*For In Vitro Diagnostic Use*

The CD30 antigen is a single chain glycoprotein, known to act as a receptor for cytokine ligand CD30L. It may play a part in the regulation of cellular growth and transformation of activated lymphoblasts.  

**Product Specific Information**  
Bond ready-to-use CD30 is recommended for use as part of an antibody panel for the identification of anaplastic large cell lymphomas and Hodgkin’s Lymphomas.  

Also available as a Novocastra concentrate, refer to page 76.

![Hodgkin’s lymphoma: immunohistochemical staining with Bond ready-to-use CD30 (JCM182) using Bond Polymer Refine Detection.](image)

**CD31**

**Clone 1A10**  
7 mL Bond ready-to-use PA0250 P (HIER)  
*For In Vitro Diagnostic Use*

CD31 antigen (PECAM-1) is a single chain transmembrane glycoprotein expressed on the surface of platelets, monocytes, granulocytes, B cells and at the endothelial intracellular junction. The molecule has an extracellular domain that contains six Ig-like homology units of C2 subclass, typical of cell-to-cell adhesion molecules. This domain is thought to mediate endothelial cell-to-cell adhesion, plays a role in endothelial contact and may serve to stabilize the endothelial cell monolayer. The properties of CD31 antigen suggest that it is involved in interactive events during angiogenesis, thrombosis and wound healing. Angiogenesis is essential for tumor growth and metastases.  

**Product Specific Information**  
Bond ready-to-use CD31 (1A10) is recommended for use in the assessment of vascular invasion in neoplastic tissues.  

Also available as a Novocastra concentrate, refer to page 77.

![Esophagus: immunohistochemical staining with Bond ready-to-use CD31 (1A10) using Bond Polymer Refine Detection.](image)
CD33

Clone PWS44
7 mL Bond ready-to-use PA0555 P (HIER)
For In Vitro Diagnostic Use

CD33 antigen is reported to appear on myelomonocytic precursor cells after CD34 antigen expression. It then continues to be expressed on both the myeloid and monocyte lineages, although it is reported to be absent on granulocytes. It has been reported that expression of CD33 is restricted to monocytes, premelocytes, myeloid blasts, some acute undifferentiated leukemias and acute lymphoblastic leukemias. The expression of CD33 antigen has been demonstrated to be an important marker for distinguishing myeloid from the lymphoid leukemias.

Also available as a Novocastra concentrate, refer to page 77.

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CD43

Clone MT1
7 mL Bond ready-to-use PA0938 P (HIER)
For In Vitro Diagnostic Use

The CD43 antigen is expressed on the membrane and in the cytoplasm of T cells and cells of myeloid lineage. The molecule itself exhibits molecular weight heterogeneity with bands of 90 to 140 kD observed on SDS-PAGE between different cell lines. Cells expressing the CD43 antigen are reported to include normal and neoplastic T cells.

Product Specific Information
This antibody may be used as a pan leukocyte marker.

Also available as a Novocastra concentrate, refer to page 79.

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CD45

Clone X16/99
7 mL Bond ready-to-use PA0042 P (HIER)
For In Vitro Diagnostic Use

The CD45 antigen is a family of five or more high molecular-weight glycoproteins generated by the alternative splicing of three exons. It is present on the majority of human leukocytes, but absent from erythrocytes and platelets. CD45 expression is necessary for signalling through the T cell receptors.

Product Specific Information
CD45 (X16/99) is recommended for use in the identification of tumors of lymphoid origin as part of a panel of antibodies.

Also available as a Novocastra concentrate, refer to page 80.
CD45RO

Clone UCHL1
7 mL Bond ready-to-use PA0146 P (HIER)
For In Vitro Diagnostic Use

The CD45RO molecule, a 180 kD isoform of CD45, is reported to be expressed on 48 percent of peripheral blood T lymphocytes, 37 percent of CD4 positive lymphocytes, 80 percent of thymocytes and on the majority of T cell malignancies. Monocytes and granulocytes show surface expression of the antigen whereas tissue macrophages exhibit cytoplasmic expression. Also available as a Novocastra concentrate, refer to page 81.

CD57

Clone NK-1
7 mL Bond ready-to-use PA0443 P (HIER)
For In Vitro Diagnostic Use

The CD57 glycoprotein, also known as HNK-1, has a molecular weight of 110 kD. It is found on a subset of mononuclear cells with natural killer activity and on neuroectodermal cells expressing myelin-associated glycoprotein. Many cells which co-express CD57 and CD8 proteins are a subset of suppressor/cytotoxic T cells. These cells play a role in the rejection of grafts in acute graft versus host disease. The CD57 molecule is not expressed on erythrocytes or platelets. Also available as a Novocastra concentrate, refer to page 82.

CD56

Clone CD564
7 mL Bond ready-to-use PA0191 P (HIER)
For In Vitro Diagnostic Use

The neural cell adhesion molecules are a family of closely-related cell surface glycoproteins thought to play a role in embryogenesis, development and contact-mediated interactions between neural cells. The CD56 antigen (NCAM) consists of four major isoforms generated by differential splicing of the RNA transcript from a single gene located on chromosome 5. The CD56 antigen is expressed on neurons, astrocytes, Schwann cells, NK cells and a subset of activated T lymphocytes and some neuroendocrine tumors. Also available as a Novocastra concentrate, refer to page 81.

CD57

Clone CD564
7 mL Bond ready-to-use PA0191 P (HIER)
For In Vitro Diagnostic Use

The neural cell adhesion molecules are a family of closely-related cell surface glycoproteins thought to play a role in embryogenesis, development and contact-mediated interactions between neural cells. The CD56 antigen (NCAM) consists of four major isoforms generated by differential splicing of the RNA transcript from a single gene located on chromosome 5. The CD56 antigen is expressed on neurons, astrocytes, Schwann cells, NK cells and a subset of activated T lymphocytes and some neuroendocrine tumors. Also available as a Novocastra concentrate, refer to page 81.

CD61

Clone 2f2
7 mL Bond ready-to-use PA0308 P (HIER)
For In Vitro Diagnostic Use

The CD61 antigen, also known as GPIIIa, is a glycoprotein that is expressed on platelets, megakaryocytes, monocytes, macrophages and endothelial cells. CD61 combines with CD41 to form the platelet glycoprotein IIb/IIIa (integrin αIIbβ3) and with CD51 to form the vitronectin receptor (integrin αVβ3).

Product Specific Information

Bond ready-to-use CD61 (2f2) is recommended for use in detecting CD61 protein expression in a variety of normal and neoplastic tissues. Also available as a Novocastra concentrate, refer to page 82.

CD61

Clone 2f2
7 mL Bond ready-to-use PA0308 P (HIER)
For In Vitro Diagnostic Use

The CD61 antigen, also known as GPIIIa, is a glycoprotein that is expressed on platelets, megakaryocytes, monocytes, macrophages and endothelial cells. CD61 combines with CD41 to form the platelet glycoprotein IIb/IIIa (integrin αIIbβ3) and with CD51 to form the vitronectin receptor (integrin αVβ3).

Product Specific Information

Bond ready-to-use CD61 (2f2) is recommended for use in detecting CD61 protein expression in a variety of normal and neoplastic tissues. Also available as a Novocastra concentrate, refer to page 82.
CD68

**Clone 514H12**
7 mL Bond ready-to-use PA0273 P (HIER)
*For In Vitro Diagnostic Use*

The CD68 antigen is an intracellular molecule, which has primarily been associated with cytoplasmic granules and, to a lesser extent, the membranes of macrophages, monocytes, neutrophils, basophils and large lymphocytes. CD68 expression has been reported in stimulated T cells, NK cells, lymphomas, sarcomas and carcinomas, and in liver and renal tubules.

**Product Specific Information**
The CD68 antigen can be identified in a variety of normal and neoplastic tissues using CD68 (514H12).

Also available as a Novocastra concentrate, refer to page 83.

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CD99

**Clone 12E7**
7 mL Bond ready-to-use PA0509 P
*For In Vitro Diagnostic Use*

CD99 antigen, a 32 kD glycoprotein, is also known as MIC2, E2, 12E7, HuLy-m6 or FMC29. CD99 antigen is reported to be expressed on cortical thymocytes and T lymphocytes and is involved in rosette formation with sheep or human erythrocytes. It is also expressed on granulosa cells of the ovary, most pancreatic islet cells, Sertoli cells of the testis and on some endothelial cells. CD99 antigen is reported to be strongly expressed on Ewing’s sarcoma cells and primitive peripheral neuroectodermal tumors.

Also available as a Novocastra concentrate, refer to page 85.

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CD79a

**Clone 11E3**
7 mL Bond ready-to-use PA0192 P (HIER)
*For In Vitro Diagnostic Use*

The CD79 complex is associated with membrane-bound immunoglobulins on B cells, with these immunoglobulins the two subunits, CD79a and CD79b constitute the B cell antigen receptor. The CD79a component is reported to first appear at the pre-B cell stage, early maturation, and persists until the plasma cell stage where it is found as an intracellular component. The CD79a antigen is reported to be expressed in the majority of acute leukemias of precursor B cell type, B cell lines, B cell lymphomas and in some myelomas. It is not present in myeloid or T cell lines.

Also available as a Novocastra concentrate, refer to page 84.

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CD138 (Syndecan 1)

**Clone M115**
New!
7 mL Bond ready-to-use PA0088 P (HIER)
*For In Vitro Diagnostic Use*

The CD138 molecule is a transmembrane heparan sulphate glycoprotein expressed at distinct stages of differentiation in normal lymphoid cells such as pre-B cells, immature B cells and Ig-producing plasma cells as well as being expressed in stratified and simple epithelia. The loss of CD138 expression from atypical cells is reported to be an early event during cervical carcinogenesis whereas CD138 antigen expression shows a close association with preserved epithelial morphology and differentiation, however, the major utility of CD138 as a marker in immunohistochemistry is the quantification of plasma cells.

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Products in this catalog are subject to regulatory approval.
The catalog is not for use in the USA.
**CDX2**

**Clone AMT28**  
7 mL Bond ready-to-use PA0535 P (HIER)  
*For In Vitro Diagnostic Use*

CDX2 is a caudal-type homeobox, intestine-specific transcription factor that is expressed early in intestinal development and may be involved in the regulation of proliferation and differentiation of intestinal epithelial cells. CDX2, as well as CDX1, is of particular interest as the intestine is the only organ that contains detectable levels of either gene product.

CDX2 is primarily expressed on the surface of the villus and in the crypts. In contrast to CDX1, intense CDX2 expression is reported to occur in all but the distal portions of the developing intestine. The loss of CDX2 has been reported to contribute towards the progression of some sporadic colorectal cancers and CDX2 may also be associated with carcinogenesis of the stomach, as expression of CDX2 mRNA progressively decreases with the transition from well differentiated to poorly differentiated gastric cancer cell lines.

Also available as a Novocastra concentrate, refer to page 89.

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**Cytokeratin 5**

**Clone XM26**  
7 mL Bond ready-to-use PA0468 P (HIER)  
*For In Vitro Diagnostic Use*

Cytokeratin 5 is closely related to Cytokeratin 6 and shares a similar tissue distribution. The antigen is found in various proportions in many non-keratinizing stratified squamous and basal epithelia and epitheliomas.

**Product Specific Information**

Cytokeratin 5 (XM26) is recommended for the detection of Cytokeratin 5 in normal and neoplastic tissues, especially in squamous cell carcinomas and, when used as part of a panel of antibodies, for the distinction of mesotheliomas from most adenocarcinomas.

Also available as a Novocastra concentrate, refer to page 95.

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**Chromogranin A**

**Clone 5H7**  
7 mL Bond ready-to-use PA0430 P (HIER)  
*For In Vitro Diagnostic Use*

Chromogranin A is a 68 kD acidic protein that is reported to be widely expressed in neural tissues and in secretory granules of human endocrine cells; eg parathyroid gland, adrenal medulla, anterior pituitary gland, islet cells of the pancreas and C cells of the thyroid. Chromogranin A expression has been reported in neuroendocrine tumors such as pituitary adenomas, islet cell tumors, pheochromocytomas, medullary thyroid carcinomas, Merkel cell tumors and carcinoids.

**Product Specific Information**

Bond ready-to-use Chromogranin A (5H7) is recommended for use as part of a panel of antibodies for the identification of tumors of neuroendocrine origin.

Also available as a Novocastra concentrate, refer to page 91.

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**Cytokeratin 7**

**Clone RN7**  
7 mL Bond ready-to-use PA0942 P (HIER)  
*For In Vitro Diagnostic Use*

Cytokeratin 7 is reported to be expressed in specific subtypes of adenocarcinoma from ovary breast and lung whereas adenocarcinomas from the gastrointestinal tract are negative.

**Product Specific Information**

Clone RN7 is recommended for use as part of an antibody panel in the differential diagnosis of carcinomas.

Also available as a Novocastra concentrate, refer to page 96.

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Cytokeratin 8

Clone TS1
7 mL Bond ready-to-use PA0567 P (HIER)
For In Vitro Diagnostic Use

Cytokeratin 8, also known as tissue polypeptide antigen (TPA), together with Cytokeratin 18, is one of the first cytokeratins expressed in the embryo and persists in adult tissues. Both cytokeratins, 8 and 18, are major components of all simple epithelia but not of stratified squamous epithelia. Cytokeratin 8, reported to be expressed in the adenocarcinomas of individuals, is also found to be present in their sera. Also available as a Novocastra concentrate, refer to page 96.

Cytokeratin 17

Clone E3
7 mL Bond ready-to-use PA0114 P (HIER)
For In Vitro Diagnostic Use

In normal tissues Cytokeratin 17 is reported to be expressed in basal cells of complex epithelia eg basal cells of pseudostratified epithelium in the trachea, larynx, bronchi, myoepithelial cells in salivary glands and sweat glands. In neoplastic tissue, Cytokeratin 17 is reported to be expressed in squamous cell carcinomas of the lung, cervix and oral cavity.

Product Specific Information
Clone E3 reacts with the human cytokeratin intermediate filament protein (46 kD) identified as Cytokeratin 17. Also available as a Novocastra concentrate, refer to page 97.

Cytokeratin 19

Clone b170
7 mL Bond ready-to-use PA0799 P (Enzyme)
For In Vitro Diagnostic Use

The smallest human cytokeratin filament protein (40 kD) has been identified as Cytokeratin 19 and has been reported to be expressed in a large number of epithelial cell types, including many ductal and glandular epithelia.

Product Specific Information
Cytokeratin 19 (b170) produces a complex heterogenous staining pattern in non-keratinizing squamous epithelia and hair follicles, with strong staining of the basal layer observed. Also available as a Novocastra concentrate, refer to page 98.

Cytokeratin 20

Clone PW31
7 mL Bond ready-to-use PA0918 P (HIER)
For In Vitro Diagnostic Use

Cytokeratin 20 is of interest due to its limited tissue expression. It is almost entirely confined to the gastric and intestinal epithelium, urothelium and Merkel cells of the skin. Adenocarcinomas of these tissues are reported to express Cytokeratin 20 whilst carcinomas from the breast, lung and ovary are negative. Cytokeratin 20 is therefore an important marker in the differential diagnosis of carcinomas.

Product Specific Information
Clone PW31 is recommended for use as part an antibody panel in the characterization tumors originating from urothelium, intestinal epithelium and Merkel cells. Also available as a Novocastra concentrate, refer to page 98.
Cytokeratin 8/18

Clone 5D3
7 mL Bond ready-to-use PA0067 P (HIER)
For In Vitro Diagnostic Use

In normal tissues, Cytokeratins 8 and 18 are reported to be expressed in all simple and glandular epithelium. In neoplastic tissues they have been shown to be expressed in adenocarcinomas and most squamous cell carcinomas.

Product Specific Information
Cytokeratin 8/18 (5D3) is recommended for use as part of an antibody panel in the identification of adenocarcinomas and most squamous cell carcinomas, but keratinizing squamous carcinomas are generally negative.

Also available as a Novocastra concentrate, refer to page 99.

Colon mucosa: immunohistochemical staining with Bond ready-to-use Cytokeratin 8/18 (5D3) using Bond Polymer Refine Detection.

Cytokeratin Multi

Clone AE1 and AE3
7 mL Bond ready-to-use PA0909 P (Enzyme)
For In Vitro Diagnostic Use

Refer to page 34 for further information about Multi-Cytokeratin.

Desmin

Clone DE-R-11
7 mL Bond ready-to-use PA0032 P (HIER)
For In Vitro Diagnostic Use

Product Specific Information
Clone DE-R-11 reacts with the 18 kD rod region of the intermediate filament protein desmin (53 kD) in both striated and smooth muscle cells. The labeling is confined to the Z bands in cardiac and striated muscle giving a characteristic striated staining pattern. It does not appear to react with any other filament proteins.

Also available as a Novocastra concentrate, refer to page 101.

Cytokeratin (High Molecular Weight)

Clone 34ßE12
7 mL Bond ready-to-use PA0134 P (Enzyme)
For In Vitro Diagnostic Use

Cytokeratin (High Molecular Weight) 34ßE12 reacts with human cytokeratin intermediate filament proteins 1, 5, 10 and 14. Expression: squamous epithelium and sweat ducts in normal skin, some pneumocytes, bronchial epithelium and mesothelium in normal lung and bile ducts in normal liver. Also ductal cells of the normal pancreas, some acinar and ductal cells of normal breast, some follicular epithelia of normal thyroid and some epithelia and mesothelium of the normal small and large bowel.

Also available as a Novocastra concentrate, refer to page 137.

Squamous cell carcinoma: immunohistochemical staining with Bond ready-to-use Cytokeratin (High Molecular Weight) using Bond Polymer Refine Detection.

DOG-1

Clone K9
7 mL Bond ready-to-use PA0219 P (HIER)
For In Vitro Diagnostic Use

Expressed on the plasma membrane of GIST (Gastro-Intestinal Stromal Tumor), it is rarely expressed in other soft tissue tumors that can often be confused with GISTs. DOG-1 (Discovered on GIST-1) immunoreactivity is reported in 97.8 percent of scorable GISTs, including all KIT negative GISTs.

Also available as a Novocastra concentrate, refer to page 101.

Gastrointestinal stromal tumor: immunohistochemical staining with Bond ready-to-use DOG-1 (K9) using Bond Polymer Refine Detection.
E-Cadherin

Clone 36B5
7 mL Bond ready-to-use PA0387 P (HIER)
For In Vitro Diagnostic Use

E-cadherin is a Ca\(^{2+}\)-dependent, transmembrane cell adhesion molecule. It plays an important role in the growth, development and the intercellular adhesion of epithelial cells. Most tumors have an abnormal architecture and any subsequent loss of adhesiveness is thought to be an important step in the development of local invasion. E-cadherin may have a role in neoplastic progression, particularly as a suppressor of invasion. In prostate cancers, for example, the expression of E-cadherin is reported to be reduced or absent in comparison with its expression in normal prostate which is uniformly strong. Reduced expression or absence of E-cadherin in addition to alpha, beta and gamma-catenin in primary breast carcinomas has also been reported and these four proteins are associated with the development of metastases. The main immunohistochemical utility of E-cadherin is to highlight differential expression of this protein in lobular and ductal carcinomas.

Also available as a Novocastra concentrate, refer to page 102.

Estrogen Receptor

Clone 6F11
7 mL Bond ready-to-use PA0151 P (HIER)
For In Vitro Diagnostic Use

Estrogen Receptor (6F11) is indicated as an aid in the prediction of prognosis for breast cancer. Clone 6F11 binds specifically to the Estrogen Receptor alpha (ER\(\alpha\)) antigen in the nuclei of cells in normal tissues that express high levels of ER; a proportion of endometrial, ovarian and myometrial cells, and normal breast ductal cells.

The dysregulation of ER\(\alpha\) is thought to contribute to breast tumorigenesis. Presence of ER\(\alpha\) in these tumors is related to an improved overall survival and favorable response to endocrine therapy such as anti-estrogen Tamoxifen.

Also available as a Novocastra concentrate, refer to page 106.

Epithelial Membrane Antigen

Clone GP1.4
7 mL Bond ready-to-use PA0035 P (HIER)
For In Vitro Diagnostic Use

Epithelial membrane antigen (EMA), also known as episialin, has a molecular weight in the range 265 to 400 kD. In normal tissues, EMA is reported to be expressed in a variety of normal epithelia with the highest expression reported at the apical portion of the ductal lining cells of mammary epithelium. A similar pattern of expression has been reported in other glandular epithelia eg sweat glands, while squamous epithelium shows an uneven pattern of antigenic expression.

Also available as a Novocastra concentrate, refer to page 105.

Factor XIIIa

Clone E980.1
7 mL Bond ready-to-use PA0449 P (HIER)
For In Vitro Diagnostic Use

Factor XIIIa, also known as fibrinoligase and fibrin-stabilizing factor, is the last enzyme generated in the blood coagulation cascade. It is a Ca\(^{2+}\)-dependent transglutaminase or transamidating enzyme which forms intermolecular gamma-glutamyl-epsilon-lysine crosslinks between fibrin molecules resulting in the mechanical stabilization of the fibrin clot and its resistance to proteolysis. Factor XIIIa may also function to stabilize cell surface molecules and membranes. Ca\(^{2+}\)-dependent trans-glutaminases with thiol active centers are widespread in animal tissues and have been associated with cell proliferation, embryonic development and growth through the proliferation of mammary stroma and epithelial elements. Normal mammary stroma, like most collagenous connective tissue contains resident populations of CD34 positive dendritic interstitial cells and scattered Factor XIIIa positive collagen-associated dendrophages. Factor XIIIa has been examined to determine its expression in normal and inflamed skin. Factor XIIIa positive cells in human skin represent a specific population of bone marrow dendritic cells, distinct from Langerhans cells which share some features common to mononuclear phagocytes. In benign skin conditions such as inflammatory dermatoses eg atopic eczema and psoriasis, an increased number of factor XIIIa positive cells in the upper dermis, closely associated with lymphocytes, has been described.

Also available as a Novocastra concentrate, refer to page 109.
Placenta: immunohistochemical staining with Bond ready-to-use Factor XIIa (E980.1) using Bond Polymer Refine Detection.

Fascin

**Clone IM20**
7 mL Bond ready-to-use PA0420 P (HIER)
*For In Vitro Diagnostic Use*

Human fascin is a 55 to 58 kDa actin-bundling protein, whose actin binding ability is regulated by phosphorylation. In normal tissues the detection of fascin is reported to be predominantly restricted to dendritic cells and in the thymus has been observed only in medullary dendritic cells. In reactive nodes, interdigitating reticulum cells of T cell zones, cells in subcapsular areas, and cells of the reticular network express fascin.

Variable expression is seen in follicular dendritic cells and endothelial cells. Lymphoid cells, myeloid cells and plasma cells do not express fascin. However, in cases of Hodgkin’s disease, including nodular sclerosis, mixed cellularity lymphocyte depletion and unclassified cases, most or all Reed Sternberg cells are reported to be positive for fascin. Fascin expression may be induced by Epstein-Barr virus (EBV) infection of B cells with the possibility that viral induction of fascin in lymphoid or other cell types must also be considered in EBV-positive cases.

Also available as a Novocastra concentrate, refer to page 110.

Galectin-3

**Clone 9C4**
7 mL Bond ready-to-use PA0238 P (HIER)
*For In Vitro Diagnostic Use*

Galectin-3 is a member of the beta-galactosidase-binding lectin family. It is involved in several biological events including binding to the basement membrane glycoprotein laminin. Cell surface galectin-3 may be involved in homotypical cell adhesion and is downregulated in colon cancer as the disease progresses. This downregulation has also been examined in breast carcinoma with a similar correlation of expression reported. Downregulation of galectin-3 could be one of the many events that enable cancer cells to interact with laminin to facilitate invasion and metastasis and may indicate activation of the invasive phenotype in various tumor types. Galectin-3 has been reported to be detected in anaplastic large cell lymphomas, whereas galectin-3 is not detected in Reed Sternberg cells or variants of Hodgkin’s disease.

Also available as a Novocastra concentrate, refer to page 112.

Breast: immunohistochemical staining with Bond ready-to-use Galectin-3 (9C4) using Bond Polymer Refine Detection.

Gastrin

**Polyclonal**
7 mL Bond ready-to-use PA0681 P
*For In Vitro Diagnostic Use*

Gastrin, a polypeptide hormone, occurs naturally in three forms: gastrin-14, gastrin-17 and gastrin-34. Both primary and secondary G cell hyperplasia are reported to be characterized by clustering of the immunoreactive cells which sometimes project buds from the mucous glands.

**Product Specific Information**

Gastrin (polyclonal) reacts with non-sulfated (I) and sulfated (II) gastrin-17 as well as gastrin-34. The antibody cross-reacts with cholecystokinin octapeptide. Gastrin (polyclonal) labels gastrin or gastrin-analogue producing cells.

Also available as a Novocastra concentrate, refer to page 113.

Stomach: immunohistochemical staining with Bond ready-to-use Gastrin (Polyclonal) using Bond Polymer Refine Detection.

Hodgkin’s lymphoma: immunohistochemical staining with Bond ready-to-use Fascin (IM20) using Bond Polymer Refine Detection.
Glial Fibrillary Acidic Protein

Clone GA5
7 mL Bond ready-to-use PA0026 P (HIER)
For In Vitro Diagnostic Use

Glial fibrillary acidic protein (GFAP) is an intermediate filament protein of 52 kD reported to be expressed in glial cells eg astrocytes and ependymal cells. In the peripheral nervous system, GFAP has been reported to be expressed in Schwann cells, enteric glial cells and satellite cells of human sensory ganglia and in neoplastic tissues GFAP has been reported to be expressed in astrocytomas and ependymomas.

Also available as a Novocastra concentrate, refer to page 114.

Glucagon

Polyclonal
7 mL Bond ready-to-use PA0594 P
For In Vitro Diagnostic Use

Glucagon expression has been reported in the endocrine cells of the pancreatic islets and also in the mucosa of the small and large intestine. Pancreatic glucagon, a peptide of 29 amino acids, has biological activities including glycogenolysis, lipolysis, gluconeogenesis and ketogenesis. These effects are all antagonistic to insulin action and, therefore, lead to increased blood sugar levels. The majority of glucagonomas are reported to arise from the pancreas and produce pancreatic glucagon. These tumors are found chiefly in the main body or tail of the pancreas.

Also available as a Novocastra concentrate, refer to page 114.

Gross Cystic Disease Fluid Protein-15

Clone 23A3
7 mL Bond ready-to-use PA0350 P (HIER)
For In Vitro Diagnostic Use

Gross cystic disease of the breast is a benign premenopausal disorder in which cysts are a predominant pathological lesion. These cysts appear to be formed from excessive apocrine cystic secretions. This fluid is composed of several glycoproteins including a unique 15 kD monomer protein, GCDFP-15. It has been reported that cytosolic analysis of normal tissue from all major organs has demonstrated GCDFP-15 in apocrine epithelia, lacrimal, ceruminous and Moll’s glands and in numerous serous cells of the submandibular, tracheal, bronchial, sublingual and minor salivary glands. Cytosol from breast carcinoma lesions are reported to contain GCDFP-15 at a wide range of concentrations. The concentration is reported to be highest in more differentiated carcinomas and GCDFP-15 shows only a few positive individual epithelial cells within lobules and small ducts in normal breast. Expression has also been reported in fibroadenomas within areas of apocrine metaplasia. GCDFP-15 and prostate specific antigen are reported to be co-expressed in androgen receptor-positive breast tumors.

Also available as a Novocastra concentrate, refer to page 116.
**Human Chorionic Gonadotrophin Hormone**

**Polyclonal**
7 mL Bond ready-to-use PA0014 P (HIER)
For In Vitro Diagnostic Use

Human chorionic gonadotrophin (hCG) is a glycoprotein hormone produced by trophoblastic cells of the placenta beginning 10 to 12 days after conception. Maintenance of the fetus in the first trimester of pregnancy requires the production of hCG, which binds to the corpus luteum of the ovary which is stimulated to produce progesterone which in turn maintains the secretory endometrium. hCG is composed of two subunits, alpha and beta. The alpha subunit of hCG is identical to the subunit of luteinising hormone, thyroid stimulating hormone and follicle stimulating hormone. The common alpha chain and the hormone-specific beta chains have molecular weights of 14 kD and 17 kD, respectively. The hCG beta-subunit is unique in the family of beta-containing glycoprotein hormones in that it contains an extension of 29 amino acids at its COOH end. It is believed that the C-terminal region of the HCG-beta subunit plays a role in the intracellular behavior of the heterodimer.

Also available as a Novocastra concentrate, refer to page 121.

![Placenta: immunohistochemical staining with Bond ready-to-use Human Chorionic Gonadotrophin Hormone (Polyclonal) using Bond Polymer Refine Detection.]

**Human Follicle Stimulating Hormone**

**Clone INN-hFSH-60**
7 mL Bond ready-to-use PA0693 P (Enzyme)
For In Vitro Diagnostic Use

Follicle stimulating hormone (FSH) is a pituitary hormone of 35 kD which is involved in the maturation of ovarian follicles and estrogen secretion in females. In males, FSH stimulates the secretion of testosterone.

**Product Specific Information**

Human Follicle Stimulating Hormone (INN-hFSH-60) recognizes the beta 2 epitope of the beta subunit of human FSH.

![Pituitary: immunohistochemical staining with Bond ready-to-use Human Follicle Stimulating Hormone (INN-hFSH-60) using Bond Polymer Refine Detection.]

**Inhibin (alpha)**

**Clone R1**
7 mL Bond ready-to-use PA0110 P (HIER)
For In Vitro Diagnostic Use

Inhibins are peptide hormones produced by the granulosa cells in female follicles and by Sertoli cells in the male seminiferous tubules. They appear to oppose the functions of activins, as inhibins and activins inhibit and activate, respectively, the secretion of follitropin by the pituitary gland. Inhibin has 2 subunits (alpha and beta) that are coded by separate genes. The alpha subunit determines whether inhibin or activin will be produced. The antibody may be of value in the differentiation of adrenocortical tumors, placental and gestational trophoblastic lesions and sex cord stromal tumors.

![Granulosa theca cell tumor: immunohistochemical staining with Bond ready-to-use Inhibin (R1) using Bond Polymer Refine Detection.]

**Human Growth Hormone**

**Polyclonal**
7 mL Bond ready-to-use PA0704 P
For In Vitro Diagnostic Use

Growth hormone (GH), somatotropin, is the primary hormone responsible for regulating overall body growth and is also important in organic metabolism. It is synthesized by acidophilic or somatotropic cells of the anterior pituitary gland. Human GH has a molecular weight of 22 kD. GH stimulates growth indirectly by promoting the liver’s production of somatomedins, which act directly on bone and soft tissue to cause growth. GH exerts direct metabolic effects on the liver, adipose tissue and muscle. In general, growth hormone enhances protein synthesis, conserves carbohydrates and uses up fat stores.

Also available as a Novocastra concentrate, refer to page 121.

![Pituitary: immunohistochemical staining with Bond ready-to-use Human Growth Hormone (Polyclonal) using Bond Polymer Refine Detection.]

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Insulin

**Clone 2D11-H5**
7 mL Bond ready-to-use PA0620 P
*For In Vitro Diagnostic Use*

Insulin is a hormone secreted by the beta cells of the islets of Langerhans in the pancreas. It promotes glycogen storage, formation of triglycerides, and synthesis of protein and nucleic acids. Reports of immunocytochemical investigation reveal the presence of insulin in the cytoplasm of certain islet tumors. However, in some instances insulin-positive granules are sparse and form a margin against the cell membrane.

Also available as a Novocastra concentrate, refer to page 125.

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**Ki67**

**Clone MM1**
7 mL Bond ready-to-use PA0118 P (HIER)

**Clone K2**
7 mL Bond ready-to-use PA0230 P (HIER)
*For In Vitro Diagnostic Use*

The Ki67 antigen is a nuclear protein which is expressed in all active parts of the cell cycle (G1, S, G2 and mitosis) but is absent in resting cells (G0). In contrast to many other cell cycle-associated proteins, the Ki67 antigen is consistently absent in quiescent cells and is not detectable during DNA repair processes. Thus, the presence of Ki67 antigen is strictly associated with the cell cycle and confined to the nucleus, suggesting an important role in the maintenance and/or regulation of the cell division cycle.

**Product Specific Information**

Bond ready-to-use Ki67 is recommended for the assessment of cell proliferation in normal and neoplastic tissues.

Also available as a Novocastra concentrate, refer to page 126.

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Luteinizing Hormone

**Clone C93**
7 mL Bond ready-to-use PA0655 P
*For In Vitro Diagnostic Use*

Luteinising hormone (LH) is a trophic hormone which modulates the secretory activity of other endocrine glands. It is produced by the anterior hypophysis of the pituitary gland. This glycoprotein hormone, like human follicle stimulating hormone and thyroid stimulating hormone, is composed of a common alpha-subunit and a specific beta-subunit which characterizes each of these hormones.

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**Macrophage Marker**

**Clone MAC387**
7 mL Bond ready-to-use PA0752 P (HIER)
*For In Vitro Diagnostic Use*

L1, a member of the S-100 family of proteins, is reported to be found on neutrophils, monocytes, certain reactive macrophages and squamous mucosal epithelia.

**Product Specific Information**

Clone MAC387 is reported to be specific for the leucocyte antigen L1.
Mast Cell Tryptase

Clone 10D11
7 mL Bond ready-to-use PA0019
For In Vitro Diagnostic Use

Mast cells contain a number of preformed chemical mediators such as histamine, chymase, carboxypeptidase and proteolytic tryptase. A substantial quantity of tryptase is reported to be found in mast cells of skin and lung and suggests this enzyme plays a major role in mast cell mediated events. In vitro studies indicate tryptase can cleave C3 to form C3a anaphylatoxin, inactivate fibrinogen as a coagulable substrate for thrombin and activate latent collagenase. Models of allergic disease in the skin, nose and lung have each indicated elevated tryptase levels. Human mast cell tryptase has been reported to be implicated as a mediator of inflammation. Mast cell degranulation in the gut causes mucus secretion, mucosal edema, increased gut permeability and may be responsible for some of the symptoms and signs of inflammatory bowel disease.

Also available as a Novocastra concentrate, refer to page 130.

Mesothelin

Clone 5B2
7 mL Bond ready-to-use PA0373
For In Vitro Diagnostic Use

Mesothelin is present on the surface of mesothelial cells, mesothelioma, epithelial ovarian cancers and some squamous cell carcinomas. Mesothelin is abundantly expressed in the kidney and in occasional epithelial cells of the trachea, tonsil and fallopian tube. The function of mesothelin is unclear but it may have a role in cellular adhesion.

Product Specific Information

Mesothelin is reported to be abundant in normal mesothelial cells from which malignant mesothelioma and ovarian cystadenocarcinomas are derived. As such, Bond ready-to-use Mesothelin (5B2) is recommended for use as part of a panel of antibodies to distinguish mesotheliomas and ovarian cystadenocarcinomas from other solid tumors.

Mesothelin (5B2) is recommended for use as part of a panel of antibodies to distinguish mesotheliomas and ovarian cystadenocarcinomas from other solid tumors.

Also available as a Novocastra concentrate, refer to page 133.

Melan A

Clone A103
7 mL Bond ready-to-use PA0233
For In Vitro Diagnostic Use

Melan A, a product of the MART-1 gene, is a melanocytic differentiation marker recognized by autologous cytotoxic T lymphocytes.

Product Specific Information

Melan A (A103) is employed in the assessment of Melan A in melanocytic lesions.

Also available as a Novocastra concentrate, refer to page 132.

MLH1 (Mismatch Repair Protein)

Clone ES05
7 mL Bond ready-to-use PA0610
For In Vitro Diagnostic Use

MLH1, a mismatch repair protein involved in maintaining the integrity of genetic information, alongside MSH2, MSH6 and PMS2. During DNA replication, strand misalignment can occur resulting in alterations to microsatellite repeats, often referred to as microsatellite instability (MSI). These defects in DNA repair pathways have been linked to human carcinogenesis. Mutations in the MLH1 gene have been reported to be found in tumors with MSI, such as some forms of colon cancer eg Hereditary nonpolyposis colon cancer (HNPCC), a subset of sporadic carcinomas and breast cancer. Loss of expression of MLH1 has also been reported in acute lymphoblastic leukemia, endometrial carcinoma, gastric carcinoma and ovarian carcinoma.

Also available as a Novocastra concentrate, refer to page 134.
Appendix: immunohistochemical staining with Bond ready-to-use MLH1 (ES05) using Bond Polymer Refine Detection.

**MSH2 (Mismatch Repair Protein)**

**Clone 25D12**  
7 mL Bond ready-to-use PA0048 P (HIER)  
For In Vitro Diagnostic Use

MSH2 is involved in the initial recognition of mismatched nucleotides during the post replication mismatch repair process. The loss of MSH2 function leads to the accumulation of replication errors, which in turn may be responsible for the multiple mutations required for multistage carcinogenesis. Mutations in mismatch repair genes have been linked to hereditary nonpolyposis colon cancer and to sporadic cancers which exhibit microsatellite instability. MSH2 is reported to be expressed in the nuclei of cells from a variety of tissues including thyroid, heart, smooth muscle and the germinal centers of lymphoid follicles. In ileum and colon, MSH2 expression has been reported in the crypts, the cells of which are undergoing rapid renewal. They are responsible for the continuous production of differentiated cells which migrate over 2 to 4 days before being sloughed into the lumen.

Also available as a Novocastra concentrate, refer to page 134.

Appendix: immunohistochemical staining with Bond ready-to-use MSH2 (25D12) using Bond Polymer Refine.

**MSH6 (Mismatch Repair Protein)**

**Clone PU29**  
7 mL Bond ready-to-use PA0597 P (HIER)  
For In Vitro Diagnostic Use

MSH6 is a 160 kDa protein which is involved in DNA mismatch repair (MMR) and recombination pathways, when heterodimerized with MSH2. Defects in mismatch repair systems can cause mutations and can cause DNA microsatellite sequences to become unstable. Microsatellite instability has been described in colorectal cancer, particularly in Hereditary Nonpolyposis Colorectal Cancer (HNPPC) where MSH6 expression, along with other MSH proteins, is disrupted. Immunohistochemical studies have reported that MSH6 is strongly expressed in the nuclei of cells in normal colonic epithelium, especially in crypts. Expression is also found in lymphocytes. Studies have also shown that MSH6 is expressed in gastric carcinomas and endometrial carcinomas. However, sometimes expression can be lost in some endometrial carcinomas and colonic carcinomas with microsatellite instability. MSH6 has been reported to be a useful marker to use in conjunction with microsatellite instability screening to identify colon tumors that may contain MMR gene mutations, such as HNPPC.

Also available as a Novocastra concentrate, refer to page 135.

Appendix: immunohistochemical staining with Bond ready-to-use MSH6 (PU29) using Bond Polymer Refine.

**Multi Cytokeratin**

**Clone AE1 and AE3**  
7 mL Bond ready-to-use PA0909 P (Enzyme)  
For In Vitro Diagnostic Use

Keratins are a family of water insoluble proteins of 40 to 70 kDa. These proteins form tonofilaments, a class of intermediate filament, in epidermis as well as in almost all other epithelia. The process of normal epidermal differentiation is characterized by a series of morphological and biochemical changes as cells progress from the germinative basal layer through the spinous and granular layers to the outer cornified layer. The 65 to 67 kDa cytokeratins are reported to be present only above the basal layer, the 58 kDa cytokeratin is reported to be expressed throughout the entire epidermis including the basal layer and the 56 kDa cytokeratin is reported to be absent from the basal layer and is normally eliminated during stratum corneum formation. The 56 and 65 to 67 kDa cytokeratins are reported to be characteristic of epidermal cells undergoing terminal differentiation and may be considered as molecular markers for keratinization.

**Product Specific Information**

Clones AE1 and AE3 are specific for the 56.5, 50, 50', 48 and 40 kDa acidic cytokeratins as well as the 65 to 67, 64, 59, 58, 56 and 52 kDa basic cytokeratins. The cocktail of clones AE1 and AE3 exhibit broad reactivity with two families of cytokeratin, acidic and basic.

Also available as a Novocastra concentrate, refer to page 136.
Multiple Myeloma Oncogene 1 (MUM-1)

**Clone EAU32**

7 mL Bond ready-to-use PA0129 P (HIER)

*For In Vitro Diagnostic Use*

MUM-1 (Multiple Myeloma Oncogene 1)/FR4/ACSAT/PiP gene was originally identified because of its involvement in the t(6;14) translocation observed in multiple myeloma, which causes the juxtaposition of the MUM-1 gene to the Ig heavy chain locus. An antibody to MUM-1 indicates that the protein is strongly expressed in late plasma cell directed stages of B cell differentiation and in activated T cells and suggests that MUM-1 may serve as a marker for lympho-hemopoietic neoplasms derived from these cells. The morphologic spectrum of MUM-1 expressing cells has been found to range from that of a centrocyte to that of a plasmablast/plasma cell. Consequently the histogenic value of MUM-1 may be to provide a marker to aid in the identification of the transition from BCL-6 positive (germinal center B cells) to CD138 positive (plasmablasts and plasma cells). MUM-1 expression occurs in a wide range of lymphoid neoplasms including a proportion of diffuse B cell lymphomas but not myeloid or extra hemopoietic neoplasms. MUM-1 is consistently expressed in myeloma cells, Reed Sternberg cells in classic Hodgkin Disease, and normal and neoplastic T cells.

Also available as a Novocastra concentrate, refer to page 136.

**Muscle Specific Actin**

**Clone HHF35**

7 mL Bond ready-to-use PA0258 P

*For In Vitro Diagnostic Use*

Actins are protein constituents of microfilaments, the ubiquitous cytoskeletal elements present in most cells. Actins can be biochemically and immunologically divided into three main subsets; alpha-actins are present in muscle tissue, beta- and gamma-actins are present in non-muscle cells and a minor subset of gamma-actins is present in muscle cells.

**Product Specific Information**

Muscle Specific Actin (PA0258) is specific for alpha- and gamma-actins of smooth muscle (42 kD) reported to be expressed in striated muscle fibers of the myocardium, skeletal muscle, arterial cell wall, smooth muscle coat of the entire gastrointestinal tract, myometrial smooth muscle, prostatic stroma and bladder wall.

Also available as a Novocastra concentrate, refer to page 138.

**Muramidase (Lysozyme)**

**Polyclonal**

7 mL Bond ready-to-use PA0391 P (Enzyme)

*For In Vitro Diagnostic Use*

Intracellular muramidase, also known as lysozyme, has been reported to be expressed in myeloid and monocyctic cells, in leukocytes and in myelo-proliferative disorders. Muramidase is also reported to be expressed in poorly differentiated leukemic monoblasts.

Also available as a Novocastra concentrate, refer to page 129.
Myeloperoxidase

**Clone 59A5**
7 mL Bond ready-to-use PA0491 P
*For In Vitro Diagnostic Use*

Myeloperoxidase is a lysosomal enzyme found in cells of the myeloid series which metabolises most of the hydrogen peroxide generated by activated phagocytes. It is a major constituent of azurophilic cytoplasmic granules that uses hydrogen peroxide to oxidise a variety of aromatic compounds and chloride ions to hypochlorous acid (HOCI), a strong oxidant. HOCI is the most bacteriocidal oxidant known to be produced by neutrophils. Myeloperoxidase is reported to be a major component in all myeloid cells, including mature granulocytes and is a superior marker to myeloperoxidase mRNA, whose level decreases with the maturation of the cell and is not detectable from the myelocyte stage onwards. Myeloperoxidase is reported to be expressed in neutrophil granulocytes and monocytes in blood, in precursors of granulocytes in the bone marrow and in Kupffer cells of the liver.

Also available as a Novocastra concentrate, refer to page 139.

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Myoglobin

**Clone MYO18**
7 mL Bond ready-to-use PA0727 P (HIER)
*For In Vitro Diagnostic Use*

Myoglobin is a cytoplasmic, single chain polypeptide of 153 amino acids that contains a single heme group. Myoglobin is reported to be expressed in skeletal and cardiac muscle but not in smooth muscle and functions as an oxygen transporting pigment.

Also available as a Novocastra concentrate, refer to page 139.

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Myosin Heavy Chain (Smooth Muscle)

**Clone S131**
7 mL Bond ready-to-use PA0493 P (HIER)
*For In Vitro Diagnostic Use*

Myosin is a contractile muscle specific protein composed of two heavy and four light chains. The myosin heavy chain has many isoforms which are specific for different muscles or fiber types, some of which are developmentally regulated. Smooth muscle myosin heavy chain (SM-MHC) is a cytoplasmic structural protein that is a major component of the contractile apparatus in smooth muscle cells. It has been reported to be specific for smooth muscle development.

Also available as a Novocastra concentrate, refer to page 140.

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Myf-4 (Rhabdomyosarcoma Marker)

**Clone LO26**
7 mL Bond ready-to-use PA0226 P (HIER)
*For In Vitro Diagnostic Use*

Rhabdomyosarcomas are a class of myoblast-derived soft tissue sarcomas that usually express a number of muscle-specific genes and primarily affect children and young adults. Differentiation of myogenic cells is controlled by a set of regulatory genes including MyoD1, myogenin, Myf-5 and Myf-6. Myf-4 is the human homolog of myogenin. Its gene product, together with that of The, accumulates in the nucleus of differentiated cells. Myf-4 has been shown to be useful in the sub typing of small round blue cell tumors.

Also available as a Novocastra concentrate, refer to page 139.
**Negative Control (Mouse)**

**Clone MOPC-21**

7 mL Bond ready-to-use PA0996

*For In Vitro Diagnostic Use*

In some tissues, non-specific binding may occur, especially in neoplastic or necrotic tissue.

**Product Specific Information**

The use of Negative (Mouse) antibody is recommended to aid in the identification of cells, tissues or tissue components, which may non-specifically bind mouse antibodies and will allow better interpretation of specific staining at the antigenic site.

![Tonsil: immunohistochemical staining with Bond ready-to-use Negative (Mouse) using Bond Polymer Refine Detection.](image)

**Negative Control (Rabbit)**

7 mL Bond ready-to-use PA0777

*For In Vitro Diagnostic Use*

In some tissues, non-specific binding may occur, especially in neoplastic or necrotic tissue.

**Product Specific Information**

The use of Negative (Rabbit) is recommended to aid in the identification of cells, tissues or tissue components, which may non-specifically bind rabbit antibodies and will allow better interpretation of specific staining at the antigenic site.

![Tonsil: immunohistochemical staining with Bond ready-to-use Negative (Rabbit) using Bond Polymer Refine Detection.](image)

**Neurofilament 200kD**

**Clone N52.1.7**

7 mL Bond ready-to-use PA0371

*For In Vitro Diagnostic Use*

Neurofilaments constitute the main structural elements of neuronal axons and dendrites. Neurofilaments are composed of three major subunits referred to as the neurofilament triplet, with molecular weights of 68 kD, 160 kD and 200 kD. Neurofilament subunits are reported to be present in neurons, neuronal processes, peripheral nerves and sympathetic ganglion cells. Within tumors, only neoplastic cells of neural origin or those exhibiting neuronal differentiation, have been reported to express neurofilaments. Also available as a Novocastra concentrate, refer to page 142.

![Cerebrum: immunohistochemical staining with Bond ready-to-use Neurofilament (N52.1.7) using Bond Polymer Refine Detection.](image)

**Neuron Specific Enolase**

**Clone 22C9**

7 mL Bond ready-to-use PA0435

*For In Vitro Diagnostic Use*

Enolase is a glycolytic enzyme catalyzing the reaction pathway between 2-phospho-glycerate and phosphoenol pyruvate. In mammals, enolase molecules are dimers composed of three distinct subunits (α, β and γ) whereas, in rats, five forms have been found. The α subunit and γ subunit are of approximately 47 kD and 45 kD, respectively. The γγ and αγ enolases are located mainly in the nervous tissue and neuroendocrine cells.

**Product Specific Information**

Clone 22C9 reacts with the γ subunit of the enolase isoenzyme. Neuron Specific Enolase (22C9) is recommended for use as part of a panel of antibodies for the identification of normal and neoplastic cells of neuronal and neuroendocrine origin. Also available as a Novocastra concentrate, refer to page 142.

![Carcinoid: immunohistochemical staining with Bond ready-to-use Neuron Specific Enolase (22C9) using Bond Polymer Refine Detection.](image)
Oct-2

Clone Oct-207
7 mL Bond ready-to-use PA0532 P (HIER)
For In Vitro Diagnostic Use

Oct-2 is a transcription factor belonging to the POU homeo-domain family that binds to the Ig gene octamer sites regulating B cell specific genes. It is dependent on the activity of B cell restricted coactivators such as BOB-1/OBF-1. Reed Sternberg (RS) cells represent the malignant cells in classical Hodgkin’s disease and are derived from germinal center B cells. In a number of these cases, cells do not express immunoglobulin due to the presence of crippling mutations within the Ig genes. As Ig gene expression in B cells also requires an interaction between octamer sites and the transactivating factors Oct-2 and BOB-1 expression represents a novel mechanism for immunoglobulin gene deregulation in RS cells. Oct-2 protein expression is not restricted to B cells, although expression levels are much higher in these cells. Germinal center B cells show higher expression for Oct-2 and BOB-1/OBF-1. Oct-2 expression is reported to be significantly greater in germinal center derived lymphomas, although other B cell lymphomas also display high levels of expression.

Also available as a Novocastra concentrate, refer to page 143.

p53 Protein

Clone DO-7
7 mL Bond ready-to-use PA0057 P (HIER)
For In Vitro Diagnostic Use

p53 protein plays a vital role in suppressing the development of cancer. The accumulation of p53 protein in response to DNA damage in vitro is well established and appears to induce growth arrest and apoptosis by the transcriptional regulation of other genes.

Product Specific Information

This monoclonal antibody recognizes both wild type and mutant forms of human p53 protein. Bond ready-to-use p53 (DO7) is recommended for determining the p53 status of a variety of carcinomas, including breast and colorectal carcinomas.

Also available as a Novocastra concentrate, refer to page 145.

Oct 3/4

Clone N1NK
7 mL Bond ready-to-use PA0934 P (HIER)
For In Vitro Diagnostic Use

Oct3/4 is a member of the POU homeodomain family of transcription factors, which is expressed by embryonic stem cells and germ cells. A critical amount of Oct3/4 levels are associated with loss of pluripotency. Oct3/4 has been proposed as a useful marker for germ cell tumors which exhibit features of pluripotentiality, including seminoma/dysembryoma and embryonal carcinoma, and establishing a germ cell origin for some metastatic tumors of uncertain primary tumor.

Also available as a Novocastra concentrate, refer to page 143.

p63

Clone 7JUL
7 mL Bond ready-to-use PA0478 P (HIER)
For In Vitro Diagnostic Use

p63 is a type II integral membrane protein predominantly localized in the rough endoplasmic reticulum. p63 is reported to be expressed in a number of normal tissues including proliferating cells of the epithelium, cervix, urothelium and prostate. p63 is reported to be expressed in most poorly differentiated squamous cell carcinomas.

Also available as a Novocastra concentrate, refer to page 72.
Pax-5

Clone 1EW
7 mL Bond ready-to-use PA0552 P (HIER)
For In Vitro Diagnostic Use

Pax genes are a family of developmental control genes that encode nuclear transcription factors and have been implicated in the control of mammalian development.

PAX-5 is a B cell specific transcription factor, that is expressed in pro B cells, pre-B, mature B cells and subsequently in all stages of B cell development until the plasma cell stage in which it is downregulated.

Also available as a Novocastra concentrate, refer to page 148.

Placental Alkaline Phosphatase

Clone 8A9
7 mL Bond ready-to-use PA0161 P (HIER)
For In Vitro Diagnostic Use

Reports indicate that Clone 8A9 stains seminomas and placenta indicating a specificity for both PLAP and PLAP-like enzyme. Placental alkaline phosphatase (PLAP) is a membrane-associated sialoglycoprotein enzyme normally present at high concentration in syncytiotrophoblasts within the placenta during the third trimester of gestation. PLAP is reported to be expressed only in normal term placenta, endocervix and fallopian tube and also in ovarian and proximal gastrointestinal tumors. PLAP expression is rare in malignant germ cell tumors. This is a distinct molecule from: A PLAP-like variant has been described which shares more than 85 percent homology with PLAP itself. PLAP-like enzyme is reported to be predominantly found in normal fetal and neonatal testis, and in thymus. It is also commonly expressed in germ cell tumors and more recently described in seminomas. Used in the detection of seminomas.

Also available as a Novocastra concentrate, refer to page 150.

Progesterone Receptor

Clone 16
7 mL Bond ready-to-use PA0312 P (HIER)
For In Vitro Diagnostic Use

Progesterone Receptor content in breast cancer is an important parameter in the prediction of, prognosis and response to endocrine therapy. Progesterone Receptor (16) is an aid in this management, prognosis and prediction of therapy outcome.

Product Specific Information

Clone 16 is specific to the A form of progesterone receptor in formalin-fixed, paraffin-embedded tissues.

Also available as a Novocastra concentrate, refer to page 152.

Prostate Specific Antigen

Clone 35H9
7 mL Bond ready-to-use PA0431 P (HIER)
For In Vitro Diagnostic Use

Prostate specific antigen is a protein of the kallikrein family of protein kinases. Distinct from Prostatic Acid Phosphatase, it has been found to be immunologically identical and biologically similar to a protein isolated from the prostate gland.

Also available as a Novocastra concentrate, refer to page 153.
Prostatic Acid Phosphatase

**Clone PASE/4LJ**
7 mL Bond ready-to-use PA0006 P
*For In Vitro Diagnostic Use*

Prostatic acid phosphatase (PAP) is an isoenzyme of acid phosphatase found in large amounts in the prostate and seminal fluid. The precise function of PAP is unknown, but it may act as a hydrolase to split phosphoryl choline in semen and also function as a transferase. Elevated serum levels of the enzyme are reported in metastatic prostatic carcinoma.

Also available as a Novocastra concentrate, refer to page 154.

Prostate adenocarcinoma: immunohistochemical staining with Bond ready-to-use Prostatic Acid Phosphatase (PASE/4LJ) using Bond Polymer Refine Detection.

S-100

**Polyclonal**
7 mL Bond ready-to-use PA0900 P (Enzyme)
*For In Vitro Diagnostic Use*

S-100 protein is reported to be expressed in neuroectodermal tissue, including nerves and melanocytes. Langerhans’ cells in skin and interdigitating reticulum cells in the paracortex of lymph nodes are also reported to express S-100 protein.

**Product Specific Information**

S-100 (polyclonal) is recommended for use in a panel of antibodies for the determination of tumors of neuroectodermal origin.

Also available as a Novocastra concentrate, refer to page 157.

Lung metastatic melanoma: immunohistochemical staining with Bond ready-to-use S-100 (Polyclonal) using Bond Polymer Refine Detection.

Protein Gene Product 9.5

**Clone 10A1**
7 mL Bond ready-to-use PA0286 P (HIER)
*For In Vitro Diagnostic Use*

Protein gene product (PGP) 9.5 is a neuron specific protein, structurally and immunologically distinct from neuron specific enolase. PGP9.5 expression has been reported in neurons and nerve fibers at all levels of the central and peripheral nervous system, in many neuroendocrine cells, in segments of the renal tubules, in spermatogonia and Leydig cells of the testis, in ova and in some cells of both the pregnant and non-pregnant corpus luteum. PGP9.5 is known to be a member of the ubiquitin C-terminal hydroxylase family and is also concentrated within inclusion bodies suggesting that such structures may be metabolically active regions of the cells.

Also available as a Novocastra concentrate, refer to page 154.

Small bowel nerve fibers: immunohistochemical staining with Bond ready-to-use Protein Gene Product 9.5 (10A1) using Bond Polymer Refine Detection.

Serotonin

**Polyclonal**
7 mL Bond ready-to-use PA0736 P (HIER)
*For In Vitro Diagnostic Use*

Serotonin (5-hydroxytryptamine, 5-HT) is reported to be a widely distributed neurotransmitter and hormone in the mammalian peripheral and central nervous system (CNS). Serotonin is formed by the decarboxylation of 5-hydroxy-tryptophan, its intermediate, which in turn is formed by hydroxylation of L-tryptophan by tryptophan hydroxylase. In the CNS, the action of serotonin is terminated by reuptake into the presynaptic terminal by specific serotonin transporters. Serotonin has been implicated in several neuropsychiatric disorders such as anxiety, depression and schizophrenia. The majority of serotonergic nerve terminals in the CNS originate in neuronal cell bodies of the Raph nuclei (dorsal, median), nucleus Raph obscurus and nucleus Raph pallidus in the brainstem which project to specific areas of the brain and spinal cord. Serotonin is thought to be an inhibitory neurotransmitter regulating a wide range of sensory, motor and cortical functions in the CNS. In the periphery, serotonin is reported to be present in neural and non-neural structures such as platelets, gastrointestinal tract (myenteric plexus, enterochromaffin cells), lungs (neuroepithelial cells), thyroid gland and spleen.

Also available as a Novocastra concentrate, refer to page 158.

Carcinoid: immunohistochemical staining with Bond ready-to-use Serotonin (Polyclonal) using Bond Polymer Refine Detection.
Smooth Muscle Actin

**Clone csm-1**
7 mL Bond ready-to-use PA0943 P

For In Vitro Diagnostic Use

Smooth muscle can be located in the vascular walls, intestinal muscularis mucosae, muscularis propria and in the stroma of many tissues. They have also been noted in the myoepithelial cells of various glands most notably the salivary and mammary glands and in neoplastic tissues such as leiomyomas and leiomyosarcomas.

Also available as a Novocastra concentrate, refer to page 57.

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Somatostatin

**Polyclonal**
7 mL Bond ready-to-use PA0331 P

For In Vitro Diagnostic Use

Somatostatin is a cyclic polypeptide hormone originally isolated from the hypothalamus and characterized by its ability to inhibit release of growth hormone from the pituitary gland. It exists in two forms, somatostatin-14, composed of 14 amino acids and somatostatin-28, a prohormone composed of 28 amino acids. In the digestive system, somatostatin has been identified in intrinsic nerves of the intestinal wall and in endocrine cells of the digestive mucosa and the pancreatic islets. The antrum, duodenum and pancreas have been reported to contain almost exclusively somatostatin-14, whereas the gastric body and the rest of the intestine contain 40 to 80 percent somatostatin-28.

**Product Specific Information**

Somatostatin (polyclonal) is specific for D cells of the mammalian pancreas and cells of the hypothalamic parvicellular region.

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Synaptophysin

**Clone 27G12**
7 mL Bond ready-to-use PA0299 P (HIER)

For In Vitro Diagnostic Use

Synaptophysin is an integral membrane glycoprotein. It is reported to occur in presynaptic vesicles of neurons in brain, spinal cord, retina and in similar vesicles of the adrenal medulla as well as in neuromuscular junctions. Synaptophysin may be involved in synaptic vesicle formation and exocytosis and as such is reported to be expressed in a wide spectrum of neuro-endocrine tumors.

**Product Specific Information**

Bond ready-to-use Synaptophysin (27G12) is recommended for the identification of tumors of neuroendocrine origin and differentiation.

Also available as a Novocastra concentrate, refer to page 160.

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Tartrate-Resistant Acid Phosphatase (TRAP)

**Clone 26E5**
7 mL Bond ready-to-use PA0093 P (HIER)

For In Vitro Diagnostic Use

Tartrate-resistant acid phosphatase (TRAP) is a basic, iron-binding protein with high activity towards phosphoproteins, ATP and 4-nitrophenyl phosphate. This isoenzyme has been reported through different applications to be expressed in human alveolar macrophages, osteoclasts, spleen and liver. Expression of TRAP is reported to be increased in the spleen and monocytes of individuals with Gaucher’s disease, Hodgkin’s disease and the sera of individuals undergoing active bone turnover. Elevated levels are also reported to be associated with various B cell and T cell leukemias and lymphomas, decidual cells, syncytiotrophoblasts and some macrophages distributed throughout maternal and embryonic tissues.

Also available as a Novocastra concentrate, refer to page 161.
Terminal Deoxynucleotidyl Transferase

**Clone SEN28**
7 mL Bond ready-to-use PA0339 P (HIER)  
*For In Vitro Diagnostic Use*

Terminal Deoxynucleotidyl Transferase (TdT) is a DNA polymerase. It is reported to be expressed in primitive T and B lymphocytes of the normal thymus and bone marrow. TdT is reported to be expressed in leukemias and acute lymphoblastic lymphomas where early and precise differentiation is crucial. The determination of TdT expression is reported to be most valuable when it is difficult to differentiate histologically between lymphoblastic lymphoma and Burkitt’s lymphoma.

**Product Specific Information**
Terminal Deoxynucleotidyl Transferase (SEN28) is recommended for use in the diagnosis and differentiation of acute lymphoblastic leukemia/lymphoma from other lymphomas.

Also available as a Novocastra concentrate, refer to page 162.

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Thyroid Stimulating Hormone

**Clone QB2/6**
7 mL Bond ready-to-use PA0776 P (Enzyme)  
*For In Vitro Diagnostic Use*

Thyroid stimulating hormone (TSH) is a pituitary hormone of 28 kD which stimulates thyroid growth and production of thyroid hormones. TSH is reported to be expressed in thyrotrophic cells of the pituitary and pituitary adenomas.

Also available as a Novocastra concentrate, refer to page 163.

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Thyroglobulin

**Clone 1D4**
7 mL Bond ready-to-use PA0025 P  
*For In Vitro Diagnostic Use*

A heavily glycosylated protein of 670 kD

Thyroglobulin is composed of two identical subunits, synthesized by the follicular epithelial cells of the thyroid.

Also available as a Novocastra concentrate, refer to page 162.

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Thyroid Transcription Factor-1

**Clone SPT24**
7 mL Bond ready-to-use PA0364 P (HIER)  
*For In Vitro Diagnostic Use*

Thyroid Transcription Factor-1 (TTF-1) plays a role in regulating genes expressed in the thyroid, lung and brain. These include the genes encoding thyroglobulin, Clara cell secretory protein and surfactant proteins. Gene targeting studies have shown TTF-1 to be essential for the proper development of the thyroid and lungs; since abnormal expression may underline a number of congenital abnormalities.

**Product Specific Information**
Thyroid Transcription Factor-1 (SPT24) is recommended for use in the classification of tumors of the thyroid and lung.

Also available as a Novocastra concentrate, refer to page 163.

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For detailed information on all products please visit our website:  
www.leica-microsystems.com
Tyrosinase

Clone T311
7 mL Bond ready-to-use PA0322 P (HIER)
For In Vitro Diagnostic Use

The biosynthesis of melanin in melanocytes involves a family of enzymes, a key member of which is tyrosinase.

Tyrosinase deficiency is associated with various forms of albinism and in particular oculocutaneous albinism. L-tyrosinase is the initial substrate for melanin biosynthesis and its conversion to dopaquinone is catalyzed by tyrosinase, whose expression is reported in melanocytes and melanomas.

Tyrosinase expression in melanocytic lesions can be assessed using Tyrosinase (T311).

Also available as a Novocastra concentrate, refer to page 167.

Villin

Clone CWWB1
7 mL Bond ready-to-use PA0106 P (HIER)
For In Vitro Diagnostic Use

Villin and the structurally-related proteins gelsolin, fragmin and severin, all regulate the framework and assembly of actin. Villin is mainly produced by epithelial cells that develop a brush border. epithelial cells of the intestinal mucosa and gall bladder, or in epithelial cells of the kidney proximal tubules and ductuli efferentes of the testes.

Villin is also reported to be found in some epithelia which lack a brush border but which are derived from embryonic gut such as duct cells of the exocrine pancreas and biliary cells of the liver. In these cell types, villin is concentrated in the apical cytoplasm. Epithelial cells of the intestinal mucosa are continually being renewed and this involves a migration of these cell types from the intestinal crypts to the tips of the villi, gradually acquiring their differentiated phenotype as they do so. The maximum production of villin occurs at the base of the villus. Villin shows tissue-specific expression, restricted to certain epithelia and their apical domains, thus indicating their polarity. The morphological loss of polarity of colonic epithelial cells is reported to be one of the most significant indicators of dysplasia or neoplasia.

Also available as a Novocastra concentrate, refer to page 170.

von Willebrand Factor

Clone 36B11
7 mL Bond ready-to-use PA0400 P (HIER)
For In Vitro Diagnostic Use

Human von Willebrand factor (or factor VIII-related antigen) is a 270 kD multimeric plasma glycoprotein. It mediates platelet adhesion to injured vessel walls and serves as a carrier and stabilizer for coagulation factor VIII.

The von Willebrand factor has functional binding domains to platelet glycoprotein Ib, glycoprotein Ib/IIIa, collagen and heparin. Von Willebrand factor is synthesized by endothelial cells and is reported to be expressed in platelets, megakaryocytes and a number of tumors, including hemagiomas, hemangiosarcomas and Kaposi’s sarcomas.

Also available as a Novocastra concentrate, refer to page 123.
Wilms’ Tumor

**Clone WT49**
7 mL Bond ready-to-use PA0562 P (HIER)
For In Vitro Diagnostic Use

Wilms’ tumor protein (WT1) has a role in transcriptional regulation and is expressed in the kidney and a subset of hematopoietic cells. Alteration of transcription factor function is a common mechanism in oncogenesis. The WT1 protein contains a DNA binding domain and any deletions or point mutations of the WT1 gene which destroy this activity result in the development of the childhood nephroblastoma Wilms’ tumor and Denys-Drash syndrome. The tumor is reported to arise from the embryonic metanephric mesenchyme cells in a disorganized array and affects 1 in 10,000 live births. Mutations of the WT1 gene are observed in only 10 to 20 percent of sporadic Wilms’ tumors, but may be present in another range of tumors derived from the urogenital tract and mesothelium. Wilms’ tumor protein is also reported to be expressed in a range of human cancers including breast, acute myeloid leukemia and mesothelioma. Wilms’ tumor protein is often used as part of a panel of antibodies to subtype small round blue cell tumors.

Also available as a Novocastra concentrate, refer to page 170.

ZAP-70

**Clone L453R**
7 mL Bond ready-to-use PA0998 P (HIER)
For In Vitro Diagnostic Use

ZAP-70 is a member of the syk family of proteins. It is expressed on T cells and NK cells and is required for the T cell receptor activation that triggers an immune response. CLL B cells that express the non-mutated immunoglobulin VH genes express levels of ZAP-70 protein that are comparable to those found in the blood T cells of healthy adults. Leukemic cells that express mutated IgVH genes generally do not express detectable levels of ZAP-70 protein and this is correlated with the high level expression of CD38. The ZAP-70 positive sub-type has been reported to be associated with a more aggressive phenotype.

Also available as a Novocastra concentrate, refer to page 171.
Bond Ready-to-Use ISH Probes

Anti-Biotin Antibody

7.5 mL ready-to-use AR0584 For In Vitro Diagnostic Use

Components

Anti-Biotin Antibody is a purified anti-biotin, IgG1 isotype. It is supplied ready-to-use.

Application

In situ hybridization (ISH) allows the detection and visualization of specific nucleic acids in tissue sections. ISH probes used for detection of DNA on the Bond contain a biotin label. The Anti-Biotin Antibody allows the linking of the probe with the detection reagents and consequently visualization of a chromogenic product by light microscopy.

Anti-Fluorescein Antibody

3.75 mL AR0833 15 mL AR0222 For In Vitro Diagnostic Use

Components

Anti-Fluorescein Antibody is a purified IgG fraction of a mouse monoclonal antibody. It is supplied ready-to-use.

Application

In situ hybridization (ISH) allows the detection and visualization of specific nucleic acids in tissue sections. ISH probes used for the detection of mRNA on Bond contain a fluorescein label. The Anti-Fluorescein Antibody allows linking of the oligonucleotide probe with the detection reagents, and consequently, visualization of a chromogenic product by light microscopy.

CMV Probe

5.5 mL PB0614 For In Vitro Diagnostic Use

Components

Ready-to-use fluorescein-conjugated oligonucleotide probe directed to human cytomegalovirus (CMV) early gene RNA transcript in formalin-fixed, paraffin-embedded tissue. Optimized for use with Bond Polymer Refine Detection (DS9800) and Anti-Fluorescein Antibody (AR0833/AR0222).

Application

CMV is a member of the Beta Herpes Virus family, transmitted via body fluids, and can establish primary infection, latent infection and subsequent viral reactivation. CMV is a common opportunistic pathogen, capable of causing serious disease in immunocompromised individuals such as AIDS patients, transplant patients and in neonates. Congenital CMV is a result of intrauterine infection and although the majority of children are asymptomatic, congenital CMV can result in sensorineural hearing loss, cognitive, motor and visual deficits and seizures.

DNA Negative Control

6.25 mL PB0731 For In Vitro Diagnostic Use

Components

DNA Negative Control is a ready-to-use reagent consisting of the hybridization solution used in the Bond DNA Probes, for use in formalin-fixed paraffin embedded tissue. Optimized for use with Bond Polymer Refine Detection (DS9800), Anti-Biotin Antibody (AR0584) and Stringency Wash (AR0633).

Application

Negative control probes should be run on patient tissue to confirm the absence of background staining resulting from non-specific interactions that would influence the test result.

DNA Positive Control

6.25 mL PB0682 For In Vitro Diagnostic Use

Components

The DNA Positive Control Probe is a probe designed to specifically hybridize to the genomic ALU repeat sequences, which represent approximately 10 percent of the human genome. It is generated with a biotin label using the same procedures as applied to the Bond DNA Probes, optimized for use with Bond Polymer Refine Detection (DS9800), Anti-Biotin Antibody (AR0584) and Stringency Wash (AR0633) in formalin-fixed paraffin embedded tissue.

Application

Positive control probes should be run on patient tissue to confirm that all reagents are working correctly and to provide information on the preservation of nucleic acids in the tissue as well as accessibility of nucleic acids to the probe.
EBER Probe

5.5 mL PB0589 P
For In Vitro Diagnostic Use

Components
Ready-to-use fluorescein-conjugated oligonucleotide probe directed to Epstein-Barr Virus encoded RNA (EBER) transcripts in formalin-fixed, paraffin-embedded tissue. Optimized for use with Bond Polymer Refine Detection (DS9800) and Anti-Fluorescein Antibody (AR0833/AR0222).

Application
Epstein-Barr Virus (EBV) is a member of the Gamma Herpes Virus family. EBV can establish both lytic infection as well as latent infection. Epstein Barr Virus encoded RNA is abundantly expressed in latent EBV infection and ISH is considered a sensitive method for the detection of latent EBV infection. Latent EBV infection is associated with several conditions including: Hodgkin’s Lymphoma, B cell Non Hodgkin’s Lymphoma, nasopharyngeal carcinoma, lymphoproliferative disorders and lymphoma in the immunosuppressed, including transplant and AIDS patients, gastric cancer and some T cell lymphomas.

HPV (subtypes 16, 18, 31, 33, 51) Probe

6.25 mL ready-to-use PB0829 P
For In Vitro Diagnostic Use

Components
HPV (16, 18, 31, 33, 51) is a ready-to-use biotin-conjugated DNA probe directed to HPV subtypes 16, 18, 31, 33 and 51, for use in formalin-fixed paraffin-embedded tissue. It has been optimized for use with Bond Polymer Refine Detection (DS9800), Anti-Biotin Antibody (AR0584) and Stringency Wash (AR0633).

Application
HPV infections have been associated with a number of malignant and benign lesions, including genital warts, anogenital cancers and oral head and neck cancers. Most notable HPV subtypes have been associated with above 95 percent of cervical cancer. As a result, HPV subtypes are broadly classified as high or low risk, depending on the incidence they are associated with cervical malignant transformation (high risk) and benign lesion development (low risk). There are 15 HPV subtypes classified as high risk, including 16, 18, 31, 33 and 51. HPV subtypes 16 and 18 are the most frequent subtypes associated with cervical carcinogenesis and are detected in up to 71 percent of cervical cancers.

HPV (subtypes 6, 11) Probe

6.25 mL ready-to-use PB0780 P
For In Vitro Diagnostic Use

Components
HPV (6,11) is a ready-to-use biotin-conjugated DNA probe directed to HPV subtypes 6 and 11, for use in formalin-fixed paraffin-embedded tissue. It has been optimized for use with Bond Polymer Refine Detection (DS9800), Anti-Biotin Antibody (AR0584) and Stringency Wash (AR0633).

Application
HPV infections have been associated with a number of malignant and benign lesions, including genital warts, anogenital cancers and oral head and neck cancers. Most notable HPV subtypes have been associated with above 95 percent of cervical cancers. As a result, HPV subtypes are broadly classified as high or low risk, depending on the incidence they are associated with cervical malignant transformation (high risk) and benign lesion development (low risk). There are 12 HPV subtypes classified as low risk, including 6 and 11, which have a low association with cervical cancer progression.
**Kappa Probe**

5.5 mL PB0645  
_For In Vitro Diagnostic Use_

**Application**

Kappa Probe is used in conjunction with Lambda Probe for the detection of antibody producing B cells in formalin-fixed, paraffin-embedded tissue. B cell neoplasms are thought to arise from a single transformed cell (monoclonal), whereas reactive states result in proliferation of a number of B cells (polyclonal). Since immunoglobulins from the same B cell contain either Kappa or Lambda light chains, light chain restriction or monoclonality can be used to make the distinction between reactive and neoplastic B cell proliferations.

**Components**

Ready-to-use fluorescein-conjugated oligonucleotide probe directed to Kappa light chain messenger RNA in formalin-fixed, paraffin-embedded tissue. Optimized for use with Bond Polymer Refine Detection (DS9800) and Anti-Fluorescein Antibody (AR0833/AR0222).

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**Lambda Probe**

5.5 mL PB0669  
_For In Vitro Diagnostic Use_

**Components**

Lambda Probe is used in conjunction with Kappa Probe for the detection of antibody producing B cells in formalin-fixed, paraffin-embedded tissue. B cell neoplasms are thought to arise from a single transformed cell (monoclonal), whereas reactive states result in proliferation of a number of B cells (polyclonal). Since immunoglobulins from the same B cell contain either Kappa or Lambda light chains, light chain restriction or monoclonality can be used to make the distinction between reactive and neoplastic B cell proliferations.

**Application**

Ready-to-use fluorescein-conjugated oligonucleotide probe directed to Lambda light chain messenger RNA in formalin-fixed, paraffin-embedded tissue. Optimized for use with Bond Polymer Refine Detection (DS9800) and Anti-Fluorescein Antibody (AR0833/AR0222) on the Bond system.

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**RNA Negative Control Probe**

5.5 mL PB0809  
_For In Vitro Diagnostic Use_

**Components**

RNA Negative Control Probe is a single oligonucleotide, designed from zebrafish DNA and analyses using Basic Local Alignment Search Tool (BLAST) analysis to confirm that the sequence bears no homology with any human sequences. Optimized for use with Bond Polymer Refine Detection (DS9800) and Anti-Fluorescein Antibody (AR0833/AR0222).

**Application**

The RNA Negative Control Probe is generated with a fluorescein label using the same procedures as applied to the other oligonucleotide probes that are used in the detection of RNA on Bond. Therefore, RNA Negative Control Probe is ideal as a negative control probe for RNA ISH on Bond.

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**RNA Positive Control Probe**

5.5 mL PB0785  
_For In Vitro Diagnostic Use_

**Components**

Ready-to-use fluorescein-conjugated oligonucleotide probe directed to the Poly(A) tail of messenger RNA in formalin-fixed, paraffin-embedded tissue. Optimized for use with Bond Polymer Refine Detection (DS9800) and Anti-Fluorescein Antibody (AR0833/AR0222).

**Application**

RNA is very susceptible to degradation by RNases, therefore, the RNA Positive Control Probe is ideally used as a screening tool to detect the preservation of mRNA in cells. Staining with the RNA Positive Control Probe should result in dark brown nuclear staining with some cytoplasmic staining, depending on the translational activity of the cell.

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**Stringency Wash**

6.25 mL AR0633  
_For In Vitro Diagnostic Use_

**Components**

The Stringency Wash Solution is a formamide mixture used with the Bond DNA Probes. This solution reduces non-specific hybridization of DNA probes.

**Application**

In situ hybridization (ISH) allows the detection and visualization of specific nucleic acids in tissue sections. The Stringency Wash Solution is intended for use with biotin conjugated DNA probes to reduce non-specific DNA hybridization in formalin-fixed, paraffin-embedded tissue using the automated Bond system.
Consumables

Bond Aspirating Probe Cleaning System

15 Cleaning Cycles CS9100
For In Vitro Diagnostic Use

The Bond Aspirating Probe Cleaning System contains reagents optimized to clean the aspirating probe of residual DAB. Sold in a standard reagent tray, the system is loaded onto Bond where a predefined cleaning protocol ensures maximum wash efficiency.

Bond Mixing Stations

5 Pack S21.1971.110

Bond Mixing Stations are reusable inserts with six vials for mixing and catalyzing chromogens prior to slide application. Fresh chromogen promotes high quality staining. Replacing the mixing stations at recommended intervals ensures that the mixed chromogen does not become contaminated.

Bond CT Cleaning Rack

1 Rack S21.2129

The Bond (CT) Covertile Cleaning Rack supports Covertiles to make cleaning simple and convenient.

Bond Open Containers 7 mL

10 Pack, minimum 200 Tests/container OP79193

Bond Open 7 mL Containers allow the use of reagents from any source on the Bond system. Each container can be refilled until a total of 40 mL has been dispensed from it. They are ideal for reagents that are consumed intermittently and have a short shelf life.

Bond Open Containers 30 mL

10 Pack, minimum 200 Tests/container OP309700

Bond Open 30 mL Containers allow the use of reagents from any source on the Bond system. Each container holds 30 mL and can be refilled until a total of 40 mL has been dispensed from it. They are ideal for high throughput reagents that are consumed on a daily basis and their use can minimize reagent preparation time.

Bond Reagent Tray

1 Tray S21.1003.110

Additional Bond Reagent Trays let laboratories setup reagents for upcoming runs while other reagent trays are in use. This reduces setup delays and improves laboratory workflow.

Bond Slide Labeler Cleaning Pen

1 Pen S21.1913.110

The Bond Slide Labeler Cleaning Pen is used to clean the print head on the Bond Slide Labeler. Regular cleaning helps ensure labels are printed clearly and correctly.

Bond Slide Labeler Printing Ribbon

1 Roll S21.1912.110

Bond Slide Labeler Printing Ribbon produces high-quality, solvent-resistant labels when printing on Bond slide labels. This assists in preserving the integrity of patient data recorded on the Bond slide labels.

Bond Slide Tray

1 Tray S21.0304.110

Additional Bond Slide Trays to allow laboratories to prepare slides while other trays are running. This reduces setup delays and improves laboratory workflow.

Bond Titration Container Inserts

50 Pack OPT9719
For In Vitro Diagnostic Use

Bond Titration Container Inserts are tubes that fit directly into the Bond Titration Containers. They enable safer use of up to 40 mL of reagent per titration container.

Bond Titration Kit

10 Titration Containers and 50 Titration Container Inserts OPT9049

The Bond Titration Kit contains Bond Titration Container Inserts and Bond Titration Containers. The kit lets users optimize primary antibody concentrations on the Bond system. The kits can be re-used for different antibodies and are designed with minimal dead volume to preserve reagent.
Bond Universal Covertile

100 Pack S21.2001.110

The Bond Universal Covertile is a patented technology that facilitates gentle, even reagent flow over tissue. It prevents reagent evaporation and minimizes waste generation. The Covertile is re-usable and can also be recycled once its staining life is over.

Bond Universal Covertile.

Bond Universal Slide Labels

3000 Labels/roll S21.2011.110

Bond Universal Slide Labels are used to record patient data and can be adhered to a slide for easy identification. The labels are resistant to most solvents so information remains intact during routine laboratory use.

Bond Universal Slide Label Covers

3000 Labels/roll S21.1985.110

Bond Universal Slide Label Covers are applied directly on top of the slide label prior to staining on the Bond system. They protect the information printed on the label against commonly used histology chemicals.

Leica Microsystems Plus Slides

20 Boxes x 72 slides/box S21.2113

Leica Microsystems Plus Slides are positively charged glass microscopic slides designed for use on the Bond system. They include defined margins to enable the accurate placement of tissue for staining in the 100 μL and the 150 μL dispense modes, which helps in maintaining the integrity of staining quality.
Create superior IHC slides with Novocastra antibodies, Novolink™ Compact Polymer™ detection systems, and ancillary reagents. For quality, consistency and efficiency, it’s time to switch to Novocastra.
A BETTER WAY TO SELECT SUPERIOR REAGENTS

Pathologists and scientists can quickly identify the antibodies they need with the Novocastra Reference Range. Each antibody clone in the range was selected for its superior performance then grouped according to its applications.

- Quality – antibodies tested in formalin-fixed, paraffin-embedded tissue
- Consistency – a complete solution including detection systems, diluents and ancillaries
- Reliability – robust mouse monoclonal antibodies

NOVOCASTRA™ REFERENCE RANGE™

You can identify Reference Range products in this catalog by looking for this symbol: Reference Range
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<td>CD30</td>
<td>JCM182</td>
<td>NCL-L-CD30-691</td>
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<td>CD33</td>
<td>PWS44</td>
<td>NCL-L-CD33</td>
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<td>CD34 (Endothelial Cell Marker)</td>
<td>GBEnd10</td>
<td>NCL-L-END</td>
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<tr>
<td>CD45</td>
<td>X16/99</td>
<td>NCL-L-CA</td>
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<td>CD56 (NCAM)</td>
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<td>CD68</td>
<td>514H12</td>
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<td>11E3</td>
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<td>CD117 (c-kit Oncoprotein)</td>
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<td>CH15</td>
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<td>Oct-297</td>
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<td>3SH8</td>
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<td>66.4.C2</td>
<td>NCL-L-RCC</td>
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<td>NCL-L-TdT-329</td>
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<td>SP272</td>
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<td>Zap-70</td>
<td>L453R</td>
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Adenomatous Polyposis Coli Protein (APC)

Clone EMM43
1 mL lyophilized NCL-APC P
See also APC (Adenomatous Polyposis Coli Protein) on page 58.

Adenovirus

Clone 10/5.1.2
1 mL lyophilized NCL-ADENO

The Adenoviridae are a family of double-stranded DNA viruses. They may cause a variety of infections involving respiratory, ocular, genito-urinary or enteric systems. Adenoviruses may cause life-threatening infections in transplant recipients, AIDS patients and immunocompromised patients.

Product Specific Information
NCL-ADENO is a pan adenovirus specific reagent. Reactivity has been confirmed with adenovirus serotypes 1 to 7, 40 and 41 as primary isolates in tissue culture. NCL-ADENO does not cross-react with tissue culture isolates of respiratory syncytial virus, influenza virus types A and B, parainfluenza virus types 1, 2, 3 and 4b, herpes simplex virus types 1 and 2, varicella-zoster virus, cytomegalovirus, mumps virus, measles virus, echovirus 19, coxsackievirus B4 virus, poliovirus types 1, 2 and 3 or negative tissue culture cells used in routine virus isolation.

Human nasopharyngeal secretion: immunofluorescence for Adenovirus using NCL-ADENO. Note intense staining of Adenovirus infected respiratory epithelial cells. Acetone-fixed cells.

Akt (Phosphorylated)

Clone LP18
1 mL, 0.1 mL liquid NCL-L-Akt-Phos P (HIER) W

Akt-1, also referred to as Protein Kinase B (PKB) or Rac alpha is a member of the Akt serin/threonine protein kinase family. It plays an important role in many biological responses including metabolism, cell survival and growth by phosphorylation and inactivating several targets including GSK 3 beta, caspase 9, BAD and the forkhead transcription factor.

Product Specific Information
NCL-L-Akt-Phos is not recommended for use with PBS, since the use of PBS-based wash buffers and possibly PBS-based antibody diluents gives increased background staining and decreased staining intensity. Proprietary reagents from Leica or TBS-based wash buffer and diluents are recommended.

ALK (Anaplastic Lymphoma Kinase) (CD246) (p80)

Clone 5A4
1 mL, 0.1 mL lyophilized NCL-ALK P (HIER) Reference Range
7 mL Bond ready-to-use PA0306 P (HIER)

Anaplastic large cell lymphoma (ALCL) is usually composed of large pleomorphic cells which are reported to express CD30 antigen and the epithelial membrane antigen (EMA). These tumor cells tend to occur in younger individuals and may be associated with cutaneous and extranodal involvement. A proportion of these cases contain a chromosomal translocation t(2;5) (p23; q35). This results in a hybrid gene encoding part of the nucleophosmin (NPM) gene joined to the cytoplasmic domain of the anaplastic lymphoma kinase (ALK) gene, giving rise to the protein, p80. Large cell lymphomas account for approximately 25 percent of all non-Hodgkin’s lymphomas in children and young adults, of which one third carries the NPM-ALK gene translocation.

Refer to page 14 for the Bond ready-to-use format.

Reference Range
### Alpha-1-Antichymotrypsin

**Polyclonal**
1 mL lyophilized NCL-A1ACp

Alpha-1-Antichymotrypsin (ACT) is an early-stage acute phase protein and a member of the serine proteinase inhibitor or serpin superfamily. The precise role of ACT is uncertain but it is thought to act as an anti-inflammatory agent inhibiting chymotrypsin, cathepsin G, mast cell chymase, neutrophil chemotaxis and superoxide anion production. ACT is synthesized primarily by hepatocytes of the liver. Lower levels of synthesis have also been discovered via immunohistochemical analysis in mast cells, endothelial cells, breast and intestinal epithelial cells. ACT also exists in the brain. Research has shown that it is found in amyloid fibrils, endothelial cells and the cytoplasm of astroglial cells in certain brain abnormalities. Further research has also shown that a major proportion of prostate-specific antigen (PSA) in serum exists complexed to ACT.

### Alpha-1-Antitrypsin

**Polyclonal**
1 mL lyophilized NCL-A1Ap

Alpha-1-antitrypsin is synthesized in the liver and is present in serum and tissue fluids where it acts as an inhibitor of proteases, particularly elastase. Its main function appears to be the neutralization of elastase released by neutrophils during an inflammatory response. Alpha-1-antitrypsin deficiency may result in uninhibited elastase-induced tissue destruction eg in the lung. Alpha-1-antitrypsin deficiency is associated with panacinar emphysema and liver disease. In the liver, alpha-1-antitrypsin deficiency may lead to neonatal hepatitis or an individual may present in later childhood or adulthood with cirrhosis.

### Alpha-Actinin

**Clone RBC2/1B6**
1 mL, 0.1 mL lyophilized NCL-alpha-ACT

Alpha-actinin is a rod-like cytoskeletal protein belonging to the same family as spectrin, dystrophin and utrophin. In skeletal muscle, alpha-actinin is located in the Z band/disc and cross-links with F-actin in this region. Muscle tissues show the presence of abundant threadlike particles, known as nemaline bodies, in the myofibers. Electron microscopy studies have shown that the nemaline rods have a lattice structure similar to that of the Z discs and the rods are thought to be lateral polymers of the Z discs.

### Alpha B Crystallin

**Clone G2JF**
1 mL, 0.1 mL lyophilized NCL-ABCrys-512

Alpha B crystallin is a lens protein that has some homology with the small heat shock proteins. It is expressed in tissues such as skeletal muscle, cardiac muscle, smooth muscle, renal tubular epithelium, Schwann cells, glial cells, thyroid epithelium, colonic epithelium and stratified squamous epithelium. Alpha B crystallin is reported to be found in ubiquitinated intermediate filament inclusion bodies, such as Lewy bodies (neurofilaments), Rosenthal fibers (glial filaments) and Mallory bodies (cytokeratins). However, it is rarely found in neurofibrillary tangles. The role of Alpha B crystallin in inclusion bodies is unknown, but it may function as an accessory protein for intermediate filament aggregation. Alpha B crystallin is reported to be expressed in various carcinomas including renal cell carcinoma.
Alpha-Catenin

**Clone 25B1**
1 mL lyophilized NCL-A-CAT F P (HIER) W

Alpha-catenin, which shows some homology with vinculin, appears to play a role in tumor invasion and metastasis through the dysfunction of E-cadherin. Normal epithelium of the esophagus, stomach and colon express alpha-catenin strongly, without exception. However, in primary tumors of these tissues its expression is frequently reduced. It has been suggested that some human cancer cells may have impaired E-cadherin-mediated cell adhesiveness as a result of the downregulation of alpha-catenin expression. Abnormalities in the expression of alpha-catenin seem to associate with malignant cellular features and disease progression in prostate cancer. In one study of several tumor-related proteins in breast cancers, it was shown that alpha and beta-catenins could be re-expressed in metastatic tissue. Re-expression of these adhesion molecules by tumor cells after release from the primary site may be important and perhaps necessary for cells to adhere in remote organs.


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Alpha-Internexin

**Clone 2E3**
1 mL lyophilized NCL-A-INTER P (HIER)

Alpha-internexin is a 66 kD protein which shares several characteristics with intermediate filament proteins. In rats, alpha-internexin is often co-purified with intermediate filaments from spinal cord and optic nerve. The protein is axonally transported together with the neurofilament triplet proteins (68, 160 and 200 kD) along the length of the optic nerve. Although the distribution of alpha-internexin is similar to the light component neurofilament (68 kD), its distribution in rat embryo is far more extensive in the early stages of development. There is also evidence that expression of alpha-internexin is heavily upregulated in damaged neurons.


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Alpha Fetoprotein

**Clone C3**
1 mL, 0.1 mL lyophilized NCL-A-FP F P 7 mL Bond ready-to-use PA0963 P

Alpha fetoprotein (AFP) is an oncofetal antigen of 70 kD found in body fluids which if detected in high concentrations has clinical implications. AFP is expressed in fetal liver but is not present under normal circumstances in healthy adult tissues. It is reported to be expressed in a proportion of germ cell tumors, with high frequency in yolk sac tumors. Refer to page 14 for the Bond ready-to-use format.


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Alpha-Methylacyl-CoA Racemase (AMACR, p504s)

**Clone EPUM1**
1 mL, 0.1 mL liquid NCL-L-AMACR P (HIER)

Alpha-methylacyl-CoA racemase (AMACR), also known as p504s, is a mitochondrial and peroxisomal enzyme that is involved in bile acid biosynthesis and beta-oxidation of branched-chain fatty acids. AMACR is essential in lipid metabolism, and is expressed in normal liver (hepatocytes), kidney (tubular epithelial cells) and gall bladder (epithelial cells). Expression has also been found in lung (bronchial epithelial cells) and colon (colonic surface epithelium). Expression is granular and cytoplasmic. AMACR expression can also be found in hepatocellular carcinoma and kidney carcinoma. Past studies have also shown that AMACR is expressed in various colon carcinomas (well, moderately and poorly differentiated) and over expressed in prostate carcinoma.

Human prostatic adenocarcinoma: immunohistochemical staining for alpha-methylacyl-CoA racemase (AMACR, p504S) using NCL-L-AMACR. Paraffin section.

For detailed information on all products please visit our website:
www.leica-microsystems.com
Alpha Smooth Muscle Actin (SMA)

**Clone αsm-1**
1 mL lyophilized NCL-SMA  F P (Enzyme)  W
7 mL ready-to-use RTU-SMA  F P (Enzyme)
7 mL Bond ready-to-use PA0943  P

Cytoplasmic actins are part of the microfilament system of cytoskeletal proteins. Smooth muscle actin is found in vascular walls, intestinal muscularis mucosae and muscularis propria and in the stroma of various tissues. It is also reported to be expressed in myofibroblasts and myoepithelial cells and antibodies to SMA are reported to be a useful tool for the identification of leiomyomas, leiomyosarcomas and pleomorphic adenomas. When such antibodies are used in a differential diagnostic situation they must be used within a panel of antibodies together with the clinical presentation data and interpreted by a pathologist.

**Product Specific Information**
Enzyme pretreatment may enhance staining in some cases.
Refer to page 41 for the Bond ready-to-use format.

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Alpha-Synuclein

**Clone KM51**
1 mL lyophilized NCL-ASYN  P (HIER)
1 mL liquid NCL-L-ASYN  P (HIER)

Alpha-synuclein is a protein of 140 amino acids and a member of the synuclein family. It shares 61 percent sequence homology with beta-synuclein and is highly conserved between vertebrate species. It does not possess a signal sequence suggesting that it is an intracellular protein. All synucleins have an unusual organization based around the eleven residue repeating motif and an alpha-helical secondary structure resembling those found in the lipid-binding domain of exchangeable apolipoproteins, including Apo E. This homology suggests a direct interaction of alpha-synuclein with membranes consistent with its affinity for synaptosomes. The function of alpha-synuclein may be to carry a target protein to the inner membrane of nerve terminals or to the outer surface of synaptic vesicles. Western blot analyses of highly purified Lewy bodies from Lewy body dementia brain material has shown full-length, partially truncated and insoluble aggregates of alpha-synuclein. Alpha-synuclein may be implicated in the formation of Lewy bodies and the selective degeneration of neurons in sporadic Parkinson’s disease and Lewy body dementia.

**Product Specific Information**
Clone KM51 is specific for alpha-synuclein and unreactive with beta-synuclein. Pretreatment of tissue sections with 98 to 100 percent formic acid must be used within a panel of antibodies together with the clinical presentation data and interpreted by a pathologist.

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Amyloid A Component

**Clone mc1**
1 mL lyophilized NCL-AAC  P

Amyloidosis is a disease characterised by the deposition of amorphous eosinophilic extracellular material in various body tissues forming confluent masses and progressively replacing the parenchymatous cells of vital organs, resulting in gradual loss of function and eventual death. Such organs become enlarged, firm, pale in colour and develop a waxy texture. It has been reported that the detection of amyloid A protein in human tissue biopsies, eg renal or rectal biopsies by immunohistochemistry, to characterise AA-type amyloidosis (secondary amyloidosis) is often worthwhile as it may be difficult to observe in haematoxylin and eosin preparations.

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Amyloid P Protein

**Clone B5**
1 mL lyophilized NCL-AMP  F P

Amyloid consists mainly of rigid, non-branching protein fibrils, together with rod-like aggregates of a pentagonal shaped glycoprotein called amyloid P protein. Amyloid P protein, also known as P component, comprises 10 percent of amyloid tissue and is present in all but the central nervous system forms of amyloid. Amyloid P protein is a constituent of normal basement membranes and the microfibrillary elastic fiber network.

**Product Specific Information**
NCL-AMP may be used for the identification of amyloid P protein in normal human tissue and in amyloid deposits. NCL-AMP is only suitable for paraffin-embedded material when the tissue has been fixed in 70 percent ethanol.

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Amyloid Precursor Protein

**Clone 3G12**
1 mL lyophilized NCL-APP-228  P (HIER)

**Clone 40.10**
1 mL lyophilized NCL-APP  P (HIER)

Alzheimer’s disease, the most common cause of dementia in the elderly, exists in both familial and sporadic forms. Genetic studies have identified three genes; beta-amyloid precursor protein (APP), Presenilin-1 and Presenilin-2 which, when mutated, can cause familial forms of Alzheimer’s disease. APP and APP-like proteins are transmembrane glycoproteins with a similar modular domain structure.

**Product Specific Information**
NCL-APP-228 and NCL-APP have been raised to the extracellular portion of APP between the Kunitz protease inhibitor domain and the beta amyloid region. This region shows the least homology with the APP-like proteins. NCL-APP-228 and NCL-APP do not cross-react with APP-like proteins. NCL-APP reacts with large pyramidal cells as well as smaller neurons, astrocytes and microglia. NCL-APP-228 reacts with late-stage neurofibrillary tangle-bearing neurons, neuritic processes surrounding senile plaques and neuritop threads in grey matter of Alzheimer’s disease brain. Unmasking in 1mM EDTA (pH8.0) in a pressure cooker may be required for up to 5 minutes in order for NCL-APP-228 to work optimally.
Anaplastic Lymphoma Kinase (ALK) (CD246) (p80)

Clone 5A4
1 mL, 0.1 mL lyophilized NCL-ALK P (HIER) W
7 mL Bond ready-to-use PA0306 P (HIER)

See also ALK (Anaplastic Lymphoma Kinase) (CD246) (p80) on page 54.

Androgen Receptor

Clone AR27
1 mL, 0.1 mL lyophilized NCL-AR-318 F P (HIER)

Clone 2F12
1 mL lyophilized NCL-AR-2F12 F P (HIER)

Clone AR27 was developed to produce superior staining to clone 2F12 on paraffin sections.

Androgen Receptor is a member of the superfamily of ligand responsive transcription regulators. The androgen receptor functions in the nucleus where it is believed to act as a transcriptional regulator mediating the action of male sex hormones (androgens). The androgen receptor has wide distribution and can be demonstrated by immunohistochemistry in several tissues eg prostate, skin, and oral mucosa. Androgen receptor has been reported in a diverse range of human tumors eg osteosarcoma and in prostatic carcinoma androgen receptor expression may be of clinical relevance. Furthermore, mutation of the gene encoding androgen receptor has been reported in prostatic carcinoma.

AP-2 Gamma

Clone GIA50
1 mL lyophilized NCL-AP2G P (HIER) W

The AP-2 transcription factors are required for normal growth and morphogenesis during mammalian development. Initial in vitro studies have also indicated that the AP-2 family of proteins are involved in the etiology of human breast cancer. The various AP-2 genes are expressed in many human breast cancer cell lines and critical AP-2 binding sites are present in both c-erbB-2 and estrogen receptor promoters. AP-2 gamma has been shown to be expressed in normal breast myoepithelial cells and to be upregulated in a proportion of breast cancer specimens. AP-2 gamma expression has been shown to be upregulated in the trophoblast lineage throughout development, suggesting a crucial role for both trophoblast development and differentiation. Gene expression and antibody studies have indicated that AP-2 gamma expression occurs in testis within oogonia/ gonadocytes and was downregulated with germ cell differentiation. Several studies have since indicated that AP-2 gamma may be useful in the identification of testicular derived tumors.

Product Specific Information

NCL-AP2G has been shown, through immunohistochemistry, ELISA studies and Western blotting to be specific for the AP-2 gamma transcription factor.

APC (Adenomatous Polyposis Coli Protein)

Clone EMM43
1 mL lyophilized NCL-APC P

The human adenomatous polyposis coli (APC) gene at locus 5q21 encodes a protein of 2,843 amino acids. A precise role for APC in the regulation of the wnt/beta-cateninin signalling pathway has been clearly recognized. APC forms molecular complexes which are able to eliminate intra-cytoplasmic beta-catening, inducing its degradation. It is expressed in the cytoplasm of epithelial and mesenchymal cell types. In the epithelium of bladder, small and large intestine, esophagus, stomach and epidermis, APC expression is restricted to regions in which cell replication has ceased and terminal differentiation has been established. Expression has been reported in lung, kidney and mammary gland endothelial, myoepithelial and duct lining epithelial cells. Some tissues such as ovary, myometrium, thyroid, parathyroid and tonsil do not express the protein. Mutations of the APC gene have been linked to the development of sporadic colorectal tumors, as well as familial adenomatous polyposis and cancers of the pancreas, stomach and esophagus. APC mutations have also been observed at significantly high frequency in the advanced stages of breast cancer suggesting a biological role in carcinogenesis.
**Apolipoprotein J (Clusterin)**

**Clone 7D1**

1 mL lyophilized NCL-CLUSTERIN  **F P** *(HIER)*

See also Clusterin (Apolipoprotein J) on page 91.

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**Apoptosis Protease Activating Factor 1**

**Polyclonal**

1 mL lyophilized NCL-APAF1  **F P** *(HIER)*

Apoptosis is one of a number of responses that may occur as a result of signal transduction pathways in the cell. One identified mechanism for initiating caspase activation requires the participation of mitochondria and involves a 130 kD protein known as apoptosis protease activating factor-1 (Apaf-1). Apaf-1 is a cytosolic protein that remains in a latent state until bound to cytochrome c (Apaf-2). Cytochrome c is commonly released from the mitochondria during apoptosis induced by many, but probably not all cell death stimuli. The resulting Apaf1/cytochrome c complex associates with the zymogen form of caspase-9 (Apaf-3) in the presence of dATP or ATP, promoting the autocatalytic activation of caspase-9. Once activated caspase-9 can then cleave and activate procaspase-3 directly, resulting in a cascade of additional caspase activation and apoptosis.

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**B Cell Marker (MB2)**

**Clone MB2**

1 mL lyophilized NCL-MB2  **F P**

MB2 is a pan B cell marker that is expressed in all B cells except mature plasma cells. It does not react with T cells. The antibody is weakly reactive with endothelial cells and several types of epithelial cells. These include epidermis (but excludes the squamous cell layer), epiteliala of breast, lung, pancreas, stomach, colon, bladder, fallopian tube and also hepatocytes and stromal cells of the ovary. MB2 has been reported to react with an uncharacterized cytoplasmic antigen found in both normal B cells and B cell lymphomas.

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**Aurora Kinase 2**

**Clone JLM28**

1 mL liquid NCL-L-AK2  **P (HIER) W**

Aurora Kinase 1 and 2 encode cell cycle-regulated serine/threonine kinases that are involved in microtubule spindle activities during mitosis and meiosis. Aurora Kinase 2, also known as STK15, BTAK, ARK1 and AIK, localizes to interphase and mitotic centrosomes and to the spindle poles. It is degraded rapidly after G2/M phase release in mammalian cells. Aurora Kinase 2 is reported to be expressed at high levels in testis and various proliferating cell lines, including HeLa cells. Aurora Kinase 2 is regulated by phosphorylation which is important both for its activity and stability. The inhibition of its activity leads to the formation of a monopolar spindle because its activity is necessary for centrosome separation. Aurora Kinase 2 overexpression leads to centrosome amplification, chromosome instability and transformation in mammalian cells. Overexpression of both active and inactive Aurora Kinase 2 can lead to polyploidy. This suggests that Aurora Kinase 2 can behave as a dominant negative mutant and inhibit other aurora kinases. When inactive kinase is expressed, however, the cells eventually die and do not become immortalized, unlike with the active kinase.

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**B Cell Specific Octamer Binding Protein-1 (BOB-1)**

**Clone TG14**

1 mL, 0.1 mL liquid NCL-L-BOB-1  **P (HIER)**

7 mL Bond ready-to-use  **PA0558 P (HIER)**

B cell specific octamer binding protein-1 (BOB-1), also known as OBF-1 and OCA-B, is a lymphocyte specific transcriptional coactivator protein. It interacts with OCT1 and OCT2 transcription factors and contributes to the transcriptional activity of octamer motifs. BOB-1 has been reported to be detectable in all B cell populations found in reactive lymphoid tissues. The strongest expression being found in germinal center B cells and plasma cells. The expression of BOB-1 in B cell tumors has been reported to be variable.

Refer to page 15 for the Bond ready-to-use format.
Bcl-2 Oncoprotein

**Clone 3.1**
1 mL, 0.1 mL lyophilized NCL-bcl-2-486 P (HIER) W

**Clone bcl-2/100/D5**
1 mL, 0.1mL lyophilized NCL-bcl-2 F P (HIER) W
1 mL liquid NCL-L-bcl-2 F P (HIER) W
7 mL ready-to-use RTU-bcl-2 F P (HIER)
7 mL Bond ready-to-use PA0117 P (HIER)

Clone 3.1 was developed to produce superior staining on paraffin sections.

Bcl-2 is a member of a family of proteins that are involved in apoptosis. Bcl-2 is an integral inner mitochondrial membrane protein of 25 kD and has a wide tissue distribution. It is considered to act as an inhibitor of apoptosis. For this reason, bcl-2 expression is inhibited in germinal centers where apoptosis forms part of the B cell production pathway. In 90 percent of follicular lymphomas a translocation occurs which juxtaposes the bcl-2 gene at 18q21, to an immunoglobulin gene. This t(14;18) translocation can deregulate gene expression and bcl-2 over-expression can be demonstrated immunohistochemically in the vast majority of follicular lymphomas.

Bcl-3 Oncoprotein

**Clone 1E8**
1 mL lyophilized NCL-Bcl-3 F P (HIER)

Bcl-3 was first identified as a putative proto-oncogene and was originally isolated through its involvement in the translocation event t(14;19) where it is highly expressed in a subset of chronic lymphocytic leukemias and other B cell neoplasms. The Bcl-3 gene product is also thought to play a role in the immune system through its interactions with the NF-kappaB family of transcription factors to enhance proliferation and to act as a transcription cofactor. More specifically, Bcl-3 oncoprotein appears to regulate the activity of homodimeric NF-kappaB p50 subunit and a closely-related homolog, p52, in a phosphorylation-dependent manner. Although to date, no immunohistochemistry data has been published, Bcl-3 mRNA is found in a number of tissues, including spleen and other lymphoid tissues.

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Bcl-6 Oncoprotein

**Clone LN22**
1 mL, 0.1 mL liquid NCL-L-Bcl-6-564 P (HIER)
7 mL Bond ready-to-use PA0204 P (HIER)

Clone LN22 was developed to produce superior staining compared to clone P1F6 on paraffin sections.

Bcl-6 is a proto-oncogene that encodes a Kruppel-type zinc-finger protein of 95 kD and shares homology with other transcription factors. Bcl-6 protein is mainly expressed in normal germinal center B cells and related lymphomas. It has been shown that the Bcl-6 proto-oncogene is involved in chromosome rearrangements at 3q27 in non-Hodgkin’s lymphomas and Bcl-6 rearrangements have also been detected in 33 to 45 percent of diffuse large B cell lymphomas. Immunohistochemistry has been reported to show the Bcl-6 gene product to be detectable in follicular lymphomas, diffuse large B cell lymphomas, Burkitt’s lymphomas and in nodular, lymphocyte predominant Hodgkin’s disease.

Refer to page 15 for the Bond ready-to-use format.
Bcl-10 Oncoprotein

**Clone DAA22**

1 mL lyophilized NCL-Bcl-10

Bcl-10 oncoprotein is an apoptotic regulatory molecule identified as a result of its direct involvement in the translocation event t(1;14) (p22;q32) of mucosa-associated lymphoid tissue (MALT) lymphomas. MALT lymphomas are the most common subset of extranodal non-Hodgkin’s lymphomas. Wild type Bcl-10 oncoprotein promotes apoptosis under normal circumstances and induces NF-kappaB activation. Mutated forms of Bcl-10 oncoprotein have been found to be associated with many common forms of cancer. The N-terminal region of Bcl-10 oncoprotein encodes a caspase recruitment domain (CARD) which is homologous with regions of several proteins involved in apoptosis. Several mutation events lead to the Bcl-10 oncoprotein becoming truncated in the region immediately downstream of the CARD. The truncated molecules do not induce apoptosis and gain a transforming function that is not present in the full length molecule. These truncated molecules are, therefore, thought to be important factors that encourage cell proliferation during tumor development. In normal tissues, Bcl-10 oncoprotein is expressed only in breast and lymphoid tissues with staining predominantly found in the cytoplasm.

**Product Specific Information**

NCL-Bcl-10 is raised to the majority of the coding region of the Bcl-10 oncoprotein.

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**Western blot:** detection of Bcl-10 oncoprotein (32 kD) using NCL-Bcl-10. Lane A, molecular weight markers. Lane B, A549 cell line immunoblotted with NCL-Bcl-10.

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**Bcl-w**

**Clone 6C1**

1 mL lyophilized NCL-Bcl-w

Bcl-w belongs to the Bcl-2 family of proteins and promotes cell survival, whereas other members such as bak and bax are antagonists and promote apoptosis. The Bcl-w gene is highly conserved between mice and man. Bcl-w protein is reported to be found in a diverse range of tissues including cerebellum, hippocampus, colon, liver, heart, stomach, skeletal muscle, testis and placenta. It is also expressed in most myeloid and a few lymphoid cell lines including those of macrophage megakaryocytic and erythroid origin. It is not expressed on B and T cell lines. Bcl-w is apparently dispensable in normal development and function of most organs but is essential for spermatogenesis.

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**bcl-x**

**Clone NC1**

1 mL lyophilized NCL-bcl-x

Bcl-x has homology with and is a member of the Bcl-2 family of proteins. Bcl-x can function as a regulator of cell death independently of bcl-2. Differential splicing of the bcl-x mRNA produces short and long variants known as bcl-x_s and bcl-x_L. These variants have different functions. Bcl-x immunoreactivity has been demonstrated in many cell types and like bcl-2, has been localized to the cytosol associated with mitochondria. Bcl-x has been demonstrated to be immunohistochemically detected in plasma cells, activated lymphocytes in interfollicular areas and a small number of lymphocytes within germinal centers. It has also been reported in Reed Sternberg cells in about 86 percent of Hodgkin’s disease cases. In normal tissues, bcl-x expression has been reported in cortical thymocytes, megakaryocytes, red blood cell precursors and some types of differentiating myeloid cells in bone marrow as well as spermatocytes and spermatids in the testes. It is also found in mammary epithelial cells, secretory and basal epithelial cells of the prostate, gastrointestinal epithelial cells and differentiated keratinocytes in the upper layers of the epidermis (but not in basal cells).
Beta-2-Microglobulin

Polyclonal
1 mL lyophilized NCL-B2Mp P (Enzyme) O

Beta-2-microglobulin, a single polypeptide chain of molecular weight 11.6 kD, is present on the surface of most nucleated cells and its expression may be decreased or lost in malignancy. Beta-2-microglobulin is the major constituent of a subtype of secondary amyloidosis which is associated with long term hemodialysis. Clinical and pathological features of this disease have been characterized. Spontaneous fractures and destructive arthropathies (articular swelling and pain in an oligoarticular distribution, along with effusions in large joints) have been related to amyloid deposition. Amyloid has been implicated in most clinical complaints of beta-2-microglobulin-related amyloid arthropathy where it is found in synovial biopsies taken from the involved joints.

Product Specific Information
NCL-B2Mp is also effective in ELISA techniques.

Beta Amyloid

Clone 6F/3D
1 mL lyophilized NCL-B-Amyloid F P

Beta amyloid is an extracellular filamentous protein deposit found in the brain. It is the major protein component of amyloid cores and neuritic plaques and is also found as a deposit in neurofibrillary tangles. In man, Alzheimer’s disease is the most common cause of senile dementia and is characterized by abnormal filamentous protein deposits in the brain. Beta amyloid deposits are also detected in Lewy body dementia, Down’s syndrome, amyloidosis (Dutch type) and in the Guam Parkinson-Dementia complex.

Product Specific Information
Pretreatment of tissue sections with 98 to 100 percent formic acid is recommended when using NCL-B-Amyloid.

Beta-Dystroglycan

Clone 43DAG1/8D5
1 mL, 0.1 mL lyophilized NCL-b-DG F W E

Dystrophin associated glycoproteins (DAGs) are a complex of at least seven proteins involved in the attachment of dystrophin to muscle membranes. The biological significance of this dystrophin/glycoprotein complex is not fully understood, but it appears to form an essential linkage between actin on the inside of the muscle fiber and muscle laminin in the basal lamina which surrounds the fiber. Beta-dystroglycan spans the muscle membrane and it has been suggested that it is the member of the complex which binds directly to dystrophin. Labeling of beta-dystroglycan may be reduced in some forms of muscular dystrophy where another component eg dystrophin or laminin, is directly affected. Labeling with an antibody to beta-spectrin to monitor membrane integrity, is an essential immunohistochemical control.
**Primary Antibodies**

**BL-CAM (CD22)**

**Clone FPC1**
1 mL, 0.1 mL lyophilized NCL-CD22-2 P (HIER)

See also CD22 (BL-CAM) on page 75.

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**Blood Coagulation Factor XIIIa (Factor XIIIa)**

**Clone E980.1**
1 mL, 0.1 mL lyophilized NCL-FXIIIa P (HIER)
7 mL Bond ready-to-use PA049 P (HIER)

See also Factor XIIIa (Blood Coagulation Factor XIIIa) on page 109.

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**BM1 (Myeloid Marker)**

**Clone BM-1**
1 mL lyophilized NCL-BM1 F P

NCL-BM1 is reactive with a 183 kD myeloid-specific DNA-binding protein expressed in human myeloid precursor cells. The DNA-binding protein is reported to be found in the cytoplasm and nucleus of normal and malignant myeloid cells. Unlike other markers, the antigen designated BM-1 appears to be restricted in its reactivity to M2 and M3 acute myelogenous leukemia (AML) subtypes.

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**BM2 (Myeloid Marker)**

**Clone BM-2**
1 mL lyophilized NCL-BM2 F P (HIER)

NCL-BM2 is reactive with a cytoplasmic antigen expressed in human granulocytes. Markers of myeloid cells are useful in the identification of different levels of cellular differentiation.

**Product Specific Information**

NCL-BM1 and NCL-BM2 react with early precursor and mature forms of human myeloid cells. NCL-BM2 is useful for the detection of myeloid leukemias and granulocytic sarcomas.

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**Bone Morphogenetic Protein 4**

**Clone 3H2**
1 mL, 0.1 mL lyophilized NCL-BMP4 P W

Bone morphogenetic protein 4 (BMP4) is one of nine structurally related BMPs belonging to the transforming growth factor beta (TGF-beta) superfamily of secreted proteins. Mature BMP4 is a dimer that binds to a multimeric transmembrane receptor with serine/threonine kinase activity. Although BMP4 was discovered because it stimulates bone formation in adult mammals, it has important roles as a signalling molecule in embryonic tissues including the developing central and peripheral nervous system, musculature and skeleton. It also participates in a signalling pathway found in insects and worms. BMP4 is implicated in fibrodysplasia ossificans progressive. It is reported to be uniquely overexpressed in lymphoblastoid cells and proosseous fibroproliferative lesions. BMPs 1 to 8 are also reported to be expressed in prostatic adenocarcinomas with BMPs 1 to 5 also expressed in both benign and prostatic hyperplasia and ocular melanoma.

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**Bromodeoxyuridine**

**Clone 85-2C8**
1 mL lyophilized NCL-BrdU F P

5-Bromodeoxyuridine (BrdU) is an analogue of thymidine. BrdU can be introduced to live proliferating cells which in turn incorporate BrdU into the DNA during S phase, prior to cell division. Immunocytochemical staining for BrdU is an accurate method for measuring cell proliferation and detects nucleated cells from different animal species which have incorporated BrdU in place of thymidine into their DNA. The detection of BrdU incorporation can be used to determine the proliferative response of cells to mitogenic stimuli and to monitor the effects of various treatments on tumors.

*Protocol included with product indicates a requirement to incubate fresh tissue fragments with bromodeoxyuridine before fixation and embedding followed by sectioning and finally antibody incubation NCL-BrdU via immunohistochemistry.

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Normal human colon biopsy incubated with BrdU and stained using NCL-BrdU. Note intense nuclear staining of a small proportion of crypt epithelial cells. Paraffin section.
CA19-9 (Sialyl Lewis α)

Clone C241:5:1:4
1 mL lyophilized NCL-CA19-9 FP (HIER)
1 mL liquid NCL-L-CA19-9 FP (HIER)
7 mL Bond ready-to-use PA0424 P (HIER)

CA19-9 is an epitope on the sialylated Lewis α carbohydrate structure. Sialylated Lewis α plays a role in cell adhesion by acting as a functional ligand for the inducible adhesion molecule E-selectin. CA19-9 and CA50 (carcinoma associated mucin antigen) are useful serum markers in the diagnosis and follow up of gastrointestinal and pancreatic cancers. In carcinoma of the pancreas, it is reported that the immunohistochemical expression of both CA19-9 and CA50 correlates with tumor differentiation where the strongest staining is observed in well differentiated tumors. These two markers are also reported in a number of benign lesions such as chronic pancreatitis.

Product Specific Information
Clone C241:5:1:4 reacts specifically with Sialyl Lewis α-containing glycolipids, showing no crossreaction with Lewis α, Lewis β, or other structurally related molecules. The epitope recognized by NCL-L-CA19-9 is designated CA19-9 and is similar to CA50 (carcinoma associated mucin antigen).

Refer to page 16 for the Bond ready-to-use format.


CA125 (Ovarian Cancer Antigen)

Clone Ov185:1
1 mL lyophilized NCL-CA125 FP (HIER)
1 mL liquid NCL-L-CA125 FP (HIER)
7 mL ready-to-use RTU-CA125 FP (HIER)
7 mL Bond ready-to-use PA0539 P (HIER)

CA125 antigen is usually associated with ovarian epithelial malignancies. Serum assays are widely used to detect this protein in the monitoring of ovarian cancers. CA125 antigen may also be detected by immunohistochemistry and expression has been found in neoplasms such as seminal vesicle carcinoma and anaplastic lymphoma. CA125 antigen is not found exclusively in malignant tumors. CA125 is also known as MUC16.

Refer to page 16 for the Bond ready-to-use format.

Calbindin

Clone KR6
1 mL lyophilized NCL-CALBINDIN P (HIER)

Calbindin is a calcium-binding protein belonging to the troponin C superfamily. It functions as a buffer of cytosolic calcium and is found in the brain, kidney, gut and pancreatic islets. In normal brain, calbindin (28 kD) has been identified in medium sized neurons of the neuropil of the matrix compartment of the striatum, the woolly fiber arrangements of the globus pallidus and the fiber structures of the pars reticula of the substantia nigra. The normal expression of calbindin is modified in patients with progressive supranuclear palsy, striatal degeneration and Huntington’s disease (HD). In HD, alterations to the dendritic arbors and spiny striatal neurons may be visualized by immunohistochemistry for calbindin. In moderate grades of HD, proliferative changes have been found in these areas and in severe grades, degenerative changes have been noted. A proportion of dendritic cells within the light zone of germinal centers are also noted to be positive for calbindin.

Human brain, cerebellum: immunohistochemical staining for calbindin using NCL-CALBINDIN. Note cytoplasmic staining of Purkinje cells and neuronal processes. Paraffin section.
Calcitonin

**Clone CL1948**  
1 mL, 0.1 mL liquid NCL-L-CALCITONIN P (Enzyme)

**Polyclonal**  
0.5 mL lyophilized NCL-CALP P  
7 mL Bond ready-to-use PA0406 P (Enzyme)

Calcitonin (CT) is a 32 amino acid peptide synthesized by the parafollicular C cells of the thyroid. It acts through its receptors to inhibit osteoclast mediated bone resorption, decrease calcium resorption by the kidney and decrease calcium absorption by the intestines. The action of calcitonin is therefore to cause a reduction in serum calcium, an effect opposite to that of parathyroid hormone. The calcitonin gene transcript also encodes the calcitonin gene-related peptide (CGRP), which is thought to be a potent vasodilator. The tissue specificity of the transcript produced depends on alternative splicing of the CT/CGRP gene transcript. In the parafollicular cells of the thyroid 95 percent of the CT/CGRP is processed and translated to produce CT, however, in neuronal cells 99 percent of the CT/CGRP RNA is translated into CGRP. The C cells of the thyroid give rise to an endocrine tumor, medullary thyroid carcinoma (MTC), which occurs in a sporadic (75 percent of cases) and hereditary form (25 percent of cases). Familial MTC is associated with C cell hyperplasia (CCH), whereas sporadic MTC is thought not to be. However, in the general population CCH is present in 20-30 percent of thyroid glands, either with normal histology, thyroiditis or follicular tumors.

Refer to page 16 for the Bond ready-to-use format.

Calpain

**Clone Calp3d/2C4**  
2.5 mL lyophilized NCL-CALP-2C4 W

**Clone Calp3c/11B3**  
2.5 mL, 1 mL lyophilized NCL-CALP-11B3 W

**Clone Calp3c/12A2**  
2.5 mL, 1 mL lyophilized NCL-CALP-12A2 W

At least seven forms of autosomal recessive muscular dystrophy (MD) have been included under the banner “limb girdle muscular dystrophy” (LGMD). These forms may be divided into two groups; those with abnormal expression of the dystrophin/glycoprotein complex and those in which labeling of the proteins in this complex is unaffected. Thus the sarcoglycanopathies (also known as LGMD types 2C, 2D, 2E and 2F) are caused by defects in the genes for gamma, alpha, beta and delta-sarcoglycan on chromosomes 13q12, 17q21, 4q12 and 5q33, respectively. Among the dystrophies in which expression of the sarcoglycans is normal, the gene responsible for LGMD2A has been identified as the chromosome 15q15-encoded muscle-specific calcium-activated neutral protease, calpain 3. Calpain 3 enzyme is only stable in human muscle when homogenized in treatment buffer immediately after harvest. (Anderson LVB et al. American Journal of Pathology. 153(4): 1169-1179 (1998)), and in homogenates containing SDS and is therefore well suited for analysis by Western blot.

**Product Specific Information**

NCL-CALP-2C4 reacts with the full-size calpain 3 (94 kD) and an additional fragment (30 kD) in human skeletal muscle. NCL-CALP-12A2 reacts with full-size protein plus apparent degradation products at approximately 60 kD. Specificity of these antibodies has been confirmed by the loss of all these bands in samples with null gene mutations. NCL-CALP-11B3 reacts with calpain 3 bands at 94 and 60 kD, pre- and post-autolyzed forms of the ubiquituous calpains 1 and 2 (μ and m-calpain) staining a group of bands between 76 and 84 kD in human skeletal muscle (Anderson LVB et al. American Journal of Pathology. 153(4): 1169-1179, (1998)). Cross-reactivities in different animals and tissues are described (see reference).

Calmodulin

**Clone 6312**  
1 mL lyophilized NCL-CALMODULIN P (HIER)

Calmodulin, a ubiquitous eukaryotic calcium binding protein, is a principal mediator of the calcium signal. It participates in signalling pathways inducing proliferation, motility and cell cycle progression. Human calmodulin is encoded by three genes CALM1, CALM2 and CALM3 located on different chromosomes. The vertebrate CALM family of genes is unique in that its members specify an identical protein. The protein itself is made up of 148 amino acids and has four calcium binding domains. As calmodulin is essential for normal cell function, it is likely that levels are tightly controlled both temporally and spatially. Immunohistochemical staining for calmodulin has been reported in the epithelia of testis, breast, stomach, prostate, gall bladder as well as in macrophages, fibroblasts and sebaceous glands within the dermis of skin. In healing skin wounds, calmodulin is found at its highest levels in maturing keratinocytes. It is noticeably abundant in epidermis close to the wound and re-epithelializing margins where calcium levels are highest. In studies of Alzheimer’s brains, calmodulin immunostaining has been reported to be lost in cortical regions where large amounts of aluminium have accumulated.
Primary Antibodies

Calponin (Basic)

Clone 26A11
1 mL, 0.1 mL lyophilized NCL-CALPONIN-B P (HIER) W
7 mL Bond ready-to-use PA0416 P (HIER)

Basic calponin (calponin-h1) is a 34 kD protein which exhibits a high degree of homology to acidic and neutral calponins at its N-terminal region. It is an actin, tropomyosin and calmodulin binding protein thought to be involved in the regulation of smooth muscle contraction. The expression of basic calponin is reported to be restricted to smooth muscle cells and is a marker of the differentiated contractile phenotype of developing smooth muscle. Vascular smooth muscle cells convert to a synthetic dedifferentiated phenotype when this protein is lost and this is a key stage in both atherosclerosis and restenosis of coronary arteries after balloon angioplasty. It is thought that basic calponin exerts its effect via the cortical actin cytoskeleton and therefore influences proliferation, the transformed phenotype and the metastatic potential of tumor cells. Basic calponin mRNA is expressed in smooth muscle of prostate, bowel and aorta whereas neutral and acidic calponin mRNAs are expressed in non-smooth muscle tissues such as heart, placenta, lung, kidney, pancreas, spleen, testis and ovary as well as in smooth muscle-containing tissues.

Refer to page 16 for the Bond ready-to-use format.

Calretinin (5A5)

Clone 5A5
1 mL, 0.1 mL lyophilized NCL-CALRETININ P (HIER)
1 mL liquid NCL-L-CALRETININ P (HIER)
7 mL ready-to-use RTU-CALRETININ P (HIER)

Calretinin is an intracellular calcium-binding protein of 31.5 kD belonging to the tropomin C superfamily characterized by a structural motif described as the EF-hand domain. Calcium is an important moderator of a number of vital physiological processes, including neuronal excitability, axonal transport, synthesis and release of some neurotransmitters, membrane permeability and enzyme activity. Calretinin is found in the nervous system and thymus. Calretinin can also be demonstrated in normal and neoplastic mesothelial cells and has been reported to be a useful marker for the identification of malignant mesotheliomas of epithelial type to differentiate these from metastases of lung adenocarcinoma where antibodies to detect calretinin are used within a panel and interpretation together with clinical data is undertaken by a qualified pathologist.

Calretinin (CAL6)

Clone CAL6
1 mL liquid NCL-L-CALRET-566 P (HIER) W
7 mL Bond ready-to-use PA0346 P (HIER)

Calretinin is a calcium-binding protein of 29 kD that is a member of the family of so-called EF-hand proteins that also includes S-100 proteins. Calretinin is reported to be abundantly expressed in neurons. Outside the nervous system, calretinin is reported to be expressed in a range of cell types including mesothelial cells, steroid producing cell, (eg adrenal cortical cells, Leydig cells, ovarian theca interna cells as well as Sertoli cells, some neuroendocrine cells, eccrine sweat glands) and other cell types. The presence of calretinin is reported to be a useful marker primarily for differentiating malignant mesothelioma from carcinomas. Other reports indicate the detection of calretinin is helpful for the differential characterization of ovarian stroma tumors. Calretinin-positive cells have also been reported in the convoluted tubules of kidney with some antibodies.

Refer to page 17 for the Bond ready-to-use format.
Carbonic Anhydrase IX

**Clone TH22**
1 mL, 0.1 mL liquid NCL-L-CAIX P (HIER) W

Carbonic anhydrase (CA) is an enzyme that assists rapid interconversion of carbon dioxide and water into carbonic acid, protons, and bicarbonate ions. Originally named MN/G250, carbonic anhydrase IX (CAIX) is a cell surface transmembrane protein, which is predominantly found in the gastrointestinal tract and gall bladder. The glandular regions of normal colon are reported to be negative, but in the case of adenocarcinoma, the glands are positive. CAIX is also reported to be expressed in common epithelial tumors such as carcinomas of the esophagus, lung, colon, kidney, cervix and non-small cell lung carcinoma. In breast carcinomas, CAIX expression has been reported to be associated with malignant tissue. Expression of CAIX is reported to be absent in normal kidney, chromophobe carcinomas or oncocytomas, however, it is specifically expressed in clear cell renal carcinomas.

Carcinoembryonic Antigen (CD66e)

**Clone 12-140-10**
1 mL lyophilized NCL-CEA-2 F P (Enzyme)
1 mL liquid NCL-L-CEA-2 F P (Enzyme)
7 mL ready-to-use RTU-CEA-2 F P (Enzyme)

**Clone II-7**
7 mL Bond ready-to-use PA0004 P (HIER)

Carcinoembryonic antigen (CEA) is a heterogeneous cell surface glycoprotein produced by cells of fetal colon. Low levels are also found on normal mucosal epithelia of the adult colon and a variety of other normal tissues. CEA is encoded by the CEA gene that is located on chromosome 19. It is a member of the CEA gene family, which in turn is a subfamily of the immunoglobulin superfamily. Cell adhesion properties are now well recognized for CEA. It is believed that the expression of this glycoprotein in conjunction with other known adhesion molecules will influence the cell-cell interaction.

Refer to page 17 for the Bond ready-to-use format.

Caspase-2

**Clone 10H2**
1 mL lyophilized NCL-CASP-2 P (HIER)

Caspases are an extended family of cysteine proteases that play critical roles in apoptosis. Caspases are synthesized as precursors known as pro-caspases and these are converted into mature enzymes by apoptotic signals. Caspase-2 is an early effector in the apoptotic cascade and precedes the activation of caspase-3. It is generally found in the nucleus, but pro-caspase-2 may also be detected in mitochondrial and cytosolic fractions. Lymphoid organs display only weak caspase-2 expression, located in sinusoidal histiocytes and thymic epithelial cells. Extra-lymphoid caspase-2 reactivity is found in particular organs like the kidney. The caspase-2/caspase-3 cascade may be inhibited by the bcl-2 oncoprotein.

**Clone JHM62**
1 mL, 0.1 mL lyophilized NCL-CPP32 P (HIER) W

See also CPP32 (Caspase-3) on page 93.
Caspase-8

**Clone 11B6**
1 mL, 0.1 mL lyophilized NCL-CASP-8 P (HIER)

The caspases represent a family of cysteine proteases that play important regulatory roles within the cell. Caspase-8, also called FLICE, has an N-terminal domain with sequence homology to the death effector domain of FADD that allows association of caspase-8 with the TNF/Fas family of receptors. This association with the cell surface death receptors has shown caspase-8 to be a proximal regulator of apoptosis. Caspase-8 is activated by association with the Fas/FADD death-inducing signalling complex to release two active subunits, p18 and p10, into the cytosol, where they activate other caspases amplifying the apoptotic signal. Caspase-8 is reported to be expressed in pancreatic tumors, high grade non-Hodgkin’s lymphomas and invasive breast carcinomas.

**Product Specific Information**

NCL-CASP-8 is raised to the p18 subunit found in caspases 8a, 8b and 8h.

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Caspase-9

**Clone 2C9B11**
1 mL, 0.1 mL lyophilized NCL-CASP-9 P (HIER) W

Caspase-9 is a member of the caspase family of cysteine proteases that has been implicated in apoptosis and cytokine processing. Caspases have been shown to be activated during normal human keratinocyte differentiation and this activation is required for the normal loss of the nucleus. In addition, this apoptotic pathway may be activated in cardiac myocytes under conditions of ischemia. In the presence of ATP, apoptotic stimuli induce proteolytic processing and activation of pro-caspase 9 by cytochrome c and Apaf-1. Activated caspase-9 cleaves downstream caspases such as caspase-3, 6 and 7 initiating the caspase cascade. Caspase-9 is essential for apoptosis during the normal development of the central nervous system. Mutations or deficiencies in caspase-9 result in resistance to apoptotic stimuli that mimic conditions in developing tumors.

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Cathepsin B

**Clone CB131**
1 mL lyophilized NCL-CATH-B P

Cathepsin B is one member of a family of proteolytic enzymes and is expressed in cytoplasmic lysosomes in different types of normal and neoplastic tissues. It is a cysteine protease and like most cathepsins is involved in cellular metabolism such as protein degradation. Immunohistochemical studies have detected expression in bowel mucosa, skin, prostate and thyroid. Staining for cathepsin B, in common with other cathepsins, may be so intense that it appears to be nuclear in some cells. A proportion of endothelial cells are positive in many tissues. This has been reported previously where it has been described as sprouting endothelial cells. In tissues containing tumors this is thought to be related to tumor progression. Cathepsin B is an important matrix-degrading protease in several human cancers including lung adenocarcinomas, squamous cell carcinomas, rectal and breast carcinomas. Cathepsin B is reported to be overexpressed in squamous cell carcinoma where undifferentiated cells are strongly positive and the more differentiated cells in tumor islands are either weakly positive or negative. The expression of cathepsin B has also been reported in melanomas where the upregulation of this enzyme was found to be a characteristic of a more invasive tumor phenotype.

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Cathepsin D

**Clone C5**
1 mL, 0.1 mL lyophilized NCL-CDm P

Cathepsins are members of the papain family of cysteine lysosomal proteases which are involved in a variety of physiological processes such as proenzyme activation, enzyme inactivation, antigen presentation, hormone maturation, tissue remodelling and bone matrix resorption. Cathepsin D is first produced in a precursor form, pro-cathepsin D (52 kD), and then processed in the cell to an intermediate form of 46 kD, then finally to the mature forms of 34 kD and 14 kD. It has been proposed that the presence of high levels of cathepsin D in breast cancer may signify a functional estrogen receptor apparatus.

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For regulated products, please refer to the catalog for appropriate labeling requirements.
Primary Antibodies

Cathepsin G

**Clone 19C3**
1 mL lyophilized NCL-CATH-G P (HIER) W

Cathepsin G expression in normal tissues is restricted to granulocytes, especially neutrophils. However, mononuclear phagocytes have been demonstrated to bind and internalize proteases from neutrophils. Cathepsin G is located in neutrophilic polymorphonuclear leukocytes which contain specialized azurophil granules together with two other serine proteases; elastase and hepsin. These three proteases may participate in the killing and digestion of engulfed pathogens and in connective tissue remodelling at sites of inflammation. Cathepsin G is also reported to be expressed in acute and chronic myeloid leukemias whereas acute lymphoblastic or chronic lymphocytic leukemias are negative for this protein.


Cathepsin L

**Clone 13C2**
1 mL lyophilized NCL-CATH-L P

Cathepsin L is a lysosomal cysteine protease which plays a major role in intracellular protein catabolism. It exhibits the most potent collagenolytic and elastinolytic activity of any of the cathepsins in vitro. It can inactivate alpha-1 protease inhibitor which controls human neutrophil elastase activity in vitro. Cathepsin L has been implicated in a number of pathological processes including myofibrial necrosis in myopathies and in myocardial ischemia and also in the renal tubular response to proteinuria. Cathepsin L is present in all normal cell types but, in general, increased expression occurs in cancers. The highest observed levels of Cathepsin L are to be found in kidney and testicular tumors, with very high levels reported to be detected in non-small cell carcinomas of the lung and above normal levels expressed in breast, ovarian, colonic, adrenal, bladder, prostate and thyroid cancers. Cathepsin L, serine protease (uPA), protease inhibitor (PAI-1) as well as other proteases play an important role in cancer invasion by their ability to destroy the surrounding extracellular matrix through their respective proteolytic activities.


Caveolin-1

**Clone 4D6**
1 mL, 0.1 mL liquid NCL-L-Caveolin-1 P (HIER)

Caveolin-1 is a major structural component of caveolae which are vesicular invaginations present on the plasma membrane of different cell types. It plays a regulatory role in several signalling pathways and is reported to be most abundantly expressed in terminally differentiated mesenchymal cells such as smooth muscle cells, adipocytes and endothelial cells. High levels are also reported in fibroblasts where a fine granular membranous and diffuse cytoplasmic staining pattern is described. In pancreatic cancer, caveolin-1 is reported to be expressed on the cell membrane and cytoplasm of cancer cells. Further studies have reported that caveolin-1 is likely to act as a tumor suppressor in some human malignancies such as sarcomas.

CCK-8 (Cholecystokinin)

**Polyclonal**
0.25 mL lyophilized NCL-CCK-8p P (Enzyme)

Cholecystokinin (CCK) was first isolated as a 33 amino acid intestinal peptide hormone that binds saturably and reversibly to distinct receptors in brain and pancreatic cell membranes. In both the brain and intestine, CCK exists in a number of molecular forms of which the C-terminal octapeptide (CCK-8) represents the most abundant molecular species. CCK, gastrin, secretin and vasoactive intestinal polypeptide belong to the gastrointestinal hormone family. CCK functions to stimulate enzyme secretion from the pancreas, gall bladder contraction, intestinal motility as well as inhibiting gastrin-induced acid secretion. CCK also serves as a neurotransmitter and modulates the action of other neurotransmitters eg dopamine, 5-HT, GABA and excitatory amino acids. CCK is distributed in several regions of the brain including the cerebral cortex, hippocampus, amygdaloid nuclei and the hypothalamus. CCK is localized mainly in peripheral nerve fibers in the myenteric and submucosal ganglia as well as in endocrine cells of the gastrointestinal tract.
Primary Antibodies

CD1a

Clone MTB1
1 mL, 0.1 mL lyophilized NCL-CD1a-235 F P (HIER)
1 mL liquid NCL-L-CD1a-235 F P (HIER)
7 mL ready-to-use RTU-CD1a-235 F P (HIER)
7 mL Bond ready-to-use PA0235 P (HIER)

Clone JPM30
1 mL, 0.1 mL lyophilized NCL-CD1a-220 F P (HIER)

CD1a is a protein of 43 to 49 kD expressed on dendritic cells and cortical thymocytes. CD1a antigen expression has been shown to be useful in differentiating Langerhans cells, powerful antigen presenting cells present in skin and epithelia, from interdigitating cells. Immunohistochemical studies for CD1a antigen have reported a reduction in epidermal Langerhans cells in graft versus host disease and the participation of CD1a antigen-positive dendritic cells in atherosclerotic lesion formation and asthmatic inflammation.

Product Specific Information
Clone MTB1 detects cortical thymocytes, Langerhans cells in epidermis, interdigitating cells of dermis and interdigitating cells of stratified squamous epithelium of tonsil. Clone MTB1 may also detect small focal groups of lymphocytes outside the germinal centers of tonsil indicating a cross-reaction with CD1b antigen. Clone JPM30 detects cortical thymocytes, Langerhans cells in epidermis, interdigitating cells of dermis, interdigitating cells of stratified squamous epithelium of tonsil but in addition it stains sweat gland ducts in the dermis and epithelial cells of small intestine indicative of cross-reactivity with CD1d antigen.

Refer to page 17 for the Bond ready-to-use format.


CD2 (LFA-2)

Clone AB75
1 mL, 0.1 mL lyophilized NCL-CD2-271 P (HIER)
1 mL liquid NCL-L-CD2-271 P (HIER)
7 mL ready-to-use RTU-CD2-271 P (HIER)
7 mL Bond ready-to-use PA0271 P (HIER)

Clone 11F11
7 mL Bond ready-to-use PA0271 P (HIER)

The CD2 antigen (LFA-2) is a monomeric 45 to 58 kD glycoprotein. It is an accessory molecule important in mediating the adhesion of activated T cells and thymocytes with antigen-presenting cells and target cells.

Refer to page 17 for the Bond ready-to-use format.


CD3

Clone LN10
1 mL, 0.1 mL liquid NCL-L-CD3-565 P (HIER)
7 mL Bond ready-to-use PA0553 P (HIER)

Clone PS1
1 mL, 0.1 mL lyophilized NCL-CD3-PS1 P (HIER) W
1 mL liquid NCL-L-CD3-PS1 P (HIER) W
7 mL ready-to-use RTU-CD3-PS1 P (HIER)

Clone UCHT1
1 mL lyophilized NCL-CD3 F C

Clone LN10 was developed to produce superior staining with PBS based buffers compared to clone PS1 on paraffin sections.

The CD3 molecule consists of five different polypeptide chains with molecular weights ranging from 16 to 28 kD. The CD3 antigen is first detected in early thymocytes and its appearance probably represents one of the earliest signs of commitment to the T cell lineage.

Product Specific Information
Clone PS1 is specific for the non-glycosylated epsilon chain of the human CD3 molecule (Chetty R and Gatter K. Journal of Pathology. 173: 303-307 (1994)). Clone LN10, our newest clone, is also specific for the non-glycosylated epsilon chain of the human CD3 molecule. Clones LN10, PS1, and UCHT1 recognize T cells in thymus, bone marrow, peripheral lymphoid tissue and blood and are all pan T cell markers.

Refer to page 18 for the Bond ready-to-use format.

CD4

Clone 4B12
1 mL, 0.1 mL lyophilized NCL-CD4-368 F P (HIER) W
1 mL liquid NCL-L-CD4-368 F P (HIER)
7 mL Bond ready-to-use PA0368 P (HIER)

Clone 1F6
1 mL, 0.1 mL lyophilized NCL-CD4-1F6 P (HIER) W
1 mL liquid NCL-L-CD4-1F6 P (HIER) W
7 mL ready-to-use RTU-CD4-1F6 P (HIER)

Clone 4B12 was developed to allow conventional protocol where endogenous peroxidase is blocked before primary antibody incubation to produce superior staining on paraffin sections.

The CD4 molecule (T4) is a single chain transmembrane glycoprotein with a molecular weight of 59 kD. The CD4 antigen is expressed on a T cell subset (helper/inducer) representing 45 percent of peripheral blood lymphocytes and at a lower level on monocytes. Most cases of cutaneous T cell lymphoma, including mycosis fungoides, express the CD4 antigen and HTLV-1 associated adult T cell leukemia/lymphoma is also generally CD4 positive.

Product Specific Information
Please note that the use of 1 percent or greater H2O2 to block endogenous peroxidase has a detrimental effect on the epitope recognized by clone 1F6. Therefore, it is recommended that endogenous peroxidase is blocked before retrieval with 0.5 percent H2O2/methanol for 10 minutes, otherwise staining intensity may be reduced.

Refer to page 18 for the Bond ready-to-use format.


CD5

Clone 4C7
1 mL, 0.1 mL lyophilized NCL-CD5-4C7 P (HIER) W
1 mL liquid NCL-L-CD5-4C7 P (HIER) W
7 mL ready-to-use RTU-CD5-4C7 P (HIER)
7 mL Bond ready-to-use PA0168 P (HIER)

CD5 antigen is reported to be expressed on 95 percent of thymocytes and 72 percent of peripheral blood lymphocytes. In lymph nodes, the main reactivity is observed on T cells. CD5 antigen is also expressed by many T cell leukemias, lymphomas, activated T cells and on a subset of B cells located primarily in the mantle zones of normal lymph nodes. CD5 antigen expression is also reported in T cell acute lymphocytic leukemias (T-ALL), some B cell chronic lymphocytic leukemias (B-CLL) as well as B and T cell lymphomas.

Refer to page 18 for the Bond ready-to-use format.

CD7

Clone LP15
1 mL, 0.1 mL liquid *NCL-L-CD7-580* P (HIER)
7 mL Bond ready-to-use *PA0266* P (HIER)

The CD7 molecule is a membrane-bound glycoprotein of 40 kD and is the earliest T cell specific antigen to be expressed in lymphocytes. CD7 antigen is also the only early marker to persist throughout differentiation. The function and role of the CD7 molecule has not yet been fully identified, although the activation of T cells with gamma/delta receptors has been proposed based on mAb-induced activation. CD7 antigen is reported to be found on the majority of peripheral blood T cells, most natural killer cells and thymocytes.

**Product Specific Information**
Clone LP15 was developed to provide superior staining to clone CD7-272 on paraffin sections.

Refer to page 18 for the Bond ready-to-use format.

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CD8

Clone 1A5
1 mL, 0.1 mL lyophilized *NCL-CD8-295* F P (HIER) W
1 mL liquid *NCL-L-CD8-295* F P (HIER) W
7 mL ready-to-use *RTU-CD8-295* F P (HIER)

Clone 4B11
1 mL, 0.1 mL lyophilized *NCL-CD8-4B11* F P (HIER) W
7 mL Bond ready-to-use *PA0183* P (HIER)

The CD8 molecule is composed of two chains and has a molecular weight of 32 kD. It is found on a T cell subset of normal cytotoxic/suppressor cells which make up approximately 20 to 35 percent of human peripheral blood lymphocytes. The CD8 antigen is reported to be detected on natural killer cells, 80 percent of thymocytes, on a subpopulation of 30 percent of peripheral blood null cells and 15 to 30 percent of bone marrow cells.

Refer to page 19 for the Bond ready-to-use format.

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Human thymus: immunohistochemical staining for CD8 antigen using NCL-CD8-295. Note intense membrane staining of T lymphocytes. Paraffin section.

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CD9 (Motility-Related Protein-1)

Clone 72F6
1 mL lyophilized *NCL-CD9* F P (HIER)

CD9 antigen is a 24 to 27 kD glycoprotein expressed on the surface of developing B lymphocytes, platelets, monocytes, eosinophils, basophils, stimulated T lymphocytes and by neurons and glial cells in the peripheral nervous system. It belongs to a family of membrane proteins termed tetraspanins which transverse the membrane four times. In pre-B cells and platelets, CD9 antigen regulates cell activation and aggregation possibly through an association with the integrin CD41/CD61 (GPIib/GPIIia). It also regulates cell motility in a variety of cell lines and appears to be an important regulator of Schwann cell behavior in the peripheral nervous system. In melanoma and breast cancer, CD9 antigen expression has been reported to occur predominantly on primary, non-metastatic tumors.

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Primary Antibodies

CD10

Clone 56C6
1 mL, 0.1 mL lyophilized NCL-CD10-270  F  P (HIER)  W
1 mL liquid NCL-L-CD10-270  F  P (HIER)  W
7 mL ready-to-use RTU-CD10-270  F  P (HIER)
7 mL Bond ready-to-use PA0270  P (HIER)

CD10 antigen, also called nephrilysin, is a 100 kD cell surface metalloendopeptidase which inactivates a variety of biologically active peptides. It was initially identified as the common acute lymphoblastic leukemia antigen (CALLA) and was thought to be tumor-specific. Subsequent studies, however, have shown that CD10 antigen is expressed on the surface of a wide variety of normal and neoplastic cells. In other lymphoid malignancies, CD10 antigen is reported to be expressed on cells of lymphoblastic, Burkitt’s and follicular lymphomas. CD10 antigen has been identified on the surface of normal early lymphoid progenitor cells, immature B cells within adult bone marrow and germinal center B cells within lymphoid tissue. It is also expressed in various non-lymphoid cells and tissues, such as breast myoepithelial cells, bile canalicular, fibroblasts, with especially high expression on the brush border of kidney and gut epithelial cells. (G. McIntosh et al. American Journal of Pathology. 154(1): 77-82 (1999)).

Refer to page 19 for the Bond ready-to-use format.


CD11c

Clone 5D11
1 mL, 0.1 mL liquid NCL-L-CD11c-563  P (HIER)
7 mL Bond ready-to-use PA0554  P (HIER)

CD11c is a member of the leukocyte integrin family of adhesion proteins. It is reported to be expressed in normal tissues, mainly on myeloid cells eg in bone marrow myelocytes, premelocytes, metamyelocytes, non-segmented and segmented neutrophils with high levels reported on tissue macrophages and monocytes and with lowest levels in granulocytes. It is also reported to be expressed on NK cells, activated T cells, lymphoid cell lines, including hairy cell leukemias and a proportion of interdigitating dendritic cells. CD11c antigen expression is reported to be a useful indicator of monocyte differentiation in the classification of acute myeloid leukemias and for the identification of hairy cell leukemias.

Refer to page 19 for the Bond ready-to-use format.


CD13

Clone 38C12
1 mL, 0.1 mL lyophilized NCL-CD13-304  P (HIER)

CD13 antigen, also known as aminopeptidase N, is a member of the type II integral membrane metalloproteases which also includes the leukocyte antigens CD10, CD26, CD73 and BP-1. CD13 antigen is a receptor for the coronaviruses which cause respiratory disease in humans and several animal species. The antigen functions as a zinc-binding metalloprotease which plays a role in cell surface antigen presentation by trimming the N-terminal amino acids from MHC class II-bound peptides. CD13 antigen is reported to be expressed on granulocytes, monocytes and their precursors, most acute myeloid leukemias and a smaller proportion of acute lymphoid leukemias. Non-hematopoietic cells which express CD13 antigen include epithelial cells, renal proximal tubules, intestinal brush border, endothelial cells, fibroblasts, brain cells, bone marrow, osteoclasts and cells lining the bile canaliculi.

Primary Antibodies

CD14

Clone 7
1 mL, 0.1 mL lyophilized NCL-CD14-223 P (HIER) W
1 mL liquid NCL-L-CD14-223 P (HIER) W

CD14 antigen is a glycosyl-phosphatidylinositol (GPI)-linked glycoprotein with a molecular weight of 55 kD. The CD14 antigen is reported to be expressed on cells of the myelomonocytic lineage including monocytes, macrophages and Langerhans cells. Low expression is also reported on neutrophils and on B cells. CD14 antigen is a receptor for bacterial lipopolysaccharide (LPS, endotoxin) and the lipopolysaccharide binding protein (LBP). LBP and CD14 antigen serve two physiological roles. These proteins act as opsonin and opsonic receptor, respectively, to promote the phagocytic uptake of bacteria or LPS-coated particles by macrophages.


CD15

Clone BY87
1 mL, 0.1 mL lyophilized NCL-CD15 F P (HIER/Enzyme)
1 mL liquid NCL-L-CD15 F P (HIER/Enzyme)
7 mL ready-to-use RTU-CD15 F P (HIER/Enzyme)

Clone Carb-1
7 mL Bond ready-to-use PA0039 P (HIER)

CD15 antigen, also known as X-hapten, is reported to be expressed on 90 percent of circulating human granulocytes, 30 to 60 percent of circulating monocytes and is absent from normal lymphocytes. The CD15 antigen is also expressed on Reed Sternberg cells of Hodgkin’s disease and some leukemias.

Product Specific Information
Please note that either enzyme pretreatment or heat induced epitope retrieval (HIER) temperature antigen unmasking using 1mM EDTA (pH8.0) solution may be used on fixed, paraffin-embedded tissue. The choice of antigen unmasking technique to provide the best result should be determined by the user.

Refer to page 19 for the Bond ready-to-use format.

CD16

Clone 2H7
1 mL, 0.1 mL lyophilized NCL-CD16 P (HIER)

CD16 antigen has a molecular weight of 50 to 70 kD and is a low affinity Fc receptor for complexed IgG, Fc/gamma RI, expressed on natural killer (NK) cells, granulocytes, activated macrophages and a subset of T cells expressing alpha-beta or gamma-delta T cell antigen receptors. The CD16 antigen exists both as a glycosyl-phosphatidylinositol (GPI)-anchored protein in polymorphonuclear cells and as a transmembrane protein in NK cells.


CD19

Clone BT51E
1 mL, 0.1 mL liquid NCL-L-CD19-163 P (HIER) W
7 mL Bond ready-to-use PA0843 P (HIER)

Clone 4G7/2E
1 mL, 0.1 mL lyophilized NCL-CD19-2 F C

Clone BT51E was developed to be effective on formalin-fixed, paraffin-embedded tissue sections.

CD19 is a member of the immunoglobulin superfamily and has two Ig like domains. It is a single chain glycoprotein present on the surface of B lymphocytes and follicular dendritic cells of the hematopoietic system. CD19 is a crucial regulator in B cell development, activation and differentiation. On B cells, CD19 associates with CD21, CD81 and CD225 (Leu-13) forming a signal transduction complex. CD19 is expressed from the earliest recognizable B cell lineage stage, through development to B cell differentiation but is lost on maturation to plasma cells.

Refer to page 20 for the Bond ready-to-use format.
Primary Antibodies

**CD20**

**Clone 7D1**
1 mL, 0.1 mL lyophilized NCL-CD20-7D1  F P (HIER)  W

**Clone MJ1**
1 mL, 0.1 mL lyophilized NCL-CD20-MJ1  F P (HIER)
7 mL Bond ready-to-use PA0906  P (HIER)

**Clone L26**
1 mL lyophilized NCL-CD20-L26  F P (HIER)  W
1 mL liquid NCL-L-CD20-L26  F P (HIER)  W
7 mL ready-to-use RTU-CD20-L26  F P (HIER)

Clone 7D1 was developed to produce superior manual staining on paraffin sections.

The CD20 antigen is a non-glycosylated phosphoprotein of approximately 33 kD which is expressed on normal and malignant human B cells and is thought to act as a receptor during B cell activation and differentiation. CD20 antigen has been reported to be expressed on normal B cells from peripheral blood, lymph node, spleen, tonsil, bone marrow, acute leukemias and chronic lymphocytic leukemias.

Refer to page 20 for the Bond ready-to-use format.

**CD21**

**Clone 2G9**
1 mL, 0.1 mL lyophilized NCL-CD21-2G9  F P (HIER)
1 mL liquid NCL-L-CD21-2G9  F P (HIER)
7 mL Bond ready-to-use PA0171  P (HIER)

CD21 antigen is a type I integral membrane glycoprotein of molecular weight 140 kD, which functions as the receptor for the C3d fragment of the third complement component. The CD21 molecule, present on mature B cells, is involved in transmitting growth-promoting signals to the interior of the B cell and acts as a receptor for Epstein-Barr virus. CD21 antigen is reported to be found in B cell chronic lymphocytic leukemias and in a subset of T cell acute lymphocytic leukemias but is absent on T lymphocytes, monocytes and granulocytes. CD21 antigen is also reported to be expressed in follicular dendritic cells and in follicular and mantle cell lymphomas, mature leukemias and lymphomas.

Refer to page 20 for the Bond ready-to-use format.

**CD22 (BL-CAM)**

**Clone FPC1**
1 mL, 0.1 mL lyophilized NCL-CD22-2 P (HIER)
7 mL Bond ready-to-use PA0249  P (HIER)

The CD22 antigen (BL-CAM) is a type 1 integral membrane glycoprotein with a molecular weight of 130 to 140 kD. It is a heterodimer of two independently expressed glycoprotein chains, present both on the membrane and in the cytoplasm of B lymphocytes. Expression of the CD22 antigen is reported to appear early in B cell lymphocyte differentiation at approximately the same stage as that of the CD19 antigen expression. Surface antigen expression is variable and may be lost upon differentiation. CD22 antigen is also reported to be strongly expressed on hairy cell leukemias. It is absent on peripheral blood T cells, T cell leukemias, granulocytes and monocytes.

Refer to page 20 for the Bond ready-to-use format.
CD23

Clone 1B12
1 mL, 0.1 mL lyophilized NCL-CD23-1B12 F P (HIER)
1 mL liquid NCL-L-CD23-1B12 F P (HIER) C
7 mL ready-to-use RTU-CD23-1B12 F P (HIER)
7 mL Bond ready-to-use PA0169 P (HIER)

The CD23 molecule is the low affinity IgE receptor found on B cells. It is a membrane glycoprotein of 45 kD and is reported to be found on a subpopulation of peripheral blood cells, B lymphocytes and on EBV-transformed B lymphoblastoid cell lines. Expression of CD23 antigen has been reported on monocytes and dendritic cells.

Refer to page 21 for the Bond ready-to-use format.

CD25 (Interleukin-2 Receptor)

Clone 4C9
1 mL, 0.1 mL lyophilized NCL-CD25-305 P (HIER)
7 mL Bond ready-to-use PA0305 P (HIER)

See also Interleukin-2 Receptor (CD25) on page 125.

CD27

Clone 137B4
1 mL lyophilized NCL-CD27 F P (HIER)

CD27 antigen, a member of the nerve growth factor/tumor necrosis factor receptor superfamily, is a type I transmembrane protein consisting of a disulfide-linked 120 kD dimer. CD27 antigen is reported to be expressed on mature thymocytes and on the majority of human peripheral blood T lymphocytes, on both CD4 positive and CD8 positive subsets. CD27 antigen is also expressed on activated B lymphocytes and a proportion of resting NK cells. Among CD4 positive cells, CD27 antigen is preferentially expressed on unprimed CD4 positive/CD45RA positive/CD45RO negative T lymphocytes while primed CD4 positive/CD45RA negative/CD45RO positive T lymphocytes express low levels of CD27. During activation, the appearance of a 32 kD soluble form results from proteolytic cleavage of the parent molecule. Soluble CD27 antigen has also been reported in cases of B cell chronic lymphocytic leukemia.

CD29

Clone 7F10
1 mL, 0.1 mL lyophilized NCL-CD29 P (HIER)

The β1 integrins are a family of structurally-related heterodimeric molecules and are composed of a β1 subunit (CD29 antigen) which is associated with 1 of 6 known alpha subunits. These impart the specificity to each of the receptors and the VLA molecules which are designated according to their alpha chain eg VLA-1 is α1/β1, VLA-2 is α2/β1. The adhesive properties of CD29 heterodimers on T cells can be regulated by cell activation, possibly through interactions between the cytoplasmic domain of CD29 antigen and the cytoskeleton. CD29 antigen is reported to be expressed on most cells including all leukocytes, although only at low levels on granulocytes. On T cells, CD29 antigen is expressed at higher levels on memory cells than on naive cells. The co-expression of CD4 and CD29 antigens is found in helper/inducer subpopulation of CD4 lymphocytes. CD29 antigen is one of several additional molecules reported to be found on the cell membrane of hepatocytes in cases of cirrhosis, alcoholic hepatitis and hepatitis C. Reduced expression of CD29 antigen together with the β2 integrin, CD11b, has been reported on peripheral blood lymphocytes from Graves’ disease patients.

CD30

Clone JCM182
1 mL, 0.1 mL liquid NCL-L-CD30-591 P (HIER) W
7 mL Bond ready-to-use PA0790 P (HIER)

Clone 1G12
1 mL, 0.1 mL lyophilized NCL-CD30 F P (HIER)
1 mL liquid NCL-L-CD30 F P (HIER)
7 mL ready-to-use RTU-CD30 F P (HIER)
7 mL Bond ready-to-use PA0153 P (HIER)

Clone 15B3
1 mL, 0.1 mL lyophilized NCL-CD30-365 F P (HIER)

Clone JCM182 was developed to be highly effective on formalin-fixed, paraffin-embedded tissue sections.

The CD30 antigen is a single chain glycoprotein with a molecular weight of 120 kD. CD30 antigen is known to act as a receptor for a cytokine ligand, CD30L, and may also play a role in the regulation of cellular growth and transformation. CD30 antigen is reported to be expressed on the surface of multinucleated Reed Sternberg cells, mononuclear Hodgkin’s cells and in the majority of anaplastic large cell lymphomas. The CD30 antigen is expressed in non-Hodgkin’s lymphoma and virally transformed cells, e.g. EBV-transformed B cells. Most T cell lymphomas are reported not to express CD30 antigen, with the exception of some pleomorphic T cell lymphomas.
Primary Antibodies

Product Specific Information
Using retrieval solutions other than that recommended for Clone JCM182 in the datasheet may increase background reactivity.
Refer to page 21 for the Bond ready-to-use format.


CD31 (PECAM-1)
Clone 1A10
1 mL, 0.1 mL lyophilized NCL-CD31-1A10 P (HIER)
7 mL Bond ready-to-use PA0250 P (HIER)

CD31 antigen (PECAM-1) is a single chain transmembrane glycoprotein with a molecular weight of 130 to 140 kD. The CD31 molecule is expressed on the surface of platelets, monocytes, granulocytes, B cells and at the endothelial intracellular junction. The molecule has an extracellular domain that contains six Ig-like homology units of C2 subclass, typical of cell to cell adhesion molecules. This domain mediates endothelial cell to cell adhesion, plays a role in endothelial contact and may serve to stabilize the endothelial cell monolayer. The CD31 molecule also has a cytoplasmic domain with potential sites for phosphorylation after cellular activation. The properties of CD31 antigen suggest that it is involved in interactive events during angiogenesis, thrombosis and wound healing. Angiogenesis is essential for tumor growth and metastases.
Refer to page 21 for the Bond ready-to-use format.


CD33
Clone PWS44
1 mL, 0.1 mL liquid NCL-L-CD33 P (HIER) W
7 mL Bond ready-to-use PA0555 P (HIER)

CD33 antigen is reported to appear on myelomonocytic precursor cells after CD34 antigen expression. It then continues to be expressed on both the myeloid and monocyte lineages, although it is reported to be absent on granulocytes. It has been reported that expression of CD33 is restricted to monocytes, promyelocytes, myeloid blasts, some acute undifferentiated leukemias and acute lymphoblastic leukemias. The expression of CD33 antigen has been demonstrated to be an important marker for distinguishing myeloid from the lymphoid leukemias.
Refer to page 22 for the Bond ready-to-use format.


CD34 (Endothelial Cell Marker)
Clone QBEnd/10
1 mL, 0.1 mL lyophilized NCL-END P (Enzyme) C
1 mL liquid NCL-L-END F P (Enzyme) C
7 mL ready-to-use RTU-END F P (Enzyme)
7 mL Bond ready-to-use PA0212 P (HIER)

CD34 antigen is a single chain transmembrane glycoprotein with a molecular weight of 110 kD. The CD34 protein is selectively expressed on human lymphoid and myeloid haemapoietic progenitor cells. The CD34 protein is also expressed on vascular endothelium.

Product Specific Information
Enzyme digestion of paraffin sections is recommended with Clone QBEnd/10 in preference to heat induced epitope retrieval as it produces stronger staining and reduces background elastin staining.
Refer to page 22 for the Bond ready-to-use format.

Human tonsil: immunohistochemical staining for CD34 antigen using NCL-END. Note intense staining of neoplastic endothelial cells and absence of staining of stromal cells. Paraffin section.
**CD35**

**Clone RLB25**
1 mL, 0.1 mL lyophilized NCL-CD35  F P (Enzyme)

The CD35 antigen, also known as CR1 or C3b/C4b R, is a transmembrane protein of 160 to 250 kD which binds complement components C3b and C4b. It mediates phagocytosis by neutrophils and monocytes of particles coated with C3b or C4b. CD35 antigen has an inhibitory effect on complement activation by both the classical and alternative pathways. CD35 antigen is reported to be found on erythrocytes, B cells, a subset of T cells, monocytes, macrophages cultured in vitro, neutrophils, eosinophils, glomerular podocytes and follicular dendritic cells. Decreased levels of CD35 antigen has been reported on B cells in patients with HIV infection.


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**CD37**

**Clone CT1**
1 mL lyophilized NCL-CD37  F P (HIER)

CD37 antigen is a member of the TM4 superfamily with a molecular weight of 40 to 52 kD. CD37 antigen was originally defined as an antigen of mature B lymphocytes where it is highly expressed. It is reported not to be expressed on pre-B cells or plasma cells and is expressed only at low level in T cells, neutrophils, monocytes and some myelomonocytic leukemia cells. NK cells, platelets and erythrocytes also do not express CD37 antigen. CD37 antigen on B cells associates non-covalently with MHC class II, CD19 and CD21 antigens and with other TM4 superfamily molecules CD53, CD81 and CD82.


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**CD38**

**Clone SPC32**
1 mL, 0.1 mL lyophilized NCL-CD38-290  F P (HIER)

1 mL liquid NCL-L-CD38-290  F P (HIER)

The CD38 molecule is a type II single transmembrane glycoprotein with a molecular weight of 46 kD. It is an ectoenzyme with the activities of ADP-ribosyl cyclase, cyclic ADP-ribose hydrolase, NAD glycohydrolase and is involved in both the formation and hydrolysis of cADPR, a second messenger that regulates the mobilization of intracellular Ca^{2+} ions. Although the CD38 molecule was originally identified as a T lymphocyte differentiation antigen, it is reported to be expressed in a wide range of cells and tissues. CD38 antigen can deliver potent growth and differentiation signals to lymphoid and myeloid cells. It is found on immature cells of the B and T cell lineages but not on most mature resting peripheral lymphocytes. It is also present on thymocytes, pre-B cells, germinal center B cells, mitogen-activated T cells, Ig-secreting plasma cells, monocytes, NK cells, erythrocytid and myeloid progenitors in the bone marrow and brain cells. CD38 antigen has also been reported in neurofibrillary tangles, the pathological indicator of Alzheimer’s disease that occurs in the neuronal perikarya and proximal dendrites.


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**CD39**

**Clone 22A9**
1 mL lyophilized NCL-CD39  P (HIER)

CD39 antigen is a transmembrane glycoprotein found on mature B lymphocytes, follicular dendritic cells, endothelial cells, activated T cells, NK cells and Langerhans cells. It is also known as E-type apyrase which hydrolyses extracellular ATP and ADP, a function important to homotypic adhesion and platelet aggression. CD39 antigen expressing cells may provide protection from the toxic effects of ATP leaked from damaged cells. CD39 antigen may enable tumor cells to reduce contact with T lymphocytes and escape immunological recognition. Increased levels of CD39 antigen expression are also reported to be associated with increased ectoATPase activity that occurs during the progression of melanomas.

For detailed information on all products please visit our website:  www.leica-microsystems.com
### CD40

**Clone 11E9**

1 mL, 0.1 mL lyophilized NCL-CD40 P (HIER) W

The CD40 antigen is a single chain glycoprotein with a calculated molecular weight of 27 kD. It is known to be a member of the tumor necrosis factor/nerve growth factor superfamily and shows a significant homology to the Hodgkin’s disease-associated antigen, CD30. The precise function of the CD40 antigen is unknown but it appears to be involved in the transduction of regulatory signals for cellular functions such as B cell proliferation and differentiation. It is also important in the prevention of apoptosis of germinal center B cells. The CD40 antigen is reported to be found on mature B cells (except plasma cells), most B cell leukemias and lymphomas, interdigitating reticulum cells, follicular dendritic cells and Reed Sternberg cells. Outside the immune system, CD40 antigen is reported to be expressed on some epithelial cells of certain carcinomas and in malignant melanomas.

### CD41 (GPIIb/IIIa)

**Clone M148**

1 mL lyophilized NCL-CD41 F

The CD41 antigen, also known as GPIIb/IIIa, is reported to be expressed early in megakaryocyte maturation and in megakaryoblastic leukemias and is absent or defective in platelets from patients with Glanzmann’s thrombasthenia. The CD41 antigen is involved in fibrinogen binding, clot retraction and platelet aggregation.

![Human tonsil: immunohistochemical staining for CD41 antigen (GPIIb/IIIa) using NCL-CD41. Note staining of aggregated platelets within the blood vessel. Frozen section.](image)

### CD42b (GPIb)

**Clone MM2/174**

1 mL lyophilized NCL-CD42b F P (HIER)

The CD42b glycoprotein, also known as GPIb, is a co-factor of ristocetin-induced aggregation and is involved in the binding of platelets to blood vessel walls. The CD42b antigen is reported to be expressed on platelets and on megakaryocytes in bone marrow and in megakaryoblastic leukemias. The absence of CD42b antigen on platelets is reported to be a possible indicator of Bernard-Soulier disease.

### CD43

**Clone MT1**

1 mL lyophilized NCL-MT1 F P (Enzyme) W

1 mL liquid NCL-L-MT1 F P (Enzyme) W

7 mL ready-to-use RTU-MT1 F P (Enzyme)

7 mL Bond ready-to-use PA0938 P (HIER)

**Clone MT1 produces superior staining on paraffin sections.**

The CD43 antigen is expressed on the membrane and in the cytoplasm of T cells and cells of myeloid lineage. The molecule itself exhibits molecular weight heterogeneity with bands of 90 to 140 kD observed on SDS-PAGE between different cell lines. Cells expressing the CD43 antigen are reported to include normal and neoplastic T cells. A small proportion of B cell chronic leukemias and centrocytic lymphomas are also reported to express CD43 antigen.

**Product Specific Information**

Enzyme pretreatment may enhance staining with clone MT1 in some cases. Refer to page 22 for the Bond ready-to-use format.

![Human mantle cell lymphoma: immunohistochemical staining for CD43 antigen using NCL-MT1. Note intense membrane staining of tumor cells. Paraffin section.](image)

### CD44 (H-CAM)

**Clone DF1485**

1 mL, 0.1 mL lyophilized NCL-CD44-2 F P (HIER) C

The CD44 antigen (H-CAM) is an 80 to 95 kD transmembrane glycoprotein with extensive O-linked glycosylation. The antigen is a cell surface receptor for hyaluronate, suggesting a role in the regulation of cell substrate interactions as well as cell migration. CD44 antigen is reported to be expressed on T cells, B cells, monocytes, granulocytes, erythrocytes and weakly on platelets. Other CD44 antigen positive cell types are reported to include epithelial cells, glial cells, fibroblasts and myocytes. Increased expression of CD44 antigen is found on some carcinomas and it has been reported that transition of tumor cell lines from non-metastatic to metastatic may be associated with changes in the expression of CD44 antigen variants.

Primary Antibodies

CD44 Variant Antibodies

**Clone VFF-327v3**
1 mL lyophilized CD44 variant 3 NCL-CD44v3 F P (HIER) W

**Clone VFF-8**
1 mL lyophilized CD44 variant 5 NCL-CD44v5 F P (HIER)

**Clone VFF-7**
1 mL lyophilized NCL-CD44v6 F P (HIER)

The CD44 molecule belongs to a family of cellular adhesion molecules found on a wide range of normal and malignant cells in epithelial, mesothelial and hemopoietic tissues. CD44 is a single gene with 20 exons, of which 10 are normally expressed to encode the basic CD44 (H-CAM) molecule. The additional 10 exons (v1 to v10) are only expressed by alternative splicing of the nuclear RNA. The expression of specific cell adhesion molecule CD44 splice variants has been reported to be associated with metastasis in certain human malignancies, such as breast cancer. A complex pattern of CD44 variant expression in different tumors compared to the CD44 expression of the normal cell of origin has been reported (Fox SB et al., Cancer Research (53): 4539-4546, 1993)). High levels of expression were observed with the variant exons by breast carcinomas that arise from breast ductal epithelium which do not normally express CD44. Conversely, normal gastrointestinal epithelium were reported to express low levels of many of the CD44 variants and the derived colon cancers expressed low and variable levels of the variants. Respiratory epithelium which expressed variants at high levels in normal cells were reported to express the same variants at similar levels in lung carcinomas.


**CD45**

**Clone X16/99**
1 mL, 0.1 mL lyophilized NCL-LCA F P (HIER) C
7 mL Bond ready-to-use PA0042 P (HIER)

**RP2/18, Clone RP2/22**
1 mL lyophilized NCL-LCA-RP F P
1 mL liquid NCL-L-LCA-RP F P
7 mL ready-to-use RTU-LCA-RP F P

The CD45 antigen (leukocyte common antigen) is a family of five or more high molecular weight glycoproteins present on the surface of the majority of the human leukocytes (including lymphocytes, monocytes and eosinophils) but absent from erythrocytes and platelets. Various isoforms of CD45 are generated by alternative splicing of three exons. Expression of CD45 is necessary for signalling through the T cell receptor. NCL-LCA-RP is a cocktail of two antibodies, clone RP2/18 and RP2/22.

**Product Specific Information**

The heat induced epitope retrieval (HIER) technique may enhance staining in some cases with NCL-LCA-RP, NCL-L-LCA-RP and RTU-LCA-RP. Refer to page 22 for the Bond ready-to-use format.


**CD45RA**

**Clone X148**
1 mL lyophilized NCL-B1 F P C

The CD45R subfamily comprises a restricted form of the leukocyte common antigen and is divided into four isoforms: CD45RA, CD45RB, CD45RC and CD45RO. The CD45RA molecule, a 220 kD isoform of CD45, is reported to be expressed on B cells, monocytes and a small proportion of T cells.
CD45RB

Clone MEM55
1 mL lyophilized NCL-CD45RB  F  P (HIER)

The CD45 molecule is reported to be found on all cells of hematopoietic origin, except erythrocytes. The various isoforms are expressed differently on various lymphoid cell types and are termed CD45RA, CD45RB, CD45RC and CD45RO. Low expression of CD45RB on CD45RO positive T lymphocytes defines a subset of highly differentiated T lymphocytes which accumulate in vivo within affected rheumatoid arthritic joints. The percentage of these cell types is also reported to be increased in the circulation of individuals with acute EBV infection and it is thought that these cells have a migratory advantage and are selectively recruited to sites of inflammation. CD45RB antigen is also reported to be found on B cells, monocytes, macrophages and is expressed weakly on granulocytes.

Product Specific Information
The heat induced epitope retrieval (HIER) technique may enhance staining in some cases.

Human stomach, B cell lymphoma: immunohistochemical staining for CD45RB antigen using NCL-CD45RB. Note intense membrane staining of neoplastic lymphoid cells. Paraffin section.

CD45RO

Clone UCHL1
1 mL, 0.1 mL lyophilized NCL-UCHL1  F  P (HIER)  C
1 mL liquid NCL-L-UCHL1  F  P (HIER)  C
7 mL ready-to-use RTU-UCHL1  F  P (HIER)
7 mL Bond ready-to-use PA0146  P (HIER)

The CD45RO molecule, a 180 kD isoform of CD45, is reported to be expressed on 48 percent of peripheral blood T lymphocytes, 37 percent of CD4 positive lymphocytes, 80 percent of thymocytes and on the majority of T cell malignancies. Monocytes and granulocytes show surface expression of the antigen whereas tissue macrophages exhibit cytoplasmic expression. The heat induced epitope retrieval (HIER) technique may enhance staining in some cases.

Refer to page 23 for the Bond ready-to-use format.


CD54 (ICAM-1)

Clone 23G12
1 mL, 0.1 mL lyophilized NCL-CD54-307  P (HIER)

See also ICAM-1 (CD54) on page 123.

CD56 (NCAM)

Clone CD564
1 mL, 0.1 mL lyophilized NCL-CD56-504  P (HIER)
7 mL Bond ready-to-use PA0191  P (HIER)

Clone 1B6
1 mL, 0.1 mL lyophilized NCL-CD56-1B6  P (HIER)  W
1 mL liquid NCL-L-CD56-1B6  P (HIER)  W
1 mL ready-to-use RTU-CD56-1B6  P (HIER)

Clone CD564 was developed to produce superior staining on paraffin sections.

The neural cell adhesion molecules are a family of closely-related cell surface glycoproteins thought to play a role in embryogenesis, development and contact-mediated interactions between neural cells. The CD56 antigen (NCAM) consists of four major isoforms generated by differential splicing of the RNA transcript from a single gene located on chromosome 5. The CD56 antigen is expressed on neurons, astrocytes, Schwann cells, NK cells and a subset of activated T lymphocytes.

Refer to page 23 for the Bond ready-to-use format.
CD57

**Clone NK-1**
1 mL, 0.1 mL lyophilized NCL-NK1  F P
7 mL ready-to-use RTU-NK1  F P
7 mL Bond ready-to-use PA0443 P (HIER)

The CD57 glycoprotein, also known as HNK-1, has a molecular weight of 110 kD. It is found on a subset of mononuclear cells with natural killer activity and on neuroectodermal cells expressing myelin-associated glycoprotein. Many cells which co-express CD57 and CD8 proteins are a subset of suppressor/cytotoxic T cells. These cells play a role in the rejection of grafts in acute graft versus host disease. The CD57 molecule is not expressed on erythrocytes or platelets.

**Product Specific Information**
Enzyme pretreatment may enhance staining in some cases.
Refer to page 23 for the Bond ready-to-use format.

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**CD62L (L-selectin)**

**Clone 9H6**
1 mL lyophilized NCL-CD62L-489 P (HIER)
See also L-selectin (CD62L) on page 128.

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**CD62P (P-selectin)**

**Clone C34**
1 mL lyophilized NCL-CD62P-367 P (HIER)
See also P-selectin (CD62P) on page 155.

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**CD63 (Melanoma Marker)**

**Clone NKI/C3**
1 mL, 0.1 mL lyophilized NCL-CD63  F P

CD63 antigen is a member of the TM4 superfamily with its structure consisting of four transmembrane regions, short cytoplasmic N and C-termini and two extracellular regions. CD63 antigen is widely distributed on the surface and interior of both hematopoietic and non-hematopoietic cells such as most sweat glands, islets of Langerhans, pituitary, pancreas, peribronchial glands, Paneth cells and prostate glands. It is reported to be strongly expressed on monocytes, macrophages and activated platelets and weakly expressed on lymphocytes and granulocytes. CD63 antigen associates non-covalently with CD9, CD81 and the integrins VLA-3, VLA-4 and VLA-6. It is reported that CD63 antigen may play a role as a tumor suppressor gene as its expression in human melanoma cells reduces tumor spread and metastasis.

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**CD66a (CEACAM1)**

**Clone 29H2**
1 mL lyophilized NCL-CD66a P (HIER)

CD66a antigen, also known as biliary glycoprotein (BGP), is a member of the carcinoembryonic antigen (CEA) family and of the immunoglobulin superfamily. CD66a, CD66b, CD66c and CD66d are known to be expressed by hematopoietic cells. CD66a antigen is also expressed in epithelia, in certain endothelia and in cells of the myeloid lineage. In liver, expression occurs in hepatocytes along the bile canalliculus. Apical membranous expression of the antigen is reported to occur in enterocytes, superficial absorptive cells of the colon, epithelia of oesophageal and Brunner’s glands, bile ducts and gall bladder, pancreatic ducts, proximal tubules of the kidney, prostate, endometrium and mammary ducts. Selective expression in endothelia is reported to occur in glomeruli and vasa recta of the kidney, small placental vessels, adrenal sinuoids, endometrium and prostate. Among the cells of the myeloid lineage, granulocytes and myelocytes express CD66a antigen. The expression of CD66a antigen has also been reported to be down-regulated in breast, endometrial, colorectal and prostate cancers. However, in one specific study of breast cancer, CD66a antigen was found not to be downregulated.
Primary Antibodies

**CD66e (Carcinoembryonic Antigen)**

**Clone 12-140-10**
1 mL lyophilized NCL-CEA-2  F P (Enzyme)
1 mL liquid NCL-L-CEA-2  F P (Enzyme)
7 mL ready-to-use RTU-CEA-2  F P (Enzyme)

See also Carcinoembryonic Antigen (CD66e) on page 67.

**CD68**

**Clone 514H12**
1 mL, 0.1 mL lyophilized NCL-CD68  F P (HIER)
1 mL liquid NCL-L-CD68  F P (HIER)
7 mL ready-to-use RTU-CD68  F P (HIER)
7 mL Bond ready-to-use PA0273  P (HIER)

**Clone KP1**
1 mL lyophilized NCL-CD68-KP1  F P (HIER)

*Clone 514H12 is the main choice of end users on paraffin sections.*

The CD68 molecule is a 110 kD intracellular glycoprotein primarily reported to be associated with cytoplasmic granules and to a lesser extent the membranes of macrophages. Markers to CD68 antigen are the most frequently used for the identification of macrophages in immunohistochemistry. However, CD68 is also found in monocytes, neutrophils, basophils and large lymphocytes. The function of the CD68 molecule is not certain but these lysosomal membrane proteins are major components and may protect the membranes from attack by acid hydrolases. It is unclear if the surface associated CD68 protein is functionally significant or due to leakage from the lysosomes. CD68 protein expression has been demonstrated in stimulated T cells and NK cells and non-haematopoietic tissues such as liver and renal tubules.

Refer to page 24 for the Bond ready-to-use format.

**CD69**

**Clone CH11**
1 mL, 0.1 mL lyophilized NCL-CD69  P (HIER)

The CD69 molecule is a type II membrane glycoprotein expressed as a disulfide-linked homodimer. The human and mouse genes for CD69 are encoded within the NK gene complex on chromosomes 12 and 6, respectively. CD69 protein is expressed mainly on activated T and B lymphocytes.

**CD71**

**Clone 10F11**
1 mL, 0.1 mL lyophilized NCL-CD71-309  P (HIER)

The CD71 molecule is a type II membrane glycoprotein with a molecular weight of approximately 180 kD. It is known as the transferrin receptor and is composed of two disulfide bonded 90 kD subunits. The CD71 molecule plays a critical role in cell proliferation by controlling the supply of iron, an essential component for many metabolic pathways, through the binding and endocytosis of transferrin, the major iron-carrying protein. CD71 protein is reported to be expressed on activated B and T cells, macrophages, proliferating cells and metabolically active cells eg neurons.

**CD72**

**Clone D748**
1 mL lyophilized NCL-CD72  P (HIER)

The CD72 molecule is a member of the type II integral membrane glycoproteins which includes other related cell surface molecules such as the asialoglycoprotein receptors, CD23 and the Kupffer cell receptor. The function of the CD72 molecule is unknown but the exposure of B cells to CD72 antibodies is reported to activate a variety of signalling pathways which can induce MHC class II expression and B cell proliferation. However, the significance of this is unclear. In addition, CD72 protein is reported to bind to and is a substrate, in vivo, of the protein tyrosine phosphatase SHP-1 which is known to regulate B cell antigen receptor (BCR) signalling. Signals from BCR help to determine B cell fate directing either proliferation, differentiation or apoptosis. CD72 protein is reported to be expressed on all cells of B cell lineage with the exception of plasma cells and weakly on human tissue macrophages.
### Primary Antibodies

**CD79a**

**Clone 11E3**
- 1 mL, 0.1 mL lyophilized NCL-CD79a-225 F P (HIER)
- 1 mL liquid NCL-L-CD79a-225 F P (HIER) C
- 7 mL Bond ready-to-use PA0192 P (HIER)

**Clone 11D10**
- 1 mL, 0.1 mL lyophilized NCL-CD79a-192 F P (HIER) C
- 1 mL liquid NCL-L-CD79a-192 F P (HIER)
- 7 mL ready-to-use RTU-CD79a-192 F P (HIER)

*Clone 11E3 was developed to produce superior staining on paraffin sections.*

The CD79 complex is a disulfide-linked heterodimer which is non-covalently associated with membrane-bound immunoglobulins on B cells. This complex of polypeptides and immunoglobulin constitute the B cell antigen receptor. The two components of this complex are designated CD79a and CD79b. The CD79a antigen is reported to first appear at the pre-B cell stage, early in maturation, and persist until the plasma cell stage where it is found as an intracellular component. The CD79a antigen is reported to be expressed in the majority of acute leukemias of precursor B cell type, B cell lines, B cell lymphomas and in some myelomas. It is not present in myeloid or T cell lines. Refer to page 24 for the Bond ready-to-use format.

**CD79b**

**Clone JS01**
- 1 mL, 0.1 mL liquid NCL-L-CD79b P (HIER)

CD79b, also known as B29 and Ig-β, is thought to function in the cellular activation and signalling that occurs when surface immunoglobulin (Ig) on B cells binds antigen or becomes cross-linked by anti-Ig antibody. This function occurs with the formation of a membrane signalling complex that is associated with Ig at the surface of B cells. CD79b, together with CD79a, forms the B cell antigen receptor (mlg) complex. CD79b expression is reported to be found in 80 to 90 percent of mature B cell neoplasms, with the exception of chronic lymphocytic leukemias.

**CD81**

**Clone 1D6**
- 1 mL lyophilized NCL-CD81 P (HIER)

CD81 antigen, also known as TAPA-1, is a member of the TM4 superfamily and is predicted to have four transmembrane regions, short cytoplasmic N and C-termini and two extracellular regions. CD81 protein has a molecular weight of 26 kD and is expressed by most cell types. Of the hematopoietic cells, CD81 protein is reported to be expressed by B and T cells, macrophages, dendritic cells, NK cells and eosinophils but not by neutrophils, platelets or erythrocytes. The CD81 protein associates non-covalently with a number of other molecules eg CD19, CD21, MHC class I and II, CD20, CD37, CD53 and CD82 in B cells and CD4, CD8 and CD82 in T cells. It also associates with the integrins CD29/CD49c (VLA-3), CD29/CD49d (VLA-4) and CD29/CD49f (VLA-6) in several other cell types. No extracellular ligand has been identified for CD81 protein and its function remains unclear, although mouse CD81 protein plays a role in early T cell development. The human CD81 molecule has been reported to be involved in cell adhesion, motility, metastasis as well as cell activation and signal transduction.
CD82

Clone 5B5
1 mL lyophilized NCL-CD82 P (HIER)

CD82 antigen, also known as KAI1 or C33 antigen, is a member of the TM4 superfamily. It is expressed in most cell types, including B and T cells, NK cells, monocytes, granulocytes and platelets but not in erythrocytes. Upon lymphocyte activation, CD82 antigen expression is reported to be strongly upregulated and, in vitro, it can transduce signals in B cells, T cells and monocytes. The expression of CD82 antigen is reported to suppress metastasis in tumor cells. In benign prostatic hyperplasia, the expression of CD82 antigen was found to be uniform in the cellular membrane of glandular epithelial cells. However, tissue from untreated prostate cancer showed more variable expression.

CD83

Clone 1H4b
1 mL, 0.1 mL lyophilized NCL-CD83 P (HIER)

CD83 antigen, a member of the immunoglobulin superfamily, is reported to be expressed on mature and activated dendritic cells. These include Langerhans cells in the skin, peripheral blood dendritic cells and interdigitating reticulum cells within the T cell zones of lymphoid organs. In early human pregnancy, decidua is reported to contain immunostimulatory CD83 antigen positive dendritic cells. CD83 antigen is reported to be expressed in Hodgkin’s disease and can be found to be expressed in most Reed Sternberg cells. In breast carcinoma, mature CD83 positive cells may be found in peripheral areas amongst T cells, which resembles dendritic/T cell clusters of secondary lymphoid organs. This is a characteristic of ongoing immune reactions where mature and activated dendritic cells are essential for the recruitment of activated tumor specific lymphocytes during carcinogenesis. Some germinal center B cells and activated peripheral lymphocytes also express CD83 antigen.

CD85 (Fas)

Clone GM30
1 mL lyophilized NCL-FAS-310 F P (HIER)

See also Fas (CD95) on page 110.

CD99

Clone PCB1
1 mL, 0.1 mL liquid NCL-L-CD99-187 P (HIER)

CD99 is a 32 kDa transmembrane glycoprotein, encoded by the MIC2 gene, which is located in the pseudoautosomal region of the human X and Y chromosomes. Recently, the MIC2 gene has been shown to encode two distinct proteins which are produced by alternative splicing of the CD99 gene transcript and are identified as bands of 30 and 32 kDa (p30/32).

Although its function is not fully understood, CD99 has been implicated in various cellular processes including homotypic aggregation of T cells, upregulation of T cell receptor and MHC molecules, apoptosis of immature thymocytes and leukocyte diapedesis. CD99 is reported to be expressed on most human tissues including cortical thymocytes, pancreatic islets cells, Leydig and Sertoli cells, virtually all hematopoietic cell types (except granulocytes), peripheral blood lymphocytes, granulose cells of the ovary, endothelial cells and basal/parabasal squamous epithelial cells. CD99 expression has been reported in a wide range of tumors, including Ewing’s sarcoma and T cell lymphoma.

Refer to page 24 for the Bond ready-to-use format.

CD105 (Endoglin)

Clone 4G11
1 mL, 0.1 mL lyophilized NCL-CD105 P (HIER)

See also Endoglin (CD105) on page 103.
CD117 (c-kit Oncoprotein)

Clone T595
1 mL lyophilized NCL-CD117 P (HIER)
1 mL liquid NCL-L-CD117 P (HIER)
7 mL ready-to-use RTU-CD117 P (HIER)

Clone 57A5D8
1 mL lyophilized NCL-cKIT F
See also c-kit Oncoprotein (CD117) on page 91.

CD123

Clone BR4MS
1 mL, 0.1 mL liquid NCL-L-CD123 P (HIER)

The CD123 antigen is also known as the alpha subunit of the human interleukin-3 receptor. It is a type I transmembrane glycoprotein and is a member of the cytokine receptor superfamily. CD123 forms a heterodimer with CD131 (the beta subunit of the interleukin-3 receptor) to form the interleukin-3 receptor, where the cytokine specificity is provided by the alpha subunit and the signal transduction function is provided by the beta subunit. The interleukin-3 receptor is reported to be expressed on monocytes, neutrophils, basophils, eosinophils, megakaryocytes, proliferation and differentiation of these cells. Outside the hematopoietic system CD123 is reported to be expressed in Leydig cells of the testis, some endothelial cells, and cells of the placenta and brain.

CD134 (OX40)

Clone 102H6
1 mL lyophilized NCL-CD134 P (HIER)

The CD134 molecule is a member of the tumor necrosis factor receptor superfamily. It was originally named MRC OX40 after the first antibody which led to its discovery. CD134 protein binds to OX40 ligand and is expressed specifically on activated T lymphocytes with maximum expression determined at twenty four hours post stimulus. In rats, CD134 protein is only expressed on activated CD4 positive T lymphocytes and in humans it is described as being found predominantly on CD4 positive cells. In mice, CD134 protein is expressed on both activated CD4 positive and CD4 positive/CD8 positive cells. The OX40 ligand binds CD134 protein on T cells and co-stimulates proliferation. Crosslinking of CD134 with OX40 ligand on activated B cells stimulates proliferation and antibody production suggesting a role in B cell differentiation into plasma cells. Functionally, the CD134 molecule is involved in T cell co-stimulation and T cell dependent antibody production.

CD137

Clone S16
1 mL lyophilized NCL-CD137 P (HIER)

CD137 antigen, a member of the tumor necrosis factor receptor family, and its ligand are reported to be expressed on activated T lymphocytes and on antigen-presenting cells, respectively. This receptor/ligand system regulates the activation, proliferation and survival of T and B lymphocytes and monocytes through bidirectional signal transduction. Human CD137 antigen is reported to be expressed on activated B cells, Reed Sternberg cells and peripheral blood monocytes but is absent from resting T cells. In nonlymphoid cells, expression has been reported in blood vessel walls, on the endothelial layer and on vascular smooth muscle cells. Soluble forms of CD137 are reported at increased levels in sera of individuals with rheumatoid arthritis. The expression of soluble CD137 lags behind that of membrane bound CD137 by approximately 24 hours and it has been proposed that as activation of lymphocytes through membrane-bound CD137 delivers a potent stimulatory signal then soluble CD137 may provide a negative control mechanism for immune responses.

CD141 (Thrombomodulin)

Clone 15C8
1 mL, 0.1 mL lyophilized NCL-CD141 F P (HIER)
See also Thrombomodulin (CD141) on page 162.
CD146 (MCAM)

**Clone N1238**  
1 mL, 0.1 mL lyophilized NCL-CD146 P (HIER) W

CD146 protein is also known as the melanoma metastasis-associated surface molecule, MUC18, A32 antigen, S-Endo-1 and the melanoma cell adhesion molecule, MCAM or Mel-CAM. Originally, the CD146 molecule was defined as a marker of tumor progression and metastasis formation in human melanoma. More recently, it has been reported to be expressed on endothelial cells, smooth muscle and cerebellar cortex. Structurally, CD146 is an integral membrane glycoprotein of 113 kD with the characteristic V-V-C2-C2-C2 immunoglobulin-like domain structure. It shares considerable homology with chicken neural adhesion molecule, chicken gicerin, goldfish neurulin and is also closely related to the human blood group glycoprotein, lutheran. Although CD146 molecule functions as a cell adhesion molecule it interacts with an as yet uncharacterized ligand. CD146 can be induced on all T cells via PHA, recall antigen, superantigen and T cell receptor/CD3 stimulation. Furthermore reports suggest that the CD146 molecule is involved in the extravasation and homing of activated T cells. CD146 protein can promote tumor progression in human melanoma, possibly through enhanced interaction between melanoma cells and endothelial cells. In contrast, CD146 protein may act as a tumor suppressor in breast carcinoma with expression frequently lost in some cases.

Human malignant melanoma: immunohistochemical staining for CD146 antigen using NCL-CD146. Note membrane staining of metastatic melanocytes and endothelial cells. Paraffin section.

CD151 (PETA-3)

**Clone RLM30**  
1 mL lyophilized NCL-CD151 P (HIER)

The CD151 molecule, also known as PETA-3/SFA, is a member of the family of tetraspanin transmembrane proteins. Tetraspanins are characterized by one small and one large extracellular loop, a small cytoplasmic loop and short amino and carboxy-terminal domains. They act as linkers between extracellular integrin alpha chain domains and intracellular signalling molecules. They are involved in a wide range of cellular processes such as cell adhesion, motility, activation, proliferation, differentiation and cancer. The CD151 molecule has been reported to be expressed in basal cells of epidermis, epithelial cells, skeletal, smooth and cardiac muscle cells, schwann cells, platelets, megakaryocytes and endothelial cells. In the small intestine, CD151 is reported to be expressed by crypt and villous enterocytes but is not detectable on the brush border. High expression of CD151 has also been reported in small lung cell carcinomas.


CD163

**Clone 10D6**  
1 mL, 0.1 mL lyophilized NCL-CD163 P (HIER)

The CD163 molecule is a type I membrane protein also known as M130 antigen, Ber-Mac3, Ki-M6 or SM4. CD163 protein is restricted in its expression to the monocytic/macrophage lineage. It is reported to be present on all circulating monocytes and most tissue macrophages except those found in the mantle zone and germinal centers of lymphoid follicles, interdigitating reticulum cells and Langerhans cells. In addition, multinucleated cells within inflammatory lesions are reported not to express CD163 protein. The protein is upregulated by glucocorticoids and downregulated by the immunosuppressant cyclosporin A and by phorbol esters, while lipopolysaccharide, an inflammatory mediator, has no influence on expression. It has been proposed that a specific release mechanism of soluble CD163 antigen by human monocytes may play an important role in modulating inflammatory processes.

CD166 (ALCAM)

**Clone MOG/07**
1 mL, 0.1 mL lyophilized NCL-CD166 P (HIER)

The human CD166 molecule, also known as activated leukocyte cell adhesion molecule (ALCAM), is a glycoprotein of 100 kD that functions as a ligand for the CD6 molecule. It is the human homolog of the chicken neural adhesion molecule, BEN/SC-1/OM-GRASP, the rat molecule, KG-CAM, and the fish protein, neurolin. The CD166 molecule is reported to be expressed by a subset of activated leukocytes. CD166/CD6 interactions may play a role in the binding of T and B cells to activated leukocytes as well as in interactions between cells of the nervous system involving neurite extension of the neurons. The CD166 molecule is also expressed in a number of other cell types including activated monocytes, epithelial cells, fibroblasts, neurons, melanoma cells and also in sweat and sebaceous glands. CD166 protein expression is reported to be upregulated in a cell line deriving from a metastasizing melanoma. It is also reported that CD166 protein may play a role in T cell development in the thymus.

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CD168 (RHAMM)

**Clone 2D6**
1 mL lyophilized NCL-CD168 F P (HIER)

The CD168 molecule, also known as RHAMM/IHABP (receptor for hyaluronic acid mediated motility/intracellular hyaluronic acid binding protein), is a ubiquitously expressed filamentous, cytoskeletal accessory protein. It is not, as originally reported, a cell surface receptor. However, in some cancers, it is reported that the expression of cell surface variants of CD168 is closely correlated with tumor progression. The CD168 molecule plays a role in cell signalling, migration and adhesion via interactions with hyaluronan, microtubules, actin, calmodulin and components of the extracellular regulated kinase (erk) signalling pathway. CD168 appears to have an important role in human sperm motility. In the brain, the CD168 molecule is reported to be expressed in the majority of neurons and in many oligodendrocytes where it has an effect on astrocyte motility, neurite migration and axonal growth. CD168 antigen is necessary for migration of smooth muscle cells after wound injury and it has been associated with adult wound fibroplasias. Reports indicate that CD168 antigen is detected at varying levels in normal breast epithelium but in breast cancers, strong expression has been observed particularly in well-differentiated grade 1 ductal carcinomas, whereas high grade cancers displayed significantly lower expression. CD168 is also reported to be expressed at low frequency in non-cancerous gastric mucosa and in 74 percent of gastric cancers where it is associated with malignant progression.

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CD205 (DEC-205)

**Clone 11A10**
1 mL liquid NCL-L-DEC205 P (HIER)

CD205 is a 205 kD integral membrane glycoprotein homologous to the macrophage mannose receptor and related receptors. It is a novel multilectin, endocytic receptor that can be used by dendritic cells and thymic epithelial cells to direct captured antigens from extracellular spaces to a specialized antigen processing compartment.

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CD243 (P-glycoprotein)

**Clone 5B12**
1 mL lyophilized NCL-PGLYm F P (HIER)

See also P-glycoprotein (CD243) on page 150.

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CD246 (Anaplastic Lymphoma Kinase) (ALK) (p80)

**Clone 5A4**
1 mL, 0.1 mL lyophilized NCL-ALK P (HIER)
7 mL Bond ready-to-use PA0306 P (HIER)

See also ALK (Anaplastic Lymphoma Kinase) (CD246) (p80) on page 54.

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cdk-activating kinase (CAK)

**Clone MO-1.1**
1 mL lyophilized NCL-CAK F W 0

Cyclin dependent kinase (cdk) activation is dependent on cyclin binding and phosphorylation of a conserved threonine residue mediated by cdk-activating kinase (CAK). Human CAK has been identified as the p40MO15 (cdk7)/cyclin H/MAT1 complex which is localized to the nucleus in vertebrates. DNA repair mechanisms and regulation of gene activity both involve CAK. NCL-CAK detects the catalytic subunit p40MO15 (cdk7).

**Product Specific Information**
NCL-CAK may also be used in immunoprecipitation techniques.
CDX2

Clone AMT28
1 mL, 0.1 mL lyophilized NCL-CDX2 P (HIER)
7 mL Bond ready-to-use PA0535 P (HIER)

CDX2 is a caudal-type homeobox, intestine-specific transcription factor that is expressed early in intestinal development and may be involved in the regulation of proliferation and differentiation of intestinal epithelial cells. CDX2, as well as CDX1, is of particular interest as the intestine is the only organ that contains detectable levels of either gene product. This pattern of restricted expression is unusual for homeobox genes. Phosphorylation of the CDX2 activation domain can modulate its function and different spatial expression patterns in the intestinal epithelium. CDX2 is primarily expressed on the surface of the villus and in the crypts. In contrast to CDX1, intense CDX2 expression is reported to occur in all but the distal portions of the developing intestine. The loss of CDX2 has been reported to contribute towards the progression of some sporadic colorectal cancers. It has been reported that CDX2 may also be associated with carcinogenesis of the stomach as expression of CDX2 mRNA progressively decreases with the transition from well differentiated to poorly differentiated gastric cancer cell lines.

Refer to page 25 for the Bond ready-to-use format.


CEACAM1 (CD66a)

Clone 29H2
1 mL lyophilized NCL-CD66a P (HIER)
See also CD66a (CEACAM1) on page 82.

Cellular Apoptosis Susceptibility Protein

Clone 30F12
1 mL lyophilized NCL-CAS F P (HIER) W

Cellular apoptosis susceptibility protein, the product of the CAS gene, is associated with microtubules and the mitotic spindle. CAS is the human homolog of the yeast chromosome-segregation gene, CSE-1. The molecular mechanism or function by which CAS is associated with cell proliferation and apoptosis is not yet fully understood but it has been proposed that the protein may play a role in the development of some leukemias and lymphomas. Aggressive non-Hodgkin’s lymphoma and Hodgkin’s disease have been reported where up to 80 percent of the malignant cells express CAS protein. These include large cell anaplastic lymphomas of T and null cell phenotype and diffuse large B cell lymphomas. Low grade non-Hodgkin’s lymphoma were reported where only 10 to 60 percent of all cells were positive. It was proposed that high expression of cytoplasmic CAS protein appeared to correlate with proliferation of normal and malignant lymphoid cells.
c-erbB-3 Oncoprotein

Clone RTJ1
1 mL lyophilized NCL-c-erbB-3 P (HIER) O

The c-erbB-3 oncprotein is a member of the type 1 growth factor receptor family which also includes c-erbB-2 and epidermal growth factor receptor (EGFR). These receptors share a common overall structure consisting of an extracellular domain, a transmembrane region and a cytoplasmic domain. The expression of c-erbB-3 oncprotein has been reported in chronic pancreatitis, exocrine pancreatic cancer and in tumors of the gastrointestinal tract.

Product Specific Information

NCL-c-erbB-3 recognizes an epitope in the cytoplasmic domain of the human c-erbB-3 oncprotein and does not cross-react with c-erbB-2 or EGFR. NCL-c-erbB-3 may also be used in immunoprecipitation techniques.

Cholecystokinin (CCK-8)

Polyclonal
0.25 mL lyophilized NCL-CCK-8p P (Enzyme)
See also CCK-8 (Cholecystokinin) on page 69.

Choline Acetyltransferase

Clone 38B12
1 mL lyophilized NCL-ChAT P (HIER)

Choline acetyltransferase (ChAT) is a 68 kD enzyme which catalyzes the synthesis of acetylcholine (ACh) from choline and acetyl coenzyme A. The human ChAT gene encodes two proteins, the 68 kD ChAT enzyme and a 27 kD protein immunologically related and coexpressed with ChAT in cholinergic neurons of the central nervous system. The smaller protein may play a role in the regulation of ACh synthesis. ChAT is expressed in cholinergic neurons, the majority of the neurons in the nucleus basalis of Meynert, large neurons in the striatum (putamen and caudate nuclei), the majority of neurons in the pedunculopontine, hypoglossal, dorsal nucleus of vagus and subgroups of neurons in Rollier’s and the medial olivary accessory nuclei. Prominent staining is observed in ribbon-like protein, distributed at the periphery of large neurons of the nucleus basalis of Meynert, the motor neurons in the hypoglossal and ambiguous nuclei.

Product Specific Information

NCL-ChAT does not label axons in the insular cortex of the internal capsule non-cholinergic structures, endothelial cells or microglia.

For detailed information on all products please visit our website:
www.leica-microsystems.com
Chromogranin A

Clone 5H7
1 mL, 0.1 mL lyophilized NCL-CHROM-430 P (HIER)
7 mL Bond ready-to-use PA0430 P (HIER)

Chromogranin A is a 68 kD acidic protein which is reported to be widely expressed in neural tissues and in secretory granules of human endocrine cells eg parathyroid gland, adrenal medulla, anterior pituitary gland, islet cells of the pancreas and C cells of the thyroid. Chromogranin A expression has been reported in neuroendocrine tumors such as pituitary adenomas, islet cell tumors, pheochromocytomas, medullary thyroid carcinomas, Merkel cell tumors and carcinoids.

Refer to page 25 for the Bond ready-to-use format.

C-jun Oncoprotein

Clone DK4
1 mL lyophilized NCL-cJUN F P (Enzyme)

C-jun is the normal cellular homolog of the transforming gene of avian sarcoma virus 17 and is a member of the early-response gene family. The c-jun oncogene encodes a nuclear protein, p38, which is a major component of the transcription factor AP1 and interacts with the c-fos oncogene product forming a transacting heterodimer. C-jun oncoprotein plays an important role in the regulation of gene expression and signal transduction processes. Alterations in c-jun expression may affect the transcriptional initiation of specific target genes and as a consequence may affect normal cell growth and function.

Clusterin (Apolipoprotein J)

Clone 7D1
1 mL lyophilized NCL-CLUSTERIN P (HIER)

Clusterin is also known as apolipoprotein J, complement lysis inhibitor, gp80, glycoprotein III, SGP-2, SP 40, TRPM2 and T64. It is a ubiquitous, multi-functional protein of 80 kD comprising of two disulfide-linked subunits, alpha and beta. It is implicated in numerous biological processes including sperm maturation, lipid transport, regulation of the complement cascade, membrane recycling, cell death, immune regulation, cell adhesion and morphological transformation. In pathological conditions, it is an amyloid associated protein co-localizing with fibrillar deposits in systemic and localized amyloid disorders. In Alzheimer’s disease, clusterin is reported to be present in amyloid plaques and cerebrovascular deposits. In breast cancers, clusterin expression is reported to be correlated with tumor size and, when upregulated, correlated inversely with apoptotic index. This suggested that clusterin expression was not a prerequisite to cellular death by apoptosis. Clusterin has also been reported to be expressed in anaplastic large cell lymphoma.
c-MET (Hepatocyte Growth Factor Receptor)

**Clone 8F11**
1 mL, 0.1 mL lyophilized NCL-cMET F P (HIER)

The c-MET gene encodes a transmembrane tyrosine kinase identified as the receptor for a polypeptide known as hepatocyte growth factor (HGF). HGF has been shown to exert a pleiotropic activity on several cell types mainly of epithelial origin. It is a powerful mitogen for hepatocytes and also stimulates the growth of other cell types including kidney tubular cells, keratinocytes and endothelial cells. Other cell types known to express c-MET include hepatocytes, microglial cells in white matter and astrocytes.

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c-myc Oncoprotein

**Clone 9E11**
1 mL, 0.1 mL lyophilized NCL-cMYC F P

The c-myc oncogene is the human cellular homolog of the avian v-myc gene found in several leukemogenic retroviruses. c-myc is a nuclear phosphoprotein, which has DNA-binding activity and is implicated in the control of normal proliferation and differentiation. Expression of c-myc in untransformed cells is growth factor dependent and essential for progression through the cell cycle. c-myc is expressed during proliferation in a wide variety of adult tissues and at all stages of embryonic development.

**Product Specific Information**
Enzyme pretreatment may enhance staining in some cases.

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Collagen Type II

**Polyclonal**
1 mL lyophilized NCL-COLL-IIp P (Enzyme)

Collagen type II is the structural protein predominantly found throughout the cartilage matrix and is also found in very small amounts in the eye. The fibrils formed by this protein are usually thinner and more delicate than collagen type I fibrils.

**Product Specific Information**
NCL-COLL-IIp reacts with type II collagen and does not cross-react with collagen types I, III, IV, V, VI, other human serum proteins or non-collagenous extracellular associated proteins.

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Collagen Type IV

**Clone PHM-12**
1 mL lyophilized NCL-COLL-IV F P (HIER+Enzyme)

In kidney, collagen IV is expressed in glomerular and tubular basement membranes and also mesangial cells and the matrix within glomeruli, the basal lamina of capillaries as well as basement membrane structures in many organs.

**Product Specific Information**
The heat induced epitope retrieval (HIER) technique followed immediately by 30 seconds of enzyme digestion produces optimal staining with this antibody. NCL-COLL-IV recognizes collagen type IV, which is a major constituent of basement membranes.

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Collagen Type VII

**Clone LH7.2**
1 mL lyophilized NCL-COLL-VII F

Collagen type VII is a basement membrane component which is the major protein in the anchoring fibrils projecting from the lamina densa into the subjacent connective tissue. Collagen type VII has been reported to be detected in the basal lamina of stratified epithelia such as epidermis, oral, oesophageal and cervical epithelium and urothelium of the bladder. Those epithelia which are composed of different cell types eg sweat gland epithelium or breast epithelium which are made up of myoepithelial cells next to glandular cells, possess a type VII collagen-containing basement membrane. Basement membranes play an important role in tumor progression. In normal breast tissue, benign breast lesions and in situ malignancies, the basement membrane always surrounds ducts and tubules whereas in invasive breast carcinomas it is often absent. Collagen type VII is reported to be a defective membrane component in the condition Recessive Dystrophic Epidermolysis Bullosa (RDEB).


Human skin: immunohistochemical staining for collagen type VII using NCL-COLL-VII. Note staining of the basal lamina of the stratified epithelium. Frozen section.
Complement Component C9

Clone 10A6
1 mL, 0.1 mL lyophilized NCL-CCC9 P (HIER)

Complement component C9 binds to the C5b-8 complex as the final protein of the membrane attack complex. After binding, it undergoes a conformational change and inserts itself into the cell membrane, forming transmembrane channels. Complement component C9 acts in a similar way to perforin, a pore forming protein found in cytotoxic T cells. Male and female reproductive tissues express and synthesize complement components, binding proteins and receptors, although the implications of this is unclear. The detection of complement component C9 has been reported in cases of acute myocardial damage at necropsy. Detection of myocardial infarction or diffuse damage can be unreliable with conventional methods of examination of the heart such as enzyme histochemistry or by the elaborate technique of quantification of contraction band necrosis.

CPP32 (Caspase-3)

Clone JHM62
1 mL, 0.1 mL lyophilized NCL-CPP32 P (HIER) W

Cysteine protease protein (CPP)-32 is a member of the interleukin-1 beta-converting enzyme (ICE) family of mammalian proteases which specifically cleaves substrates at the C-terminal side of aspartic acid residues. Members of this family have been implicated in apoptosis and CPP32 (caspase-3) is thought to act as a control mediator of programmed cell death in mammalian cells. CPP32 is synthesized as an inactive 32 kD proenzyme and is processed during apoptosis to its active form which is responsible for the cleavage of poly (ADP-ribose) polymerase (PARP), actin and sterol regulatory element binding protein (SREBP). CPP32 is reported to be found in epithelial cells of skin, renal proximal tubules and collecting ducts, epithelioreticular cells of the thymus and bronchial, colonic and salivary duct epithelia. Chondrocytes, bone osteocytes, megakaryocytes, mature neutrophils of bone marrow and plasma cells of the tonsil, lymph node and bone marrow are also reported to express CPP32 antigen.

Cyclin A

Clone 6E6
1 mL lyophilized NCL-CYCLIN A P (HIER) W C

Cyclins are proteins that vary in abundance and are associated with and activate cyclin dependent kinases (cdk) at different stages of the cell cycle. Cyclin A, more commonly defined as A2, a protein of 60 kD, binds independently to a cdc-related kinase, cdk2, in S to G2 phase and cdc2/cdk1 in G2 to M phase, leading to enzyme activation. Cyclin A is detectable in S phase, increasing during cell cycle progression to G2 phase and may prove useful as a marker of proliferation. Cyclin A is reported to be expressed in normal human epidermis and various proliferative skin diseases including psoriasis, seborrhoeic keratosis and squamous cell carcinoma. The majority of breast tumors reported with elevated fractions of cells expressing cyclins A, B and E have been shown to have increased proliferative status.

Cyclin B1

Clone 7A9
1 mL, 0.1 mL lyophilized NCL-CYCLIN B1 P (HIER) W C

Cyclin B protein acts in a similar way to cyclin A, as regulatory subunits of p34/cdc2/cdk1 affecting the G2 to M phase transition. Cyclin B expression is, therefore, restricted to a specific short period of the cell cycle with cyclin B1 expression detected earlier and peaking in concentration before cyclin B2 expression. Cyclin B positive cells, indicated by cytoplasmic staining, in proliferating tissue are reported to represent a subset of Ki67 positive cells.

Product Specific Information

Please note that methacarn fixation produces optimal staining.
Primary Antibodies

Cyclin D1

Clone P2D11F11
1 mL, 0.1 mL lyophilized
NCL-CYCLIN D1-GM P (HIER/Enzyme) W
1 mL liquid NCL-L-CYCLIN D1-GM P (HIER/Enzyme) W
7 mL ready-to-use RTU-CYCLIN D1-GM P (HIER/Enzyme)

Cyclin D1, a protein of 36 kD, is also known as PRAD1 or bcl-1. Maximum expression of cyclin D1 occurs at a critical point in mid to late G1 phase of the cell cycle. The cyclin D1 gene, located on 11q13 has been reported to be overexpressed in mantle cell lymphomas due to the chromosomal translocation t(11;18). It has also been observed in approximately 30 percent of breast cancers.

Cyclin D3

Clone DCS-22
1 mL lyophilized NCL-CYCLIN D3 F P (HIER/Enzyme) W

The D-type cyclins are a family of proteins which function primarily by regulating the activity of cyclin dependent kinases in the G1 phase of the cell cycle. Cyclin D3, a protein of 34 kD, shares 53 percent sequence homology with cyclin D1. Cyclin D3 expression is reported to be induced later than cyclin D1 in G1 phase of the cell cycle. When complexed with cyclin dependent kinases, cyclin D3 shows activity characteristic of other D-type cyclins. However, an increase in cyclin D3 expression with an absence of kinase activity has been observed in terminally differentiated, quiescent cells, suggesting an additional role for cyclin D3.

Cyclin E

Clone 13A3
1 mL, 0.1 mL lyophilized NCL-CYCLIN E F P (HIER) W

Cyclin E was identified as a protein which would complement cyclin mutations in yeast and mammalian cells. Overexpression of cyclin E shortens the length of the G1 phase, accelerating progression of the cell cycle into S phase. The activity of cyclin E is mediated through its activation of cyclin dependent kinase 2 (cdk2) protein and is modulated by the presence of cyclin dependent kinase inhibitors such as p16.

Western blot detection of human cyclin E (50 kD) using NCL-CYCLIN E. Lane A, molecular weight markers. Lane B, thymidine blocked MDA-MB-157 cell line immunoblotted with NCL-CYCLIN E.

Cyclin G

Clone 11C8
1 mL lyophilized NCL-CYCLIN G P (HIER) W

Cyclin G, a member of the cyclin family, is one of a number of proteins which is a transcriptional target of the tumor suppressor, p53. Cyclin G appears to be upregulated from early G1 to G1/S phase and is reported to be constitutively expressed throughout the cell cycle in T and B cell lines. In contrast, in stimulated peripheral T cells, cyclin G mRNA levels are highest in early G1 phase and decline during cell cycle progression. Cyclin G expression levels parallel p53 protein expression in murine B lymphocytes, however, in several human Burkitt lymphomas and tissues of p53 null mice, cyclin G expression levels can be both inverse to that of p53 levels or expressed independently of p53 protein. In damaged neurons, an increase in cyclin G mRNA expression has been shown in the early stages of nerve regeneration and in situ hybridization has demonstrated cyclin G expression in a restricted group of mature neurons, particularly in the telencephalon and the thalamus. This constitutive expression in some cell types suggests that cyclin G may have a function different from the other members of the cyclin group and that cyclin G expression is not predominantly regulated by p53 protein.
Cyclooxygenase-2

Clone 4H12
1 mL, 0.1 mL lyophilized NCL-COX-2 P (HIER)

Cyclooxygenase-2 is a mitogen-inducible form of cyclooxygenase (prostaglandin-endoperoxide synthase) which is expressed in response to various inflammatory stimuli, including UV radiation and by T cell receptor triggering in peripheral blood. It is an inducer of angiogenesis and plays a role in normal keratinocyte differentiation. Immunohistochemical staining for cyclooxygenase-2 increases in the more differentiated, suprabasal keratinocytes of normal skin. Squamous cell carcinomas derived from differentiated epidermis express cyclooxygenase-2 whereas basal cell carcinomas are negative. In Crohn’s disease and ulcerative colitis, cyclooxygenase-2 is strongly expressed in the upper crypts, surface epithelial cells and in the mononuclear cells of the lamina propria. It is expressed in both epithelial and interstitial cells of adenomatous polyps and colon adenocarcinomas. It is also expressed in a high proportion of oesophageal squamous cell carcinomas and adenocarcinomas as well as in most cases of prostatic adenocarcinoma. In Alzheimer’s disease, expression of cyclooxygenase-2 is reported to be upregulated in the frontal cortex regions.

Cytokeratin 1

Clone 34\(\beta\)B4
0.5 mL lyophilized NCL-CK1 F P (HIER)

Intermediate filaments, distinctive cytoskeletal components present in virtually all mammalian cells are distinguished from other cytoskeletal structures such as microtubules and microfilaments on the basis of filament diameter and protein composition. Keratins are a complex class of intermediate filaments with molecular weights ranging from 40 to 70 kD. At least 20 different human cytokeratin peptides have been individually characterized and catalogued. Cytokeratin 1 has a molecular weight of 68 kD and is present in complex epithelium.

Product Specific Information
NCL-CK1 reacts with squamous epithelium.

Cytokeratin 4

Clone 6B10
0.5 mL lyophilized NCL-CK4 F P (HIER) W

Cytokeratin 4 is a 59 kD cytokeratin intermediate filament protein. It is found in non-cornifying squamous epithelium such as that of the superficial and intermediate epithelial cells of the esophagus, ectocervix, tongue, vagina, larynx, pharynx, epiglottis, anus as well as the superficial cells of the cornea. Cytokeratin 4 is also reported to be expressed in the suprabasal cells of the urinary bladder transitional epithelium, in single cells and cell groups of sweat glands, prostatic ducts and in cylindrical, ciliated bronchial epithelial cells. Cytokeratin 4 is reported to be in squamous cell carcinomas derived from several non-cornified stratified epithelia.

Product Specific Information
NCL-CK4 is a chain-specific antibody. It is of particular use in the characterization of certain complex epithelia.

Cytokeratin 5

Clone XM26
1 mL, 0.1 mL lyophilized NCL-CK5 F P (HIER) W
1 mL liquid NCL-L-CK5 F P (HIER) W
7 mL ready-to-use RTU-CK5 F P (HIER)
7 mL Bond ready-to-use PA0468 P (HIER)

Cytokeratins are a large family of cytoskeletal proteins found in epithelial cells. They are coordinately synthesized in pairs so that at least one member of each family is expressed in each epithelial cell. Cytokeratins assemble into obligatory heteropolymers composed of type I (acidic) and type II (basic) polypeptides to form higher order tetramers and protofilaments. Basal cells of human epidermis express acidic keratin 14 and basic cytokeratin 5. Cytokeratin 5 is a 58 kD protein that is closely related to cytokeratin 6. They share similar tissue distribution and are found in various proportions in many non-keratinizing stratified squamous epithelia eg tongue mucosa, as well as in basal epithelia of trachea, basal cells of epidermis, hair follicles, sebaceous and sweat glands of skin, luminal cells of the mammary gland, basal cells of prostate, urethelium, vagina and endocervical mucosa. Cytokeratins 5 and 6 are also expressed in basal cell epitheliomas, squamous cell carcinomas of skin, tongue, epiglottis and of the rectal-anal region. Point mutations in the cytokeratin 5 gene at locus 12q11-q13 can cause various types of epidermolysis bullosa simplex. Cytokeratin 5 is also reported to be expressed in most epithelial and biphasic mesotheliomas. Clone XM26 is specific for the 58 kD intermediate filament protein known as cytokeratin 5. It is not cross-reactive with cytokeratin 6. Refer to page 25 for the Bond ready-to-use format.

Reference Range
Primary Antibodies

Cytokeratin 6

Clone LHK6B
1 mL lyophilized NCL-CK6 F

Cytokeratins are precisely regulated in tissue and little is known about the molecular mechanisms underlying this regulation. However, the expression pattern of cytokeratin 6 is known to be particularly complex. It is found in hair follicles, suprabasal cells of a variety of internal stratified epithelia, in epidermis, in both normal and hyperproliferative situations. Epidermal injury results in activation of keratinocytes which produce and respond to growth factors and cytokines and become migratory. Activated keratinocytes express a specific pair of cytokeratins, 6 and 16. Furthermore, cytokeratin 6 is reported to be expressed in approximately 76 percent of head and neck squamous cell carcinomas. The expression of cytokeratin 6 has been particularly associated with differentiation.

Product Specific Information
NCL-CK6 reacts with the human cytokeratin intermediate filament protein (56 kD) identified as cytokeratin 6.

Cytokeratin 7

Clone RN7
1 mL, 0.1 mL liquid NCL-L-CK7-560 P (HIER) Reference Range
7 mL Bond ready-to-use PA0942 P (HIER)

Clone OV-TL 12/30
1 mL lyophilized NCL-CK7-OVTL F P (HIER/Enzyme) W
1 mL liquid NCL-L-CK7-OVTL F P (HIER/Enzyme) W
7 mL ready-to-use RTU-CK7-OVTL F P (HIER/Enzyme)

Clone RN7 was developed to produce superior staining on paraffin sections.

Cytokeratins are intermediate filament proteins present in epithelial cells. They are expressed in a tissue-specific manner in normal organs and the tumors that arise from them. Cytokeratin 7 belongs to the neutral basic type B subfamily of cytokeratins. Its distribution is confined to glandular and transitional epithelia. Cytokeratin 7 is reported to be expressed in abundance in cultured bronchial and mesothelial cells but only at lower levels in cultured epidermal cells. The predicted amino acid sequence of this keratin has revealed a striking difference between this keratin and the type II keratins expressed in epidermal cells. Cytokeratin 7 has been reported in adenocarcinomas of the lung, breast, endometrium, ovary, thyroid as well as in carcinomas of the bladder and chromophobe renal cell carcinoma. Cytokeratin 7 and Cytokeratin 20 expression have been reported to show characteristic patterns on primary and metastatic lung and colorectal adenocarcinomas.

Product Specific Information
Where clone OV-TL 12/30 can produce unwanted staining of endothelial cells, clone RN7 does not stain these cell types. The choice of epitope retrieval, heat or enzyme, to provide the best result with clone OV-TL 12/30 should be determined by the user. Clones RN7, OV-TL 12/30 and LP5K react with the human cytokeratin intermediate filament protein (54 kD) identified as cytokeratin 7.

Refer to page 25 for the Bond ready-to-use format.

Cytokeratin 8

Clone TS1
1 mL, 0.1 mL lyophilized NCL-CK8-TS1 F P (HIER)
1 mL liquid NCL-L-CK8-TS1 F P (HIER)
7 mL ready-to-use RTU-CK8-TS1 F P (HIER)
7 mL Bond ready-to-use PA0567 P (HIER)

Cytokeratin 8, also known as tissue polypeptide antigen (TPA), together with cytokeratin 18, is one of the first cytokeratins expressed in the embryo and persists in adult tissues. Both cytokeratins, 8 and 18, are major components of all simple epithelia but not of stratified squamous epithelia. Cytokeratin 8, reported to be expressed in the adenocarcinomas of individuals, is also found to be present in their sera.

Product Specific Information
Clone TS1 reacts with human cytokeratin intermediate filament protein (52.5 kD) identified as cytokeratin 8.

Refer to page 26 for the Bond ready-to-use format.

Reference Range


For detailed information on all products please visit our website: www.leica-microsystems.com

Products in this catalog are subject to regulatory approval. This catalog is not for use in the USA.
Cytokeratin 10

Clone LHP1
1 mL lyophilized NCL-CK10  F P (Enzyme)

Cytokeratin 10 is found in suprabasal layers of keratinizing stratified epithelia. It is also found in a variable number of cells in suprabasal layers of non-keratinizing stratified epithelia and is reported to be expressed in more differentiated areas of some squamous carcinomas. Cytokeratin 10 is found in various normal epithelia, including the anal canal, foot sole epidermis and epidermises of other locations. Cytokeratin 10 is reported to be expressed in ductal carcinoma of breast and squamous cell carcinoma of the ano-rectal region.

Product Specific Information
NCL-CK10 reacts with the human cytokeratin intermediate filament protein (56.5 kD) identified as cytokeratin 10.

Cytokeratin 13

Clone KS-1A3
0.5 mL lyophilized NCL-CK13  F P (HIER) W

Cytokeratin 13 is expressed as a major component of squamous, non-keratinised epithelium, transitional epithelium, pseudostratified epithelium and myoepithelium. It is reported to be expressed in carcinomas of the trachea, apocrine and eccrine sweat glands, salivary glands, reserve cells of endocervical glands, bladder, ectocervix, tongue, esophagus, anal canal and the basal layer of keratinised epidermis.

Product Specific Information
NCL-CK13 reacts with the acidic intermediate filament protein (54 kD) identified as cytokeratin 13.

Cytokeratin 14

Clone LL002
1 mL, 0.1 mL lyophilized NCL-LL002  F P (HIER)  Reference Range
1 mL liquid NCL-L-LL002  F P (HIER)

Cytokeratins 14 and 5 are useful to distinguish stratified epithelial cell types from simple epithelial cell types. Cytokeratin 14 has been reported to be expressed in neoplasms of squamous cell origin.

Product Specific Information
Clone LL002 reacts with the human cytokeratin intermediate filament protein (50 kD) identified as cytokeratin 14.

Cytokeratin 15

Clone LHK15
1 mL, 0.1 mL lyophilized NCL-CK15  F P (HIER)

Cytokeratin 15 is a 52 kD intermediate filament protein expressed only in basal keratinocytes of stratified squamous epithelium, fetal epidermis and fetal nail. It is a type I keratin and does not appear to have a natural type II expression partner. All trichoepitheliomas, derived from hair follicle stem cells, and approximately twenty five percent basal cell carcinomas are reported to express cytokeratin 15. Squamous cell carcinomas are reported not to express cytokeratin 15.

Product Specific Information
NCL-CK15 reacts with the human cytokeratin intermediate filament protein (54 kD) identified as cytokeratin 15.

Reference Range

New!
Cytokeratin 18

Clone DC-10
1 mL, 0.1 mL lyophilized NCL-CK18  F P (HIER)
Cytokeratin 18 is normally co-expressed with cytokeratin 8 and is found in most simple ductal and glandular epithelia.

Product Specific Information
NCL-CK18 reacts with the acidic cytokeratin intermediate filament protein (45 kD) identified as cytokeratin 18. Cytokeratin 18 is reported not to be expressed in stratified squamous epithelium on most squamous cell carcinomas.

Cytokeratin 19

Clone b170
1 mL, 0.1 mL lyophilized NCL-CK19  F P (Enzyme)
7 mL Bond ready-to-use PA0799 P (Enzyme)
The smallest human cytokeratin filament protein (40 kD) has been identified as cytokeratin 19 and has been reported to be expressed in a large number of epithelial cell types, including many ductal and glandular epithelia.

Product Specific Information
NCL-CK19 produces a complex heterogenous staining pattern in non-keratinizing squamous epithelia and hair follicles, with strong staining of the basal layer observed.
Refer to page 26 for the Bond ready-to-use format.

Cytokeratin 20

Clone PW31
1 mL, 0.1 mL liquid NCL-L-CK20-561 P (HIER)
7 mL Bond ready-to-use PA0918 P (HIER)
Clone CK205
1 mL lyophilized NCL-CK20-543 P (HIER)
Clone K 20.8
1 mL lyophilized NCL-L-CK20 P (HIER/Enzyme) W
1 mL liquid NCL-L-CK20 P (HIER/Enzyme) W
7 mL ready-to-use RTU-CK20 P (HIER/Enzyme)

Clone PW31 was developed to produce superior staining on paraffin sections.
Cytokeratin 20 has been demonstrated to be almost entirely confined to the gastric and intestinal epithelium, urothelium and Merkel cells of the skin. Cytokeratin 20 is less acidic than other type I cytokeratins and is of interest due to its restricted tissue expression. In normal tissue, cytokeratin 20 is expressed in intestinal epithelium, gastric foveolar epithelium, a number of endocrine cells in the upper portions of the pyloric glands, urothelium and Merkel cells in epidermis. In tumors it is reported, there is a marked difference in the expression of cytokeratin 20 within different carcinomas. Neoplasms expressing cytokeratin 20 are derived from normal epithelia which themselves expressed cytokeratin 20. Colorectal carcinomas consistently express cytokeratin 20, while gastric adenocarcinomas express cytokeratin 20 to a lesser degree. Adenocarcinomas of the gall bladder and bile duct, ductal cell adenocarcinomas of the pancreas, mucinous ovarian tumors, Merkel cell tumors and transitional cell carcinomas have also been reported to express cytokeratin 20.

Refer to page 26 for the Bond ready-to-use format.
Cytokeratin (5/18)

Clone C-50
1 mL lyophilized NCL-C50 F P (HIER)
Cytokeratin 18 is reported to be expressed by simple epithelial cells and a wide range of epithelial-derived tumors. Cytokeratin 5 is reported to be expressed by basal cells and suprabasal cells of stratified epithelium.

Product Specific Information
NCL-C50 reacts with human cytokeratin intermediate filament proteins of 58 kD and 45 kD, identified as cytokeratins 5 and 18 respectively. However, the recognition of cytokeratin 5 on paraffin sections using NCL-C50 may be variable.

Cytokeratin (5/6/18)

Clone LP34
1 mL lyophilized NCL-LP34 F P (Enzyme) C
1 mL liquid NCL-LP34 F P (Enzyme) C
7 mL ready-to-use RTU-LP34 F P (Enzyme)
Cytokeratins 5, 6 and 18 are reported to be expressed in a broad range of human epithelial tissues, from simple glandular epithelia to stratified squamous epithelia. These include epithelial cells that are ectodermal, mesodermal, or endodermal in origin. These cytokeratins have been reported to be expressed in tumor cells of epithelial origin and less commonly of mesothelial origin. Non-epithelial tumors such as lymphomas do not express these cytokeratins.

Product Specific Information
Clone LP34 reacts with human cytokeratin intermediate filament proteins 5, 6 and 18 on frozen tissue. The recognition of cytokeratin 18 on paraffin sections using clone LP34 may be variable.

Cytokeratin, Multi

Clone AE1, Clone AE3 cocktail
1 mL, 0.1 mL lyophilized NCL-AE1/AE3 F P (HIER)
1 mL liquid NCL-AE1/AE3 F P (HIER)
7 mL ready-to-use RTU-AE1/AE3 F P (HIER)
7 mL Bond ready-to-use PA0909 P (Enzyme)
See also Multi-Cytokeratin on page 136.

Cytokeratin, Multi (1/5/10/14)

Clone 34βE12
1 mL, 0.1 mL lyophilized NCL-CK34BE12 F P (HIER) W
7 mL ready-to-use RTU-CK34BE12 F P (HIER)
7 mL Bond ready-to-use PA0134 P (Enzyme)
See also Multi-Cytokeratin 1/5/10/14 on page 137.

Cytokeratin, Multi (4/5/6/8/10/13/18)

Clone C-11
1 mL lyophilized NCL-C11 F P (HIER)
See also Multi-Cytokeratin (4/5/6/8/10/13/18) on page 137. (4/5/6/8/10/13/18).
Cytokeratin, Multi (5/6/8/18)

Clone 5D3, Clone LP34 cocktail
1 mL, 0.1 mL lyophilized NCL-CK5/6/8/18  F P (Enzyme)
1 mL liquid NCL-L-CK5/6/8/18  F P (Enzyme)
7 mL ready-to-use RTU-CK5/6/8/18  F P (Enzyme)
See also Multi-Cytokeratin (5/6/8/18) on page 137.

Cytomegalovirus Antibodies

Clone 2, Clone 6 cocktail
1 mL, 0.1 mL lyophilized Cytomegalovirus (pp65 antigen) NCL-CMVpp65  P (HIER) W I

Clone QB1/42
1 mL lyophilized Cytomegalovirus (early antigen) NCL-CMV-EA  F P (HIER)

Clone QB1/06
1 mL lyophilized Cytomegalovirus (late antigen) NCL-CMV-LA  F P (HIER)

Cytomegalovirus (CMV) is an opportunistic pathogen infecting lung, kidney, gut and other organs in situations where an individual is immunologically immature, such as the fetus and neonate. Infection also occurs in immunosuppressed individuals eg transplant recipients, individuals undergoing chemotherapy and those with HIV infection. The typical course of an active CMV infection in the immunosuppressed individual is reported to be characterized by a period of pp65 antigenaemia which correlates with viral replication. This may be observed over some weeks and begins before the onset of clinical symptoms. Following the isolation of CMV strains in cell culture, early viral proteins are expressed in the cell nucleus, within 3 to 24 hours of infection. After 48 to 72 hours, a number of late viral proteins may be demonstrated in the nucleus and cytoplasm of infected cells.

Product Specific Information

NCL-CMVpp65 is a pool of 2 unique monoclonal antibodies suitable for the detection of the pp65 antigen in cyospin preparations.

Daxx

Clone 36H11
1 mL lyophilized NCL-DAXX P (HIER)
Daxx binds the death domain of Fas and links this receptor to an apoptosis pathway involving the activation of Jun N-terminal kinase (JNK). The human homolog of Daxx enhances Fas-mediated apoptosis probably by modulating the transcription of genes involved in Fas-induced caspase activation and apoptosis. The Fas-binding domain of Daxx is a dominant negative inhibitor of both Fas-induced apoptosis and JNK inactivation, while the FADD death domain partially inhibits death but not JNK activation. The Daxx apoptotic pathway is sensitive to both bcl-2 and dominant negative JNK pathway components and acts cooperatively with the FADD pathway. Therefore, Daxx and FADD define two distinct pathways downstream of Fas. Daxx mRNA is widely expressed in human tissues such as heart, brain, lung, liver, skeletal muscle, kidney, pancreas and placenta. The human Daxx gene has been mapped to 6p21.3 in the major histocompatibility complex (MHC) region. Its location may help in understanding the genetic basis of autoimmune diseases. In cells, the protein is found in the nucleus and to a lesser extent in the cytoplasm.

DEC-205 (CD205)

Clone 11A10
1 mL liquid NCL-L-DEC205  P (HIER) P (HIER)
See also CD205 (DEC-205) on page 88.
Deleted in Colorectal Cancer Protein

**Clone DM51**
1 mL lyophilized NCL-DCC P (HIER)

The deleted in colorectal cancer (DCC) gene located on chromosome 18 is a tumor suppressor gene that encodes a transmembrane protein structurally similar to NCAM. The highest reported expression of this protein can be found in axons of the central and peripheral nervous systems where it functions as a netrin receptor required for the guidance of the developing axons. The DCC gene is reported to be expressed in most epithelial tissues where the protein may participate in the regulation of cell to cell or cell to substratum interaction. In normal colon, DCC expression is restricted to the mucosa with intense granular cytoplasmic staining in the crypts, particularly in the goblet cells. Altered DCC expression may be the result of allelic loss which is reported to occur in more than 70 percent of colorectal carcinomas, localized mutations, aberrant splicing of transcripts or allele-specific loss of transcripts. The DCC gene has also been reported to be inactivated in pancreatic, gastric, breast, prostatic and brain cancers and also in some leukemias. The expression of DCC protein is reduced in these cancers by 36 to 50 percent. In astrocytic tumors and colorectal carcinomas reduced expression of DCC protein is reported.


Deleted in Pancreatic Cancer Locus 4 Protein

**Clone JM56**
1 mL lyophilized NCL-DPC4 P (HIER)

Deleted in pancreatic cancer locus 4 (DPC4) is a tumor suppressor gene reported to be frequently mutated or deleted in pancreatic and metastatic colon cancers. DPC4, also known as Smad4, acts as a cofactor that binds transforming growth factor-beta receptor-activated Smad2 and Smad3 generating transcriptional complexes which translocate to the nucleus to participate in sequence-specific DNA-binding and transcriptional activation. Mutation or deletion of the DPC4 gene is reported in 50 percent of pancreatic ductal adenocarcinomas and a subset of acute myelogenous leukemias, biliary tract carcinomas, ovarian, colon and breast cancers. The expression of DPC4 protein has been reported to be a sensitive and specific marker for DPC4 gene alterations in pancreatic carcinomas. Loss of DPC4 expression occurs late in the neoplastic progression which leads to the development of infiltrating pancreatic cancer when it is histologically recognizable as a carcinoma. The continued expression of DPC4 protein is reported in pancreatic intraductal papillary mucinous neoplasms (IPMN) and suggests genetic differences in tumorigenesis from ductal carcinomas.

Normal human small intestine: immunohistochemical staining for desmin using NCL-DCC. Note granular cytoplasmic staining of muscle cells in the muscularis externa. Paraffin section.

Desmin

**Clone DE-R-11**
1 mL, 0.1 mL lyophilized NCL-DES-DERII F P (Enzyme) W
1 mL liquid NCL-L-DES-DERII F P (Enzyme) W
7 mL ready-to-use RTU-DES-DERII F P (Enzyme)
7 mL Bond ready-to-use PA0032 P (HIER)

**Product Specific Information**

NCL-DES-DERII reacts with an 18 kD rod piece of the intermediate filament protein desmin (53 kD) in muscle cells. The antibody does not appear to recognize other intermediate filament proteins. In normal tissues, Clone DE-R-11 reacts with both striated (skeletal and cardiac) and smooth muscle cells. The labeling is confined to the Z bands in skeletal and cardiac muscle giving a characteristic striated appearance.

Refer to page 27 for the Bond ready-to-use format.

Normal human small intestine: immunohistochemical staining for desmin using NCL-DES-DERII. Note cytoplasmic staining of muscle cells in the muscularis externa. Paraffin section.

**DOG-1**

**Clone K9**
1 mL, 0.1 mL liquid NCL-L-DOG-1 P (HIER)
7 mL Bond ready-to-use PA0219 P (HIER)

**Reference Range**

DOG-1, a 986 amino acid protein of unknown function, is expressed predominantly on the plasma membrane of gastrointestinal stromal tumors (GISTs) and is rarely expressed in other soft tissue tumors, which, due to appearance, can be confused with GISTs. Reactivity for DOG-1 has been reported to be found in 97.8 percent of scorable GISTs, including all KIT negative GISTs. Reactivity for DOG-1 has been suggested to aid in the identification of GISTs, including Platelet-Derived Growth Factor Receptor Alpha mutants that fail to express KIT antigen.

**Product Specific Information**

The use of PBS-based diluents may result in increased background staining. Refer to page 27 for the Bond ready-to-use format.

Dysferlin

**Clone Ham1/7B6**
1 mL, 0.1 mL lyophilized NCL-Hamlet F P W

**Clone Ham3/17B2**
1 mL, 0.1 mL lyophilized NCL-Hamlet-2 F P (HIER) W

Dysferlin is the protein product of the 2p13 gene that is defective in individuals with Limb-Girdle Muscular Dystrophy type 2B (LGMD2B) and Miyoshi Myopathy (MM). Dysferlin is normally localized to the muscle plasma membrane. In individuals with LGMD2B and MM, immunoreactivity to dysferlin is reported to be severely reduced or lost, depending on the type of mutation. Individuals with other neuromuscular conditions demonstrate normal labeling patterns.

**Product Specific Information**
NCL-Hamlet may require heat induced epitope retrieval in some cases. Labeling with an antibody to beta-spectrin, to monitor membrane integrity, is an essential immunohistochemical control.

Dystrophin Antibodies

**Clone Dy4/6D3**
2.5 mL, 1 mL lyophilized Dystrophin (Rod Domain)
NCL-DYS1 F W E

**Clone Dy8/6C5**
2.5 mL, 1 mL lyophilized Dystrophin (C-terminus)
NCL-DYS2 F W E

**Clone Dy10/12B2**
2.5 mL, 1 mL lyophilized Dystrophin (N-terminus)
NCL-DYS3 F W E

**Clone 13H6**
1 mL lyophilized Dystrophin (C-terminus)
NCL-DYSA P (HIER)

**Clone 34C5**
1 mL lyophilized Dystrophin (N-terminus)
NCL-DYSB P (HIER)

Duchenne Muscular dystrophy (DMD) is the most severe of the muscular dystrophies resulting in progressive muscular wasting and death. Dystrophin is the 427 kD protein product of the DMD/BMD gene located on the X chromosome at position Xp2. Western blotting and immunohistochmistry are the two established methods for the detection of abnormalities of dystrophin expression in muscle samples.

**Product Specific Information**
NCL-DYS1, NCL-DYS2 and NCL-DYS3 map within amino acids 1181-1388, 3669-3685 and 321-494, respectively, on the dystrophin molecule. The immunolabeling patterns for NCL-DYS1, NCL-DYS2 and NCL-DYS3 are similar. NCL-DYSA is raised to a region of the dystrophin molecule, upstream from the C-terminal region and NCL-DYSB is raised to a region of the N-terminus of the dystrophin molecule. NCL-DYSA and NCL-DYSB will be of particular interest in the investigation of archived formalin-fixed, paraffin-embedded material. Labeling with an antibody to beta-spectrin, to monitor membrane integrity, is an essential immunohistochmical control.

E-Cadherin

**Clone 36B5**
1 mL, 0.1 mL lyophilized NCL-E-Cad P (HIER)
7 mL ready-to-use RTU-E-Cad P (HIER)
7 mL Bond ready-to-use PA0387 P (HIER)

E-cadherin is a Ca²⁺-dependent, transmembrane cell adhesion molecule. It plays an important role in the growth, development and the intercellular adhesion of epithelial cells. Most tumors have an abnormal architecture and any subsequent loss of adhesiveness is thought to be an important step in the development of local invasion. E-cadherin may have a role in neoplastic progression, particularly as a suppressor of invasion. In prostate cancers, for example, the expression of E-cadherin is reported to be reduced or absent in comparison with its expression in normal prostate which is uniformly strong. Reduced expression or absence of E-cadherin in addition to alpha, beta and gamma-catenin in primary breast carcinomas has also been reported and these four proteins are associated with the development of metastases. The main immunohistochmical utility of E-cadherin is to highlight differential expression of this protein in lobular and ductal carcinomas.

Refer to page 28 for the Bond ready-to-use format.

Human skeletal muscle: immunohistochemical staining for dystrophin using NCL-DYSA. Note membrane staining of normal muscle fibers (A) and reduced and variable staining of muscle fibers in an individual with Duchenne and Becker muscular dystrophy (B). Paraffin section.

Elastin

**Clone BA-4**

0.5 mL lyophilized NCL-ELASTIN **P (Enzyme)**

Elastin is a polymeric protein found in connective tissue which imparts the property of elasticity to vertebrate elastic tissue. It is synthesized and secreted as a soluble, single-chain protein (tropoelastin) which undergoes a number of post-ribosomal modifications prior to its organization into an elastic fiber in the extracellular space. Once secreted, tropoelastin molecules are joined covalently via chemical modification and cross-linking of specific lysyl residues to form the mature insoluble elastin. Ultrastructurally, it is predominantly an amorphous material which may change its morphology with ageing and different disease states. The abnormal accumulation of elastic tissue in blood vessels is found in atherosclerosis and hypertension. Genetic defects in the elastin molecule are reported to lead to inherited diseases such as Marfan's syndrome, pseudoaxanthoma elasticum and the Buschke-Ollendorf syndrome.

Human aorta: immunohistochemical staining for elastin using NCL-ELASTIN. Note extracellular staining within the arterial wall. Paraffin section.

Emerin

**Clone 4G5**

1 mL, 0.1 mL lyophilized NCL-EMERIN **F P (HIER)**

Emery-Dreifuss muscular dystrophy (EDMD) is a late onset X-linked recessive disorder characterized by slowly progressing contractures, wasting of skeletal muscle and cardiomyopathy usually presented as heart block. Contractures are seen in the elbows, Achilles tendons and postcervical muscles with humero-peroneal distribution early in the course of the disease. The STA gene, at Xq28 locus, encodes a serine-rich 34 kD protein, emerin, which is ubiquitous in tissues and is found in highest concentration in skeletal and cardiac muscle. Emerin is localized in the nuclear membrane of normal muscle cells and its deficiency plays a crucial part in the pathology of EDMD.

**Product Specific Information**

NCL-EMERIN is of use in the detection of the normal STA gene product.

Human skeletal muscle: immunohistochemical staining for emerin using NCL-EMERIN. Note perinuclear staining of all cell nuclei. Paraffin section.

Endoglin (CD105)

**Clone 4G11**

1 mL, 0.1 mL lyophilized NCL-CD105 **P (HIER)**

CD105, also known as Endoglin, is an endothelial homodimeric membrane glycoprotein containing the peptide sequence RGD which is a recognition motif for adhesion receptors of the integrin family. It has been proposed that endoglin is a TGF-beta receptor. CD105 antigen is reported to be expressed on endothelial cells of capillaries, arterioles and venules in a variety of tissues and at low levels on acute lymphoblastic and myelocytic leukemia cells. ENDOGLIN expression may be of interest in the study of monocyte differentiation into macrophages, studies of cellular adhesion of circulating blood cells and in the lysis of CD105 positive cells in the presence of complement.

Normal human ovary: immunohistochemical staining for endoglin using NCL-CD105. Note membrane staining of cells in both the theca interna and theca externa. Paraffin section.

Endothelial Cell Marker (CD34)

**Clone QBEnd/10**

1 mL, 0.1 mL lyophilized NCL-END **F P (HIER) W**

Refer to page 77 for further information about CD34.

Endothelin-1 Receptor (ETA)

**Clone RJT24**

1 mL, 0.1 mL liquid NCL-L-ETA **P (HIER)**

Endothelins (ET) are potent vasoconstrictive peptides originally isolated from vascular endothelial cells. Their biological effects are mediated through two different receptors, endothelin-1-selective endothelin receptor (ETA) and the non-selective receptor sub-type (ETB). Analysis of mRNA by Northern blotting reported high levels in aorta, lung, atrium, colon and placenta with moderate levels in the cerebral cortex, cerebellum, ventricle, kidney, adrenal glands and duodenum, whereas liver was negative. Studies using immunohistochemistry have reported the presence of ETA in medial smooth muscle of arteries, full-term placenta, normal and diseased gall bladder and ovarian luteinized granulosa cells. ETA has also been reported to have a role in gastric ulcer healing and in the development of neural-crest derived cells.
Enterovirus

**Clone 5-D8/1**

1 mL lyophilized enterovirus (unconjugated)
NCL-ENTERO W 1 0

Enteroviruses are a large family of viruses whose main site of infection is the alimentary tract. Dissemination via the bloodstream is the likely route of spread to the wide range of target organs susceptible to infection. Most enterovirus infections are subclinical in young children. However, they can cause a wide range of syndromes involving many of the body systems eg myocarditis, respiratory and neonatal diseases.

**Product Specific Information**

NCL-ENTERO recognizes an epitope on the VP1 peptide, which is highly conserved within the Enterovirus group, except for Hepatitis A virus. The antibody reacts with most echovirus strains (except some strains of echovirus 22 and 23), Poliovirus and Enterovirus strains. No reaction is observed with tissue culture grown strains of Respiratory syncytial virus, Parainfluenza virus types 1, 2, 3 and 4b, Herpesvirus types 1 and 2, Influenza virus types A and B, Mumps virus, Measles virus, Varicella-zoster virus, Cytomegalovirus and negative tissue culture cells routinely used in virus isolation.

Envoplakin

**Clone CENV-1**

1 mL lyophilized NCL-ENV0 F P (HIER)

Envoplakin is a membrane-associated precursor of the epidermal cornified envelope which is a layer of transglutaminase cross-linked protein deposited under the plasma membrane of keratinocytes in the outermost layers of the epidermis. The envoplakin protein (210 kD) is expressed in keratinizing and non-keratinizing stratified squamous epithelia but not in simple epithelia or non-epithelia. The human envoplakin gene (EVPL) has been localized to the region of the tylosis oesophageal cancer gene (TOCG) on 17q25 and is physically linked to D17S1603. This sequence-tagged site segregates with the autosomal dominant human disease focal non-epidermolytic palmoplantar keratosis which is associated with an increased risk of oesophageal cancer. This chromosomal localization of the envoplakin gene, the homology of the encoded protein to keratin-binding proteins and its expression in epidermal and oesophageal keratinocytes all raise the possibility that loss of envoplakin function could be responsible for this form of palmoplantar keratoderma.

Epidermal Growth Factor Receptor

**Clone EGFR.25**

1 mL, 0.1 mL lyophilized (Cytoplasmic Domain)
NCL-EGFR-384 F P (HIER)
1 mL liquid (Cytoplasmic Domain)
NCL-L-EGFR-384 F P (HIER)

**Clone EGFR.113**

1 mL, 0.1 mL lyophilized (Extracellular Domain)
NCL-EGFR F P (HIER)
1 mL liquid (Extracellular Domain) NCL-L-EGFR F P (HIER)

Epidermal growth factor receptor (EGFR) is a transmembrane protein receptor of 170 kD with tyrosine kinase activity. Increased levels of EGFR are reported to be linked with malignant transformation of squamous cells eg in squamous cell carcinoma of the lung, head, neck, skin, cervix and esophagus. EGFR may also play a role in the development and progression of hepatocellular carcinomas where recurrence rates are higher in EGFR-positive cases. This correlation has similarly been reported in colorectal cancers where EGFR, produced by tumor cells, plays an important role in the invasiveness and proliferation of colorectal cancers. The majority of published studies of EGFR expression in human breast cancer has similarly shown an association with EGFR expression where it is inversely related to estrogen receptor status.

**Product Specific Information**

Clone EGFR.25 is raised to the cytoplasmic domain of the EGFR molecule whereas clone EGFR.113 is raised to the extracellular domain.
Epithelial Membrane Antigen

**Clone GP1.4**
1 mL, 0.1 mL lyophilized NCL-EMA  F P
1 mL liquid NCL-L-EMA  F P
7 mL ready-to-use RTU-EMA  F P
7 mL Bond ready-to-use PA0035 P (HIER)

Epithelial membrane antigen (EMA), also known as episialin, is reported to be expressed in a variety of normal and neoplastic epithelia. It has been reported that markers to CD45 (LCA) when used in conjunction with markers to EMA are useful in labelling cells of lymphoid origin whereas the combination of anti-cytokeratin antibodies together with EMA is useful to characterize cells of epithelial origin. EMA is also notably described to be expressed in a subset of Hodgkin's lymphomas.

Refer to page 28 for the Bond ready-to-use format.

Epithelial-Related Antigen

**Clone MOC-31**
1 mL lyophilized NCL-MOC-31  F P (HIER)

NCL-MOC-31 reacts with an epithelial antigen of 40 kD present on most normal and malignant epithelia. MOC-31 is reported to be assigned to a group of antibodies known as SCLC-Cluster 2 which react with an epithelial antigen determined at the Second International Workshop on Small Cell Lung Cancer (SCLC) Antigens. A characteristic of this antibody has been reported (Edwards C and Oates J, Journal of Clinical Pathology. 48: 626-630 (1995)). Further testing has shown that either a pressure cooker (121°C) method or a heated water bath method (90°C for 60 minutes) utilizing 0.01M citrate buffer (pH6.0) provides the strongest staining patterns on formalin-fixed, paraffin-embedded tissue. It is recommended that for best results customers try both methods as described on the data sheet.

Epithelial Specific Antigen

**Clone VU-1D9**
1 mL, 0.1 mL lyophilized NCL-ESA  F P (Enzyme) W
7 mL ready-to-use RTU-ESA  F P (Enzyme)

Epithelial specific antigen (ESA) is a 40 kD cell surface glycoprotein. It is reported to be expressed in the majority of human epithelial cells and is rarely expressed in mesothelial cells.

Epstein-Barr virus (early antigens)

**Clone G3-E31**
1 mL lyophilized Epstein-Barr virus (early antigen diffuse) NCL-EADE31 P (HIER) W O

Epstein-Barr virus (EBV) early antigens are a group of non-structural proteins, the synthesis of which do not require viral DNA replication. At least two forms of early antigen have been identified on the basis of their distribution in the cell, namely diffuse and restricted. The early antigen diffuse is expressed during the early lytic phase of virus replication, most notably in keratinocytes of hairy cell leukoplasia.

**Product Specific Information**

NCL-EADE31 recognizes EBV early antigen diffuse (50 to 52 kD), encoded by the BMRF-1 open reading frame. NCL-EARF2 recognizes EBV early antigen restricted (85 kD). NCL-EADE31 and NCL-EARF2 react with formalin-fixed, paraffin-embedded cells eg EBV-transformed B95-8 and RAJI cells using heat induced epitope retrieval (HIER) with citrate buffer (pH6.0).

Epstein-Barr virus transformed B95-8 cells: immunocytochemical staining for early antigen diffuse non-structural protein using NCL-EADE31. Note intense staining of infected cells only where early virus replication is underway. Paraffin-embedded cells.

Reference Range


Human appendix: immunohistochemical staining for epithelial specific antigen using NCL-ESA. Note membrane staining of epithelial cells only. Paraffin section.


Epstein-Barr virus transformed B95-8 cells: immunocytochemical staining for early antigen diffuse non-structural protein using NCL-EADE31. Note intense staining of infected cells only where early virus replication is underway. Paraffin-embedded cells.
Epstein-Barr virus-Induced Gene 3 Protein

Clone EL8
1 mL lyophilized NCL-EBI-3 F P (HIER)

Epstein-Barr virus (EBV)-associated Hodgkin’s lymphoma (HL) and nasopharyngeal carcinoma (NPC) usually occurs in individuals without clinically apparent deficiencies in anti-viral immunity. Despite expressing viral proteins, both tumors are apparently able to escape EBV-specific immunity in vivo. EBI-3 is an EBV-induced cytokine homologous to the interleukin 12 p40 subunit which can heterodimerize with the interleukin 12 p35 subunit. Researchers have suggested that EBI-3 protein may function to antagonize interleukin 12 and to inhibit the development of a Th1 immune response. It has been reported that EBI-3 protein is strongly expressed in Hodgkin’s Reed Sternberg (RS) cells in approximately 96 percent of HL cases, independently of the EBV status of the tumor cells. EBI-3 protein has also been reported to be detected in a small percentage of epithelial tumor cells of NPC biopsies but not in Burkitt’s lymphomas. EBI-3 protein may be an additional component of the repertoire employed by Hodgkin’s RS cells to inhibit and effect anti-tumor or anti-viral immune response. EBI-3 protein expression has also been reported in spleen, tonsil, mature dendritic cells, colonic mucosa and at high levels in full term placenta.

Epstein-Barr virus (nuclear antigen 2)

Clone PE2
1 mL, 0.1 mL lyophilized NCL-EBV-PE2 F W

Epstein-Barr virus (EBV) nuclear antigen 2 (EBNA2) is an EBV-encoded nuclear protein of 82 kD. EBNA2 is essential for growth transformation of B lymphocytes and has been shown to modulate the activity of several viral and cellular promoters.

Estrogen Receptor

Clone 6F11
2 mL lyophilized NCL-ER-6F11/2 F P (HIER) W C
2 mL liquid NCL-L-ER-6F11/2 F P (HIER) W C
1 mL, 0.1 mL lyophilized NCL-ER-6F11 F P (HIER) W C
1 mL liquid NCL-L-ER-6F11 F P (HIER) W C
7 mL ready-to-use RTU-ER-6F11 F P (HIER) W
7 mL Bond ready-to-use PA0151 P (HIER)

Estrogen receptor (ER) content of breast cancer tissue is an important parameter in the prediction of prognosis and response to endocrine therapy. The introduction of highly specific monoclonal antibodies to ER has allowed the determination of receptor status of breast tumors to be carried out in routine histopathology laboratories.

Product Specific Information


Refer to page 28 for the Bond ready-to-use format.
THE RESULTS ARE CLEAR
Leica Microsystems’ Estrogen Receptor (clone 6F11) and Progesterone Receptor (clone 16) antibodies are available in IVD format as an aid in the management, prognosis and prediction of therapy outcome of breast cancer.
• IVD labeled for increased diagnostic confidence
• Validated for clinical use
• Multiple formats – Novocastra liquid concentrate, Novocastra ready-to-use and Bond™ ready-to-use

ER AND PR ANTIBODIES
Estrogen and Progesterone Receptor Antibodies (duo packs)

Clone 6F11 and Clone 1A6
2 × 1 mL lyophilized NCL-ER/PGR-312d/1 F P (HIER) W
2 × 0.5 mL lyophilized NCL-ER/PGR-312d F P (HIER) W
2 × 1 mL lyophilized NCL-ER/PGRd/1 F P (HIER) W
2 × 0.5 mL lyophilized NCL-ER/PGRd F P (HIER) W

Product Specific Information
For convenience, Leica Microsystems offer two antibodies in one pack. NCL-ER/PGR-312d/1 and NCL-ER/PGRd/1 are 2 × 1 mL unit alternatives to the 2 × 0.5 mL duo packs and are recommended as a more economic option for high volume users of these antibodies.

Estrogen Receptor (beta)

Clone EMR02
1 mL lyophilized NCL-ER-beta P (HIER) W

Estrogen Receptor alpha (ERα) and beta (ERβ) are the translated products of separate genes located on different chromosomes. Although both isoforms share a high degree of amino acid homology, the role of the conserved domains demonstrate specific functions. The A/B region, D domain and F domains are notably distinct in sequence. ERα is the highly characterized estrogen receptor cloned originally from a human breast cancer cell line with ERβ more recently identified in rodents and now in humans. ERβ is reported to be expressed as multiple isoforms. ERβ, unlike ERα, is widely expressed being found in normal adult tissues of ovary, fallopian tube, lung, kidney, brain, heart, prostate and testis.

Ets-1 Oncoprotein

Clone 1G11
1 mL, 0.1 mL lyophilized NCL-ETS-1 F P (HIER) W

The proto-oncogene c-Ets-1 is a transcription factor known to regulate expression of a number of genes involved in extracellular matrix remodelling. The processes of tumor invasion and metastasis are thought to depend on the increased proteolytic activity of the invading tumor cells that may involve matrix metalloproteinases, cathepsins B and D and plasminogen activator in the metastatic cascade. Ets-1 interacts with the urokinase-type plasminogen activator gene enhancer and with the promoters of stromelysin-1 (MMP3) and collagenase-1 (MMP1) gene which may implicate it in this process. Ets-1 is reported to be absent from normal gastric epithelium, but is expressed in approximately 60 percent of gastric carcinomas and oral squamous cell carcinomas. The Ets-1 proto-oncogene is also preferentially expressed in lymphoid cells, where it is essential for the maintenance of the normal pool of resting T and B cells. Ets-1 expression level and distribution are differentially controlled in resting, activated and apoptotic lymphocytes.

Excitatory Amino Acid Transporter 2

Clone 1H8
1 mL lyophilized Excitatory Amino Acid Transporter 2 NCL-EAAT2 F P (HIER)

Human excitatory amino acid transporters (EAATs) are members of a family of high affinity sodium-dependent transporter molecules that regulate neurotransmitter concentrations at the excitatory glutamatergic synapses of the mammalian central nervous system. It is reported that these proteins are thought to reduce extracellular glutamate concentration, thereby modulating synaptic signalling to replenish glutamate levels and prevent glutamate induced excitotoxicity. A decrease in glutamate transporter activity has been associated with amyotrophic lateral sclerosis and excitotoxicity may be causal or exacerbating in neurodegenerative diseases, including cerebral ischemia and epilepsy. EAAT1 is reported to be prominently expressed in the cerebellum, frontal cortex, hippocampus and basal ganglia, is a potent antagonist and also appears to specifically block amino acid transport mediated by EAAT2.
EZH2 (Enhancer of Zeste Homolog 2 (Drosophila))

**Clone 6A10**
1 mL, 0.1 mL liquid NCL-L-EZH2 **P (HIER)** **W**

Polycomb-group proteins (PcG) such as EZH2 (Enhancer of Zeste Homolog 2 (Drosophila)) form multimeric gene repressing complexes involved in axial patterning, hematopoiesis and cell cycle regulation. PcG proteins ensure correct embryonic development by expressing homeobox genes as well as contributing to the regulation of lymphopoiesis.

**Product Specific Information**
NCL-L-EZH2 stains optimally when used in TBS-based wash buffer and diluent systems.

Factor VIII-Related Antigen (von Willebrand Factor)

**Clone 36B11**
1 mL, 0.1 mL lyophilized NCL-vWF **F P (HIER)**
1 mL liquid NCL-L-vWF **F P (HIER)**
7 mL Bond ready-to-use PA0400 **F P (HIER)**

See also Human von Willebrand Factor (Factor VIII-related antigen) on page 123.

Factor XIIIa (Blood Coagulation Factor XIIIa)

**Clone E980.1**
1 mL, 0.1 mL lyophilized NCL-FXIIIa **P (HIER)**
7 mL Bond ready-to-use PA0449 **P (HIER)**

Factor XIIIa also known as fibrinoligase and fibrin-stabilizing factor, is the last enzyme generated in the blood coagulation cascade. It is a Ca2+-dependent transglutaminase or transamidating enzyme which forms intermolecular gamma-glutamyl-epsilon-lysine crosslinks between fibrin molecules resulting in the mechanical stabilization of the fibrin clot and its resistance to proteolysis. Factor XIIIa may also function to stabilize cell surface molecules and membranes. These Ca2+-dependent transglutaminases with thiol active centers are widespread in animal tissues and have been associated with cell proliferation, embryonic development and growth through the proliferation of mammary stroma and epithelial elements. Normal mammary stroma, like most collagenous connective tissue contains resident populations of CD34 positive dendritic interstitial cells and scattered factor XIIIa positive collagen-associated dendrophages.

Factor XIIIa has been examined to determine its expression in normal and inflamed skin. Factor XIIIa positive cells in human skin represent a specific population of bone marrow dermal dendritic cells, distinct from Langerhans cells which share some features common to mononuclear phagocytes. In benign skin conditions such as inflammatory dermatoses eg atopic eczema and psoriasis, an increased number of factor XIIIa positive cells in the upper dermis, closely associated with lymphocytes, has been described.

Refer to page 28 for the Bond ready-to-use format.

Fas-Associated Death Domain Protein

**Clone 64A6**
1 mL lyophilized NCL-FADD **F P (HIER)**

Fas-Associated Death Domain Protein (FADD), also known as Mort-1, is a cytoplasmic death domain-containing protein (23 kD) which interacts with the intracellular death domain of Fas and initiates apoptosis. The interaction of FADD and Fas through their C-terminal death domains unmasks the N-terminal effector domain of FADD allowing it to recruit caspase-8 to the Fas signalling complex and thereby activating a cysteine protease cascade. The end result of this pathway is a cell death mechanism characterized by nuclear and cytoplasmic condensation and DNA fragmentation. FADD exists in the cytoplasm of normal cells but does not induce cell death unless present in high concentration. It has been reported to be expressed in mammalian testis where it is implicated in the modulation of testicular homeostasis by controlling germ cell apoptosis. FADD is also reported to be downregulated in hepatocellular carcinomas, tumors known to be resistant to Fas-mediated apoptosis.

Human fetus: immunohistochemical staining for Fas-associated death domain protein using NCL-FADD. Note intense membrane and cytoplasmic staining of developing fetal skin, internal components and organs. Paraffin section.
Fas-Associated Phosphatase-1

**Clone AC21**
1 mL lyophilized NCL-FAP-1 P (HIER)

Fas-associated phosphatase-1 (FAP-1) is a protein tyrosine phosphatase that interacts with the cytosolic, negative regulatory domain of Fas and inhibits Fas-mediated apoptosis. FAP-1 expression is reported to be expressed in normal renal tubules, skeletal muscle, myocardium, pituitary gland, parathyroid gland, pancreatic islets, hepatocytes, testicular germ cells, prostatic glands, neurons, endometrial glands, trophoblasts, bronchial epithelial cells and some types of gastrointestinal epithelial cells. Expression is highest in these tissues but variable expression of FAP-1 is reported in breast, stomach, colon and lung carcinomas as well as in several types of sarcoma. The expression of FAP-1 in normal tissues is reported to partly overlap with Fas expression which may suggest that FAP-1 has an important role in the regulation of apoptosis.

Normal human thyroid: immunohistochemical staining for Fas-associated phosphatase-1 using NCL-FAP-1. Note intense cytoplasmic staining of thyroid epithelial cells. Paraffin section.

Fas (CD95)

**Clone GM30**
1 mL lyophilized NCL-FAS-310 P (HIER)

Fas is a 48 kD transmembrane glycoprotein. It is a member of the nerve growth factor receptor/tumor necrosis factor superfamily. This cell surface molecule mediates receptor-triggered apoptosis (programmed cell death). During embryonic and postembryonic development, many cells die by means of apoptosis. This plays a major role in determining morphological and functional maturity in a variety of systems, including the formation of the neural network and clonal deletion of autoreactive T cells. Apoptosis is accompanied by condensation of the cytoplasm, loss of plasma membrane microvilli and extensive degradation of chromosomal DNA into oligomers of about 180 base pairs. The Fas antigen is reported to be expressed on the surface of various cell types, including activated T and B lymphocytes and T lymphoblastoid cell lines.

Human small intestine: immunohistochemical staining for Fas antigen (CD95) using NCL-FAS-310. Note membrane staining of absorptive epithelial cells. Paraffin section.

Fascin

**Clone IM20**
1 mL, 0.1 mL lyophilized NCL-FASCIN P (HIER) W
7 mL Bond ready-to-use PA0420 P (HIER)

Human fascin is a 55 to 58 kD actin-bundling protein, whose actin binding ability is regulated by phosphorylation. In normal tissues the detection of fascin is reported to be predominantly restricted to dendritic cells and in the thymus has been observed only in medullary dendritic cells. In reactive nodes, interdigitating reticulum cells of T cell zones, cells in subcapsular areas, and cells of the reticular network express fascin. Variable expression is seen in follicular dendritic cells and endothelial cells. Lymphoid cells, myeloid cells and plasma cells do not express fascin. However, in cases of Hodgkin’s disease, including nodular sclerosis, mixed cellularity lymphocyte depletion and unclassified cases, most or all Reed Sternberg cells are reported to be positive for fascin. Fascin expression may be induced by Epstein-Barr virus (EBV) infection of B cells with the possibility that viral induction of fascin in lymphoid or other cell types must also be considered in EBV-positive cases.

Refer to page 29 for the Bond ready-to-use format.

Fas Ligand

**Clone 5D1**
1 mL lyophilized NCL-FAS-L P (HIER) W

Fas ligand, a cell surface molecule belonging to the tumor necrosis factor family, binds to its receptor Fas, thus inducing apoptosis. Various cells express Fas, whereas Fas ligand is reported to be expressed predominantly on activated T cells. Fas and Fas ligand are involved in the downregulation of immune reactions as well as T cell-mediated cytotoxicity. It is known that tumor necrosis factor (TNF) works as a cachectin and mediates septic shock, so like TNF, Fas ligand may work as an agent that causes tissue damage. The Fas/Fas ligand system has been implicated both in maintaining immune privilege and also as a key regulator in spermatogenesis.

Human prostate: immunohistochemical staining for Fas ligand using NCL-FAS-L. Note membrane and cytoplasmic staining of glandular epithelial cells. Paraffin section.
Feline Calicivirus (capsid protein)

**Clone 1G9**
0.5 mL lyophilized NCL-1G9  

The Caliciviridae are a family of positive-stranded RNA viruses of unique morphology characterized by a series of cup-like depressions on the surface of the virus. Feline Calicivirus (FCV) is a ubiquitous pathogen of cats producing a variety of clinical symptoms, including oral ulceration, upper respiratory tract infection and polyarthritis. FCV has a genome of 7.7kb which encodes several proteins.

**Product Specific Information**
NCL-1G9 detects one of these, a capsid protein of 62 kD.

**Western blot:** detection of feline Calicivirus (FCV) capsid protein (62 kD) using NCL-1G9. Lane A, molecular weight markers. Lane B, CRFK cells infected with FCV immunoblotted with NCL-1G9.

Fibronectin

**Clone 568**
1 mL, 0.1 mL lyophilized NCL-FIB F P

Fibronectins are glycoproteins composed of two 200 kD disulfide-linked subunits. They are found in basement membranes and in the extracellular connective tissue matrix. Fibronectins are bound to the surface of cells by members of a family of cellular adhesion molecules, the integrins. A number of fibronectin isotypes exists as a result of multiple splicing of mRNA, producing a glycoprotein of numerous domains and repeat sequences. These domains correlate with the binding of bacteria, cells, collagen, heparin and a variety of other macromolecules. Cellular fibronectin has been reported to be widely expressed in the stroma of many malignant tumors.

**Product Specific Information**
NCL-FIB is specific for the cell attachment domain of human fibronectin. Enzyme pretreatment may enhance staining in some cases.

Filaggrin

**Clone 15C10**
1 mL lyophilized NCL-FILAGGRIN P (HIER)

Filaggrins are an important class of the intermediate filament-associated proteins which interact with keratin intermediate filaments (IFs) of terminally differentiating mammalian epidermis. A precursor molecule of filaggrin, profilaggrin, accumulates in the epidermis as keratohyalin granules which, in mouse, is phosphorylated and incapable of interaction with IFs. At the time of terminal differentiation, the precursor is proteolytically processed by excision of the linker to individual filaggrin molecules which are then able to interact with keratin IFs. Filaggrins exhibit wide species variations and their aberrant expression has been reported in a number of human keratinizing disorders such as parakeratosis, psoriasis and molluscum contagiosum. Filaggrin also appears to be a target molecule for rheumatoid arthritis-specific auto-antibodies in humans.

Normal human skin: immunohistochemical staining for filaggrin using NCL-FILAGGRIN. Note intense cytoplasmic staining of terminally differentiated keratinocytes. Paraffin section.

Filamin

**Clone PM6/317**
1 mL lyophilized NCL-FIL F P (HIER) W

Filamin functions as a crosslinking protein forming a flexible link between two actin filaments in muscle. It is composed of two identical polypeptide chains each joined to the other at one end, with an actin binding site at the other.

**Product Specific Information**
NCL-FIL cross-reacts with rabbit, chicken, guinea pig and rat filamin.

Western blot: detection of filamin protein (250 kD) using NCL-FIL. Lane A, Rainbow™ molecular weight markers (Amersham Life Science). Lane B, MRC-5 cells immunoblotted with NCL-FIL.
Primary Antibodies

Folate Receptor Alpha

Clone BN3.2

1 mL, 0.1 mL liquid NCL-L-FRalpha P (HIER)

Folate is a basic component of cell metabolism and DNA synthesis and repair. It is involved in essential one-carbon transfer reactions and is a vitamin required by both normal and tumor cells. Folate entry into cells is facilitated via two different systems: the reduced folate carrier, which utilizes a bidirectional anion-exchange mechanism, and the folate receptor system. Folate receptor alpha is a membrane-bound member of the folate receptor family, facilitating folate transport via a mechanism termed potocytosis where the receptor is internalized and then recycled back to the cell membrane. Staining patterns are both membrane and cytoplasmic due to this mechanism. Members of the folate receptor family share highly conserved sequences in the open reading frames, but differ in amino acids in the 5’ untranslated regions and as a consequence can differ in function and tissue expression. Folate receptor alpha expression is reported to be highly restricted in normal tissues and only selectively overexpressed in a limited number of epithelial malignancies.

Galectin-1

Clone 25C1

1 mL, 0.1 mL lyophilized NCL-GAL1 P (HIER) W

Galectin-1 is a member of the beta-galactoside-binding family and is a pleiotropic dimeric protein of 14 kD participating in a variety of normal and pathological processes, including cancer progression. Galectin-1 can affect the proliferation of normal and malignant cells. Inhibition of cell growth is observed in a lactose-dependent manner as lower concentrations of the lectin stimulate cell proliferation. Galectin-1 may also be implicated in the induction of apoptosis of activated T cells through the binding of exogenous galectin-1 to CD45 molecules present on the surface of lymphocytes. Galectin-1, reported to be present either at the surface of cancer cells or accumulated around these cells could act as an immunological shield to protect against a T cell immune response and provide an advantage for survival. Galectin-1 is reported to be expressed by a variety of malignant tumors including thyroid carcinoma. In colon carcinomas, the progressive overexpression of galectin-1 has been reported to be demonstrated during the evolution from normal to malignant cell type. Galectin-1 has not been detected in the cells of normal prostate, prostatic intra-epithelial neoplasia or prostatic carcinoma cells. However, galectin-1 is reported to be detectable in the stroma and associated fibroblasts of these tissues and is significantly increased in the tumor-associated stroma compared with non-neoplastic gland-associated stroma in a proportion of these. Three laminin binding proteins, galectin-1 together with galectin-3 and laminin receptor have been shown to effect similar qualitative and quantitative cell surface changes in cancer cells allowing them to cross basement membranes during metastatic spread. These changes in expression are reported in breast, colon, ovarian and uterine cancers.

Folypolyglutamate Synthetase

Clone AS2

1 mL, 0.1 mL liquid NCL-L-FPGS P (HIER)

Folic acid is a water soluble vitamin, essential for normal cell growth and replication. Eukaryotes, however are unable to synthesize folates and therefore require an external source. Following uptake by the cell, folates are retained within the cell by polyglutamation, catalyzed by folypolyglutamate synthetase (FPGS). Folates act as carriers of one carbon units, which are vital for the biosynthesis of purines, thymidylate and hence DNA replication. Polyglutamation by FPGS increases binding of folate co-factors to enzymes of folate biosynthesis, prevents efflux of folate co-factors from the cell and allows the accumulation of folates required for glycine synthesis in the mitochondria. FPGS also plays an important role in the cellular retention of folate analogs/antifolates and is reported to play a role in the selective cytotoxicity of such compounds used for the treatment of human cancers.

Galectin-3

Clone 9C4

1 mL, 0.1 mL lyophilized NCL-GAL3 P (HIER) W

7 mL Bond ready-to-use PA0238 P (HIER) Novel

Galectin-3 is a member of the beta-galactosidase-binding lectin family. It is involved in several biological events including binding to the basement membrane glycoprotein laminin. Cell surface galectin-3 may be involved in homotypical cell adhesion and is downregulated in colon cancer as the disease progresses. This downregulation has also been examined in breast carcinoma with a similar correlation of expression reported. Downregulation of galectin-3 could be one of the many events that enable cancer cells to interact with laminin to facilitate invasion and metastasis and may indicate activation of the invasive phenotype in various tumor types. Galectin-3 has been reported to be detected in anaplastic large cell lymphomas, whereas galectin-3 is not detected in Reed Sternberg cells or variants of Hodgkin’s disease.

Refer to page 29 for the Bond ready-to-use format.
**Primary Antibodies**

**Gamma-Catenin**

**Clone 11B6**

1 mL lyophilized NCL-G-CAT  **F P (HIER) W**

Cell to cell adhesion is mediated by cadherins which form a complex with catenins. Gamma-catenin or plakoglobin, is a major cytoplasmic protein of 82 kDa that occurs in soluble and membrane-associated forms. The down-regulation of cadherins and catenins has been detected in many types of human carcinomas and has been reported to be associated with tumor progression. E-cadherin and the catenins are reported to be expressed in normal epithelium as well as urothelium. E-cadherin plays a primary role in the maintenance of epithelial integrity where its decrease or loss of expression is reported to be strictly associated with neoplastic progression in a variety of human carcinomas, including bladder carcinoma. The combined decrease in expression of gamma-catenin, beta-catenin and E-cadherin is found at the invasive front of both grade 2 and some grade 1 carcinomas, further supporting a link with the aggressive behavior of those cancer cells. In thyroid carcinomas, catenins are also reported to be downregulated at cell to cell junctions. Gamma-catenin expression is reported to be partially or totally lost in the majority of papillary, follicular and anaplastic thyroid carcinomas.

**GAP43**

**Clone 1G7**

1 mL lyophilized NCL-GAP43  **P**

Growth associated phosphoprotein 43 (GAP43) is a major protein of neuronal growth cones and certain presynaptic terminals. It is a candidate for involvement in both axon growth and synaptic plasticity. It has been reported that in several neuronal systems, GAP43 expression is higher in neurons that are extending axons, either during development or regeneration of injured axons found in intact adult neurons. GAP43 is the best characterized of the growth associated proteins and although its normal action in vivo is unclear, GAP43 can bind calmodulin, inhibit phosphatidylinositol phosphate kinase, be phosphorylated by protein kinase C, affect neurotransmitter release and enhance filopodia in non-neuronal cells.

**Gastrin**

**Polyclonal**

0.5 mL lyophilized NCL-GASp  **F P**

7 mL Bond ready-to-use PA0681  **P New**

Gastrin, a polypeptide hormone, occurs naturally in three forms: gastrin-14, gastrin-17 and gastrin-34. Both primary and secondary G cell hyperplasia are reported to be characterized by clustering of the immunoreactive cells which sometimes project buds from the mucous glands.

**Product Specific Information**

NCL-GASp reacts with non-sulfated (I) and sulfated (II) gastrin-17 as well as gastrin-34. The antibody cross-reacts with cholecystokinin octapeptide. NCL-GASp labels gastrin or gastrin-analogue producing cells.

Refer to page 22 for the Bond ready-to-use format.

**Geminin**

**Clone EM6**

1 mL liquid NCL-L-Geminin  **P (HIER)**

Geminin is a protein of 209 amino acids thought to be involved in the control of DNA replication via the interaction with Cdt1. Geminin is not found in the G1 phase of the cell cycle, but is first expressed in the G1 to S transition phase, with expression levels rising through the rest of the cell cycle and levels reaching a maximum during mitosis. It has been proposed that Geminin may be a tumor suppressor protein. Geminin is reported to be expressed in proliferating lymphocytes and epithelial cells eg germinal centers in tonsil as well as in colon, spermatocytes, seminiferous tubules of the testes, within the basal layers of the squamous epithelium of the skin and breast. Geminin is reported to be upregulated in cancers such as non-Hodgkin’s lymphoma, B cell lymphoma, breast carcinoma and colon carcinoma.

**Normal human stomach: immunohistochemical staining for gastrin using NCL-GASp. Note intense cytoplasmic staining of the gastric mucosa. Paraffin section.**

**Human chronic lymphocytic leukemia: immunohistochemical staining for Geminin using NCL-L-Geminin. Note intense nuclear staining of proliferating neoplastic cells. Paraffin section.**
Giardia intestinalis

**Clone 9D5.3.1**
1 mL, 0.1 mL lyophilized NCL-GI P (HIER)

Giardia intestinalis (formerly Giardia lamblia) is a flagellated protozoan, which infects humans via contaminated water supplies, causing illnesses ranging from acute severe bloody diarrhoea, through moderate enteritis, chronic diarrhoea with malabsorption, to asymptomatic excretion. The remarkable hardness of the cyst form and the low numbers required to infect make the epidemiology uncertain, although water-based infections are the most common.

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Glial Fibrillary Acidic Protein

**Clone GA5**
1 mL, 0.1 mL lyophilized NCL-GFAP-GA5 F P
7 mL Bond ready-to-use PA0026 P (HIER)

Glial fibrillary acidic protein (GFAP) is an intermediate filament protein of 52 kD reported to be expressed in glial cells eg astrocytes and ependymal cells. In the peripheral nervous system, GFAP has been reported to be expressed in Schwann cells, enteric glial cells and satellite cells of human sensory ganglia and in neoplastic tissues GFAP has been reported to be expressed in astrocytomas and ependymomas.

**Product Specific Information**
When using NCL-GFAP-GA5 the heat induced epitope retrieval (HIER) technique may improve staining in some cases.
Refer to page 30 for the Bond ready-to-use format.

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Glucagon

**Polyclonal**
0.5 mL lyophilized NCL-GLUCp F P

**Polyclonal**
7 mL Bond ready-to-use PA0594 P (HIER)

Glucagon expression has been reported in the endocrine cells of the pancreatic islets and also in the mucosa of small and large intestine. Pancreatic glucagon, a peptide of 29 amino acids, has biological activities including glycogenolysis, lipolysis, gluconeogenesis and ketogenesis. These effects are all antagonistic to insulin action and, therefore, lead to increased blood sugar levels. The majority of glucagonomas are reported to arise from the pancreas and produce pancreatic glucagon. These tumors are found chiefly in the main body or tail of the pancreas.
Refer to page 30 for the Bond ready-to-use format.

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Glucocorticoid Receptor

**Clone 4H2**
1 mL lyophilized NCL-GCR P (HIER) W

The glucocorticoid receptor of molecular weight 90 kD has three main functional regions; the N-terminal modulating region, the DNA binding region and the C-terminal steroid binding region. The glucocorticoid receptor is reported to be widely distributed and expressed in many cultured cell lines eg CEM-C7. Glucocorticoid receptor is reported to be expressed in neoplastic cells of chronic lymphocytic leukemia (CLL). Two isoforms of glucocorticoid receptor exist; alpha and beta, with the alpha form usually the most abundant. The control of gene expression by glucocorticoids has been widely studied as a model for transcriptional regulation. Glucocorticoid receptors are reported to induce or repress the expression of genes in response to glucocorticoids, mediating such processes as cell growth, differentiation and apoptosis. Glucocorticoid receptors may also form a complex with heat shock protein 90 and in certain instances render the non-ligand bound receptor transcriptionally inactive.

**Product Specific Information**
NCL-GCR is raised to the N-terminal modulating region.

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Products in this catalog are subject to regulatory approval.
This catalog is not for use in the USA.
Glutathione S-Transferase (GST) Antibodies

**Clone 38H11**
1 mL lyophilized Glutathione S-Transferase (alpha)
NCL-GSTal-436

**Clone 10H6**
1 mL lyophilized Glutathione S-Transferase (mu)
NCL-GSTMu-437

**Clone LW29**
1 mL, 0.1 mL lyophilized Glutathione S-Transferase (pi)
NCL-GSTpi-438

The glutathione S-transferases (GSTs) are a multigene family of isoenzymes which catalyze the conjugation of glutathione to electrophilic substrates. These enzymes are involved in the detoxification of both endogenous and exogenous electrophiles which can react with cellular components such as DNA. The modification of DNA by reactive compounds can initiate carcinogenesis and the GSTs are believed to play a role in neutralizing carcinogens. The cytosolic GST isoenzymes have been classified into four evolutionary classes; alpha, mu, pi and theta. These isoenzymes are reported to be singly or multi-expressed in a variety of normal tissues, including stomach, bowel, brain, heart, liver, pancreas, breast, kidney and skin at differing levels. In gastric cancers, the levels of GSTalpha and pi are reported to differ from normal gastric tissue with GSTalpha showing decreased levels and GSTpi increased levels. High levels of GSTpi are reported in some breast cancer cells and have been associated with chemotherapeutic agents. Likewise, in human lung squamous cell carcinomas, high levels of GSTpi are reported to be associated with resistance to the drug cisplatin. The expression of GSTmu has been reported to be high in acute myeloid leukemias. GSTmu is also known to play a role in detoxification of epoxides released from cigarette smoke.

Gonadotropin-Releasing Hormone Receptor

**Clone A9E4**
1 mL lyophilized NCL-GnRHR F P (HIER)

Gonadotropin-releasing decapeptide hormone is the key mediator in the integration of the neural and endocrine systems. It regulates the reproductive cycle in both sexes. Gonadotropin-releasing hormone (GnRH) stimulates the gonadotrophs of the anterior pituitary to secrete luteinizing hormone as well as follicle stimulating hormone via specific receptors. The presence of high-affinity binding sites for GnRH has been reported in luteal and granulosa cells as well as in ovarian cell membrane preparations. These receptors have similar binding characteristics to those of GnRH receptors in the anterior pituitary.

**Product Specific Information**
NCL-GnRHR is specific for the extracellular domain of the GnRH receptor.

GPIb (CD42b)

**Clone MM2/174**
1 mL lyophilized NCL-CD42b F P (HIER)

See also CD42b (GPIb) on page 79.

GPIIb/IIIa (CD41)

**Clone M148**
1 mL lyophilized NCL-CD41 F

See also CD41 (GPIIb/IIIa) on page 79.

GPIIIa (CD61)

**Clone 2f2**
1 mL, 0.1 mL lyophilized NCL-CD61-308 F P (HIER)
7 mL Bond ready-to-use PA0308

See also CD61 (GPIIIa) on page 82.

Granulysin

**Clone RJT48**
1 mL liquid NCL-L-Granulysin P (HIER)

Granulysin is a member of the Saposin-like protein (SAPLIP) family. It is a lytic protein made up of two fragments, 15 kD and 9 kD, reported to be expressed selectively by NK cells and activated T cells. Granulysin protein is highly homologous to a porcine antimicrobial and antitumor protein called NK lysine and to amebapores, polypeptides used by amoebae to kill bacterial prey. Granulysin disrupts artificial liposomes and cell membranes, damages mitochondria and activates caspase 9 to induce apoptosis in nucleated cells.


Gross Cystic Disease Fluid Protein-15

**Clone 23A3**
1 mL, 0.1 mL lyophilized NCL-GCDFP15 P (HIER)
1 mL liquid NCL-L-GCDFP15 P (HIER)
7 mL ready-to-use RTU-GCDFP15 P (HIER)
7 mL Bond ready-to-use PA0350 P (HIER)

Gross cystic disease of the breast is a benign premenopausal disorder in which cysts are a predominant pathological lesion. These cysts appear to be formed from excessive apocrine cystic secretions. This fluid is composed of several glycoproteins including a unique 15 kD monomer protein, GCDFP15. It has been reported that cytosolic analysis of normal tissue from all major organs has demonstrated GCDFP15 in apocrine epithelia, lacrimal, ceruminous and Moll’s glands and in numerous serous cells of the submandibular, tracheal, bronchial, sublingual and minor salivary glands. Cytosol from breast carcinoma lesions are reported to contain GCDFP15 at a wide range of concentrations. The concentration is reported to be highest in more differentiated carcinomas and GCDFP15 shows only a few positive individual epithelial cells within lobules and small ducts in normal breast. Expression has also been reported in fibroadenomas within areas of apocrine metaplasia. GCDFP15 and prostate specific antigen are reported to be co-expressed in androgen receptor-positive breast tumors.

Refer to page 30 for the Bond ready-to-use format.

Granzyme B

**Clone 11F1**
1 mL, 0.1 mL lyophilized NCL-GRAN-B P (HIER)
1 mL liquid NCL-L-GRAN-B P (HIER)
7 mL ready-to-use RTU-GRAN-B P (HIER)
7 mL Bond ready-to-use PA0291 P (HIER)

Granzymes are neutral serine proteases which are stored in specialized lytic granules of cytotoxic T lymphocytes (CTL) and in natural killer (NK) cells. These CTL and NK cells are heavily involved in the elimination of neoplastic and virally infected cells. Secretory granules containing perforin and granzymes are instrumental in undertaking cytolytic activity. Granzyme B is understood to enter a target cell through a perforin pore-formed channel to induce DNA fragmentation and apoptosis. Granzyme B has also been described in neoplastic CTL and NK cells.

Refer to page 30 for the Bond ready-to-use format.

H-CAM (CD44)

**Clone DF1485**
1 mL, 0.1 mL lyophilized NCL-CD44-2 F P (HIER)

See also CD44 (H-CAM) on page 79.
Prokaryotes and eukaryotes express a variety of heat shock proteins (Hsps) in response to stress, including sublethal heat shock, exposure to heavy metals, hormones and viral infection. Hsp27 (27 kDa) is the most common small Hsp found in man. In breast tissue, it is reported that expression of Hsp27 is taken as evidence of a functional estrogen receptor pathway.

**Protein Specific Information**

NCL-HSP27 is reactive with Hsp27 in man, mouse and rat.

**Heat Shock Protein 70**

**Clone 8B11**

1 mL lyophilized NCL-HSP70 P (HIER)

The response of cells or organisms to stress, such as exposure to heat or chemicals, is associated with the induction of heat shock proteins. Heat shock protein 70 (Hsp70) is reported to have a protective role in ischemic disease, inflammation, infection and a potential role in antigen processing as well as a possible regulatory role in cytokine biosynthesis. Hsp70 exists in the cell in equilibrium between its free state, in the cytoplasm, and its bound state, protecting proteins in the nucleolus, perhaps either by helping refold some of the unfolded ribosomal proteins or by solubilizing the denatured ribosomal proteins to facilitate their turnover. During recovery from heat shock and as the nucleoli begin to return to their normal activities, most of the Hsp70 returns to the cytoplasm.

**Product Specific Information**

NCL-HSP70 is reactive with Hsp70 and heat shock cognate 70 (Hsc70) in man, mouse and rat.

**Heat Shock Protein 90**

**Clone JPB24**

1 mL lyophilized NCL-HSP90 P (HIER) W

Heat shock proteins are highly conserved proteins in nearly all organisms and are induced by various kinds of stress, including non-physiological temperatures. Heat shock protein 90 (Hsp90) is associated with the folding of signal-transducing proteins such as steroid hormone receptors and protein kinases. Hsp90 forms several discrete subcomplexes, each containing distinct groups of co-chaperones that function in these folding pathways. Hsp90 has been reported to be expressed in epithelial cells, mononuclear cells, giant cells, nerve cells and endothelial cells of small vessels. Hsp90 expression has been reported to be correlated with sex steroid receptor status in endometrial carcinomas. In breast cancer, MHC class I expression is reported to correlate with nuclear localization of Hsp90.

**Heat Shock Protein 105**

**Clone 58F12**

1 mL lyophilized NCL-HSP105 P (HIER) W

Heat shock protein 105 (Hsp105) exists as two isoforms; alpha and beta which belong to the Hsp105/Hsp110 protein family. Hsp105 acts as both a chaperone to prevent thermal aggregation of proteins and as a regulator of mammalian cells. The Hsp105 isoforms are reported to be found in the cytoplasm but not in the nucleoli under non-stressed and stressed conditions. In rodents, Hsp105 isoforms are reported to be moderately expressed in the adrenal glands, spleen, liver and heart and both are markedly increased after heat shock. In the testis, Hsp105 is specifically localized in the cytoplasm of germ cells but may translocate to the nucleus after heat shock. The most abundant expression of Hsp105 occurs in the brain with nuclear and cytoplasmic expression in nearly all neurons, oligodendrocytes, microglia and astrocytes. Increased expression reported during embryogenesis suggests that Hsp105 may have an important role during mouse development.

**Product Specific Information**

NCL-HSP105 is reactive with Hsp105 and heat shock cognate 105 (Hsc105) in man, mouse and rat.
Primary Antibodies

Helicobacter pylori

Clone ULC3R P (Enzyme)
1 mL, 0.1 mL liquid NCL-L-Hpylori
Helicobacter pylori is a motile, helix-shaped Gram-negative, microaerophilic, bacterial pathogen which is capable of converting from a spiral form to a coccoid form to favor its survival. Almost 50 percent of the world’s population, approaching 100 percent in some countries, are infected. There are numerous strains of Helicobacter pylori which can be grouped into two broad families, type I and type II, based on their expression of the hopQ allele. Type I and type II strains are reported to express VacA (vacuolating toxin) responsible for vacuolation of gastric epithelial cells and induction of apoptosis. Type I strains are reported to express CagA protein which is associated with deregulation of intercellular signalling pathways and initiation of pathogenesis (virulent strains) and are closely related to gastric diseases such as peptic ulceration, gastric ulceration, chronic gastritis, mucosa-associated lymphoid tissue (MALT) lymphoma and intestine type gastric adenocarcinomas. Type II strains are reported not to express CagA proteins. HopE is a 31 kD porin protein which is part of a family of 32 outer membrane proteins present in Helicobacter pylori bacteria. HopE is highly conserved in Helicobacter pylori strains, but not among other strains of the Helicobacter genus.

Product Specific Information
Clone ULC3R, unlike polyclonal antibodies to Helicobacter pylori, does not cross-react with Campylobacter jejuni (a gastric bacterium which causes infectious diarrhoea). Clone ULC3R also exhibits more defined staining of H. pylori bacteria than NCL-HPp. The antibody clone ULC3R, will be useful to identify and differentiate patients that need antibiotic eradication of the bacterium from those patients who are at a higher risk of developing clinical disease related to H. pylori infection.

Hepatitis B virus Antibodies

Clone LF161
1 mL, 0.1 mL lyophilized Hepatitis B virus (core antigen) NCL-HBcAg-506 P

Clone 1044/341
1 mL lyophilized Hepatitis B virus (surface antigen) NCL-HBsAg-2 P (Enzyme)

Hepatitis B virus is one of an expanding list of hepatitis viruses. The complete infective virion is a 42nm particle (Dane particle). The infective virion consists of a core of double stranded DNA, a specific DNA polymerase and structural proteins surrounded by an outer envelope, Hepatitis B surface antigen (HBsAg). The nucleocapsid contains two serologically distinct antigens; core antigen and ‘e’ antigen. Core antigen is localized predominantly within the nucleus of infected hepatocytes, whereas ‘e’ antigen is found in the cytoplasm of infected hepatocytes. A significant proportion of carriers infected with the Hepatitis B virus may develop persistent infection, chronic hepatitis of various types, cirrhosis and possible primary hepatocellular carcinoma.

Product Specific Information
NCL-HBcAg-506 recognizes core antigen which is localized predominantly within the nucleus. NCL-HBsAg-2 reacts with surface antigen.

Hepatitis C virus (NS3)

Clone MMM33
1 mL, 0.1 mL lyophilized NCL-HCV-NS3 F P (HIER)

Hepatitis C virus (HCV) is the leading cause of blood-borne and community acquired non-A, non-B hepatitis. HCV infection has been estimated to affect about 3 percent of the population worldwide. Higher prevalence occurs in high-risk groups, which include individuals with a history of intravenous drug abuse and those multiply transfused before the introduction of mass screening of donated blood for viral antibodies. The virus persists in approximately 80 percent of those infected. Twenty percent of individuals with chronic infection progress to cirrhosis after an average of 20 years. Hepatocellular carcinoma is a significant risk in these, occurring in around 3 percent annually. Virus antigen has been reported in the cytoplasm of hepatocytes of infected individuals by immunohistochemistry although the sensitivity of detection of antigen has varied from study to study.

Product Specific Information
NCL-HCV-NS3 is a monoclonal antibody raised against a recombinant NS3 protein.
Hepatocyte Growth Factor Receptor (c-MET)

Clone 8F11
1 mL, 0.1 mL lyophilized NCL-cMET F P (HIER)

See also c-MET (Hepatocyte Growth Factor Receptor) on page 92.

Hepatocyte Specific Antigen

Clone OCH1E5
1 mL, 0.1 mL lyophilized NCL-HSA P

Hepatoblastoma is reported to be the most common primary tumor of the liver in children. The distinction of hepatoblastoma, especially the embryonal type, from other small round cell tumors of childhood can sometimes be difficult. It is reported that the detection of specific hepatocyte antigens, alpha fetoprotein or carcinoembryonic antigen are expressed in normal and malignant fetal hepatocytes.

Product Specific Information

NCL-HSA recognizes an uncharacterized antigen present in both adult and fetal normal hepatocytes to produce a distinct granular cytoplasmic staining.

Human liver, hepatitis B positive: immunohistochemical staining for hepatocyte specific antigen using NCL-HSA. Note granular cytoplasmic staining in a proportion of hepatocytes. Paraffin section.

HER-2 (c-erbB-2 Oncoprotein) Antibodies

Clone 5A2
1 mL lyophilized HER-2 (internal domain) NCL-c-erbB-2-316 F P

Clone CB11
1 mL, 0.1 mL lyophilized HER-2 (internal domain) NCL-CB11 F P C
1 mL liquid HER-2 (internal domain) NCL-L-CB11 F P C
7 mL ready-to-use HER-2 (internal domain) RTU-CB11 F P
60 Tests Oracle HER2 Bond IHC System TA9145

Clone 10A7
1 mL, 0.1 mL lyophilized HER-2 (external domain) NCL-CBE-356 P W
1 mL liquid HER-2 (external domain) NCL-L-CBE-356 P W
7 mL ready-to-use HER-2 (external domain) RTU-CBE-356 P

Clone CBE1
1 mL, 0.1 mL lyophilized HER-2 (external domain) NCL-CBE1 F P (HIER)

Polyclonal
0.2 mL lyophilized HER-2 (internal domain) NCL-PC11 F P

The c-erbB-2 oncoprotein is closely-related in structure to the epidermal growth factor receptor and is a member of a large family of cell surface growth factor receptors. c-erbB-2 oncoprotein is reported to be detectable in a proportion of breast and other adenocarcinomas as well as transitional cell carcinomas. c-erbB-2 oncoprotein is present in a wide variety of cell types in a range of normal human fetal and adult tissues, including breast, stomach and ovary.

Product Specific Information

NCL-c-erbB-2-316, NCL-CB11, NCL-L-CB11, NCL-PC11 and RTU-CB11 all detect the internal domain of the c-erbB-2 oncoprotein. NCL-CBE-356, NCL-L-CBE-356, NCL-CBE1 and RTU-CBE-356 detect the external domain of the c-erbB-2 oncoprotein. NCL-CB11 is effective with no pretreatment on fixed, paraffin-embedded tissue but the use of the heat induced epitope retrieval (HIER) technique may enhance staining in some cases. To obtain optimal staining on frozen tissue, Carnoy’s fixative is recommended.

For more information on the Oracle HER2 Bond IHC System see page 11.
Heregulin

**Clone P137**
1 mL lyophilized NCL-HEREG P (HIER)

Heregulins or neuregulins are a family of proteins known to interact with and activate the tyrosine kinase receptor c-erbB-2 in association with c-erbB-3 or c-erbB-4. Heregulin is reported to induce in vitro chemoinvasion and chemotaxis of breast cancer cells as well as growth in an anchorage dependent and independent manner.

**Product Specific Information**
NCL-HEREG is raised to the alpha form of the heregulin protein.

Herpes simplex virus Antibodies

**Clone 20.7.1**
1 mL lyophilized Herpes simplex virus (type 1) NCL-HSV-1 P (Enzyme) I

**12.3.4, Clone 1.1.1**
1 mL lyophilized Herpes simplex virus (type 2) NCL-HSV-2 I

Infection with Herpes simplex virus (HSV) is extremely common and pathogenesis can vary depending on a variety of factors. These include age, immune status of the individual, the antigenic type of infecting virus (HSV type 1 or 2) and the site of infection. Primary infections with HSV are generally asymptomatic but they tend to be more severe than recurrent productive disease.

**Product Specific Information**
NCL-HSV-1 is HSV type 1 specific and does not cross-react with tissue culture grown HSV type 2 strains. NCL-HSV-2 is HSV type 2 specific and does not cross-react with tissue culture grown strains of HSV type 1.

HGH (Human Growth Hormone)

**Polyclonal**
0.25 mL lyophilized NCL-HGH F P
7 mL Bond ready-to-use PA0704 P

See also Human Growth Hormone (HGH) on page 121.

HGM-45M1 (Human Gastric Mucin)

**Clone 45M1**
1 mL, 0.1 mL lyophilized NCL-HGM-45M1 F P (HIER)

See also Human Gastric Mucin (HGM-45M1) on page 121.

HLA Class II (DR) Antigen

**Clone LN-3**
1 mL, 0.1 mL lyophilized NCL-LN3 F P

HLA-DR is an MHC Class II antigen that maps to chromosome 6. It is a heterodimer composed of 2 non-covalently associated glycoproteins of about 35 kD (alpha, heavy) and 27 kD (beta, light). Both chains are comprised of two Ig-like domains and have transmembrane sequences and short cytoplasmic tails. It is reported to be expressed mainly on antigen-presenting cells (monocytes/macrophages and dendritic cells), B cells and some activated T cells. Expression has also been reported on thymic epithelial cells.

HMB45 (Melanoma Marker)

**Clone HMB45**
1 mL lyophilized NCL-HMB45 F P (Enzyme)

The HMB45 antigen has also been identified in retinal pigment epithelium (RPE) but is reported to be reactive only with the transient prenatal and infantile RPE. No reaction is reported to be observed with intradermal nevi and normal adult melanocytes and non-melanocytic cells. Tumor cells of epithelial, lymphoid, glial and mesenchymal origin are reported to be negative. This clone is well described in the literature. It is indicated to label an intracytoplasmatic antigen in the majority of melanosomas and other tumors demonstrating melanoma/melanocytic differentiation. The clone is also reported to react with junctional and blue nevus cells. (Bacchi CE et al., A Review. Applied Immunohistochemistry. 4:73-85 (1996)).
Human Chorionic Gonadotrophin (alpha)

**Clone 4E12**
1 mL lyophilized NCL-HCG-alpha  **F P (HIER)**

The human chorionic gonadotrophin alpha (hCGa) gene has now been identified as an estrogen receptor alpha (ERα) responsive gene in breast cancer cells. It encodes the common alpha subunit of the four secreted glycoprotein hormones, hCG, LH, FSH and TSH. The common alpha chain and the hormone-specific beta chains have molecular weights of 14 kD and 17 kD, respectively. hCGa is expressed as part of hCG in normal placenta and as part of LH, FSH and TSH in the pituitary gland. hCGa mRNA is reported to be detected in normal pregnant women and in the peripheral blood mononuclear cells of patients with trophoblastic disease. Additionally, hCG is reported to be detected in seminomatous and non-seminomatous testicular cancers as well as in its free alpha and beta subunits. Independent studies suggest that approximately half of ERα positive breast cancers express hCGa.


Human Chorionic Gonadotrophin (beta)

**Polyclonal**
1 mL lyophilized NCL-HCGp  **F P (Enzyme)**
7 mL Bond ready-to-use  **PA0014 P (HIER)**

Human chorionic gonadotrophin (hCG) is a glycoprotein hormone produced by trophoblastic cells of the placenta beginning 10 to 12 days after conception. Maintenance of the fetus in the first trimester of pregnancy requires the production of hCG, which binds to the corpus luteum of the ovary which is stimulated to produce progesterone which in turn maintains the secretory endometrium. hCG is composed of two subunits, alpha and beta. The alpha subunit of hCG is identical to the subunit of lutetising hormone, thyroid stimulating hormone and follicle stimulating hormone. The common alpha chain and the hormone-specific beta chains have molecular weights of 14 kD and 17 kD, respectively. The hCG beta-subunit is unique in the family of beta-containing glycoprotein hormones in that it contains an extension of 29 amino acids at its COOH end. It is believed that the C-terminal region of the HCG-beta subunit plays a role in the intracellular behavior of the heterodimer.

**Product Specific Information**

NCL-HCGp was raised to the isolated beta-chain of human chorionic gonadotrophin and reacts with placental trophoblasts. NCL-HCGp shows a slight cross-reaction with lutetising hormone and may, therefore, stain gonadotrophin and reacts with placental trophoblasts. NCL-HCGp shows a slight cross-reaction with lutetising hormone and may, therefore, stain

Human Gastric Mucin (HGM-45M1)

**Clone 45M1**
1 mL, 0.1 mL lyophilized NCL-HGM-45M1  **F P (HIER)**

Many of the cancer associated antigens have been identified as mucin antigens. The expression of these antigens are associated with the earliest steps in mucin glycosylation which in turn is associated with several diseases. Human Gastric mucin is found on the surface of gastric epithelium of the normal gastrointestinal tract. The "gastric mucins" include Muc-1, Muc-5AC and Muc-6 glycoproteins.

**Product Specific Information**

NCL-HGM-45M1 recognizes the mucin epitope located in the peptide core of gastric mucin, fulfilling a similar function to the antibody, NCL-MUC-1-CORE. Thiol reduction (using 2-mercaptoethanol) completely destroys this epitope, which is partially lost following trypsin proteolysis but is stable upon periodate oxidation.

Human Growth Hormone (HGH)

**Polyclonal**
0.25 mL lyophilized NCL-HGH  **F P**
7 mL Bond ready-to-use  **PA0704 P**

Growth hormone (GH), somatotropin, is the primary hormone responsible for regulating overall body growth and is also important in organic metabolism. It is synthesized by acidophilic or somatotropic cells of the anterior pituitary gland. Human GH has a molecular weight of 22 kD. GH stimulates growth indirectly by promoting the liver’s production of somatomedins, which act directly on bone and soft tissue to cause growth. GH exerts direct metabolic effects on the liver, adipose tissue and muscle. In general, growth hormone enhances protein synthesis, conserves carbohydrates and uses up fat stores.

Refer to page 31 for the Bond ready-to-use format.

Human Herpesvirus (type 8) (latent nuclear antigen)

**Clone 13B10**
1 mL, 0.1 mL lyophilized NCL-HHV8-LNA  **P (HIER) W**

Human herpesvirus type 8 (HHV8), is the proposed etiological agent of Kaposi’s sarcoma (KS). It is reported that HHV8 has been demonstrated in KS tissues by immunohistochemistry, in situ PCR and also in situ hybridization. HHV8 encodes a latent nuclear antigen (LNA) which is the product of the viral gene orf 73. LNA is capable of forming a complex with retinoblastoma susceptibility gene product which may be related to its oncogenic activity. HHV8 has been reported to be expressed in multicentric Castleman’s disease (MCD) and in angioimmunoblastic lymphadenopathies. The localization of HHV8 in subcapsular spindle cell proliferations, which is where early intranodal KS begins, and endothelial cells in Castleman’s disease may explain the link between intranodal KS and MCD. In MCD, HHV8 is reported to be expressed in mantle zone large immunoblastic B cells.
Primary Antibodies

Human Neutrophil Defensins (1/2/3)

Clone D21
1 mL lyophilized NCL-DEFENSIN P (HIER)

Defensins are antimicrobial agents which together with serprocidins, lysozyme, bacterecins, protegrins and indolicidin have been isolated from neutrophil and macrophage granules. Defensins are synthesized as 93 to 98 amino acid pre-propeptides. In fully differentiated phagocytes, virtually all of the cellular defensin exists as processed mature peptide. Neutrophil defensins are stored in azurophil granules which discharge their contents into microbe-containing phagosomes through the process of phagosome/granule fusion. Paneth cells of the small intestine are also reported to secrete defensins, as well as lysozyme into the crypt lumen which may limit local microbial proliferation and colonization. These peptides may also exert chemotactic and immunomodulating effects in host defence and inflammation. The three principle human neutrophil defensin peptides, HNP 1, 2 and 3, are reported to be unique to neutrophils and account for 99 percent of the defensin content in these cells. Activation of neutrophils leads to a rapid release of HNP which may also be measured in plasma and other body fluids in infection and inflammation.

Human Securin

Clone DCS-280.2
1 mL lyophilized NCL-SECURIN P (HIER)

Human securin (hsecurin), also known as pituitary tumor-transforming gene-1 (PTTG) product, is required for chromosomal stability in human cells. Abnormalities of chromosome number are reported to be amongst the most common genetic aberrations in cancer. The mechanisms for regulating mitotic chromosome transmission in mammalian cells are, therefore, of great interest. Human cells without an hsecurin gene lose chromosomes at a high rate. These losses have been linked to abnormal anaphases during which cells undergo repeated unsuccessful attempts to segregate their chromosomes. Therefore, human securin is essential for the maintenance of euploidy. The expression of hsecurin is reported to correlate with cell proliferation in a cell cycle-dependent manner in both normal tissues and in several tumor types. hsecurin specifically binds to Ku, the regulatory subunit of the DNA-dependent protein kinase. Ku and hsecurin associate both in vitro and in vivo. DNA double-strand breaks prevent Ku/hsecurin association showing that genome damaging events can result in the induction of pathways that activate DNA repair mechanisms and halt cell cycle progression. It has also been proposed that hsecurin connects DNA-damage response pathways with sister chromatid separation delaying mitosis while DNA repair occurs.

Human Spasmolytic Polypeptide

Clone GE16C
1 mL lyophilized NCL-HSP P (HIER)

Human spasmolytic polypeptide (HSP) is a member of the trefoil peptide family which is reported to be expressed in discrete regions of the body, most notably the gastrointestinal tract. In the stomach, HSP is reported to be localized to foveolar and surface epithelium, pyloric glands and mucous neck cells.
Human von Willebrand Factor  
(Factor VIII-related antigen)  

**Clone 36B11**  
1 mL, 0.1 mL lyophilized NCL-vWF  
1 mL liquid NCL-L-vWF  
7 mL Bond ready-to-use PA0400  

Human von Willebrand factor (or factor VIII-related antigen) is a 270 kD multimeric plasma glycoprotein. It mediates platelet adhesion to injured vessel walls and serves as a carrier and stabilizer for coagulation factor VIII. The von Willebrand factor has functional binding domains to platelet glycoprotein Ib, glycoprotein Ib/IIIa, collagen and heparin. von Willebrand factor is synthesized by endothelial cells and is reported to be expressed in a number of tumors of vascular origin.  

Refer to page 43 for the Bond ready-to-use format.

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Hypoxia Inducible Gene 2 Protein  

**Clone HX34Y**  
1 mL, 0.1 mL liquid NCL-L-HIG2  

The gene encoding hypoxia-inducible gene 2 protein (HIG2) is one of the transcriptional targets for the activated beta-catenin/Tcf-4 complex and its product functions as an autocrine growth factor that enhances cell growth. This gene encodes a trans-membrane protein of 7 kD molecular weight that was found to be expressed exclusively in renal cell carcinomas (RCC) and fetal kidney. Reports indicate that ELISA analysis of clinical samples identified secretion of HIG2 protein into plasma of RCC patients even at an early stage of tumor development. HIG2 expression is reported to be expressed at higher levels in ovarian clear cell carcinomas when compared to those of clear cell renal tumors.

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Immunoglobulin A  

**Clone N1CLA**  
1 mL, 0.1 mL liquid NCL-L-IgA  

Clone N1CLA was developed to produce reduced background staining that is associated with polyclonal antibodies on paraffin sections.  

IgA is a member of the antibody class of the immunoglobulin superfamily. There are several classes and subclasses (isotypes) of antibody, the antibody isotype being defined by the immunoglobulin heavy chain present in the molecule. The basic structure of an immunoglobulin molecule consists of two identical heavy chains (γ, ι, κ, λ, α, ε) and two identical light chains, either kappa or lambda. IgA contains the α-chain and may be present in a serum or secretory form. In serum, 90 percent of IgA is monomeric, while in its secretory form it is the main immunoglobulin found in secretions including tears, saliva, intestinal and bronchial mucus, sweat, colostrum, and secretions from the prostate and respiratory epithelia, where it has the job of defending exposed external surfaces of the body against attack from micro organisms. Secretory IgA is synthesized locally by plasma cells and dimerized intracellularly with a cysteine-rich J-chain.

**Product Specific Information**  
Clone N1CLA was developed to produce reduced background staining that is associated with polyclonal antibodies on paraffin sections.
Immunoglobulin D

Clone DRN1C
1 mL, 0.1 mL liquid NCL-L-IgD P (HIER) W

Clone DRN1C was developed to produce reduced background staining that is associated with polyclonal antibodies on paraffin sections.

IgD, together with IgM, are the major immunoglobulins expressed on the surface of B cells where it seems they may operate as mutually interacting antigen receptors for the control of lymphocyte activation and suppression. The greater susceptibility of IgD to proteolysis in combination with antigen could well be implicated in such a function.

Product Specific Information

The use of PBS-based diluents may result in increased background staining. Clone DRN1C was developed to produce reduced background staining that is associated with polyclonal antibodies on paraffin sections.

Immunoglobulin G

Clone RWP49
1 mL, 0.1 mL liquid NCL-L-IgG P (HIER) W

Clone RWP49 was developed to produce reduced background staining that is associated with polyclonal antibodies on paraffin sections.

The human immunoglobulins consist of two identical heavy chains (~50 kDa) and two identical light chains, which are linked together by disulfide bonds. The light chains can be either kappa or lambda. The five immunoglobulins IgA, IgD, IgE, IgG and IgM differ in their heavy chains, and IgA and IgM differ as they can occur in polymeric forms. The heavy chain of IgG is named the gamma-chain. In humans, IgG consists of four sub classes that differ only marginally in their amino acid composition. Antibodies to IgG have been reported to be useful in the identification of plasma cells, lymphoid cells containing IgG and classifying B cell derived neoplasms. The normal B cell population is polyclonal, expressing a range of different immunoglobulins. In contrast, the majority of B cell neoplasms are characterized by the proliferation of monoclonal cells expressing one type of light chain, whereas more than one type of heavy chain can be expressed by the same cell. IgG positive neoplasms include hairy cell leukemia, splenic lymphoma and follicular lymphoma.

Immunoglobulin M

Clone 8H6
1 mL, 0.1 mL liquid immunoglobulin M NCL-L-IgM P (HIER) W

Clone 8H6 was developed to produce reduced background staining that is associated with polyclonal antibodies on paraffin sections.

IgM, together with IgD, is the major immunoglobulin expressed on the surface of B cells and normally constitutes about 10 per cent of serum immunoglobulin. IgM antibody is prominent in early immune responses to most antigens and predominates in certain antibody responses such as ‘natural’ blood group antibodies.

Immunoglobulin Antibodies

Polyclonal
1 mL lyophilized immunoglobulin A NCL-IgAp P (Enzyme) W

Polyclonal
1 mL lyophilized immunoglobulin D NCL-IgDp P (Enzyme)

Polyclonal
1 mL lyophilized immunoglobulin G NCL-IgGp P (Enzyme) W

Polyclonal
1 mL lyophilized immunoglobulin M NCL-IgMp P (Enzyme) W

The basic structure of immunoglobulin (Ig) molecules is a tetramer of two light chains and two heavy chains linked by disulfide bonds. There are two types of light chains, kappa and lambda, each composed of a constant domain (CL) and a variable domain (VL). There are five types of heavy chains: alpha, delta, epsilon, gamma and mu, all consisting of a variable domain (VH) and three (in alpha, delta and gamma) or four (in epsilon and mu) constant domains (CH1 to CH4).

Product Specific Information

NCL-IgAp, NCL-IgDp, NCL-IgGp and NCL-IgMp have each been solid-phase absorbed to remove cross-reactivity.
Inhibins and activins are members of the transforming growth factor beta (TGFβ) family of cytokines. Inhibins are heterodimers consisting of a common α-subunit linked to either a βA subunit (α-βA, forming inhibin A) or a βB subunit (α-βB, forming inhibin B). Activins share the β-subunit with the inhibins and may be homo or heterodimers of β-subunits forming activin A (βA-βA), activin AB (βA-βB) or activin B (βB-βB). The expression of the α-subunit, and therefore of inhibins appears to be more restricted than that of the β-subunit, and therefore of activins. Inhibins and activins play a role in the regulation of pituitary follicle stimulating hormone (FSH) secretion. The actions of inhibins and activins are thought to oppose one another, with inhibins suppressing FSH secretion and activins stimulating FSH secretion. Inhibins are secreted by granulosa cells in female follicles and Sertoli cells of the testis in the male. Inhibins are thought to have local regulatory roles in a variety of tissues, in addition to the ovary, including the brain, adrenal glands, bone marrow, fetus and placenta.

Interleukin-2 Receptor (CD25)

CD25 antigen, the alpha subunit of interleukin-2 receptor, is a single-chain glycoprotein with a molecular weight of 55 kD. Following the activation of T cells with antigen or mitogen in the presence of the monokine interleukin-1, interleukin-2 (IL-2) is rapidly synthesized and secreted. In response to this a subpopulation of T cells expresses high affinity receptors for IL-2. These cells proliferate, expanding the T cell population which is capable of mediating helper, suppressor and cytotoxic functions. IL-2 receptor is not exclusively found on T cells and is reported to be expressed on HTLV-transformed T and B cells, EBV-transformed B cells, myeloid precursors and oligodendrocytes. It is absent on thymocytes, resting T cells, non-activated B cells and null cells. IL-2 receptor expression is reported to be associated with inflammatory and malignant conditions, lymphoid neoplasia, autoimmune diseases and allograft rejection. Refer to page 21 for the Bond ready-to-use format.

Interleukin 6

IL-6 is a multifunctional cytokine that is secreted by both lymphoid and nonlymphoid cells. It plays a key role in immune responses, hematopoiesis and is an important cytokine in cell proliferation and differentiation. It may also play an important role as an autocrine growth factor in metastatic prostate cancer. IL-6 has been reported to play a role in secretion or release of pituitary hormone in pituitary hormone secreting cells and adenomas. In addition, IL-6 has been suggested to have a trophic effect in nerve cells and to have a direct pathogenic role in CNS disorders. There are an increasing number of reports that cytokines of the IL-6 family play an important regulatory role in heart physiology.

Insulin

Insulin is a hormone secreted by the beta cells of the islets of Langerhans in the pancreas. It promotes glycogen storage, formation of triglycerides, and synthesis of protein and nucleic acids. Reports of immunocytochemical investigation reveal the presence of insulin in the cytoplasm of certain islet tumors. However, in some instances insulin-positive granules are sparse and form a margin against the cell membrane. Refer to page 32 for the Bond ready-to-use format.
Involucrin

**Clone SY5**
1 mL, 0.1 mL lyophilized NCL-INV F P (Enzyme)

Involucrin is a precursor (120 kD) of the epidermal cornified envelope which becomes cross-linked during envelope assembly. Involucrin is expressed in a range of stratified squamous epithelia, including the cornea which lacks a distinct cornified layer and is expressed when differentiation is terminated. In normal dermis, involucrin is expressed in the upper cornified layer. However, in pathological conditions, involucrin expression is altered eg in psoriasis and other benign epidermal hyperplasias, where involucrin expression is found closer to the basal layer. Expression of involucrin is abnormal in squamous cell carcinomas and premalignant lesions.

**Product Specific Information**
When using NCL-INV, enzyme pretreatment may enhance staining in some cases.

Kappa Light Chain

**Clone CH15**
1 mL, 0.1 mL liquid NCL-L-KAP-581 P (HIER) Reference Range

**Clone kp-53**
1 mL lyophilized NCL-KAP F P W

**Clone L1C1**
1 mL, 0.1 mL lyophilized NCL-KAP-L1C1 F P (Enzyme)

_Tonsil: immunohistochemical staining for Kappa Light Chain using NCL-L-KAP-581. Note cytoplasmic staining of plasma cells. Paraffin section._

Immunoglobulins are polypeptides and comprise five major classes; immunoglobulin G (IgG), IgA, IgM, IgD and IgE. Each immunoglobulin consists of two identical heavy (H) chains and two identical light (L) chains. These are also subdivided into sub classes eg IgG1. There are two classes of light chain; kappa and lambda. The ratio of kappa chains and light chains varies between Ig classes and sub classes, but is also species specific. In humans, approximately 60 percent of light chains are kappa. However, in any particular immunoglobulin molecule the light chain will be either kappa or lambda. B cells contain either kappa or lambda mRNA.

Polyclonal

**Clone L1C1**
1 mL, 0.1 mL lyophilized NCL-Ki67-MM1 F P (HIER) Reference Range

**Clone K2**
7 mL Ready-to-use PA0230 P (HIER)

The Ki-67 antigen is a human nuclear protein, which is expressed in all active parts of the cell cycle (G1, S, G2 and mitosis), but absent in resting cells (G0). In contrast to many other cell cycle-associated proteins, the Ki67 antigen is consistently absent in quiescent cells and is not detectable during DNA repair processes. Thus, the presence of Ki67 antigen is strictly associated with the cell cycle and confined to the nucleus, suggesting an important role of this structure in the maintenance and/or regulation of the cell division cycle.

Refer to page 32 for the Bond ready-to-use format.

Kip2 (p57 Protein)

**Clone 25B2**
1 mL, 0.1 mL lyophilized NCL-p57 P (HIER)

Cyclin dependent kinases are positive regulators of cell proliferation. p57 protein acts as a tumor suppressor to counter this. It is closely-related to other CDKIs such as p21 protein (CIP1) and p27 protein (Kip1) as they share a common structural N-terminal domain for binding to CDK/cyclin complexes and inhibiting their kinase activity. Human p57 protein is found on chromosome 11p15.5, a region which is reported to be a common site for loss of heterozygosity in certain sarcomas, Wilms’ tumors and tumors associated with the Beckwith-Wiedemann syndrome. There is increasing interest in p57 as a marker in Gestational disease. Gestational trophoblastic disease refers to a spectrum of proliferative disorders of the placental trophoblast, with a wide range of histologic appearances and clinical behaviors. Recent developments in changes in the criteria for histologic diagnosis of these lesions due to earlier clinical diagnosis have been reviewed Hui P et al., Advantages in Anatomical Pathology. 12(3): 116-125 (2005) and the ability to make more accurate diagnoses due to the introduction of newer antibodies such as p57 is discussed.
Lambda Light Chain

Clone SHL53
1 mL, 0.1 mL liquid NCL-L-LAM-578 P (HIER) Reference Range

Clone HP-6054
1 mL, 0.1mL lyophilized NCL-LAM F P W

Polyclonal
1 mL lyophilized NCL-LAMp P (Enzyme) W

The basic structure of an immunoglobulin molecule consists of two identical heavy chains, either γ, μ, α, δ or ε, and two identical light chains, either kappa or lambda. Any heavy chain can associate with either light chain but on any immunoglobulin molecule both light chains are of the same type. The ratio of kappa and lambda light chains varies between Ig classes and subclasses. In a polyclonal population the ratio of kappa to lambda bearing B cells is approximately 2:1, with individual B cells thought to express kappa or lambda light chains, never both. The majority of kappa and lambda chains are bound to heavy chain immunoglobulin, however in normal individuals low levels of free light chain are present in serum. The occurrence of a mixture of kappa and lambda chain expressing cells suggests a polyclonal population and a reactive or nonneoplastic proliferation of B cells.

Lamin

Clone 636
1 mL, 0.1 mL lyophilized lamin A/C NCL-LAM-A/C F P (HIER) W

The nuclear lamina is a karyoskeletal structure composed of intermediate filament type proteins called lamins. It underlies the inner nuclear membrane and confers mechanical stability to the nuclear envelope. The human lamina consists of four major types of lamin, namely A, B1, B2 and C. The loss of lamin A expression has been reported to occur in small cell lung cancers.

Product Specific Information
NCL-LAM-A/C reacts with lamins A and C in human, cow and pig tissues.

Laminin

Clone LAM-89
0.5 mL lyophilized NCL-LAMININ F P (Enzyme)

Laminin is a large (850 kD) disulfide-bonded heterotrimer, cross-shaped, glycoprotein which is organized within the meshwork of basement membranes such as those associated with epithelia, surrounding blood vessels, nerves and underlying pial sheaths of the brain. It is reported to be expressed in the extracellular matrix in sites other than basement membranes during early stages of development and is localized to specific types of neurons in the central nervous system during both embryonic and adult development. Laminin interacts with receptors on cell surfaces, an interaction which results in changes in the behavior of cells such as attachment to a substrate, migration and neurite outgrowth during embryonic development and regeneration.

Langerin

Clone 12D6
1 mL, 0.1 mL lyophilized NCL-LANGERIN P (HIER)

Langerin is a type II transmembrane C-type lectin which has mannose-binding specificity. It is a 40 kD protein restricted to Langerhans cells that is involved in the internalization of cell surface material in these immature dendritic cells. Dendritic cells are antigen-presenting cells that are required for initiation of a specific T cell-driven immune response. These cells are found in nonlymphoid tissue as immature cells whose primary function is to capture antigen through specialized surface membrane endocytic structures or through macropinocytosis. The dendritic cells migrate to secondary lymphoid tissue and mature into efficient antigen presenting cells. A part of the maturation process includes the loss of adhesion receptors such as E-cadherin and the disappearance of Birbeck granules. Although Langerin is reported to be located on the cell surface, it can be rapidly internalized following ligand capture into Birbeck granules. In fact, Langerin is a potent inducer of membrane superimposition and zipping leading to Birbeck granule formation. In reports it has been suggested that the induction of Birbeck granules is a consequence of the antigen-capture function of Langerin allowing passage into these organelles and providing access to a non-classical antigen processing pathway.

Human placenta: immunohistochemical staining for laminin using NCL-LAMININ. Note staining of basement membranes of blood vessels. Paraffin section.
LFA-2 (CD2)

**Clone AB75**
- 1 mL, 0.1 mL lyophilized NCL-CD2-271 P (HIER)
- 1 mL liquid NCL-L-CD2-271 P (HIER)
- 7 mL ready-to-use RTU-CD2-271 P (HIER)

See also CD2 (LFA-2) on page 70.

**Linker for Activation of T Cells**

**Clone 3.8**
- 1 mL liquid NCL-L-LAT F P (HIER)
- 7 mL ready-to-use RTU-LAT F P (HIER)

Stimulation of the T cell antigen receptor (TCR) results in the activation of several protein tyrosine kinases (PTKs) associated with the TCR. These activated PTKs phosphorylated tyrosine residues on multiple protein substrates. This phosphorylation results in the activation of enzymes such as phospholipase C gamma or creates sites of binding for proteins involved in the activation cascade. Linker for activation of T cells (LAT) is an integral membrane protein (36 to 38 kD) which plays an important role in linking engagement of the TCR to the biochemical events of T cell activation. LAT is a substrate of activated ZAP-70 and Syk PTKs. It binds following tyrosine phosphorylation, Grb2, PLC-gamma1 and other critical signalling molecules recruiting them to the plasma membrane. This has the effect of enhancing the phosphorylation of tyrosine residues required for enzymatic activation and promoting the formation of protein complexes. LAT mRNA is found in NK cells and mast cells. LAT protein has been reported to be detected in thymus and peripheral lymphoid tissues such as T cell areas in lymph nodes and spleen. In the small intestine, intra-epithelial T cells also express LAT, and in bone marrow, LAT is expressed by T lymphocytes in interstitial spaces and also by platelets and megakaryocytes. LAT is reported not to be expressed in B cells, macrophages, plasma cells, monocytes, epithelial histiocytes and dendritic cells.

LMP-1 (Epstein-Barr virus)

**CS1, CS2, CS3, Clone CS4**
- 1 mL, 0.1 mL lyophilized NCL-EBV-CS1-4 F P (Enzyme)

See also Epstein-Barr virus (LMP-1) on page 106.

L-selectin (CD62L)

**Clone 9H6**
- 1 mL lyophilized NCL-CD62L-489 P (HIER)

The CD62L antigen is also known as Leu-8, TQ1, LAM1, MEL-14 antigen, lymph node homing antigen and L-selectin. It mediates the tethering and rolling of leukocytes on endothelial surfaces and also contributes to the recruitment of leukocytes from the blood to areas of inflammation. CD62L antigen is also important for the homing of naive lymphocytes to peripheral lymph nodes and Peyer’s patches and can also mediate neutrophil to neutrophil interactions via the recognition of CD162 antigen. CD62L antigen is reported to be expressed on the surface of mantle zone B lymphocytes in different lymphoid sites but is absent on germinal center B cells. It is also expressed on a proportion of T cells in peripheral lymph nodes, mucosal lymphoid sites and spleen. Non-lymphocytic staining has been reported on Langerhans cells, follicular dendritic cells in tonsil, neutrophils, monocytes and on macrophages in the thymus. Ligands for CD62L are expressed not only in specific vascular endothelium in lymph nodes and Peyer’s patches but also in extravascular tissues such as brain white matter, the choroid plexus and in kidney distal tubuli.

Lung Resistance-Related Protein (110 kD)

**Clone 9D6**
- 1 mL lyophilized NCL-LRRP P (HIER) W

Multidrug-resistant cancer cell lines are reported to frequently overexpress the 100 kD lung resistance protein (LRP) also known as lung resistance-related protein (LRRP). The overexpression of LRRP in acute myeloid leukemias, multiple and ovarian carcinomas has been reported. LRRP functions as a major vault transporter protein where vaults are multi-subunit structures which may be involved in nucleocytoplasmic transport. LRRP is overexpressed in P-glycoprotein negative multidrug-resistant tumor cell lines of different histogenetic origins and show an ATP-dependent drug accumulation effect. LRRP is also reported to be expressed in normal tissues, with expression being highest in epithelial cells with secretory and excretory functions such as bronchial cells and intestinal epithelial cells.
Lymphocyte Activation Gene-3 Protein (CD223)

Clone 12H6
1 mL lyophilized NCL-LAG-3 P (HIER)

Lymphocyte activation gene-3 (LAG-3) is a member of the immunoglobulin superfamily. It is a major histocompatibility (MHC) class II ligand that is evolutionarily-related to the CD4 molecule and is expressed in activated T and natural killer (NK) lymphocytes. It is reported that it may play a role in regulating the evolving immune response. LAG-3 is associated with the CD3/TCR complex, CD8 and MHC class II molecules where the resultant supramolecule may arise from an organisation in raft microdomains, a phenomenon known to regulate early events of T cell activation. LAG-3 expression is reported to be up-regulated by certain cytokines eg IL-2, IL-12 and not by others eg IL-4, IL-6, IL-10, TNF-alpha and -beta and IFN-gamma.

Mac-1 (CD11b)

Clone 44
1 mL lyophilized NCL-CD11b F

See also CD11b (Mac-1) on page 73.

Macrophage Marker (LN-5)

Clone LN-5
1 mL lyophilized NCL-LN5 F P (Enzyme)

Different types of lymphomas of true histiocytic origin can be characterized with various panels of antibodies. Expression of different phenotypes in so-called true histiocytic lymphoma and malignant histiocytosis has been observed but all express a group of markers that includes LN5. Hsu SM et al. American Journal of Pathology. 138(6):1389-404 (1991).

Product Specific Information
Clone LN-5 stains the cytoplasm of macrophages and histiocytes in hematopoietic organs. The heat induced epitope retrieval (HIER) technique may enhance staining in some cases.

Lysozyme (Muramidase)

Polyclonal
1 mL lyophilized NCL-MURAM P (Enzyme) W
7 mL Bond ready-to-use PA0391 P (Enzyme) New

Intracellular muramidase, also known as lysozyme, has been reported to be expressed in myeloid and monocytic cells, in leukocytes and in myelo-proliferative disorders. Muramidase is also reported to be expressed in poorly differentiated leukemic monoblasts.

Refer to page 35 for the Bond ready-to-use format.

Macrophage Marker (MAC387)

Clone MAC387
1 mL lyophilized NCL-MAC387 F P (Enzyme)
7 mL Bond ready-to-use PA0752 P (HIER)

L1, a member of the S-100 family of proteins, is reported to be found on neutrophils, monocytes, certain reactive macrophages and squamous mucosal epithelia.

Product Specific Information
Clone MAC387 is reported to be specific for the leucocyte antigen L1.

Refer to page 32 for the Bond ready-to-use format.
MAGE-1

**Clone 6C1**
1 mL lyophilized NCL-MAGE-1 P (HIER)

The human MAGE gene products are recognised by major histocompatibility complex-restricted cytotoxic T lymphocytes. MAGE-1, also known as tumor rejection antigen, is a target for immunotherapy in patients with hepatocellular carcinoma (HCC). MAGE-1 is reported to be expressed in about 60 per cent of HCC cases. Other studies utilising reverse transcriptase-PCR and southern blot hybridisation techniques have reported MAGE genes to be expressed in malignant tumors and pre-cancerous lesions but not in benign tumors.

Maspin

**Clone EAW24**
1 mL, 0.1 mL lyophilized NCL-MASPIN P (HIER)

Maspin, or mammary-specific serpin, is a tumor suppressor protein of 42 kD that belongs to the serine proteinase inhibitor (serpin) family. It is reported to be expressed in normal breast and prostatic epithelial cells but is downregulated in carcinomas derived from these cell types. The expression of maspin is controlled at the transcriptional level by a combination of elements including Ets, AP-1 and p53. The tumor suppressor activity of maspin may depend on its ability to inhibit angiogenesis. In breast myoepithelial cells, maspin is predominantly a soluble cytoplasmic protein which associates with secretory vesicles and is present at the cell surface. The loss of maspin in breast tumors is reported to be a progressive process and expression decreases with increasing malignancy of primary tumors and is absent from lymph node and distant metastases. In rats, maspin mRNA has been detected in mammary gland, vagina, bladder, thymus, small intestine, ventral prostate, seminal vesicles and thyroid, but is absent from heart, lung, liver, brain and kidney.

Mast Cell Chymase

**Clone CC1**
1 mL lyophilized NCL-MCC P (HIER)

Chymase is an enzyme found in human mast cells and acts as a mediator of inflammation and matrix remodelling. Mast cells are present in most human tissues and have themselves been implicated in angiogenesis, inflammation and fibrosis. Mast cells are not a single cell type but represent a highly heterogenous population. Subpopulations differ in their responsiveness to various secretagogues, their susceptibility to pharmacological control by anti-allergic drugs and also the extent to which they may be histologically stained using basic dyes. Mast cells may contain both chymase and tryptase in their secretory granules (MC_{TC}) or tryptase only (MC_{T}) without chymase. The MC_{TC} population normally predominates at connective tissue sites and is also most abundant in skin, heart, gastrointestinal submucosa and respiratory submucosa tissues. The MC_{T} cells are most numerous in mucosal tissues. Chymase, one of the major secretory products of MC_{TC} cells, may alter cytokine bioavailability by activating the interleukin-1b (IL-1b) precursor, degrading IL-4 and liberating membrane-bound stem cell factor. It could also participate in matrix remodelling by activating procollagenase and control blood flow by generating angiotensin II. In animal models, chymase has also been shown to increase microvascular permeability and promote the accumulation of inflammatory cells.

Mast Cell Tryptase

**Clone 10D11**
1 mL, 0.1 mL lyophilized NCL-MCTRYP-428 P
7 mL Bond ready-to-use PA0019 P

Mast cells contain a number of preformed chemical mediators such as histamine, chymase, carboxypeptidase and proteolytic tryptase. A substantial quantity of tryptase is reported to be found in mast cells of skin and lung and suggests this enzyme plays a major role in mast cell mediated events. In vitro studies indicate tryptase can cleave C3 to form C3a anaphylatoxin, inactivate fibrinogen as a coaguable substrate for thrombin and activate latent collagenase. Models of allergic disease in the skin, nose and lung have each indicated elevated tryptase levels. Human mast cell tryptase has been reported to be implicated as a mediator of inflammation. Mast cell degranulation in the gut causes mucus secretion, mucosal edema, increased gut permeability and may be responsible for some of the symptoms and signs of inflammatory bowel disease.

Refer to page 33 for the Bond ready-to-use format.
Matrix Metalloproteinase Antibodies

Clone 17B11
1 mL, 0.1 mL lyophilized Matrix Metalloproteinase 2
NCL-MMP2-507 P (HIER)

Clone 15W2
1 mL, 0.1 mL lyophilized Matrix Metalloproteinase 9
NCL-MMP9-439 F P

Clone 5E4
1 mL lyophilized Matrix Metalloproteinase 10
NCL-MMP10 P (HIER)

Clone 9F6
1 mL lyophilized Matrix Metalloproteinase 19
NCL-MMP19 P

The matrix metalloproteinases (MMPs) are a family of zinc-containing enzymes, which are involved in the degradation of different components of the extracellular matrix and tissue remodelling. MMPs are expressed widely during growth and development. The MMPs have been classified into collagenases, gelatinases and stromelysins, based on the in vitro substrate specificity. More recently, several MMPs have been identified as membrane-type specific and matrilysin families. MMPs are multidomain proteins and are secreted as inactive precursors which are activated by cleavage of an N-terminal pro-peptide. The major natural inhibitors of MMPs are tissue inhibitors of matrix metalloproteinases (TIMPs) which complex with MMPs and are involved in regulating the activity and activation of individual MMPs. MMP2 (also known as gelatinase A) is able to initiate degradation of type IV collagen. MMP9 degrades collagen type IV, a major component of extracellular matrix. MMP9 is also reported to be expressed in normal kidney tubules, hepatocytes, spermatids, myocytes, stomach parietal cells, prostatic columnar epithelium and uterine cells. MMP10 is also known as stromelysin-2 and has a wide range of substrates including proteoglycan, laminin, fibronectin, collagen IV, collagen IX and the telopeptides of other collagens. However, some of the more recently identified MMPs, such as MMP19 - which cleaves aggrecan and cartilage oligomeric protein, and has several novel structural features, do not fall into these traditional groupings. MMP19 is reported to be expressed mainly in placenta, lung, pancreas, ovary, spleen, intestine, breast tissue, smooth muscle, capillary walls and the endothelial layers of large and medium sized blood vessels.

MB2 (B Cell Marker)

Clone MB2
1 mL lyophilized NCL-MB2 F P
See also B Cell Marker (MB2) on page 59.

MCAM (CD146)

Clone N1238
1 mL, 0.1 mL lyophilized NCL-CD146 P (HIER) W
See also CD146 (MCAM) on page 87.

Mcl-1

Clone 38G3
1 mL lyophilized NCL-Mcl-1 P

The Mcl-1 gene encodes a protein of approximately 37 kD which shares significant homology with bcl-2, a protein which blocks programmed cell death. Mcl-1 protein has been shown to inhibit apoptosis in cells treated with agents such as UV irradiation or etoposide. Like bcl-2, Mcl-1 protein can interact with Bax, inhibiting Bax-induced cell death and promoting cell viability. Although Mcl-1 protein prolongs cell viability, it does not prevent eventual cell death. Mcl-1 protein is reported to be expressed in epithelial cells in a variety of tissues including prostate, breast, endometrium, epidermis, stomach, small intestine, colon and respiratory tract.
MDM2 Protein

Clone 1B10
1 mL, 0.1 mL lyophilized NCL-MDM2 F (HIER)

The human phosphoprotein homolog of the murine double minute 2 (MDM2) gene, with a molecular weight of 90 kD (p90), forms a complex with both mutant and wild type p53 protein. The MDM2 gene product interacts with p53 protein inhibiting p53-mediated transactivation. Overexpression of MDM2 overcomes wild type p53 mediated suppression of transformed cell growth. MDM2 amplification is reported to be observed in some soft tissue sarcomas, osteosarcomas and high grade malignant gliomas.

Product Specific Information
NCL-MDM2 reacts with the human homolog of MDM2.

Melanoma Marker (CD63)

Clone NKI/C3
1 mL, 0.1 mL lyophilized NCL-CD63 F (HIER)

See also CD63 (Melanoma Marker) on page 82.

Melanoma Marker (HMB45)

Clone HMB45
1 mL, 0.1 mL lyophilized NCL-HMB45 F (Enzyme)

See also HMB45 (Melanoma Marker) on page 120.

Merosin Laminin Alpha 2 Chain

Clone Mer3/22B2
1 mL lyophilized NCL-MEROSIN F

The dystrophin-glycoprotein complex is localized to the muscle membrane. Several members of this complex are reported to be implicated in muscular dystrophy. Dystrophin expression is altered in Duchenne and Becker muscular dystrophy and four types of limb girdle muscular dystrophy are caused by mutations in the genes for alpha, beta, gamma and delta-sarcoglycan. An extracellular member of this complex is alpha-dystroglycan and linked to this, in the extracellular matrix, is laminin. The muscle specific form of laminin, merosin, is composed of three chains: alpha 2, beta 1 and gamma 1. Mutations in the chromosome 6 encoded gene for the laminin alpha 2 chain of merosin are responsible for a form of congenital muscular dystrophy (CMD). Merosin negative CMD is characterized by a severe clinical phenotype and is associated with white matter changes on brain imaging.

Product Specific Information
NCL-MEROSIN reacts with the 300 kD fragment of merosin (Sewry et al. Muscle and Nerve Supplement. 7, S109: (1998)) labeling with an antibody to beta-spectrin to monitor membrane integrity, is an essential immuno-histochemical control.

Melanoma Marker (CD63)

Clone NKI/C3
1 mL, 0.1 mL lyophilized NCL-CD63 F (HIER)

See also CD63 (Melanoma Marker) on page 82.

Melanoma Marker (HMB45)

Clone HMB45
1 mL, 0.1 mL lyophilized NCL-HMB45 F (Enzyme)

See also HMB45 (Melanoma Marker) on page 120.

Merosin Laminin Alpha 2 Chain

Clone Mer3/22B2
1 mL lyophilized NCL-MEROSIN F

The dystrophin-glycoprotein complex is localized to the muscle membrane. Several members of this complex are reported to be implicated in muscular dystrophy. Dystrophin expression is altered in Duchenne and Becker muscular dystrophy and four types of limb girdle muscular dystrophy are caused by mutations in the genes for alpha, beta, gamma and delta-sarcoglycan. An extracellular member of this complex is alpha-dystroglycan and linked to this, in the extracellular matrix, is laminin. The muscle specific form of laminin, merosin, is composed of three chains: alpha 2, beta 1 and gamma 1. Mutations in the chromosome 6 encoded gene for the laminin alpha 2 chain of merosin are responsible for a form of congenital muscular dystrophy (CMD). Merosin negative CMD is characterized by a severe clinical phenotype and is associated with white matter changes on brain imaging.

Product Specific Information
NCL-MEROSIN reacts with the 300 kD fragment of merosin (Sewry et al. Muscle and Nerve Supplement. 7, S109: (1998)) labeling with an antibody to beta-spectrin to monitor membrane integrity, is an essential immuno-histochemical control.

Human skeletal muscle: immunohistochemical staining for merosin using NCL-MEROSIN. Note membrane staining of normal muscle fibers (A) and absence of staining of muscle fibers in an individual with chromosome 6-linked congenital muscular dystrophy (B). Frozen sections. Photographs supplied courtesy of Dr Louise V B Anderson.
Mesothelin

**Clone 5B2**
1 mL lyophilized NCL-MESO  F P (HIER)
1 mL liquid NCL-L-MESO  F P (HIER)
7 mL ready-to-use RTU-MESO  F P (HIER)
7 mL Bond ready-to-use PA0373  P (HIER)

Mesothelin is a glycosyl-phosphatidylinositol-linked (GPI) glycoprotein of 40 kD present on the surface of mesothelial cells, mesotheliomas, epithelial ovarian cancers and some squamous cell carcinomas. It is synthesized as a 69 kD precursor which is enzymatically processed into an N-terminal secreted form of 30 kD and the GPI-linked membrane-bound form of 40 kD. The secreted form is identical to the megakaryocyte potentiating factor, but it is the GPI-linked membrane-bound form which has generated interest. Mesothelin is abundantly expressed in the kidney and in occasional epithelial cells of the trachea, tonsil and fallopian tube. The function of mesothelin is unclear but it may have a role in cellular adhesion. Mesothelin is reported to be abundant in the normal mesothelial cells from which malignant mesotheliomas and ovarian cystadenocarcinomas are derived.

Refer to page 33 for the Bond ready-to-use format.

Human mesothelioma: immunohistochemical staining for mesothelin using NCL-MESO. Note intense membrane staining of tumor cells. Paraffin section.

Microphthalmia Transcription Factor (MITF)

**Clone 34CA5**
1 mL lyophilized NCL-MITF  F P (HIER)
1 mL, 0.1 mL liquid NCL-L-MITF  F P (HIER)

Microphthalmia transcription factor (MITF) gene product, a nuclear transcription factor of the basic-helix-loop-helix type, is thought to play a role in the regulation of genes encoding the enzymes necessary for melanogenesis. These include tyrosinase, TRP-1 and TRP-2. MITF is critical for the embryonic development and postnatal viability of melanocytes. The melanocyte-specific isoform of microphthalmia transcription factor MITF-M, is reported to be expressed in normal and malignant melanocytes. The other isoforms, MITF-A, MITF-C and MITF-H, differ structurally at the N-terminus from MITF-M.

**Product Specific Information**
Clone 34CA5 is reported to be reactive with the MITF-M isoform.

Human malignant melanoma: immunohistochemical staining for microphthalmia transcription factor using NCL-L-MITF. Note nuclear staining of melanoma cells. Paraffin section.

Minichromosome Maintenance Protein Antibodies

**Clone CRCT2.1**
1 mL, 0.1 mL lyophilized Minichromosome Maintenance Protein 2 NCL-MCM2  P (HIER)

**Clone JCC07**
1 mL lyophilized Minichromosome Maintenance Protein 3 NCL-MCM3  P (HIER)

**Clone CRCT5.1**
1 mL lyophilized Minichromosome Maintenance Protein 5 NCL-MCM5  P (HIER)  W

**Clone DCS-141.1**
1 mL lyophilized Minichromosome Maintenance Protein 7 NCL-MCM7  P (HIER)  W

Minichromosome maintenance (MCM) proteins have been reported to play an essential part in eukaryotic DNA replication. Each of the MCM proteins have DNA-dependent ATPase motifs in their central domain which are conserved from yeast to mammals. Both ATPase activity and helicase activity, which displaces oligonucleotides annealed to single-stranded circular DNA, are associated with an MCM protein complex. Levels of MCM proteins generally increase in a variable manner as normal cells progress from G0 into G1/S phase of the cell cycle. In the G0 phase, MCM2 and MCM5 proteins are reported to be much less abundant than the MCM7 and MCM3 proteins. Therefore, MCM proteins are not present in stoichiometric amounts and only a proportion of the molecules actively participate in cell cycle regulation as part of MCM complexes. Oncoprotein E6 of the human papillomavirus (HPV), associated with cervical cancer (HPV-16 and -18), degrades the tumor suppressor protein p53, but also seems to have p53-independent transforming functions. E6 was reported to bind to the C-terminal region of the human MCM7 protein causing chromosomal abnormalities in human cells expressing E6 proteins of oncogenic HPVs.

**Product Specific Information**
NCL-MCM2, NCL-MCM3, NCL-MCM5 and NCL-MCM7 are specific for minichromosome maintenance proteins 2, 3, 5 and 7, respectively.
Primary Antibodies

Minichromosome Maintenance Protein 6

Clone KAT82

1 mL, 0.1 mL liquid NCL-L-MCM6 P (HIER) W

Minichromosome maintenance protein 6 (MCM6) is one of the six members of the MCM family, involved in the initiation of DNA replication. The binding of MCM proteins appears to make chromatin competent for replication, as MCM-free chromatin is unable to replicate. MCM6 is detectable in nucleosols or bound to nuclear chromatin during the G1, S and G2 phases of the cell cycle and bound to chromatin in the cytoplasm during mitosis. MCM6 is reported to be undetectable during the G0 phase. Due to its role as a replication licensing factor, MCM6 is thought to represent a marker of proliferating cells, with a similar expression pattern to Ki67 during the cell cycle (G1, S, G2 and M). However, reports suggest that MCM6 is expressed during the early G1 phase, when Ki67 is undetectable, therefore suggesting that a subset of proliferating cells in early G1 phase which are undetectable with Ki67 antibodies may be detectable with an MCM6 antibody.

Mismatch Repair Protein (MLH1)

Clone ES05

1 mL, 0.1 mL liquid NCL-L-MLH1 P (HIER) 7 mL Bond ready-to-use PA0610 P (HIER)

MLH1, a mismatch repair protein involved in maintaining the integrity of genetic information, alongside MSH2, MSH6 and PMS2. During DNA replication, strand misalignment can occur resulting in alterations to microsatellite repeats, often referred to as microsatellite instability (MSI). These defects in DNA repair pathways have been linked to human carcinogenesis. Mutations in the MLH1 gene have been reported to be found in tumors with MSI, such as some forms of colon cancer e.g. Hereditary nonpolyposis colon cancer (HNPCC), a subset of sporadic carcinomas and breast cancer. Loss of expression of MLH1 has also been reported in acute lymphoblastic leukemia, endometrial carcinoma, gastric carcinoma and ovarian carcinoma.

Refer to page 33 for the Bond ready-to-use format.

Mismatch Repair Protein (MSH2)

Clone 25D12

1 mL lyophilized NCL-MSH2 P (HIER) 7 mL Bond ready-to-use PA0048 P (HIER)

Human mismatch repair protein 2 (MSH2) is involved in the initial recognition of mismatched nucleotides during the post replication mismatch repair process. Therefore, the loss of MSH2 function leads to the accumulation of replication errors, which in turn may be responsible for the multiple mutations required for multistage carcinogenesis. Mutations in mismatch repair genes have been linked to hereditary nonpolyposis colon cancer and to sporadic cancers which exhibit microsatellite instability. MSH2 is reported to be expressed in the nuclei of cells from a variety of tissues including thyroid, heart, smooth muscle and the germinal centers of lymphoid follicles. In ileum and colon, MSH2 expression has been reported in the crypts, the cells of which are undergoing rapid renewal. They are responsible for the continuous production of differentiated cells which migrate over 2 to 4 days before being sloughed into the lumen.

Refer to page 34 for the Bond ready-to-use format.
Mismatch Repair Protein (MSH6)

Clone PU29
1 mL, 0.1 mL liquid NCL-L-MSH6 P (HIER) 7 mL Bond ready-to-use PA0597 P (HIER)

MSH6 is a 160 kD protein which is involved in DNA mismatch repair (MMR) and recombination pathways, when heterodimerized with MSH2. Defects in mismatch repair systems can cause mutations and can cause DNA microsatellite sequences to become unstable. Microsatellite instability has been described in colorectal cancer, particularly in Hereditary Nonpolyposis Colorectal Cancer (HNPCC) where MSH6 expression, along with other MSH proteins, is disrupted. Immunohistochemical studies have reported that MSH6 is strongly expressed in the nucleus of cells in normal colonic epithelium, especially in crypts. Expression is also found in lymphocytes. Studies have also shown that MSH6 is expressed in gastric carcinomas and endometrial carcinomas. However, sometimes expression can be lost in some endometrial carcinomas and colonic carcinomas with microsatellite instability. MSH6 has been reported to be a useful marker to use in conjunction with microsatellite instability screening to identify colon tumors that may contain MMR gene mutations, such as HNPCC.

Product Specific Information
The use of PBS-based diluents may result in increased background staining. Refer to page 34 for the Bond ready-to-use format.

Mitogen-Activated Protein Kinase Kinase 4

Clone 7A6
1 mL lyophilized NCL-MKK4 P (HIER)

Mitogen-activated protein kinase kinase 4 (MKK4) is a member of the MAP kinase kinase family which directly phosphorylates and activates the c-Jun N-terminal kinases (JNK) in response to cellular stresses and proinflammatory cytokines. MKK4, like MKK3, also phosphorylates and activates the p38/HOG kinase. MKK4 activates mitogen-activated protein kinases (MAPKs) which are involved in the transduction of extracellular signals for growth factors or environmental stresses which usually result in cell growth and differentiation. MKK4 mRNA has been reported to be expressed in many human tissues including skeletal muscle and brain with lower expression in heart, placenta, kidney, liver, pancreas, and in the cytoplasm and nucleus of normal gastric epithelia. The deletion and mutation of the MKK4 gene, reported in human pancreatic lung, breast, testicle and colorectal cancer cell lines and in a proportion of gastric, prostatic, pancreatic, biliary and breast carcinomas, suggests that it might have a role as a suppressor of tumorigenesis or metastasis.

Mismatch Repair Protein (PMS2)

Clone M0R4G
1 mL, 0.1 mL liquid NCL-L-PMS2 P (Enzyme) W

Postmeiotic segregation increased 2 (PMS2), also known as PMS1 protein homologue 2, is a DNA mismatch repair (MMR) protein. The PMS2 gene family members are found in clusters on chromosome 7. PMS2 is a 96 kDa mismatch repair protein closely related to MLH1, MLH3 and PMS1, which are homologs of the bacterial mutL gene. The PMS2 protein forms a heterodimer with the MLH1 protein which is then activated in the presence of ATP; this complex coordinates the binding of other proteins that repair DNA errors arising during cell preparation for cell division.

The loss of PMS2 expression in tumors can be helpful in identifying hMLH1 mutation carriers and identify their suitability for mutation analysis.

PMS2 gene defects account for a small but significant proportion of colorectal cancers and for a substantial proportion of tumors with microsatellite instability. PMS2 is associated with cases of the dominantly inherited disorder Hereditary Non-Polyposis Colon Cancer (HNPCC) but more clearly associated with a variation of HNPCC known as Turcot syndrome.
Motility-Related Protein-1 (CD9)

Clone 72F6
1 mL lyophilized NCL-CD9 F P (HIER)
See also CD9 (Motility-Related Protein-1) on page 72.

Muc Glycoprotein Antibodies

Clone Ma552
1 mL lyophilized muc-1 core glycoprotein
NCL-MUC-1-CORE F P (HIER)

Clone Ma695
1 mL lyophilized muc-1 glycoprotein
NCL-MUC-1 F P (HIER)

Clone Ccp58
1 mL, 0.1 mL lyophilized muc-2 glycoprotein
NCL-MUC-2 F P (HIER)

Clone CLH2
1 mL, 0.1 mL lyophilized muc-5AC glycoprotein
NCL-MUC-5AC P (HIER)

Clone CLH5
1 mL, 0.1 mL lyophilized muc-6 glycoprotein
NCL-MUC-6 P (HIER)

Mucins are heavily glycosylated proteins which constitute the major components of mucus covering the surface of epithelial tissues. Nine distinct epithelial mucin genes (Muc-1, 2, 3, 4, 5AC, 5B, 6, 7 and 8) have been identified. Various immunohistochemical and in situ hybridization studies have reported that these mucins are differentially expressed in epithelia with cell-type specificity. The normal gastric mucosa shows cell-type specific expression of Muc-1, Muc-5AC and Muc-6 glycoproteins. Muc-1 and Muc-5AC are found in superficial epithelium and Muc-6 glycoprotein in the deep glands. Muc-1 and Muc-5AC glycoproteins are reported to be expressed in many epithelia but Muc-6 glycoprotein is mainly expressed in gastric mucosa. In addition, Muc-2 glycoprotein is not expressed in normal gastric mucosa. In gastric cancer, alterations in mucin polypeptide expression have been reported, including the loss of expression of Muc-5AC glycoprotein, increased mucin heterogeneity, glycosylation changes and the expression of simple mucin-type carbohydrates.

Multiple Myeloma Oncogene 1 (MUM-1)

Clone EAU32
1 mL, 0.1 mL liquid NCL-L-MUM1 P (HIER)
7 mL Bond ready-to-use PA0129 P (HIER)

The MUM-1 (multiple myeloma oncogene 1) gene was originally identified because of its involvement in the t(6;14) translocation observed in multiple myeloma, which causes the juxtaposition of the MUM-1 gene to the Ig heavy chain locus. MUM-1 is expressed in late plasma cell directed stages of B cell differentiation and in activated T cells, suggesting that MUM-1 may serve as a marker for lympho-hemopoietic neoplasms derived from these cells. The morphologic spectrum of MUM-1 expressing cells has been found to range from that of a centrocyte to that of a plasmablast/plasma cell. Consequently the histogenic value of MUM-1 may be to provide a marker to aid in the identification of the transition from BCL-6 positive (germinal center B cells) to CD138 positive (immunoblasts and plasma cells). MUM-1 expression occurs in a wide range of lymphoid neoplasms including a proportion of diffuse B cell lymphomas but not myeloid or extra-hemopoietic neoplasms. MUM-1 is consistently expressed in myeloma cells, Reed Sternberg cells in classic Hodgkin Disease, and activated and neoplastic T cells.

Refer to page 35 for the Bond ready-to-use format.

Multi-Cytokeratin

Clone AE1, Clone AE3
1 mL lyophilized NCL-AE1/AE3 F P (HIER)
1 mL liquid NCL-L-AE1/AE3 F P (HIER)
7 mL ready-to-use RTU-AE1/AE3 F P (HIER)
7 mL Bond ready-to-use PA0909 P (Enzyme)

Keratins are a family of water insoluble proteins of 40 to 70 kD. These proteins form tonofilaments, a class of intermediate filament, in epidermis as well as in almost all other epithelia. The process of normal epidermal differentiation is characterized by a series of morphological and biochemical changes as cells progress from the germinative basal layer through the spinous and granular layers to the outer cornified layer. The 65 to 67 kD cytokeratins are reported to be present only above the basal layer, the 58 kD cytokeratin is reported to be expressed throughout the entire epidermis including the basal layer and the 56 kD cytokeratin is reported to be absent from the basal layer and is normally eliminated during stratum corneum formation. The 56 and 65 to 67 kD cytokeratins are reported to be characteristic of epidermal cells undergoing terminal differentiation and may be considered as molecular markers for keratinization.

Product Specific Information

Clones AE1 and AE3 are specific for the 56.5, 50, 50’, 48 and 40 kD acidic cytokeratins as well as the 65 to 67, 64, 59, 58, 56 and 52 kD basic cytokeratins. The cocktail of clones AE1 and AE3 exhibit broad reactivity with two families of cytokeratin, acidic and basic.

Refer to page 34 for the Bond ready-to-use format.
Multi-Cytokeratin (4/5/6/8/10/13/18)

Clone C-11
1 mL lyophilized NCL-C11  F P (HIER)
Cytokeratins 4, 5, 6, 8, 10, 13 and 18 are differentially expressed between a variety of normal, reactive and neoplastic epithelia and also simple epithelium and both basal and suprabasal layers of cornifying and non-cornifying squamous epithelium.
NCL-C11 is reported to react with human cytokeratins 4, 5, 6, 8, 10, 13 and 18.

Multi-Cytokeratin 1/5/10/14

Clone 34βE12
1 mL lyophilized NCL-CK34BE12  F P (HIER) W
7 mL ready-to-use RTU-CK34BE12  F P (HIER)
7 mL Bond ready-to-use PA0134  P (Enzyme)
NCL-CK34βE12 reacts with human cytokeratin intermediate filament proteins 1, 5, 10 and 14. The antibody is reported to react with squamous epithelium and sweat ducts in normal skin, some pneumocytes, bronchial epithelium and mesothelium in normal lung and bile ducts in normal liver. It also reacts with ductal cells of the normal pancreas, some acinar and ductal cells of normal breast, some follicular epithelia of normal thyroid and some epithelia and mesothelium of the normal small and large bowel.
Refer to page 27 for the Bond ready-to-use format.

Multi-Cytokeratin (5/6/8/18)

5D3, Clone LP34
1 mL, 0.1 mL lyophilized NCL-CK5/6/8/18  F P (Enzyme)
1 mL liquid NCL-L-CK5/6/8/18  F P (Enzyme)
7 mL ready-to-use RTU-CK5/6/8/18  F P (Enzyme)
Product Specific Information
NCL-CK5/6/8/18, NCL-L-CK5/6/8/18 and RTU-CK5/6/8/18 react with human cytokeratins 5, 6, 8 and 18. These products are cocktails of monoclonal antibodies designed to recognize cytokeratins reported to be expressed in almost all epithelial tissues.

Multidrug Resistance-Associated Protein Antibodies

Clone 33A6
1 mL, 0.1 mL lyophilized Multidrug Resistance-associated Protein 1 NCL-MRP1  P (HIER)
Clone DTX1
1 mL lyophilized Multidrug Resistance-associated Protein 3 NCL-MRP3  P (HIER)
The human multidrug resistance-associated protein (MRP) gene family contains at least 6 members designated MRP1 to 6. MRP1 is a phosphoprotein of 1831 amino acids and is expressed in a variety of cell types. MRP1 mRNA has been demonstrated in lung, testis and peripheral blood mononuclear cells but was not detected in placenta, brain, salivary gland, liver, uterus and spleen. The protein has been expressed in the epithelium and glands of nasal respiratory mucosa. MRP3 is a 190 to 200 kD integral membrane protein which is an organic anion transporter effective in transporting chemotherapeutic drugs such as MTX, etoposide and teniposide. Northern blotting of various human tissues has indicated MRP3 to be expressed in liver, colon, pancreas and at lower levels in the kidney. MRP5 mRNA is reported to be expressed in almost all tissues, especially skeletal muscle and brain with lower expression observed in liver, adrenal gland, placenta, ovary and pancreas.
Muramidase (Lysozyme)

Polyclonal
1 mL lyophilized NCL-MURAM P (Enzyme) W
7 mL Bond ready-to-use PA0391 P (HIER) New!

Intracellular muramidase, also known as lysozyme, has been reported to be expressed in myeloid and monocytic cells, in leukocytes and in myeloproliferative disorders. Muramidase is also reported to be expressed in poorly differentiated leukemic monoblasts.

Refer to page 35 for the Bond ready-to-use format.
See also Lysozyme (Muramidase) on page 129.

Primary Antibodies

Muscle Specific Actin

Clone SC28 New!
1 mL, 0.1 mL liquid NCL-L-MSA-594 P W

Clone HHF35
1 mL lyophilized NCL-MSA F P W
7 mL Bond ready-to-use PA0258 P

Muscle Specific Actin (MSA) is a highly conserved, ubiquitous protein found in muscle and some non-muscle cells. Actins can be divided into three subsets, alpha actins found in muscle tissue cells, beta and gamma actins found in non-muscle cells and a small subset of gamma actins also found in muscle tissue cells. In normal tissues, expression is found in striated fibers of skeletal muscle, smooth muscle in arteries, veins and pericytes of smaller arteries, muscle in bowel, myometrium of the uterus, prostatic stroma, capsule cells of liver, kidney, lymph node and spleen, the myoepithelial layers of mammary ducts and glands, eccrine sweat glands and salivary glands. Expression is not found in epithelial cells, lymphoid cells, macrophages, connective tissue and neuronal cells. In neoplastic tissues, expression can be found in soft tissue tumors with muscle differentiation e.g. leiomyomas, leiomyosarcomas and rhabdomyosarcomas of varying subtypes. Non-muscle sarcomas, carcinomas, melanomas and lymphomas do not express muscle specific actin.

Product Specific Information
NCL-L-MSA-594 was developed to outperform NCL-MSA in immunohistochemistry.

Refer to page 35 for the Bond ready-to-use format.

Myelin Basic Protein

Clone 7H11
1 mL, 0.1 mL lyophilized NCL-MBP (HIER)

Myelin basic protein is reported to account for about 30 percent of the proteins in myelin found in the central nervous system. It can induce experimental allergic encephalomyelitis (EAE), a T-lymphocyte mediated disease due to delayed-type hypersensitivity; though each animal species appears to respond to a different fragment of the 170 amino acid polypeptide. Four different isoforms have been identified through cDNA cloning. All four of these variants are identical except for the insertion or deletion of two peptide fragments encoded by exons 2 and 5. Myelin basic protein is reported to be expressed in oligodendrocytes, myelin of white matter in the brain and spinal cord and in peripheral nerves, though it is expressed less abundantly in gray matter.

Product Specific Information
NCL-MBP was raised to guinea pig myelin basic protein and is reactive with human myelin basic protein.

Mycobacterium tuberculosis

Clone 1.1/3/1
1 mL lyophilized NCL-MT W

The re-emergence of tuberculosis itself, the significant increase in non-tuberculous mycobacterial infections in the immunosuppressed and the changing epidemiology of childhood mycobacterial lymphadenitis make it important to confirm the mycobacterial etiology of tissue granulomata whenever possible.

Product Specific Information
NCL-MT is raised to the 38 kD antigen of the mycobacterium tuberculosis complex (MTBC). NCL-MT reacts with several mycobacterial species, in Western blotting, including Mycobacterium tuberculosis, other members of the MTBC and Mycobacterium avium-intracellulare.
Myeloid Marker (BM1)

*Clone BM-1*
1 mL lyophilized NCL-BM1  **F** **P**
See also BM1 (Myeloid Marker) on page 63.

Myeloid Marker (BM2)

*Clone BM-2*
1 mL lyophilized NCL-BM2  **F** **P** (HIER)
See also BM2 (Myeloid Marker) on page 63.

Myeloperoxidase

*Clone 59A5*
1 mL, 0.1 mL lyophilized NCL-MYELO  **P**
7 mL Bond ready-to-use PA0491 **P** (HIER)  **New!**

Myeloperoxidase is a lysosomal enzyme found in cells of the myeloid series which metabolises most of the hydrogen peroxide generated by activated phagocytes. It is a major constituent of azurophilic cytoplasmic granules that uses hydrogen peroxide to oxidise a variety of aromatic compounds and chloride ions to hypochlorous acid (HOCl), a strong oxidant. HOCl is the most bacteriocidal oxidant known to be produced by neutrophils. HOCl reacts with proteins to form cytotoxic chloramines. Myeloperoxidase is reported to be a major component in all myeloid cells, including mature granulocytes and is a superior marker to myeloperoxidase mRNA, whose level decreases with the maturation of the cell and is not detectable from the myelocyte stage onwards. Myeloperoxidase is reported to be expressed in neutrophil granulocytes and monocytes in blood, in precursors of granulocytes in the bone marrow and in Kupffer cells of the liver.

Refer to page 36 for the Bond ready-to-use format.

Human bone marrow, granulocytic sarcoma: immunohistochemical staining for myeloperoxidase using NCL-MYELO. Note intense cytoplasmic staining of malignant myeloid cells. Paraffin section.

Myoglobin

*Clone MYO18*
1 mL, 0.1 mL lyophilized NCL-MYOGLOBIN  **P** **W**
7 mL Bond ready-to-use PA0727 **P** (HIER)

Myoglobin is a cytoplasmic, single chain polypeptide of 153 amino acids that contains a single heme group. Myoglobin is reported to be expressed in skeletal and cardiac muscle but not in smooth muscle and functions as an oxygen transporting pigment.

Refer to page 36 for the Bond ready-to-use format.

Human adult skeletal muscle: immunohistochemical staining for myoglobin using NCL-MYOGLOBIN. Note cytoplasmic staining of muscle fibers. Paraffin section.

Myogenin (Myf-4)

*Clone LO26*
1 mL, 0.1 mL lyophilized NCL-Myf-4  **P** (HIER) **W**
1 mL liquid NCL-L-Myf-4  **P** (HIER) **W**
7 mL Bond ready-to-use PA0226 **P** (HIER)

Rhabdomyosarcomas are a class of myoblast-derived soft tissue sarcomas that usually express a number of muscle-specific genes and primarily affect children and young adults. Differentiation of myogenic cells is controlled by a set of regulatory genes including MyoD1, myogenin, Myf-5 and Myf-6. Myf-4 is the human homolog of myogenin. Its gene product, together with that of Myf-3, accumulates in the nucleus of differentiated cells.

Refer to page 36 for the Bond ready-to-use format.

Human rhabdomyosarcoma: immunohistochemical staining for Myf-4 protein using NCL-L-Myf-4. Note staining of a proportion of tumor cell nuclei. Paraffin section.
Myosin Heavy Chain Antibodies

**Clone S131**
1 mL, 0.1 mL lyophilized Myosin Heavy Chain (smooth muscle) NCL-MHC-Sm  F P (HIER)
7 mL Bond ready-to-use PA0493 P (HIER)

**Clone RNMy2/9D2**
1 mL, 0.1 mL lyophilized Myosin Heavy Chain (developmental) NCL-MHCd  F

**Clone WB-MHCf**
1 mL, 0.1 mL lyophilized Myosin Heavy Chain (fast) NCL-MHCf  F

**Clone WB-MHCn**
1 mL, 0.1 mL lyophilized Myosin Heavy Chain (neonatal) NCL-MHCn  F

**Clone WB-MHCs**
1 mL, 0.1 mL lyophilized Myosin Heavy Chain (slow) NCL-MHCs  F

Myosin is a contractile muscle specific protein composed of two heavy and four light chains. The myosin heavy chain has many isoforms which are specific for different muscles or fiber types, some of which are developmentally regulated. Smooth muscle myosin heavy chain (SM-MHC) is a cytoplasmic structural protein that is a major component of the contractile apparatus in smooth muscle cells. It has been reported to be specific for smooth muscle development.

Refer to page 36 for the Bond ready-to-use format.

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### Myotilin

**Clone RS034**
1 mL lyophilized NCL-MYOTILIN  F P (HIER)

The myotilin gene on chromosome 5q31 encodes a 498 amino acid polypeptide with a molecular weight of 57 kDa. Myotilin is a structural protein of sarcomeric Z discs and sarcolemma in human skeletal and cardiac muscle. It is homologous to palladin and titin in the two C-terminal Ig-domains and also to palladin in its unique serine-rich N-terminal region. Myotilin interacts with alpha-actinin, actin and gamma-filamin. A missense mutation in the myotilin gene is associated with limb-girdle muscular dystrophy 1A (LGMD1A), an autosomal dominant disease characterized by proximal limb weakness. It is highly conserved between human and mouse with its expression being more widespread in the embryo than in the adult. Expression of myotilin has been reported in adult skeletal and cardiac muscle with variable expression reported in the peripheral nervous system, lung, liver and kidney.

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### Napsin A

**Clone IP64**
1 mL, 0.1 mL liquid NCL-L-NapsinA  P (HIER)

Napsin A has a specific function in normal alveolar epithelium and is proposed to play a role in the proteolytic processing of surfactant precursors. Napsin A is reported to be predominantly expressed in lamellar bodies of type II pneumocytes, secondary lysosomes of alveolar macrophages, respiratory epithelium of terminal and respiratory bronchioles, plasma cells, within a subset of lymphocytes in normal lung as well as in epithelial cells of renal tubules in normal kidney and is weakly expressed in normal spleen. Past studies have also reported that Napsin A is expressed in 90 percent of primary lung adenocarcinomas.

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N-Cadherin

Clone IAR06
1 mL, 0.1 mL liquid NCL-L-N-Cad P (HIER)

N-Cadherin is a member of the cadherin family of calcium dependent cell adhesion molecules. The classical cadherins include the E, N, R, P and VE-Cadherins which are believed to be expressed in a tissue specific manner. The classical cadherins have a characteristic structure comprising an extra cellular calcium-binding domain, consisting of five repeats, a transmembrane domain and a highly conserved cytoplasmic domain, which mediates interactions with cytoskeletal components of the cell via interactions with intracellular proteins including the catenins. Cadherins play an important role in cell-cell adhesion, and are implicated in segregation and aggregation of tissues during development. N-Cadherin is reported to be expressed in various cell types including neural, myocardial and mesenchymal cells. During tumor progression increased N-Cadherin expression concomitant with the loss of E-Cadherin expression is one of the features of the epithelial to mesenchymal transition, which is associated with increased tumor invasion and poor prognosis. N-Cadherin has been proposed as a useful marker in a panel of antibodies to differentiate mesotheliomas from adenocarcinomas.

NCAM (CD56)

Clone CD564
1 mL, 0.1 mL lyophilized NCL-CD56-564 P (HIER)

Clone 1B6
1 mL, 0.1 mL lyophilized NCL-CD56-1B6 P (HIER) W
1 mL liquid NCL-L-CD56-1B6 P (HIER) W
7 mL ready-to-use RTU-CD56-1B6 P (HIER) W

See also CD56 (NCAM) on page 81.

Nerve Growth Factor Receptor (gp75)

Clone 7F10
1 mL, 0.1 mL lyophilized NCL-NGFR P (HIER)

Nerve growth factor receptor (NGFR) is a member of the nerve growth factor (NGF) tumor necrosis factor (TNF) superfamily of receptors. Nerve growth factor is important for the development, differentiation and survival of neurons and its action is mediated by the binding of two distinctive cell surface receptors; the high- affinity NGF R (TrkA ) and the low-affinity NGF R (gp75). The functional role of gp75 has not yet been fully elucidated. In vitro, unbound gp75 has been shown to promote neural cell death, whereas, binding of gp75 by NGF ligand or antibody has been shown to inhibit gp75-induced cell death. NGFR (gp75) is reported to be expressed in neuronal axons, Schwann cells and perineurial cells of peripheral nerves and in non-neural cells that includes myoepithelial cells of breast, salivary and sweat glands, outer root sheath cells of hair follicles, adventitia of mature blood vessels and a lymphocyte subpopulation in the spleen and lymph node. NGFR has also been reported to be expressed in a proportion of pheochromocytomas, paragangliomas and tumors of peripheral nerve sheath differentiation.

Product Specific Information

NCL-NGFR is raised to the gp75 low-affinity NGFR protein.

Neuroblastoma Marker

Clone NB84a
1 mL lyophilized NCL-NB84 F P C

Neuroblastoma is a complex malignant disease in children. This tumor of the sympathetic nervous system, derived from pathologically maturing neural crest progenitor cells, is unique among pediatric cancers because of spontaneous regressions and catecholamine excretions. In a major study, Mietten M et al., indicated the NB84 monoclonal antibody to be a useful reagent to separate neuroblastoma from other small round cell tumors. Most of the undifferentiated neuroblastomas in their study (21 of 22) and all 83 differentiated neuroblastomas reacted with NB84, but none of these tumors were CD99 positive. Compared with synaptophysin, NB84 was more sensitive, although less specific, in the identification of neuroblastoma in formaldehyde-fixed tissue. In addition to neuroblastoma, skeletal and extraskeletal Ewing’s sarcoma and medulloblastoma showed NB84 reactivity in approximately 20 percent of cases and 50 percent of desmoplastic small round cell tumors showed positive cells, usually in smaller numbers than the neuroblastomas. The NB84 reactivity was seen slightly more commonly in morphologically defined (rosette-positive) cases of peripheral primitive neuroectodermal tumors than in Ewing’s sarcoma. However, the NB84 positivity did not correlate with the expression of other neural markers (neurofilament proteins, CD57, and synaptophysin) in these tumors. All other small round cell tumors including rhabdomyosarcomas, Wilms’ tumors, and lymphomas were NB84 negative (Miettinen M et al., Am J Surg Pathol. 22(3):327-32 (1998)).

Product Specific Information

Enzyme pretreatment may enhance staining in some cases.
Neurofilament Antibodies

**Clone DA2**
1 mL lyophilized Neurofilament 68 kD
NCL-NF68-DA2  F P (HIER)

**Clone NR4**
1 mL lyophilized Neurofilament 68 kD
NCL-NF68  F P (HIER)

**Clone RT97**
1 mL lyophilized Neurofilament 200 kD
NCL-NF200  F P

**Clone N52.1.7**
1 mL lyophilized Neurofilament 200 kD
NCL-NF200-N52  F P (HIER)
7 mL Bond ready-to-use PA0371  P (HIER)

Neurofilaments constitute the main structural elements of neuronal axons and dendrites. Neurofilaments are composed of three major subunits referred to as the neurofilament triplet, with molecular weights of 68 kD, 160 kD and 200 kD. Neurofilament subunits are reported to be present in neurons, neuronal processes, peripheral nerves and sympathetic ganglion cells. Within tumors, only neoplastic cells of neural origin or those exhibiting neuronal differentiation, have been reported to express neurofilaments.

Refer to page 37 for the Bond ready-to-use format.

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Neuron Specific Enolase

**Clone 22C9**
1 mL lyophilized NCL-NSE-435  P W
7 mL Bond ready-to-use PA0435  P (HIER)

**Clone 5E2**
1 mL lyophilized NCL-NSE2  F P W
1 mL liquid NCL-L-NSE2  F P W
7 mL ready-to-use RTU-NSE2  F P

Enolase is a glycolytic enzyme catalysing the reaction pathway between 2-phosphoglycerate and phosphoenol pyruvate. In mammals, enolase molecules are dimers composed of three distinct subunits (α, β and γ) whereas, in rats, five forms have been found. The α subunit and γ subunit are of approximately 47 kD and 45 kD, respectively. The γβ and αγ γ enolases are located mainly in the nervous tissue and neuroendocrine cells.

**Product Specific Information**
Clone 2C9 was developed to produce superior staining on paraffin sections. Clone 22C9 reacts with the γ subunit of the enolase isoenzyme. Clone 5E2 reacts with the 47 kD component of the gamma-gamma enolase isoenzyme.

Refer to page 37 for the Bond ready-to-use format.

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Nitric Oxide Synthase Antibodies

**Clone NOS-125**
1 mL lyophilized Nitric Oxide Synthase-1
NCL-NOS-1  P (HIER)

**Clone RN5**
1 mL lyophilized Nitric Oxide Synthase-3
NCL-NOS-3  F P (HIER)

Human nitric oxide synthases are a family of enzymes responsible for the synthesis of nitric oxide from L-arginine and molecular oxygen. There are at least three nitric oxide synthases; NOS-1, also known as neuronal NOS or nNOS, NOS-2, which is referred to as inducible NOS or iNOS and NOS-3, also known as endothelial NOS or eNOS. As suggested by their nomenclature, these enzymes have different cellular distribution and are subjected to different regulatory mechanisms. NOS-3 is reported to be constitutively expressed and produces picomolar quantities of nitric oxide (NO) which play a role in signal transmission resulting in physiological effects. In the gastrointestinal tract, NO is reported to play a protective role where it has direct microbiocidal properties and acts as a first line of mucosal defence in the stomach. The function of NO in tumor development, promotion and progression is unclear. The effects may be both beneficial but also detrimental to those individuals with gastric cancer where it is reported that NO supports tumor progression through the creation of neovasculature.

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Human spinal cord, lumbar: immunohistochemical staining for the 68 kD neurofilament using NCL-NF68-DA2. Note intense cytoplasmic staining of perikarya and neuronal axons. Paraffin section.

Human small intestine: immunohistochemical staining for nitric oxide synthase-1 using NCL-NOS-1. Note cytoplasmic staining of enteric ganglia. Paraffin section.
nm23 Protein

**Clone 37.6**
1 mL lyophilized NCL-nm23  F  P  W

The nm23 gene was first identified by differential screening of mouse-derived melanoma cell lines of high and low metastatic potential. Two human homologs of the nm23 gene have been isolated and designated nm23-H1 and nm23-H2. The products of these genes have been identified as nucleoside diphosphate kinase A (NDPK-A) and nucleoside diphosphate kinase B (NDPK-B), respectively. nm23-H1 and nm23-H2 are metastasis-suppressor genes implicated in the control of the metastatic process of malignant cells.

**Product Specific Information**
NCL-nm23 reacts with H1 strongly and only weakly with the H2 homolog.

NS3 (Hepatitis C virus)

**Clone MMM33**
1 mL, 0.1 mL lyophilized NCL-HCV-NS3  F  P (HIER)

See also Hepatitis C virus (NS3) on page 118.

Nucleoporin (88 kD)

**Clone JRC1**
1 mL lyophilized NCL-Nup88  P (HIER)  W

Nuclear pore complexes are large, elaborate macromolecular structures that mediate bidirectional nucleocytoplasmic traffic. In vertebrates, nuclear pore complexes are made up of 50 to 100 proteins called nucleoporins (Nup). The 88 kD nucleoporin (Nup88) is associated with a dynamic subcomplex of oncogenic nucleoporin CAN/Nup 214. Nup88 may be regarded as a widely distributed proliferation marker that is reported to be overexpressed in oncogenesis and development. In cell lines, it is localized at the nuclear membrane. In malignancies, the protein is reported to be overexpressed with a perinuclear and cytoplasmic distribution. In hyperplasia, benign tumors and most normal tissues, Nup88 is reported to be either weakly expressed or undetectable.

Oct-2

**Clone Oct-207**
1 mL, 0.1 mL lyophilized NCL-OCT2  F  P (HIER)  Reference Range
7 mL Bond ready-to-use  PA0532  P (HIER)

Oct-2 is a transcription factor belonging to the POU homeo-domain family that binds to the Ig gene octamer sites regulating B cell specific genes. It is dependent on the activity of B cell restricted coactivators such as BOB.1/BOB.1. Oct-2 protein expression is not restricted to B cells, although expression levels are much higher in these cells. Reports indicate that germinal center B cells shows higher expression for Oct-2 and BOB.1. In addition, Oct-2 expression is reported to be significantly greater in germinal center derived lymphomas, although other B cell lymphomas also display high levels of expression. Reed Sternberg (RS) cells represent the malignant cells in classical Hodgkin’s disease and are derived from germinal center B cells. In a number of these cases, cells do not express immunoglobulin due to the presence of crippling mutations within the Ig genes. As Ig gene expression in B cells also requires an interaction between octamer sites and the transactivating factors Oct-2 and BOB.1, the absence of both Oct-2 and BOB.1 expression represents a novel mechanism for immunoglobulin gene deregulation in RS cells.

Refer to page 38 for the Bond ready-to-use format.

**Clone Oct-207**
1 mL, 0.1 mL lyophilized NCL-OCT2  F  P (HIER)  Reference Range
7 mL Bond ready-to-use  PA0532  P (HIER)

Oct-2 is a transcription factor belonging to the POU homeo-domain family that binds to the Ig gene octamer sites regulating B cell specific genes. It is dependent on the activity of B cell restricted coactivators such as BOB.1/BOB.1. Oct-2 protein expression is not restricted to B cells, although expression levels are much higher in these cells. Reports indicate that germinal center B cells shows higher expression for Oct-2 and BOB.1. In addition, Oct-2 expression is reported to be significantly greater in germinal center derived lymphomas, although other B cell lymphomas also display high levels of expression. Reed Sternberg (RS) cells represent the malignant cells in classical Hodgkin’s disease and are derived from germinal center B cells. In a number of these cases, cells do not express immunoglobulin due to the presence of crippling mutations within the Ig genes. As Ig gene expression in B cells also requires an interaction between octamer sites and the transactivating factors Oct-2 and BOB.1, the absence of both Oct-2 and BOB.1 expression represents a novel mechanism for immunoglobulin gene deregulation in RS cells.

Refer to page 38 for the Bond ready-to-use format.


Oct-3/4

**Clone N1NK**
1 mL, 0.1 mL liquid NCL-L-Oct3/4  P (HIER)  W
7 mL Bond ready-to-use  PA0934  P (HIER)

Oct3/4 is a member of the POU homeodomain family of transcription factors, which is expressed by embryonic stem cells and germ cells. A critical amount of Oct3/4 levels are associated with loss of pluripotency. Oct3/4 has been proposed as a useful marker for germ cell tumors which exhibit features of pluripotentiality, including seminoma/dysgerminoma and embryonal carcinoma, and establishing a germ cell origin for some metastatic tumors of uncertain primary tumor.

Refer to page 38 for the Bond ready-to-use format.

Osteonectin

**Clone 15G12**
1 mL, 0.1 mL lyophilized NCL-O-NECTIN P (HIER) W

Osteonectin (ON), also known as BM-40 or SPARC (secreted protein, acidic and rich in cysteine) is a multifunctional glycoprotein (32.5 kD) involved with tissue mineralization as well as extracellular matrix modelling. ON is the most abundant glycoprotein secreted by human osteoblasts in developing bone and odontoblasts of developing teeth. ON mRNA and protein have been reported to be expressed in non-mineralized tissues such as steroid-producing cells of the adrenal glands, suprabasal layers of the epidermis, glomeruli in the kidney, bronchi of the lung, megakaryocytes and large vessels. This organ-specific distribution of ON in non-mineralized tissues suggests a role during human development. It is also reported to be expressed in osteosarcomas, at high levels in osteoblastic osteosarcomas and at low levels in osteoid formation of the diffuse deposition type.

Osteopontin

**Clone OP3N**
1 mL, 0.1 mL lyophilized NCL-O-PONTIN P (HIER)

Osteopontin is a 34 kD extracellular matrix protein with a cell binding domain. Other molecules which share this domain include fibronectin, vitronectin and a variety of other extracellular proteins that bind members of the integrin family of cell surface receptors. Osteopontin was originally identified as a major component of the non-collagenous organic bone matrix, however, it has subsequently been demonstrated in a wide range of normal adult tissues and body fluids. It is a multifunctional protein involved in bone mineralization, cell adhesion, cell migration, chronic inflammatory disease and transformation. Osteopontin is reported to be linked to tumorigenesis and metastasis in several experimental animal models and human cancers. In breast carcinomas, demonstrated by RT-PCR and in situ hybridization studies, expression was confined to tumor cells. It is also reported to be expressed in normal breast, including vascular endothelial cells, macrophages, myoepithelial cells, osteosarcomas but not in lymphoid tumors. Other studies using in situ hybridization have shown expression in the epithelium of gastrointestinal tract, gall bladder, pancreas, urinary and reproductive tracts, lung, salivary and sweat glands. Ganglion cells in the bowel also express osteopontin as do macrophages, T cells and NK cells upon activation. Expression of osteopontin in vascular smooth muscle and endothelium may be triggered by atherosclerosis, vascular calcification and by hypertension.

Ovarian Cancer Antigen (CA125)

**Clone Ov185:1**
1 mL lyophilized NCL-CA125 F P (HIER) 
1 mL liquid NCL-L-CA125 F P (HIER) 
7 mL ready-to-use RTU-CA125 F P (HIER) 
7 mL Bond ready-to-use PA0539 P

See also CA125 (Ovarian Cancer Antigen) on page 64.

OX40 (CD134)

**Clone 102H6**
1 mL lyophilized NCL-CD134 F P (HIER)

See also CD134 (OX40) on page 86.

p21 (WAF1 Protein)

**Clone 4D10**
1 mL, 0.1 mL lyophilized NCL-WAF-1 P (HIER) 
1 mL liquid NCL-L-WAF-1 P (HIER)

See also WAF1 Protein (p21, C1P1) on page 170.

p27 Protein

**Clone 1B4**
1 mL, 0.1 mL lyophilized NCL-p27 P (HIER) W

p27 protein, also known as kinase inhibitory protein 1 (Kip1), binds to cyclin E/cdk2 complexes (but not to cdk2 alone) and is detected in purified extracts of growth-arrested cells. p27 protein constrains cell proliferation by setting the threshold level of cyclin E necessary to activate cdk2. The 27 kD protein is also present in proliferating cells but only in a sequestered form when it is unavailable to interact with cyclin E/cdk2 complexes. It is likely that cyclin D complexed with catalytically inactive cdk4 is sufficient to sequester p27 protein and titrate its function. The presence of bound p27 protein in proliferating cells suggests that its role may not be restricted to inducing cell cycle arrest but to also set the cyclin E threshold for execution of the G1 to S phase transition during each mitotic cycle.
p53 Protein

Clone IMX25
1 mL lyophilized NCL-p53-505 P (HIER) W
7 mL Bond ready-to-use PA0057 P (HIER)

p53 protein plays a vital role in suppressing the development of cancer. The accumulation of p53 protein in response to DNA damage in vitro is well established and appears to induce growth arrest and apoptosis by the transcriptional regulation of other genes. In irradiated mice, p53 protein accumulates in splenocytes, thymocytes and osteocytes, though not in hepatocytes. Mouse T3T3 cells express high levels of phenotypically characteristic wild type p53 protein which carries two missense mutations. The range of antigenic sites in mouse p53 protein and human p53 protein is very similar.

Product Specific Information
NCL-p53-505 is raised to the same recombinant mouse p53 protein as the polyclonal, NCL-p53-CM5p. It reacts with rat and mouse p53 protein.
Refer to page 38 for the Bond ready-to-use format.

Mouse T3T3 cells: immunohistochemical staining for p53 mouse protein using NCL-p53-505. Note intense nuclear staining of a proportion of T3T3 cells. Paraffin section.

p53 Protein (1801)

Clone PAb 1801
1 mL, 0.1 mL lyophilized NCL-p53-1801 F P (HIER) W C

The gene for p53 is located on chromosome 17p, a frequent site of allelic loss in many tumors. It has been reported that a high proportion of breast and colon carcinomas show immunostaining for p53 protein and expression of p53 protein.

Product Specific Information
Clone PAb 1801 recognizes both wild type and mutant forms of human p53 protein under denaturing and non-denaturing conditions.


p53 Protein (BP53-12)

Clone BP53-12
1 mL lyophilized NCL-p53-BP F P W

p53 protein plays a vital role in suppressing the development of cancer. The accumulation of p53 protein in response to DNA damage in vitro is well established and appears to induce growth arrest and apoptosis by the transcriptional regulation of other genes.

Product Specific Information
Clone BP53-12 recognizes both wild type and mutant forms of human p53 protein under denaturing and non-denaturing conditions. The heat induced epitope retrieval technique may improve staining in some cases.


p53 Protein (CM1)

Polyclonal
0.2 mL lyophilized NCL-p53-CM1 F P (HIER) W

Mutation of the p53 protein may represent the commonest genetic event in human malignancy. In colonic tumors, p53 protein has been reported to be overexpressed in 47 percent of carcinomas and only 9 percent of adenomas. No expression has been reported in normal mucosa.

Product Specific Information
This polyclonal antibody recognizes both wild type and mutant forms of human p53 protein under denaturing and non-denaturing conditions. NCL-p53-CM1 is less sensitive to overfixation than clone DO-7.

p53 Protein (CM5)

**Polyclonal**

0.2 mL lyophilized NCL-p53-CM5p **P (HIER) W**

The accumulation of p53 protein in response to genotoxic stress in vitro is well established and appears to induce growth arrest and apoptosis by the transcriptional regulation of other genes and possibly by other direct mechanisms.

**Product Specific Information**

NCL-p53-CM5p is specific for mouse and rat p53 protein.

![Western blot: detection of p53 protein (53 kD) using NCL-p53-CM5p. Lane A, molecular weight markers. Lane B, T3T3 mouse cell line immunoblotted with NCL-p53-CM5p.](image)

p53 Protein (DO-1)

**Clone DO-1**

1 mL lyophilized NCL-p53-DO1 **F P (HIER) W**

In man, the p53 gene is located on the small arm of chromosome 17. Alterations of the p53 tumor suppressor gene are a common feature of human malignancies. A normal function of this gene is to induce apoptosis after DNA damage and, therefore, its activation can permit the survival of cells that have sustained genetic damage.

**Product Specific Information**

Clone DO-1 recognizes both wild type and mutant forms of human p53 protein under denaturing and non-denaturing conditions. The epitope to which NCL-p53-DO1 maps is sited at the N-terminus at amino acids 20 – 25.

![Human colonic adenocarcinoma: immunohistochemical staining for p53 protein using NCL-p53-DO1. Note intense nuclear staining of tumor cells. Paraffin section.](image)

p53 Protein (Phosphospecific)

**Clone FP3-2**

1 mL lyophilized NCL-p53-PHOS **P (HIER) W**

p53 protein plays a vital role in suppressing the development of cancer. Post-translational modification by phosphorylation has been proposed to be an important regulatory mechanism of p53 function. Several p53 phosphorylation sites fall within or closely flank a number of functional domains within the p53 molecule including transcriptional transactivating, DNA binding and oligomerization sequences. Several p53 protein mutants are less phosphorylated than wild type p53 protein when expressed in vivo which may suggest that phosphorylation positively regulates DNA binding. However, other experiments have also suggested that phosphorylation may also negatively regulate DNA binding.

**Product Specific Information**

NCL-p53-PHOS is specific for the phosphorylated site on human p53 protein at Ser392 within the non-specific DNA binding/oligomerization region. The functional significance of phosphorylation at this site only, remains unclear.

![Human colonic adenocarcinoma: immunohistochemical staining for p53 protein using NCL-p53-PHOS. Note intense nuclear staining of tumor cells. Paraffin section.](image)
p57 Protein (Kip2)

Clone 25B2
1 mL, 0.1 mL lyophilized NCL-p57 P (HIER)
See also Kip2 (p57 Protein) on page 128.

p63 Protein

Clone 7JUL
1 mL, 0.1 mL lyophilized NCL-p63 F P (HIER)
7 mL Bond ready-to-use PA0478 P (HIER)

p63 is a member of the p53 gene family and encodes for at least six major isotypes with transactivating, death-inducing activities (TAp63) and also dominant-negative activities (deltaNp63). p63 protein is reported to be expressed in a variety of normal human and mouse tissues, including proliferating cells of epithelium, cervix, urothelium and prostate. p63 protein is also reported to be expressed in most poorly differentiated squamous cell carcinomas. In epithelial cells, the dominant isotype, deltaNp63, lacks an acidic N-terminus corresponding to the transactivating domain of p53. The deltaN-isotype is also reported to be abundantly expressed in nasopharyngeal carcinomas. p83 protein is required for prostate development and, in mice, it is essential for limb and epidermal morphogenesis. The human p63 gene is mutated in children with the disease Ectrodactyly Ectodermal Dysplasia and Facial Clefts syndrome. In contrast to the p53 gene, the p63 gene is rarely mutated in human cancer. p63 protein is reported not to be expressed in prostate adenocarcinoma but altered expression is a frequent event in bladder carcinogenesis.

Product Specific Information
Clone 7JUL is raised to a prokaryotic recombinant fusion protein corresponding to a region (aa319-410) common to six isoforms of the p63 molecule.
Refer to page 38 for the Bond ready-to-use format.

p73 Protein (alpha)

Clone 24
1 mL lyophilized NCL-p73 F P (HIER)
p73 protein was the first identified homolog of the tumor suppressor gene, p53. Overproduction of p73 protein reported in p53-defective tumor cells, activates p53-responsive promoters. This results in the induction of apoptosis but its function in tumor development is unclear. Alternative splicing produces at least six known p73 mRNA species resulting in p73 isoforms; alpha, beta, gamma, delta, epsilon and zeta. The relative expression level of each splice variant may modulate p73 transcriptional and growth suppression activity. p73 protein expression is reported to be low in normal tissues eg normal squamous epithelium. Elevated expression has been shown by RT-PCR and/or western blotting in a number of tumors including approximately 40 percent of breast carcinomas, 80 percent of lung tumors, 50 percent of ovarian tumors and 30 percent of hepatocellular carcinomas.

p80 (Anaplastic Lymphoma Kinase) (ALK) (CD246)

Clone 5A4
1 mL, 0.1 mL lyophilized NCL-ALK P (HIER)
7 mL Bond ready-to-use PA0306 P (HIER)
See also ALK (Anaplastic Lymphoma Kinase) (CD246) (p80) on page 54.

Papillomavirus Antibodies

Clone 5A3
2 mL, 0.1 mL lyophilized Papillomavirus (type 18) NCL-HPV18 F P (HIER)
Clone 4C4
2 mL, 0.1 mL lyophilized Papillomavirus (types 6, 11,18) NCL-HPV-4C4 F P (HIER)

Infection with specific types of human Papillomavirus (HPV) has been associated with an increased risk of developing cervical neoplasia. HPV types 6 and 11 have been associated with relatively benign diseases such as genital warts but types 16 and 18 are the causative agents of cervical, vaginal and vulvar malignancies.

Product Specific Information
NCL-HPV18 is specific for the L1 coat protein of HPV type 18. NCL-HPV-4C4 is specific for HPV types 6, 11 and 18.
Parathyroid Hormone

**Clone 105G7**
1 mL, 0.1 mL lyophilized NCL-PTH-488 P

The parathyroid glands are small, oval, endocrine glands closely associated with the thyroid gland. The parathyroid glands regulate serum calcium and phosphate levels via parathyroid hormone (parathormone). Parathyroid hormone raises serum calcium levels directly, by increasing the rate of osteoclastic reabsorption and promoting breakdown of the bone matrix, and indirectly, by increasing the renal tubular reabsorption of calcium ions and inhibiting the reabsorption of phosphate ions from the glomerular filtrate, and finally, by promoting the absorption of calcium from the small intestine. Parathyroid hormone is the most important regulator of blood calcium levels and is essential to life, whereas calcitonin appears only to provide a complementary mechanism for fine adjustment. Chief cells are the most abundant cells in the parathyroid gland and are responsible for the secretion of parathyroid hormone. Antibodies to parathyroid hormone together with antibodies to thyroglobulin are useful in studies to differentiate parathyroid-derived lesions from thyroid-derived lesions.

Parvalbumin (Alpha)

**Clone 2E11**
1 mL lyophilized NCL-PARVALBUMIN P (HIER)

Alpha and beta parvalbumins are low molecular weight, water-soluble, calcium-binding proteins. The protein is found in a subset of fast-spiking inhibitory GABAergic interneurons with a Ca2+ buffering capacity that reduces the Ca2+ -dependent K+ outward current. Unlike other Ca2+ binding proteins, parvalbumin-containing neurons appear to co-localize only with corticotropin-releasing factor and not with other neuropeptides associated with GABA such as somatostatin, neuropeptide Y and cholecystokinin. Neurons which contain parvalbumin appear to be resistant to ischemia, epilepsy and N-methyl-D-aspartate receptor agonists due to their ability to buffer increase in intracellular calcium. Alpha and beta parvalbumins are reported to be expressed in different human tissues with the alpha form highly expressed in extracts of human cerebellum, weakly in kidney and not in skeletal muscle, thymus, lung, placenta, heart, liver and diaphragm. The beta form of parvalbumin has been detected only in preterm placenta. These expression patterns differ significantly between human and rodent species with these differences also reflected with some members of the S-100 family of Ca2+ binding proteins. Within the cerebellum, alpha parvalbumin is reported to be localized to Purkinje, basket, stellate and Golgi cells. In cases of spinocerebellar ataxia-1 (SCA-1), the number of Purkinje cells expressing alpha parvalbumin is reported to be much reduced, which may reflect biochemical changes preceding Purkinje degeneration.

**Product Specific Information**

NCL-PARVALBUMIN does not detect parvalbumin in preterm placenta indicating its specificity for the alpha form of this protein.

Parvovirus B19

**Clone R92F6**
1 mL, 0.1 mL lyophilized NCL-PARVO F P

Parvovirus B19 is a small, single-stranded DNA virus which causes erythema infectiosum also known as ‘slapped cheek syndrome’. Clinically, this is a febrile disease in children, often epidemic, with a facial maculopapular rash causing flushed cheeks. In individuals with erythrocyte abnormalities, such as sickle cell anaemia, Parvovirus B19 can cause hemolytic complications where the virus replicates in bone marrow cells and inhibits erythropoiesis. Parvovirus B19 has also been implicated with spontaneous abortion in humans.

**Product Specific Information**

NCL-PARVO is specific for the viral antigens, VP1 (84 kD) and VP2 (58 kD).

Pax-5

**Clone 1EW**
1 mL liquid NCL-L-PAX-5 P (HIER) W
7 mL Bond ready-to-use PA0552 P (HIER)

Pax genes are a family of developmental control genes that encode nuclear transcription factors and have been implicated in the control of mammalian development. Pax-5 is a B cell specific transcription factor that is expressed in pro B cells, pre-B and mature B cells, and subsequently in all stages of B cell development until the plasma cell stage in which it is downregulated.

**Product Specific Information**

The use of H2O2 to block endogenous peroxidase has been shown to have a detrimental effect on the epitope recognized by Clone 1EW. It is, therefore, critical that blocking with H2O2 should be carried out after application of the primary antibody with solutions of no greater than 3 percent, otherwise staining intensity will be reduced.

Refer to page 39 for the Bond ready-to-use format.

**P-Cadherin**

**Clone 56C1**

1 mL lyophilized NCL-P-Cad  F P (HIER) W
1 mL liquid NCL-L-P-Cad  F P (HIER) W

P-cadherin, like E-cadherin, is a Ca$^{2+}$-dependent cell adhesion molecule and has a fundamental role in maintaining the integrity of multicellular structures. It is responsible for selective cell to cell adhesion. P-cadherin expression is reported to be restricted and the protein is only detected in the basal or parabasal layers of stratified epithelia. P-cadherin may contribute to the maintenance of the epithelial phenotype and be involved in the final stage of tumor progression in epidermal carcinomas. Changes in the pattern of P-cadherin expression have also been reported in breast and melanocytic cancers.

Human placenta: immunohistochemical staining for P-cadherin using NCL-L-P-Cad. Note intense membrane staining of cytotrophoblasts. Paraffin section.

**Peripherin**

**Clone PJM50**

1 mL lyophilized NCL-PERIPH  F P (HIER) W

Peripherin is a 57 kD type III intermediate filament protein that is expressed in peripheral neurons, including enteric ganglion cells. Peripherin is expressed in the developing peripheral nervous system and is highly enriched in neuronal derivatives of the neural crest. The expression or absence of peripherin may be used to demonstrate abnormalities of the enteric nervous system. The assessment of the density of ganglion cells is of importance in Hirschsprung’s disease (HD)-related disorders. Peripherin is also reported to be expressed in neural crest derived tumors such as neuroblastomas and ganglioneuroblastomas.

Human small bowel: immunohistochemical staining for peripherin using NCL-PERIPH. Note intense cytoplasmic staining of enteric ganglion cells and neural elements. Paraffin section.

**PECAM-1 (CD31)**

**Clone 1A10**

1 mL, 0.1 mL lyophilized NCL-CD31-1A10  P (HIER)
7 mL Bond ready-to-use PA0250  P (HIER)

See also CD31 (PECAM-1) on page 77.

Human follicular lymphoma: immunohistochemical staining for perforin using NCL-PERFORIN. Note focal granular staining of occasional cytotoxic T lymphocytes. Paraffin section.

**Perforin**

**Clone 5B10**

1 mL, 0.1 mL lyophilized NCL-PERFORIN  P (HIER)

Perforin is a pore-forming protein found in cytoplasmic granules of cytotoxic T-lymphocytes (CTLs). CTLs bind to cells which express foreign antigens and induce them to lyse. Perforin forms circular lesions on the target cell membrane similar to those induced by complement. Perforin and C9 share a high degree of homology particularly at the membrane spanning region. Perforin is reported to be constitutively expressed in human CD3 negative, CD56 positive NK cells, CD3 positive large granular lymphocytes and gamma/delta T cells. This expression is significantly induced in CD8 positive T cells but to a lesser extent in gamma/delta T cells and NK cells. The induction of perforin mRNA is partially blocked by the immunosuppressive drug cyclosporin A.
Primary Antibodies

PETA-3 (CD151)

Clone RLM30
1 mL lyophilized NCL-CD151 P (HIER)
See also CD151 (PETA-3) on page 87.

P-glycoprotein (CD243)

Clone 5B12
1 mL lyophilized NCL-PGLYm F P (HIER)
The resistance of tumor cells to cytotoxic chemotherapeutic drugs is a major problem in the treatment of cancer. Studies have linked the presence of a 170 to 180 kD cell membrane protein, P-glycoprotein, with resistance to a wide range of lipophilic chemotherapeutic drugs, a phenomenon known as multidrug resistance. P-glycoprotein is reported to be expressed in transporting epithelia of several normal tissues, including liver, kidney, colon, adrenal and brain.

Placental Alkaline Phosphatase

Clone 8A9
1 mL, 0.1 mL lyophilized NCL-PLAP-8A9 F P (HIER)
1 mL liquid NCL-L-PLAP-8A9 F P (HIER)
7 mL ready-to-use RTU-PLAP-8A9 F P (HIER)
7 mL Bond ready-to-use PA0161 P (HIER)
Placental alkaline phosphatase (PLAP) is a membrane-associated sialoglycoprotein enzyme normally present at high concentration in syncytiotrophoblasts within the placenta during the third trimester of gestation. The expression of PLAP was originally thought to be restricted to term placenta but a human PLAP-like variant has been described which shares more than 85 percent homology with PLAP itself. This high degree of homology between PLAP and PLAP-like enzyme together with cross-reacting antibodies has led to some confusion of the distribution of PLAP and PLAP-like enzyme in various tissues. PLAP is reported to be expressed only in normal term placenta, endocervix and fallopian tube and also in ovarian and proximal gastrointestinal tumors. PLAP expression is rare in malignant germ cell tumors. PLAP-like enzyme is reported to be predominantly found in normal fetal and neonatal testis, and in thymus. It is also commonly expressed in germ cell tumors and more recently described in seminomas.

Product Specific Information
Reports indicate that clone 8A9 stains seminomas and placenta indicating a specificity for both PLAP and PLAP-like enzyme.
Refer to page 39 for the Bond ready-to-use format.

Plasma Cell Marker

Clone LIV3G11
1 mL lyophilized NCL-PC P (Enzyme)
The plasma cell is the resultant terminal stage of B cell differentiation and apart from morphological features may be distinguished from other B cells by their lack of surface HLA class I and class II antigens, surface immunoglobulin, Fc and C3 receptors or presence of intracytoplasmic immunoglobulin. There have been some interesting studies where non-Hodgkin’s lymphomas have been differentiated from plasmacytomas and myelomas based on plasma cell markers (Seeegmiller et al., American Journal of Clinical Pathology. 127(2):172-174 (2007)).

Plasminogen Activator Inhibitor (Type 1)

Clone TJA6
1 mL, 0.1 mL lyophilized NCL-PAI-1 P
Plasminogen activator inhibitor (Type 1, PAI-1) is a 48 kD protein which inhibits the conversion of plasminogen to plasmin. It is the principal inhibitor of the plasminogen activators t-PA and u-PA. PAI-1 is structurally related to the serine protease inhibitor (serpin) superfamily. The serpins are known to undergo a conformational rearrangement upon cleavage of the reactive central peptide bond (P1-P1’) and it is this conformational difference between the active and cleaved forms which determine their reactivity. The PAI-1 protein is reported to be overexpressed in a number of malignancies including ovarian cancers and derived cell lines, endometrial cancers, cervical cancer, malignant brain cancers, nasopharyngeal carcinomas, breast tumors, head and neck squamous cell carcinomas and gastric cancers. PAI-1 is also reported to be expressed by endothelial cells and is stored in platelets.

Human ovarian adenocarcinoma: immunohistochemical staining for plasminogen activator inhibitor type 1 using NCL-PAI-1. Note intense cytoplasmic staining of malignant tumor cells. Paraffin section.

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Products in this catalog are subject to regulatory approval.
This catalog is not for use in the USA.
Platelet-Derived Endothelial Growth Factor

Clone P-GF.44C
1 mL, 0.1 mL lyophilized NCL-PDEGF P (HIER) W

Angiogenesis, the formation of new blood vessels from an existing vascular bed, is a complex multi-step process. It is controlled by a number of angiogenic factors, one of which is platelet-derived endothelial growth factor (PDEGF) also shown to be thymidine phosphorylase (TP). Angiogenesis is tightly regulated and is observed only transiently during reproduction, development and wound healing. PDEGF is reported to be expressed in the nucleus and cytoplasm, the highest expression being described in macrophages, stromal cells, glial cells and some epithelia. No expression is reported in gastro-intestinal epithelium, smooth muscle, adrenal glands, lung and testis. The high expression in macrophages and skin may be important for total body thymidine homeostasis.

Western blot: detection of platelet-derived endothelial growth factor (53 kD) using NCL-PDEGF. 
Lane A, molecular weight markers. Lane B, human tonsil immunoblotted with NCL-PDEGF.

Pneumolysin

Clone 9.1/2/3/6
1 mL lyophilized NCL-SPNm W

Pneumolysin is a 53 kD species-specific protein produced by all important strains of Streptococcus pneumoniae (pneumococcus), an organism which causes a wide range of human disease, from sinusitis and pneumonia to septicemia and meningitis.

Western blot: detection of pneumolysin (53 kD) using NCL-SPNm. Lane A, molecular weight markers. Lanes B to E, Streptococcus pneumoniae culture-positive sputum samples. Lane F, Streptococcus pneumoniae culture-negative but pneumolysin PCR-positive nasopharyngeal secretion. Lane G, Streptococcus pneumoniae culture-positive fluid from an infected joint.

Polyomavirus

Clone 3.1.1
1 mL, 0.1 mL lyophilized Polyomavirus (JC/BK viruses) NCL-JCBK I O

JC virus, a Polyomavirus of the Papovaviridae was first isolated from the brain of an individual with a rare demyelinating condition. JC and BK viruses are oncogenic in newborn hamsters and transform mammalian cells in vitro but there is no evidence that they cause human cancer. JC virus is ubiquitous in humans and may be occasionally shed in the urine without any apparent symptoms during pregnancy or immunosuppression. Unlike BK virus, also a Polyomavirus, JC virus may cause a lethal disease, progressive multifocal leukoencephalopathy (PML). PML is a rare subacute demyelinating disease of the CNS which is seen mainly as a complication of advanced disseminated malignant conditions such as Hodgkin’s disease or chronic lymphocytic leukemia and also in HIV infection or following immunosuppression for organ transplantation. The target cell of JC virus is the oligodendrocyte in which the virus undergoes a lytic productive infection. JC virus may be cultured from infected urine or brain in human fetal glial cells or detected directly in biopsy or post-mortem tissue.

Product Specific Information

NCL-JCBK, specific for both JC virus and BK virus, is effective in immunocytochemistry. NCL-JCBK does not cross-react with Respiratory syncytial virus, Param influenza virus types 1, 2, 3 and 4b, Adenovirus, Varicella-zoster virus, Herpes simplex virus types 1 and 2, Mumps virus, Measles virus, echovirus 19, Coxsackie B4 virus, Poliovirus types 1, 2 and 3 and Influenza virus types A and B.

Prealbumin

Polyclonal
1 mL lyophilized NCL-PREp F P (Enzyme)

Prealbumin, also known as transthyretin, is a 55 kD molecule synthesized in the liver. Prealbumin serves as a transport protein for thyroid hormones and vitamin A. Variant prealbumin has been identified as the major fibril subunit protein in several hereditary forms of systemic amyloidosis, including familial amyloid polyneuropathy types I and II.

Clone 16
2 mL lyophilized NCL-PGR-312/2 P (HIER) W
1 mL, 0.1 mL lyophilized NCL-PGR-312 P (HIER) W
2 mL liquid NCL-L-PGR-312/2 P (HIER) W
1 mL liquid NCL-L-PGR-312 P (HIER) W
7 mL ready-to-use RTU-PGR-312 P (HIER)
7 mL Bond ready-to-use PA0312 P (HIER)

Clone 1A6
2 mL lyophilized NCL-PGR/2 P (HIER) W
1 mL, 0.1 mL lyophilized NCL-PGR P (HIER) W
1 mL liquid NCL-L-PGR P (HIER) W
7 mL ready-to-use RTU-PGR P (HIER)

Clone 16 was developed to produce superior staining on paraffin sections.

The human progesterone receptor (PR) is expressed as two isoforms, PRA (94 kD) and PRB (114 kD), which function as ligand-activated transcription factors. These two isoforms are transcribed from distinct estrogen receptor (ER)-inducible promoters within a single copy PR gene. The PRA form is a truncated version of the PRB form, lacking the first 164 N-terminal amino acids. In humans, PRA acts as a transdominant repressor of the transcriptional activity of PRB, glucocorticoid receptor, ER, androgen receptor and mineralocorticoid receptor. PRB functions mainly as a transcriptional activator. PRB is expressed strongly in endometrial glandular and stromal nuclei in the proliferative phase of the menstrual cycle and weakly during the secretory phase and early pregnancy.

Product Specific Information
Clone 1A6 reacts with a homologous region to both the A and B forms of PR. Clone 16 is specific for a region of the N-terminus of the A form of PR. The precise epitope has not been mapped but it reacts with both A and B forms of PR by Western blot but only with the A form by immunohistochemistry. This suggests that the epitope is inaccessible in the native folded B form of the protein.

Refer to page 39 for the Bond ready-to-use format.

Progesterone Receptor

Progesterone and Estrogen Receptor Antibodies (duo packs)

Clone 6F11, Clone 1A6
2 x 1 mL lyophilized NCL-ER/PRGd/1 F P (HIER) W
2 x 0.5 mL lyophilized NCL-ER/PGRd F P (HIER) W

Clone 6F11, Clone 16
2 x 1 mL lyophilized NCL-ER/PGR-312d/1 F P (HIER) W
2 x 0.5 mL lyophilized NCL-ER/PGR-312d F P (HIER) W

See also Progesterone and Estrogen Receptor Antibodies (duo packs) on page 152.

Proinsulin

Clone 1G4
1 mL lyophilized NCL-PROIN-1G4 P (HIER)

Preproinsulin is converted to proinsulin by the action of a signal peptidase in the lumen of the endoplasmic reticulum within pancreatic beta cells. The proinsulin is then transported from the endoplasmic reticulum to the Golgi apparatus and is further modified by the action of various enzymes to yield the mature hormone, insulin. Insulinomas exhibit many structural features in common with normal beta cells. Studies of proinsulin and insulin have reported proinsulin/insulin expression patterns to vary greatly among those tumors and no correlation seems to exist between the expression staining patterns and a particular histological tumor type. A diffuse expression pattern may be observed for proinsulin which differs from the crescent-shaped perinuclear staining seen in normal beta cells suggesting abnormalities in the prohormone processing. This may be observed in about 50 percent of insulinomas.

Proliferating Cell Nuclear Antigen

Clone PC10
1 mL, 0.1 mL lyophilized NCL-PCNA P W C
1 mL liquid NCL-L-PCNA P W C

Proliferating cell nuclear antigen (PCNA) is a 36 kD protein which is highly conserved between species. PCNA functions as a co-factor for DNA polymerase delta in S phase and also during DNA synthesis associated with DNA damage repair mechanisms. The PCNA molecule has a half-life in excess of 20 hours, and therefore, may be detected in non-cycling cells eg those in G0 phase.

Product Specific Information
Heat induced epitope retrieval using 10mM citrate buffer (pH6.0) may improve staining on overfixed tissues, but due to increased sensitivity using this technique, care must be taken with the interpretation of results. Staining is reduced (and may be abolished) if sections are baked onto glass slides. Air drying overnight onto 3-aminopropyltriethoxysilane (Apes) coated slides may produce improved results.
Prostate Specific Antigen

**Clone 35H9**
1 mL, 0.1 mL lyophilized NCL-PSA-431
7 mL Bond ready-to-use PA0431 P (HIER)

**Clone PSA 28/A4**
1 mL liquid NCL-L-PSA-28A4 F P
7 mL ready-to-use RTU-PSA-28A4 F P

Clone 35H9 was developed to produce superior staining on paraffin sections.

Prostate specific antigen (PSA) is a 34 kDa protein belonging to the kallikrein family of serine proteases and was originally isolated and purified from human seminal plasma. It was found to be immunologically identical and biologically similar to a protein isolated from the prostate gland. PSA is distinct from prostatic acid phosphatase. Low levels of expression of PSA have been reported in non-prostatic tissues and tumors such as breast carcinomas.

Refer to page 39 for the Bond ready-to-use format.

Prostate Specific Membrane Antigen

**Clone 1D6**
1 mL liquid NCL-L-PSMA P (HIER)

The prostate specific membrane antigen (PSMA) is expressed as a 750 amino acid glycoprotein but may also be found as PSM, a form of the protein missing the first 57 amino acids. PSMA has two enzymatic activities, one as a prostate-specific integral membrane folate hydrolase and the other as a carboxypeptidase. Reports suggest that PSMA expression may correlate with tumor burden and serve as an indicator of metastatic involvement. The cellular localization of PSMA contrasts with that of prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) that are secreted proteins.

Prostate Tumor Overexpressed Protein 1

**Clone 17C6**
1 mL lyophilized NCL-PTOV1 P (HIER)

The gene prostate tumor overexpressed protein 1, or PTOV1, was discovered following the search for molecular markers of progression in prostate cancer. The prostate in ageing males is highly susceptible to benign and malignant proliferative changes. A number of genetic and molecular alterations are responsible for the phenotypic conversion of normal or hyperplastic prostate cells into malignant, invasive cells. In the most common form of prostate cancer, carcinomatous cells arise as multifocal lesions against a background of hyperplastic tissue, called the zone of benign peripheral hyperplasia. PTOV1 is reported to be expressed at significantly higher levels in prostate cancers than in benign prostatic hyperplasia or in normal prostate tissue. In addition, PTOV1 protein is overexpressed in premalignant cells from prostatic biopsies such as those with prostate intra-epithelial neoplasia and in advanced-stage prostate cancer cells. PTOV1 protein is located mainly in the cytoplasm with juxtanuclear positivity in tumor cells. The detection of a 1.8kb PTOV1 transcript has been reported in normal human brain, heart, skeletal muscle, kidney and liver and at lower levels in normal prostate.
Prostatic Acid Phosphatase

**Clone PASE/4LJ**
1 mL liquid NCL-L-PAP F P
7 mL Bond ready-to-use PA0006 P (HIER)

Prostatic acid phosphatase (PAP) is an isoenzyme of acid phosphatase found in large amounts in the prostate and seminal fluid. The precise function of PAP is unknown, but it may act as a hydrolase to split phosphoryl choline in semen and also function as a transferase. Elevated serum levels of the enzyme are reported in metastatic prostatic carcinoma.

Refer to page 40 for the Bond ready-to-use format.

Prostate adenocarcinoma: immunohistochemical staining with Prostatic Acid Phosphatase (PASE/4LJ) using Bond Polymer Refine Detection.

Prostatic Inhibin Peptide

**Clone 4A6A6**
1 mL lyophilized NCL-PIP P

Prostatic inhibin peptide (PIP), a 10.7 kD follicle stimulating hormone suppressing molecule, is synthesized and secreted by the prostate gland. PIP has been reported to be expressed in primary prostatic tumors and their metastases. PIP has also been reported to be expressed in the serum and urine of patients with prostatic cancer. PIP expression is unaffected by reduced or absent androgens unlike both PSA and PAP whose expression is dependent on androgens.

Prostate adenocarcinoma: immunohistochemical staining with prostatic inhibin peptide using NCL-PIP. Note cytoplasmic staining of glandular epithelium. Paraffin section.

Protein Gene Product 9.5

**Clone 10A1**
1 mL, 0.1 mL lyophilized NCL-L-PGP9.5 F P (HIER) W
1 mL liquid NCL-L-PGP9.5 F P (HIER) W
7 mL Bond ready-to-use PA0286 P (HIER)

Protein gene product (PGP) 9.5 is a neuron specific protein, structurally and immunologically distinct from neuron specific enolase. The protein which has a molecular weight of 27 kD was first identified by high resolution two dimensional PAGE. PGP9.5 expression has been reported in neurons and nerve fibers at all levels of the central and peripheral nervous system, in many neuroendocrine cells, in segments of the renal tubules, in spermatogonia and Leydig cells of the testis, in ova and in some cells of both the pregnant and non-pregnant corpus luteum. PGP9.5 is known to be a member of the ubiquitin C-terminal hydroxylase family and is also concentrated within inclusion bodies suggesting that such structures may be metabolically active regions of the cells.

Refer to page 40 for the Bond ready-to-use format.

Human breast carcinoma: immunohistochemical staining for prostatic inhibin peptide using NCL-PIP. Note cytoplasmic staining of glandular epithelium. Paraffin section.

pS2 Protein

**Polyclonal**
0.5 mL lyophilized NCL-pS2 F P

pS2, also known as pNR-2, was first identified by differential screening of cDNA libraries from estrogen responsive breast cancer cell lines. In normal tissue, pS2 protein is reported to be expressed in gastric mucosa, small intestinal mucosa and normal breast epithelium. pS2 is estrogen regulated in breast cancer cell lines and may have some growth factor activity. In malignant epithelial tumors, pS2 has been reported to be expressed in gastric carcinomas and gynecological cancers. The pS2 mRNA and protein are expressed predominantly in estrogen receptor positive breast cancers.

**P-selectin (CD62P)**

**Clone C34**
1 mL lyophilized NCL-CD62P-367 P (HIER)

The CD62P antigen (140 kD), also known as P-selectin, mediates the interaction of activated platelets with neutrophils and monocyes and is responsible for the rolling attachment of neutrophils to activated endothelium. CD62P antigen binds to the carbohydrate structures Sialyl-Lewis^x^ on neutrophils and to galactosyl ceramides on neutrophils and tumor cells. A soluble CD62P antigen inhibits the integrin-mediated adhesion of activated neutrophils to endothelium.


**PTEN**

**Clone 28H6**
1 mL, 0.1 mL lyophilized NCL-PTEN P (HIER)

PTEN, also known as MMAC1 or TEP1, is a tumor suppressor gene which encodes a multifunctional phosphatase which is expressed almost ubiquitously and regulates the cell cycle, apoptosis and possibly cell adhesion. PTEN also interacts with the focal adhesion kinase (FAK) reducing FAK phosphorylation affecting cell adhesion, spreading and recognition. In addition, PTEN may prevent resistance to apoptosis by dephosphorylating phosphatidylinositol 3, 4, 5-triphosphate. Deletions and mutations to PTEN occur in a range of cancers including breast cancer, malignant melanoma, endometrial carcinoma, bladder carcinoma, small cell lung carcinoma and endometrial ovarian cancer. Germline mutations of PTEN are found in Cowden syndrome which leads to a predisposition for breast and thyroid cancers. Loss of PTEN gene expression is reported to occur in both breast and prostate cancer.


**Renal Cell Carcinoma Marker**

**Clone 66.4.C2**
1 mL, 0.1 mL lyophilized NCL-RCC P (Enzyme)

In the normal kidney, a 200 kD glycoprotein is localized within the brush border of the pars convoluta and pars recta segments of the proximal renal tubule and on the luminal surface of Bowman’s capsule adjoining the outgoing proximal tubule. The glycoprotein, gp200, is also reported to be expressed on the luminal surface of breast lobules and ducts, the luminal surface of the epididymal tubular epithelium and within the colloid of thyroid follicles. Reports indicate gp200 antigen to be expressed in approximately 93 percent of primary and 84 percent of metastatic renal cell carcinomas.

**Product Specific Information**

NCL-RCC is specific for a proximal nephrogenic renal antigenic site on the carbohydrate domain of gp200.

**Respiratory syncytial virus**

**Clone 5H5N, 5A6, IC3 cocktail**
2 mL lyophilized NCL-RSV3 F P (HIER) I

Respiratory syncytial virus (RSV) is the most important respiratory pathogen of childhood and is responsible for approximately 50 percent of all cases of bronchiolitis and 25 percent of all cases of pneumonia during the first few months of life. Approximately one percent of babies who develop an RSV infection between two and six months die, particularly those with congenital heart defects, bronchopulmonary dysplasia, low birth weight or immunodeficiency. The virus is also associated with significant lower respiratory disease in elderly and immunosuppressed individuals in whom mortality rates may be high. Multiple types and subtypes of RSV cocirculate in the population.

**Product Specific Information**

NCL-RSV3 is a cocktail of four antibodies. NCL-RSV3 does not cross-react with Parainfluenza virus types 1, 2, 3 and 4b, Adenovirus, Mumps virus, Measles virus, Influenza virus types A and B, Poliovirus types 1, 2 and 3, Coxsackie B4 virus, echovirus 19, Varicella-zoster virus, Cytomegalovirus and Herpes simplex virus types 1 and 2.
Retinoblastoma Gene Protein

Clone 13A10
1 mL, 0.1 mL lyophilized NCL-RB-358 F P (HIER) W
1 mL liquid NCL-L-RB-358 F P (HIER) W

Clone 1F8
1 mL lyophilized NCL-RB F P (HIER) W

Clone 13A10 was developed to produce superior staining on paraffin sections.

Retinoblastoma (Rb) is a rare tumor of the retina associated with mutations of chromosome 13. The nuclear phosphoprotein encoded by the Rb tumor suppressor gene is present in many cells and may indirectly regulate cell growth by activating the transcription factor ATF-2. Activation of ATF-2 initiates expression of TGF-beta2, which in turn inhibits transcription of genes affecting cell growth. Bilateral mutation of the Rb gene may potentially play a role in the development of a number of malignant tumors.

Product Specific Information
NCL-RB-358 was raised to the N-terminal region of the Rb gene protein.

ret Oncoprotein

Clone 3F8
1 mL, 0.1 mL lyophilized NCL-RET P (HIER)

The ret proto-oncogene encodes a cell surface glycoprotein belonging to a member of the receptor tyrosine kinase family and is located on chromosome 10q11.2. Three main 3' splice isoforms have been characterized from papillary thyroid carcinomas, themselves originating from thyroid epithelial cells. ret expression is reported in several regions of the central nervous system; in the developing cranial nerve ganglia and a subset of cells within dorsal root ganglia, in motor neurons in the spinal cord and hindbrain, in neuroretina and the growing tips of the renal collecting ducts in developing kidney. Some individuals with Hirschsprung’s disease have severe developmental abnormalities of the kidney and these phenotypic abnormalities may be linked with mutations of ret proto-oncogene. About 70 percent of individuals who carry one of the documented ret mutations that predispose to multiple endocrine neoplasia type II (MENII) will develop thyroid C cell derived tumors in their lifetime.

Product Specific Information
NCL-RET was raised to the intracellular domain of the molecule, present in all isoforms of the protein. Mutations are reported to occur upstream of this domain.

RHAMM (CD168)

Clone 2D6
1 mL lyophilized NCL-CD168 F P (HIER)

Refer to page 88 for further information about CD168.
Primary Antibodies

S-100

Clone S1/61/69
1 mL, 0.1 mL lyophilized NCL-S100 F P

Polyclonal
1 mL lyophilized NCL-S100p F P
1 mL liquid polyclonal NCL-L-S100p F P
7 mL ready-to-use RTU-S100p F P
7 mL Bond ready-to-use PA0900 P (Enzyme)

S-100A and S-100B proteins are two members of the S-100 family of proteins. S-100A is composed of an alpha and beta chain whereas S-100B is composed of two beta chains. S-100 protein is reported to be expressed in neuroectodermal tissue, including nerves and melanocytes. Langerhans cells in skin and interdigitating reticulum cells in the paracortex of lymph nodes are also reported to express S-100 protein. It is noteworthy that S-100 protein is highly soluble and may be eluted from frozen tissue during immunohistochemical procedures.

Product Specific Information

NCL-S100 is specific for the A form of S-100 and so is not recommended for the staining of neural elements. NCL-S100p, NCL-L-S100p and RTU-S100p may require enzyme pretreatment in some cases and are also reactive with S-100 protein from cow, chicken, pig, dog, cat, monkey, horse, mouse and rat. NCL-S100 may require heat induced epitope retrieval (HIER) in some cases.

Refer to page 40 for the Bond ready-to-use format.

S100A7 (Psoriasin)

Clone 3DC
1 mL liquid NCL-L-S100-A7 P (HIER)

S100A7, also known as psoriasin, is a member of the S-100 gene family of calcium binding proteins which regulate a variety of intracellular and extracellular processes. It is largely, although not entirely, reported to be confined to stratified squamous epithelium. Reports indicate that in breast cancer, high levels of S100A7 are associated with estrogen and progesterone receptor negative status and nodal metastasis. It is also reported to be expressed in abnormal keratinization in squamous cell carcinoma.

Human malignant melanoma: immunohistochemical staining for S100A7 using NCL-L-S100A7. Note intense staining of tumor cells. Paraffin section.

Sarcoglycan Antibodies

Clone Ad1/20A6
1 mL, 0.1 mL lyophilized sarcoglycan, alpha (adhalin) NCL-a-SARC F W E
1 mL liquid sarcoglycan, alpha (adhalin) NCL-L-a-SARC F W E

Clone βSarc1/5B1
1 mL, 0.1 mL lyophilized sarcoglycan, beta NCL-b-SARC F E
1 mL liquid sarcoglycan, beta NCL-L-b-SARC F E

Clone δSarc3/12C1
1 mL lyophilized sarcoglycan, delta NCL-d-SARC F W

Clone 35DAG/21B5
1 mL, 0.1 mL lyophilized sarcoglycan, gamma NCL-g-SARC F E

In normal skeletal muscle, dystrophin, the protein product of the gene which is defective in Duchenne and Becker muscular dystrophy, is attached to the muscle membrane via a complex of at least seven proteins (dystrophin associated glycoproteins, DAGs). Dystrophin-deficient muscle shows a generalized reduction in DAG labeling. Recent studies have shown that expression of different members of the dystrophin glycoprotein complex are altered in several types of muscular dystrophy: the picture is complex and disease classification is currently under review. For example, individuals with LGMD2D have mutations in the gene for alpha-sarcoglycan, those with LGMD2E have mutations in the beta-sarcoglycan gene, and those with LGMD2F have mutations in the delta-sarcoglycan gene. Also, many individuals with severe childhood autosomal recessive muscular dystrophy (SCARMD) show defective expression in the sarcoglycan subgroup of complex proteins which includes alpha-sarcoglycan (adhalin) and gamma sarcoglycan. As the sarcoglycans function together as a subcomplex, individuals with mutations in any one of the sarcoglycan genes usually show reduced expression for the whole group, but the reduction may be most severe for the mutated single protein. Labeling for beta-spectrin is necessary to monitor membrane integrity.

Western blot: detection of alpha-sarcoglycan (50 kD) using NCL-L-a-SARC. Lane A, molecular weight markers. Lane B, human muscle extract immunoblotted with NCL-L-a-SARC.
Sarcoplasmic or Endoplasmic Reticulum Ca\(^{2+}\) ATPase (SERCA) Antibodies

**Clone IID8**

0.5 mL lyophilized NCL-SERCA2  F P

ATP-dependent calcium pumps are responsible in part for the maintenance of low cytoplasmic free Ca\(^{2+}\) ion concentrations. The ATP pumps that are located in intracellular organelles are encoded by a family of structurally related enzymes termed the sarcoplasmic or endoplasmic reticulum Ca\(^{2+}\) ATPases (SERCA). The SERCA1 gene is exclusively expressed in type II (fast) skeletal muscle. The SERCA2 gene is subject to tissue dependent processing which is responsible for the generation of two specific isoforms. SERCA2a muscle-specific isoform is reported to be expressed in type I (slow) skeletal, cardiac and smooth muscle whilst the SERCA2b isoform is reported to be expressed in all cell types. The SERCA3 gene is less well characterized and is found in non-muscle cells.

Serotonin

**Polyclonal**

0.5 mL lyophilized NCL-SEROTp  P
7 mL Bond ready-to-use PA0736  P (HIER)

Serotonin (5-hydroxytryptamine, 5-HT) is reported to be a widely distributed neurotransmitter and hormone in the mammalian peripheral and central nervous system (CNS). Serotonin is formed by the decarboxylation of 5-hydroxy-tryptophan, its intermediate, which in turn is formed by hydroxylation of L-tryptophan by tryptophan hydroxylase. In the CNS, the action of serotonin is terminated by reuptake into the presynaptic terminal by specific serotonin transporters. Serotonin has been implicated in several neuropsychiatric disorders such as anxiety, depression and schizophrenia. The majority of serotoninergic nerve terminals in the CNS originate in neuronal cell bodies of the Raphe nuclei (dorsal, median), nucleus Raphe obscurus and nucleus Raphe pallidus in the brainstem which project to specific areas of the brain and spinal cord. Serotonin is thought to be an inhibitory neurotransmitter regulating a wide range of sensory, motor and cortical functions in the CNS. In the periphery, serotonin is reported to be present in neural and non-neural structures such as platelets, gastrointestinal tract (myenteric plexus, enterochromaffin cells), lungs (neuroepithelial cells), thyroid gland and spleen.

Refer to page 40 for the Bond ready-to-use format.

**Sialyl Lewis\(^{-}\) (CA19-9)**

**Clone C241:5:1:4**

1 mL lyophilized NCL-CA19-9  P (HIER)
1 mL liquid NCL-L-CA19-9  P (HIER)

Refer to page 64 for further information about CA19-9.

**SM22 alpha**

**Clone 10H12**

1 mL liquid NCL-L-SM22a  P (HIER)  W

SM22 alpha, also known as smooth muscle cell specific protein, is reported to be expressed at high levels in various tissues such as intestine, lung and uterus. It shares structural homology with the regulatory protein, calponin. SM22 alpha expression has been reported in most tissues that contain smooth muscle in both vascular and visceral forms. It is also reported to be expressed in some rare malignant tumors such as malignant fibrous histiocytomas.

**SMA (Alpha Smooth Muscle Actin)**

**Clone αsm-1**

1 mL lyophilized NCL-SMA  P (Enzyme)  W
7 mL ready-to-use RTU-SMA  P (Enzyme)
7 mL Bond ready-to-use PA0943  P

Refer to page 57 for further information about Alpha Smooth Muscle Actin.
Primary Antibodies

Snap-25
Clone SP12
0.5 mL lyophilized NCL-SNAP-25 P (HIER) W

The release of neurotransmitters from neurons is regulated by exocytosis of synaptic vesicles. Exocytosis is mediated by a complex consisting of membrane components of both the synaptic vesicle and the synaptic plasma membrane. Synaptosomal-associated protein of 25 kD (SNAP-25) is a plasmalemmal protein and is one of four proteins which are thought to make up an initial docking complex for regulated exocytosis. SNAP-25 lacks a transmembrane domain, but is linked to the membrane by palmitoylated cysteine residues in the central region of the molecule. SNAP-25 has been reported to be expressed in tumor cells of prolactinomas, growth hormone secreting tumors and the granule cell layer and molecular layers of the cerebellum.

Superoxide Dismutase (Cu/Zn)
Clone 30F11
1 mL lyophilized NCL-SOD1 P (HIER) W

Superoxide dismutase (SOD) is an enzyme which catalyzes the dismutation of superoxide anion to oxygen and hydrogen peroxide. These enzymes are metalloproteins classified according to the metal ion which is a necessary cofactor for enzymic activity. Their function is to act as a cellular defence mechanism against oxidative damage caused by superoxide radicals produced as a by-product of aerobic metabolism. Almost all eukaryotic cells have a mitochondrial and cytoplasmic SOD. The cytoplasmic enzyme is a dimer of identical subunits with each subunit containing one Zn and one Cu atom, the latter being involved as an electron acceptor in the dismutation reaction. The distribution of cells containing the copper/zinc SOD enzyme (SOD1) in the hippocampi from normal humans and individuals with Alzheimer’s disease (AD) has been studied. Reports indicated a higher level of SOD1 in subsets of hippocampal neurons, pyramidal and granule cells, in AD. The gene for SOD1 is carried on chromosome 21 and in Down’s syndrome, increased SOD1 activity reflects a gene dosage effect where high levels of SOD1 mRNA have been identified. These individuals develop an accelerated ageing of the brain and histopathological changes are reminiscent to that of AD.

Surfactant Precursor Protein B
Clone 19H7
1 mL, 0.1 mL lyophilized NCL-SPPB P (HIER)

Pulmonary surfactant is a phospholipid-rich mixture that reduces the surface tension at the alveolar air-liquid interface, providing alveolar stability necessary for normal ventilation. Four distinct proteins which have been isolated from pulmonary surfactant are SP-A, SP-B, SP-C and SP-D. Surfactant precursor protein B (pro-SP-B) with a molecular weight of 42 kD undergoes proteolytic processing resulting in a 9 kD non-collagenous hydrophobic pulmonary surfactant, SP-B. SP-B mRNA has been detected in both type II cells and in bronchiolar epithelial cells of adult human, mouse, rat and rabbit lung. Pro-SP-B protein and SP-B mRNA have been reported to be found in approximately 60 percent and 53 percent of pulmonary adenocarcinomas, respectively, with expression noted in adenocarcinomas with acinar, papillary, bronchoalveolar and solid growth patterns. Squamous cell and large cell carcinomas of the lung and nonpulmonary adenocarcinomas are reported not to express pro-SP-B or SP-B.

Western blot: detection of human beta-spectrin (253 kD in muscle) using NCL-SPEC1. Lane A, molecular weight markers. Lane B, urea extract of human muscle immunoblotted with NCL-SPEC1.

Surfactant Precursor Protein B


Spectrin Antibodies

Clone RBC2/3D5
1 mL lyophilized Spectrin (recommended for human use) NCL-SPEC1 F W E

Clone RBC1/5B1
1 mL lyophilized Spectrin (broad spectrum) NCL-SPEC2 F

Spectrin is a cytoskeletal protein which has some structural homology with dystrophin, the protein that is defective in Duchenne and Becker muscular dystrophy. Subtle membrane damage frequently occurs during the excision and freezing of muscle samples. Labeling for spectrin is necessary to monitor membrane integrity. It is reported that fibers which show negative labeling for both dystrophin and spectrin are damaged (or in the early stages of regeneration), whereas fibers which are negative for dystrophin but positive for spectrin reflect true abnormalities of dystrophin expression.

Product Specific Information

NCL-SPEC1 and NCL-SPEC2 recognize the beta chain of spectrin in erythrocytes and muscle. NCL-SPEC1 reacts with human beta-spectrin whereas NCL-SPEC2 reacts moderately with human beta-spectrin and weakly with rabbit, rat, mouse and dog beta-spectrin.
Primary Antibodies

Surfactant Protein A

Clone 32E12
1 mL, 0.1 mL lyophilized NCL-SP-A P (HIER)

Pulmonary surfactant plays a critical role in maintaining the structural integrity of the respiratory epithelium by reducing surface tension during expiration. It is a lipoprotein complex which is synthesized and secreted into the alveoli of the lung by type II pneumocytes. Lung surfactant protein-A (SP-A) is a major phospholipid-associated glycoprotein in surfactant and is a member of the C-type lectin superfamily that also inhibits lipid secretion and enhances the uptake of phospholipid by alveolar type II cells. Levels of SP-A in amniotic fluid are reported to reflect the degree of fetal lung maturity and inadequate levels of surfactant at birth, a frequent occurrence in premature infants, results in respiratory failure. In individuals with lung adenocarcinomas, high concentrations of SP-A have been reported in pleural effusions except in poorly differentiated lung adenocarcinomas where a significant decrease of SP-A immunoreactivity has been reported (Zamecnik J and Kodek R. Virchows Arch. 440(4): 353-61 (2002).

Synaptic Vesicle Protein 2

Clone 15E11
1 mL lyophilized NCL-SV2 P (HIER)

Synaptic vesicle protein 2 (SV2) is an integral membrane glycoprotein. It is required for normal neurotransmission and may play a role in the regulation of calcium-stimulated exocytosis. SV2 exists in three isoforms, SV2A, SV2B and SV2C, each containing 12 transmembrane spanning regions. SV2 proteins are reported to be among the most abundant and conserved components of synaptic vesicles in vertebrates. They are present on all small synaptic vesicles independent of transmitter type. SV2A and SV2B are reported to be widely distributed in the nervous system, whereas SV2C is only observed in a small number of neurons in a few areas of the brain. In the brain, SV2A is reported to be expressed at the highest levels in subcortical regions, whereas the highest level of expression of SV2B is in the cortex and hippocampus. SV2 is also reported to be expressed on secretory vesicles of neuroendocrine cells in the gastrointestinal tract, pancreas, anterior pituitary gland, thyroid, parathyroid and adrenal medulla and also in exocrine chief cells of gastric mucosa.

Product Specific Information

NCL-SV2 is raised to the N-terminal cytoplasmic region of the SV2A isoform.

Synaptophysin

Clone 27G12
1 mL, 0.1 mL lyophilized NCL-SYNAP-299 F P (HIER) W
1 mL liquid NCL-L-SYNAP-299 F P (HIER) W
7 mL ready-to-use RTU-SYNAP-299 F P (HIER)
7 mL Bond ready-to-use PA0299 P (HIER)

Synaptophysin is an integral membrane glycoprotein with a molecular weight of 38 kD. It is reported to occur in presynaptic vesicles of neurons in brain, spinal cord, retina, in similar vesicles of the adrenal medulla as well as in neuromuscular junctions. Synaptophysin may be involved in synaptic vesicle formation and exocytosis. Synaptophysin is reported to be expressed in a wide spectrum of neuroendocrine tumors including neuroblastomas, ganglioneuroblastomas, pheochromocytomas, chromaffin and non-chromaffin paragangliomas. Synaptophysin is also reported to be expressed in neuroendocrine tumors of epithelial type including pituitary adenomas, islet cell tumors, medullary carcinomas of thyroid, parathyroid adenomas, carcinoids of the bronchopulmonary and gastrointestinal tracts, neuroendocrine carcinomas of the bronchopulmonary and gastrointestinal tract and neuroendocrine carcinomas of the skin.

Refer to page 41 for the Bond ready-to-use format.
Breast carcinoma showing neuroendocrine differentiation: immunohistochemical staining for synaptophysin using NCL-SYNAP-299. Note cytoplasmic staining of tumor cells. Paraffin section.

**Synuclein, Alpha**

**Clone KM51**

1 mL liquid NCL-L-ASYN P (HIER)

Refer to page 57 for further information about Alpha-Synuclein.

**Tartrate-Resistant Acid Phosphatase (TRAP)**

**Clone 26E5**

1 mL, 0.1 mL lyophilized NCL-TRAP P (HIER)  
7 mL Bond ready-to-use PA0093 P (HIER)  

Tartrate-resistant acid phosphatase (TRAP) is a basic, iron-binding protein with high activity towards phosphoproteins, ATP and 4-nitrophenyl phosphate. This isoenzyme has been reported through different applications to be expressed in human alveolar macrophages, osteoclasts, spleen and liver. Expression of TRAP is reported to be increased in the spleen and monocytes of individuals with Gaucher’s disease, Hodgkin’s disease and the sera of individuals undergoing active bone turnover. Elevated levels are also reported to be associated with various B cell and T cell leukemias and lymphomas, decidual cells, syncytiotrophoblasts and some macrophages distributed throughout maternal and embryonic tissues.

Refer to page 41 for the Bond ready-to-use format.

Human osteoclastoma: immunohistochemical staining for tartrate-resistant acid phosphatase using NCL-TRAP. Note intense cytoplasmic staining of osteoclasts. Paraffin section.

**Tau**

**Clone Tau-2**

1 mL, 0.1 mL lyophilized NCL-Tau-2 P (HIER)  

The brain tissues from individuals with Alzheimer’s disease are characterized by an abundance of neurofibrillary tangles, neuropi threads and abnormal neurites in senile plaques. Tangles represent dense accumulations of ultrastructurally distinct paired helical filaments whose major component is a microtubule-associated tau protein.

**Product Specific Information**

NCL-Tau-2, raised against the bovine tau protein, cross-reacts with the phosphorylated form of human tau protein.


**Tenascin C**

**Clone 49**

1 mL lyophilized NCL-TENAS-C F P (HIER+Enzyme)  

Tenascin is a high molecular weight glycoprotein which has a unique molecular structure containing domains homologous to epidermal growth factor, fibronectin and fibrinogen. There are at least five members of the tenascin family, tenascin C (TN-C), TN-R, TN-X, TN-Y and TN-W4. Tenascin C was originally called tenasin. Tenasin itself was previously known as myotendinous antigen and is thought to play a role in organizing the growth of the extracellular matrix eg in wound healing. In addition, the presence of tenasin on type III fibers on the inner periosteum and outer cortex of bone appears to be important for normal osteogenesis. The expression of tenasin is reported to correlate with cell proliferation and migration. Like fibronectin, tenasin is a cell-substrate adhesive molecule that shares the ‘arginine-glycine-aspartic acid’ sequence necessary for ligand recognition by most integrins.

**Product Specific Information**

The heat induced epitope retrieval (HIER) technique followed immediately by 30 seconds of enzyme digestion produces optimal staining with NCL-TENAS-C.

Human breast carcinoma: immunohistochemical staining for tenascin using NCL-TENAS-C. Note intercellular matrix staining around malignant cells. Paraffin section.
Terminal Deoxynucleotidyl Transferase

**Clone SEN28**
1 mL, 0.1 mL lyophilized NCL-Tdt-339 P (HIER) W
1 mL liquid NCL-L-Tdt-339 P (HIER) W
7 mL ready-to-use RTU-Tdt-339 P (HIER)
7 mL Bond ready-to-use PA0339 P (HIER)

Terminal deoxynucleotidyl transferase (TdT) is a DNA polymerase of 58 kD located in the cell nucleus which catalyzes the polymerization of deoxynucleotides at the 3' hydroxyl ends of oligo or polydeoxynucleotide initiators and functions without a template. TdT is reported to be expressed in primitive T and B lymphocytes of the normal thymus and bone marrow. The identification of TdT-positive cell populations in primary and secondary lymphoid organs during maturation of the immune system is one area of interest but it is the reported occurrence of high levels of enzyme activity in white blood cells and bone marrow in certain leukemias which is of particular interest. Early and precise differentiation of lymphoblastic lymphoma is crucial. TdT is reported to be expressed in lymphoblastic lymphomas and leukemias. The determination of TdT expression is reported to be most valuable when it is difficult to differentiate histologically between lymphoblastic lymphoma and Burkitt’s lymphoma.

Refer to page 42 for the Bond ready-to-use format.

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Thymus and Activation-Regulated Chemokine

**Clone 6SN**
1 mL lyophilized NCL-TARC P (HIER)

The attraction of leukocytes to sites of inflammation is a process controlled by chemokines. Chemokines are a group of proteins of 8 to 10 kD that are divided into four families based on their first two cysteine residues in the conserved motif. Thymus and activation-regulated chemokine (TARC) functions as a selective chemoattractant for T cells which express a class of receptors binding TARC with high affinity and specificity. TARC has been identified as the specific ligand for the CC chemokine receptor 4 (CCR4) which is preferentially expressed at high levels in activated T helper 2 (Th2) cells. It is reported to be constitutively expressed in the dendritic cells of the thymus and transiently in activated peripheral blood mononuclear cells. It is present in the cell cytoplasm with frequent paranuclear condensation. Reports indicate that TARC is overexpressed in nodular sclerosis (NS) and mixed cellularity (MC) classical Hodgkin’s disease but not in non-Hodgkin’s lymphomas, anaplastic large cell lymphomas and large B cell lymphomas with CD30 positivity. Reed Sternberg cells of NS and MC Hodgkin’s lymphomas show high levels of TARC protein. Furthermore, in classical Hodgkin’s disease, TARC’s ability to attract activated T cells by strong association to the chemokine receptor, CCR4, may explain the characteristic T cell infiltrate. It has also been suggested that TARC may also play a role in platelet activation, via CCR4, seen in Th2-associated diseases such as asthma and atopic dermatitis.

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Thrombomodulin (CD141)

**Clone 15C8**
1 mL, 0.1 mL lyophilized NCL-CD141 F P (HIER)

Thrombomodulin is a transmembrane glycoprotein of 75 kD which can accelerate the activation of protein C. Activated protein C functions as an anticoagulant by combining with protein S to inactivate factors Va and VIIIa of the blood coagulation pathway and by binding thrombin. Several factors regulate thrombomodulin expression. Downregulation of thrombomodulin may be induced by the cytokine interleukin-1, tumor necrosis factor and endotoxin. Agents which increase cyclic AMP such as forskolin may upregulate thrombomodulin activity in endothelial cells. Thrombomodulin has been identified within a number of normal tissues. These include the lining cells of arteries, veins, capillaries and the lymphatics as well as mesothelial cells, meningeal lining cells, synovial cells, syncytiotrophoblasts, megakaryocytes and platelets. It is reported that in oral squamous cell carcinomas, the reduction of thrombomodulin expression may play a role in metastasis. Thrombomodulin protein is reported to be absent from most pulmonary adenocarcinomas but is expressed in malignant pleural mesotheliomas, vascular tumors and choriocarcinomas.

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Thyroglobulin

**Clone 1D4**
1 mL liquid NCL-L-THY F P
7 mL Bond ready-to-use PA0025 P

Thyroglobulin is a heavily glycosylated protein of 670kD composed of two identical subunits and is synthesized by the follicular epithelial cells of the thyroid. Thyroglobulin provides iodination sites for the formation of the thyroid hormones.

Refer to page 42 for the Bond ready-to-use format.
Thyroid Peroxidase

Clone AC25
1 mL liquid NCL-L-TPO P (HIER)
Thyroid Peroxidase gene expression is under the regulation of thyroid stimulating hormone (TSH). In normal thyroid, expression of Thyroid Peroxidase (TPO) described immunohistochemically is reported to produce a diffuse, fine, granular cytoplasmic stain in all follicular cells. Some studies have shown qualitative, as well as quantitative differences in thyroid peroxidase expression in thyroid cancer compared to normal tissue.

Product Specific Information
NCL-L-TPO stains optimally when used in TBS-based wash buffer and diluent systems.

Thyroid Stimulating Hormone

Clone QB2/6
1 mL lyophilized NCL-TSH F P (Enzyme)
7 mL Bond ready-to-use PA0776 P (Enzyme)
Thyroid stimulating hormone (TSH) is a pituitary hormone of 28 kD which stimulates thyroid growth and production of thyroid hormones. TSH is reported to be expressed in thyrotrophic cells of the pituitary and pituitary adenomas. Refer to page 42 for the Bond ready-to-use format.

Thyroid Transcription Factor-1

Clone SPT24
1 mL, 0.1 mL lyophilized NCL-TTF-1 F P (HIER) W
1 mL liquid NCL-L-TTF-1 F P (HIER) W
7 mL Bond ready-to-use PA0364 P (HIER)
Thyroid transcription factor-1 (TTF-1) is a member of the homeodomain transcription factor family and plays a role in regulating genes expressed within the thyroid, lung and brain. These include thyroglobulin, thyroid peroxidase, Clara cell secretory protein and surfactant proteins. Human TTF-1 is a single polypeptide of 371 amino acids sharing 98 percent homology with the equivalent rat and mouse proteins. TTF-1 functions by binding to specific recognition sites in a manner that may be regulated by both the redox and phosphorylation status of the protein. In addition to its role as a tissue-specific transcriptional activator in adult organs, TTF-1 may also function in organogenesis. Gene targeting studies have shown TTF-1 to be essential for the proper development of the thyroid and lungs and abnormal expression may underline a number of congenital abnormalities. TTF-1 has been reported to be expressed in greater than 90 percent of pulmonary small cell carcinomas and in 75 percent of pulmonary non-small cell carcinomas but it is not expressed in typical pulmonary carcinoids. TTF-1 is also reported to be expressed in papillary, follicular carcinomas and goitre, a non-malignant swelling of the thyroid, but not in anaplastic thyroid carcinomas. Refer to page 42 for the Bond ready-to-use format.
Tissue Inhibitor of Matrix Metalloproteinase Antibodies

**Clone 6F6a**
1 mL lyophilized Tissue Inhibitor of Matrix Metalloproteinase 1 NCL-TIMP1-485 P (HIER) W

**Clone 46E5**
1 mL lyophilized Tissue Inhibitor of Matrix Metalloproteinase 2 NCL-TIMP2-487 P (HIER) W

**Clone 18D12b**
1 mL lyophilized Tissue Inhibitor of Matrix Metalloproteinase 3 NCL-TIMP3 F P

The tissue inhibitors of metalloproteinas (TIMPs) are natural inhibitors of matrix metalloproteinas (MMPs), a group of zinc-binding endopeptides involved in degradation of the extracellular matrix (ECM). The remodelling of the ECM in a controlled fashion is essential during normal development and is a feature of physiological remodelling such as in wound healing. Tumor cell invasion and metastasis closely correlate with the activities of two MMPs, MMP2 and MMP9, both of which degrade type IV collagen in basement membranes. TIMPs constitute a family of at least four types of protein of which two of these are expressed in a wide variety of cell types. Although TIMP2 inhibits all types of activated MMPs to varying degrees, it is known to preferentially inhibit MMP2. TIMP2 also binds to proMMP9 and proMMP2 to form stable complexes in which activation of the proenzymes occur. Studies have revealed that TIMP2 can inhibit the invasive potential of tumor cells in vitro and their metastatic phenotype in vivo. TIMP3 is secreted into the ECM and complexes with MMP1, 3, 7, 9, 13, 14 and 15 deactivating them irreversibly. TIMP3 mRNA is highly expressed in placenta but is also reported to be found in the heart, kidney, lung, pancreas, uterus and skeletal muscle with low levels in the brain. In early placenta, TIMP2 and TIMP3 mRNAs are reported to be found in cells of cytotrophoblastic columns and decidua membrane. In endometrium, TIMP3 is reported to be expressed in luminal epithelium, glands, stroma, endothelial cells and vascular smooth muscle cells. In adult rat cerebellum, TIMP3 is reported to be expressed in Purkinje cell somata and processes. TIMP3 is expressed by fibroblast-like cells in ulcerated intestinal wall and in surrounding vessels and sweat glands during wound healing in skin. In breast carcinoma, TIMP3 mRNA expression is described in fibroblastic cells within the tumor stroma adjacent to cancer cells.

TNFR1-Associated Death Domain Protein

**Clone 18A11**
1 mL lyophilized NCL-TRADD P (HIER)

TNFR1-Associated Death Domain Protein is also known as TRADD. Death receptors of the TNF receptor family contain an intracellular death domain that serves to recruit adaptor proteins such as TRADD and FADD and cysteine proteases such as caspase-8. TRADD is a 34 kDa protein containing a death domain within its C-terminus which associates with the death domain of TNFR1. Activation of TNFR1 or overexpression of TRADD induces two opposite signalling pathways, caspase activation of apoptosis induction and NF-kappaB activation for anti-apoptosis gene upregulation. Stat1 directly interacts with TNFR1 and TRADD, but not with FADD, and acts as a TNFR1-signalling molecule to suppress NF-kappaB activation. TRADD is also known to interact with the Epstein-Barr virus (EBV) latent membrane protein 1 (LMP1), the major oncogene of EBV. Human TRADD is reported to be constitutively expressed at low levels in all tissues, while mouse TRADD mRNA is expressed at higher levels in spleen, lung, liver and kidney and at lower levels in brain, skeletal muscle and tests.

TNF-Related Apoptosis-Inducing Ligand (TRAIL)

**Clone 27B12**
1 mL lyophilized NCL-TRAIL P (HIER)

TRAIL (TNF-related apoptosis-inducing ligand), or APO-2L, is a 281 amino acid cytotoxic protein closely related to Fas/APO-1 ligand with the characteristic structure of a type II membrane protein. TRAIL induces extensive apoptosis in lymphoid as well as nonlymphoid tumor cell lines. Two TRAIL membrane receptors, DR4 and DR5, have been identified which are capable of mediating apoptosis and are distinct from Fas/APO-1 and TNF receptors. TRAIL induced apoptosis in target cells is mediated by the activation of caspases. Normal tissues are resistant to TRAIL as they are reported to express high levels of decoy membrane receptors, DcR1/TRID and DcR2/TRUNDD which antagonize TRAIL-induced apoptosis. TRAIL induces apoptosis in a number of different tumor cell types because most transformed cells express little DcR1. TRAIL mRNA is expressed in spleen, lung, prostate, ovary and bowel with little expression in testis, heart, skeletal muscle and pancreas. TRAIL protein is reported to be expressed on CD4 and CD8 positive T lymphocytes following activation and is also predominant in first trimester placental syncytiotrophoblasts as well as Hofbauer cells.
Human prostatic carcinoma: immunohistochemical staining for TNF-related apoptosis-inducing ligand using NCL-TRAIL. Note cytoplasmic staining of a proportion of malignant cells. Paraffin section.

Topoisomerase I

Clone 1D6
1 mL lyophilized NCL-TOPO I F P (HIER)

Topoisomerases are nuclear enzymes involved in a variety of cellular activities such as chromosomal condensation, DNA replication, transcription, recombination and segregation at mitosis. Human topoisomerase I is a 100 kD protein capable of relaxing positively and negatively supercoiled DNA by performing a transient single-stranded nick which is then re-ligated at the end of the reaction. It has been shown that the enzyme is located in regions of the genome that are undergoing active RNA synthesis where it probably reduces superhelical stresses in the DNA enabling RNA polymerase to function properly. In normal eukaryotic cells, DNA topoisomerase I does not show relevant fluctuations across the cell cycle, unlike DNA topoisomerase II alpha. Both DNA topoisomerases I and II have been found to be targets of autoantibodies in the sera of individuals with certain autoimmune diseases eg systemic lupus erythematosus and also of some anti-tumor drugs and antibiotics. Elevated levels of DNA topoisomerase I, detected by $^{32}$P transfer assays, have been reported in colorectal tumors compared with normal colon mucosa as a result of increased transcription or mRNA stability.

Product Specific Information
The use of phosphate-containing wash buffers or diluents with NCL-TOPO I has an adverse effect on staining. Only Tris-containing wash buffers or diluents should be used.

Toxoplasma gondii P30 Antigen

Clone TP3
1 mL lyophilized NCL-TG P (HIER)

Toxoplasma gondii is a ubiquitous protozoan parasite which can infect healthy humans, often asymptptomatically, but may also cause severe congenital defects in the fetus and life-threatening infection in immunocompromised hosts. It has been shown that P30, also referred to as SAG-1, the major surface antigen of Toxoplasma gondii tachyzoites is involved in the first steps of invasion. This antigen has been reported to have generated interest as a potential subunit for vaccine production. P30 is a highly conserved antigen between most strains of Toxoplasma gondii.
Transforming Growth Factor Beta

**Clone TGFB17**
1 mL, 0.1 mL lyophilized NCL-TGFB P (HIER)

Transforming growth factor beta (TGFB) is a potent cell regulatory polypeptide homodimer of 25 kD. It variably affects cell growth, differentiation and other aspects of cellular metabolism such as extracellular matrix production. Its effect depends upon the cell type and other growth factors present but in general, TGFB inhibits the growth of epithelial cells and stimulates the growth of mesenchymal cells. Most breast lesions, benign and malignant, involve abnormal proliferation and altered architecture of stromal and/or epithelial elements. Inflammatory cells present in the earliest lesions of progressive systemic sclerosis (PSS) are reported to release TGFB possibly resulting in chemotactic recruitment of additional chronic inflammatory cells. Platelets, a rich source of TGFB, are known to exhibit aggregability and may contribute to the etiology of PSS.

![Human breast carcinoma: immunohistochemical staining for transforming growth factor beta using NCL-TGFB. Note cytoplasmic staining of tumor cells. Paraffin section.](image1)

Transforming Growth Factor Beta Receptor (Type 1)

**Clone 8A11**
1 mL, 0.1 mL lyophilized NCL-TGFB1 P (HIER)

Transforming growth factor beta (TGFB) is a potent cell regulatory polypeptide homodimer of 25 kD. It variably affects cell growth, differentiation and other aspects of cellular metabolism such as extracellular matrix production. Its effect depends upon the cell type and other growth factors present but in general, TGFB inhibits the growth of epithelial cells and stimulates the growth of mesenchymal cells. Most breast lesions, benign and malignant, involve abnormal proliferation and altered architecture of stromal and/or epithelial elements. Platelets, a rich source of TGFB, are known to exhibit aggregability and may contribute to the etiology of PSS.

![Human colon, ulcerative colitis: immunohistochemical staining for transforming growth factor beta receptor (type 1) using NCL-TGFB1. Note membrane staining of a proportion of epithelial cells and lymphocytes. Paraffin section.](image2)

Troponin Antibodies

**Clone 1A2**
1 mL lyophilized troponin C NCL-TROPC P

**Clone T1/61**
1 mL lyophilized troponin C NCL-TROPT F P (Enzyme) W

Troponin comprises three protein subunits, troponin C, troponin I and troponin T. It is a contractile protein which comprises 5 percent of muscle proteins. Troponin C, an 18 kD protein, binds calcium and is responsible for regulating the process of thin filament activation during skeletal muscle contraction. Troponin I, a 21 kD protein, is the inhibitory subunit of the complex and troponin T is responsible for binding the troponin subunits to tropomyosin, a 66 kD protein that links the troponin complex to the actin helix. The troponin C gene is reported to be expressed in three distinct striated muscle lineages; cardiac myocytes, embryonic fast skeletal myotubules and adult slow skeletal myocytes. Reports have indicated that cardiac myofibers from cardiomyopathic rodent models display decreased Ca^{2+} sensitivity and that this property is a result of an alteration in the troponin/tropomyosin regulatory complex in the fibers.

**Product Specific Information**

NCL-TROPT reacts with human and chicken fast muscle troponin, but not slow muscle troponin T.

![Human skeletal muscle: immunohistochemical staining for troponin T using NCL-TROPT. Note intense staining of fast muscle fibers. Paraffin section.](image3)

Tuberin

**Clone 3B4**
1 mL lyophilized NCL-TUBERIN P (HIER)

Tuberin is the 180 kD protein product of the tuberous sclerosis (TSC-2) gene located on chromosome 16. Tuberous sclerosis is an autosomal disorder known as phakomatosis which is characterized by the widespread development of benign growths, usually described as hamartomata, in many tissues and organs. Tuberin is widely expressed at low levels in most human tissues, with increased expression in cortical neurons, cerebellar Purkinje cells, motor neurons of the spinal cord, pancreatic islet B cells, cardiac muscle and small blood vessels of the kidney and skin.

![Human cerebellum: immunohistochemical staining for tuberin using NCL-TUBERIN. Note cytoplasmic staining of Purkinje cells. Paraffin section.](image4)

For detailed information on all products please visit our website:
www.leica-microsystems.com

Products in this catalog are subject to regulatory approval.
This catalog is not for use in the USA.
**Tubulin Beta II**

**Clone KNY-379**
1 mL lyophilized NCL-TUB-B2 P (HIER) W

Tubulin beta II is one of four subunits of tubulin. Tubulin is one of the most widespread classes of multiprotein families where alpha and beta subunits are used in the construction of microtubules. Studies in rats report that tubulin beta II represents a significant proportion of beta tubulin expressed in the adrenal gland, brain and testis. In fetal tissues, this isoform has been reported in skeletal muscle as well as in brain. Expression has also been reported in migrating neuroblasts, peripheral nerves, ganglion cells and sensory organs of the developing rat nervous system and in developing skeletal and smooth muscle cells, chondrocytes and vascular endothelia.

**Product Specific Information**
Clone KNY-379 does not cross-react with vimentin or nestin.

**Tyrosinase**

**Clone T311**
1 mL lyophilized NCL-TYROS F P (HIER)
1 mL liquid NCL-L-TYROS F P (HIER)
7 mL ready-to-use RTU-TYROS F P (HIER)
7 mL Bond ready-to-use PA0322 P (HIER)

The biosynthesis of melanin within melanocytes involves a family of enzymes, a key member of which is tyrosinase. Tyrosinase deficiency is associated with various forms of albinism and in particular oculocutaneous albinism. L-tyrosine is the initial substrate for melanin biosynthesis and its conversion to dopaquinone is catalyzed by tyrosinase whose expression is reported in melanocytes and melanomas.

**Product Specific Information**
NCL-L-TRAF-1 stains optimally when used in TBS-based wash buffer and diluent systems.

**Tumor Necrosis Factor Receptor-Associated Factor 1**

**Clone 7C11**
1 mL liquid NCL-L-TRAF-1 P (HIER)

TNF receptor-associated factors (Traf) are a family of proteins that bind to surface receptors forming signalling complexes with additional proteins that mediate some cellular responses. Traf-1 can homodimerize or heterodimerize with other Traf proteins leading to the activation of some transcription factors such as nuclear factor kappa B and Jun-N-kinase. The activation of nuclear factor kappa B is known to act in concert with additional proteins to suppress TNF-alpha mediated apoptosis. The expression of this protein is reported to be induced by Epstein-Barr Virus (EBV).

**Product Specific Information**
NCL-L-TRAF-1 stains optimally when used in TBS-based wash buffer and diluent systems.
Tyrosinase-Related Protein-1

Clone G3E6
1 mL lyophilized NCL-TRP-1 P (HIER)

Tyrosinase-related protein-1 (TRP-1) is a member of a family of proteins which are involved in melanin biosynthesis. The catalytic function of TRP-1 has not been fully resolved but the enzyme appears to be important in the oxidation of 5,6-dihydroxyindole-2-carboxylic acid to form a high molecular weight pigmented biopolymer. In mammals, there are two basic types of melanin, the brown-black eumelanin and the reddish-yellow phaeomelanin. The concentrations of each are variable and are not related to skin type. In skin exposed to suberythemal doses of UVB, an increase in the number of melanocytes expressing TRP-1 and TRP-2 is reported with no increase in the number of tyrosinase-expressing melanocytes. In normal, untreated skin the number of melanocytes that express either TRP-1, TRP-2 or tyrosinase are similar irrespective of skin type. TRP-1 is also reported to be expressed in more than 50 percent of choroidal melanocytes in the adult eye.

Ubiquitin

Clone FPM1
1 mL lyophilized NCL-UBIQm P

Polyclonal
1 mL lyophilized NCL-UBIQ F P

Ubiquitin, a small protein consisting of 76 amino acids, has been reported to be found in all eukaryotic cells studied. It is one of the most conserved proteins known. Ubiquitin is required for ATP-dependent, non-lysosomal intracellular protein degradation, which eliminates most intracellular defective proteins as well as normal proteins with a rapid turnover. Degradation involves covalent binding of ubiquitin to the protein to be degraded and it is believed that in this way ubiquitin acts to label the protein for disposal by intracellular proteases. The most abundant ubiquitin-protein conjugate, however, is ubiquitin-histone H2A. This conjugate is not degraded. Since such ubiquitinated histones are present primarily in actively transcribed chromosomal regions, ubiquitin may play a role in regulation of gene expression.

Tyrosine Hydroxylase

Clone 1B5
1 mL, 0.1 mL lyophilized NCL-TH P (HIER) W

Tyrosine hydroxylase is the first enzyme in catecholamine (CA) biosynthesis and catalyzes the conversion of L-tyrosine to L-DOPA. Tyrosine hydroxylase is reported to be expressed in all CA neurons. Despite the abundant data about the distribution of catecholaminergic neurons in a wide variety of species, data on their distribution in the human brain is less comprehensive. However, one such study has reported that tyrosine hydroxylase products in the substantia nigra were restricted to neural bodies, axons and dendrites. These in turn were restricted to the third decade of life and their number increased in this location with age. This finding may be related to ageing of melanin-pigmented neurons.

Product Specific Information

NCL-TH is reactive with tyrosine hydroxylase in human, mouse and rat brain tissue.

Utrophin

Clone DRP3/20C5
2.5 mL, 1 mL lyophilized NCL-DRP2 F E

Utrophin, located on chromosome 6, is a ubiquitously expressed homologue of dystrophin and is known as dystrophin-related protein. In normal muscle, utrophin is restricted to neuromuscular junctions. However, in dystrophin-deficient muscle, utrophin expression is reported to be upregulated and appears around the periphery of most fibres. Utrophin has a role as a cell anchoring molecule. The amino terminal region of utrophin binds to the actin cytoskeleton, acting as an intracellular anchor whereas the carboxyl terminal regions bind to a group of proteins anchored in the cell membrane.

Varicella-zoster virus

Clone C90.2.8
1 mL lyophilized Varicella-zoster virus NCL-VZV P I

Varicella-zoster virus is a member of the alphaherpesvirinae. It is responsible for two ubiquitous diseases: varicella (chickenpox), an exanthem of childhood, and herpes zoster (shingles), a disabling disease of the elderly and immunocompromised individuals.

Product Specific Information

NCL-VZV is specific for Varicella-zoster virus and does not cross-react with Respiratory syncytial virus, Parainfluenza virus types 1, 2, 3 and 4b, Adenovirus, Herpes simplex virus types 1 and 2, Influenza virus types A and B, Mumps virus, Measles virus, echovirus 19, Coxsackie B4 virus and Poliovirus types 1, 2 and 3.
Vascular Endothelial Growth Factor Receptor-3

**Clone KLT9**
1 mL liquid NCL-L-VEGFR-3  P

VEGFR-3 (FLT4) is a receptor tyrosine kinase similar in structure to VEGFR-1 and VEGFR-2 but does not bind VEGF. However, the two known ligands have a high degree of homology to VEGF and are known as VEGF-C and VEGF-D. VEGFR-3 is reported to be found in many tissues including lung, intestine, brain and placenta (syncytiotrophoblasts). Throughout embryogenesis, VEGFR-3 mRNA is expressed in most endothelial cells, whilst being restricted to lymphatic vessels later in development. It appears to play an important role in the normal development of blood and lymphatic vessels. In tumors, expression has been reported in blood capillary endothelium and VEGFR-3 is thought to be involved in angiogenesis during tumor growth.


VE-Cadherin (CD144)

**Clone 33E1**
1 mL liquid NCL-L-VE-Cad  P (HIER)

Vascular endothelial cadherin (VE-Cadherin) is a calcium dependant molecule involved in the adhesion cells to the extracellular matrix. VE-Cadherin is localized to the intracellular junctions of endothelial layers, such as those of blood and lymphatic vessels and placenta. VE-Cadherin is unique among the adherin proteins as it is expressed only in the endothelial layers. VE-Cadherin has been reported to be used to identify tumors derived from endothelial tissue.

Human angiosarcoma: immunohistochemical staining for VE-Cadherin using NCL-L-VE-Cad. Note staining of malignant endothelial cells. Paraffin section.

Vesicular Monoamine Transporter (VMAT) Antibodies

**Clone RMT77**
1 mL, 0.1 mL liquid Vesicular Monoamine Transporter 1 (VMAT1) NCL-L-VMAT1  P (HIER)

**Clone NN 136**
1 mL, 0.1 mL liquid Vesicular Monoamine Transporter 2 (VMAT2) NCL-L-VMAT2  P (HIER)

Vesicular monoamine transporters (VMAT1 and VMAT2) mediate monoamine accumulation from the cytoplasm into storage organelles. They are dependent on a vacuolar ATPase-generated proton gradient to transport the cationic amine substrates into the storage organelle in exchange for protons. VMAT1 is a glycoprotein, located in the membranes of secretory granules/vesicles and is expressed in enterochromaffin (EC) cells and adrenal chromaffin cells. The presence of secretory vesicles is reported in tumor cells and is regarded as evidence of neuroendocrine differentiation. Demonstration of secretory granules in tumor cells has been reported using electron microscopy or immunohistochemistry. Specific hormone production cannot always be demonstrated in endocrine tumors, whose origin and biological behavior may be difficult to determine. Vesicular monoamine transporter (VMAT2) mediates the monoamine accumulation from the cytoplasm into storage organelles and is located in the membranes of the secretory granules/vesicles. VMAT2 is reported to be coexpressed in all chromaffin cells of the adrenal medulla. It is also reported to be expressed in gastric enterochromaffin-like cells, beta cells of the pancreas, Langerhans cells of the skin and a population of central, peripheral and enteric neurons.

Human infiltrating carcinoid of the bowel: immunohistochemical staining for vesicular monoamine transporter 1 (VMAT1) using NCL-L-VMAT1. Note intense cytoplasmic staining of malignant cells. Paraffin section.
Villin

**Clone CWWB1**
1 mL, 0.1 mL lyophilized NCL-VILLIN F P (HIER) W
1 mL liquid NCL-L-VILLIN F P (HIER) W
7 mL Bond ready-to-use PA0106 P (HIER)

Villin and the structurally-related proteins gelsolin, fragmin and severin, all regulate the framework and assembly of actin. Villin is unique among these proteins in its ability to cross-link actin filaments into bundles, a process observed only at low Ca²⁺ concentration. Villin is composed of three domains. The first two domains are homologous and the third domain is called the “headpiece”. This “headpiece” region is located at the C-terminus. Villin is mainly produced by epithelial cells that develop a brush border. Cells producing villin are reported to be found either in the epithelial cells of the intestinal mucosa and gall bladder, or in epithelial cells of the kidney proximal tubules and ductuli efferentes of the tests. However, villin is also reported to be found in some epithelia which lack a brush border but which are derived from embryonic gut such as duct cells of the exocrine pancreas and biliary cells of the liver. In these cell types, villin is concentrated in the apical cytoplasm. Epithelial cells of the intestinal mucosa are continually being renewed and this involves a migration of these cell types from the intestinal crypts to the tips of the villi, gradually acquiring their differentiated phenotype as they do so. The maximum production of villin occurs at the base of the villus. Villin, therefore, shows tissue-specific expression being restricted to certain epithelia and their apical domains, thus indicating their polarity. The morphological loss of polarity of colonic epithelial cells is reported to be one of the most significant indicators of dysplasia or neoplasia.

Refer to page 43 for the Bond ready-to-use format.

Vimentin

**Clone SRL33**
1 mL, 0.1 mL liquid NCL-L-VIM-572 P (HIER) W
7 mL Bond ready-to-use PA0033 P (HIER)

**Clone V9**
1 mL, 0.1 mL lyophilized NCL-VIM-V9 F P (HIER) W
1 mL liquid NCL-L-VIM-V9 F P (HIER) W
7 mL ready-to-use RTU-VIM-V9 F P (HIER)

**Clone VIM 3B4**
1 mL lyophilized NCL-VIM F P (Enzyme) W

Eukaryotic cells contain a number of types of cytoplasmic filamentous proteins, microtubule, microfilaments and intermediate-sized filaments (IF). Vimentin, a 57 kD protein that is an intermediate filament is reported to be expressed in most cells of mesenchymal origin, including fibroblasts, endothelial cells, smooth muscle, melanocytes as well as T and B lymphocytes.

Refer to page 43 for the Bond ready-to-use format.

WAF1 Protein (p21, C1P1)

**Clone 4D10**
1 mL, 0.1 mL lyophilized NCL-WAF-1 P (HIER) W
1 mL liquid NCL-L-WAF-1 P (HIER) W

The gene encoding WAF1, also termed p21, is transcriptionally regulated by the suppressor protein, p53. Overexpression of WAF1 is growth suppressive, possibly by inhibiting the activity of cyclin/CDK complexes. One consequence of WAF1 binding to cyclin/CDK complexes is the inhibition of Rb protein phosphorylation. Induction of WAF1 expression requires wild type p53 activity in cells undergoing p53 dependent G1 arrest or apoptosis. Mutation of the p53 gene is a common event in human cancer and results in the failure to produce WAF1. The effect of this may lead to uncontrolled cell proliferation.

Refer to page 43 for the Bond ready-to-use format.

Wilms’ Tumor

**Clone WT49**
1 mL, 0.1 mL liquid NCL-L-WT1-562 P (HIER) W
7 mL Bond ready-to-use PA0562 P (HIER) W

Wilms’ tumor protein (WT1) has a role in transcriptional regulation and is expressed in the kidney and a subset of hematopoietic cells. Alteration of transcription factor function is a common mechanism in oncogenesis. The WT1 protein contains a DNA binding domain and any deletions or point mutations of the WT1 gene which destroy this activity result in the development of the childhood nephroblastoma Wilms’ tumor and Denys-Drash syndrome. The description of WT1 involvement in nephroblastoma is not clear. Expression of WT1 protein by immunohistochemistry is never observed (or exceptionally rare) in breast cancer and negativity is considered a useful marker to distinguish breast carcinoma metastases from serous ovarian primary carcinomas. This is at variance with observations regarding mRNA in these tumors, but this is a still unresolved and complex issue.

**Product Specific Information**

Endothelial cells are prevalently negative using clone WT49. These cells are otherwise immunoreactive with clone 6FH2.

Refer to page 44 for the Bond ready-to-use format.
Zap-70

**Clone L453R**

1 mL, 0.1 mL liquid NCL-L-ZAP-70 P (HIER) W

7 mL Bond ready-to-use PA0998 P (HIER)

ZAP-70 is a member of the syk family of proteins. It is expressed on T cells and NK cells and is required for the T cell receptor activation that triggers an immune response. CLL B cells that express the non-mutated immunoglobulin V_H genes express levels of ZAP-70 protein that are comparable to those found in the blood T cells of healthy adults. Leukemic cells that express mutated IgVH genes generally do not express detectable levels of ZAP-70 protein and this is correlated with the high level expression of CD38. The ZAP-70 positive sub-type has been reported to be associated with a more aggressive phenotype.

Refer to page 44 for the Bond ready-to-use format.
MANUAL DETECTION SYSTEMS

Don’t compromise – to get the most from your Novocastra primary reagents, always rely on Novolink™ detection, Novocastra diluent, and Novocastra ancillary reagents.
Novolink Polymer Detection Systems

The Novolink Polymer Detection Systems utilize a novel Compact Polymer technology. Therefore, the problem of non-specific staining that can occur with Streptavidin/Biotin detection systems due to endogenous biotin does not occur. Novolink Polymer Detection Systems contain pre-diluted, reagents in color coded bottles for ease of use and ultimate convenience. These systems can be used for the visualization of mouse IgG, mouse IgM and rabbit IgG primary antibodies. These detection systems contain Peroxidase Block, Protein Block, Post Primary Block, Novolink Polymer, DAB Chromogen, Novolink DAB Substrate Buffer (Polymer) and Hematoxylin.

**Novolink Polymer Detection System (RE7150-K) staining for cytokeratin 5 with NCL-L-CK5 on breast carcinoma. Paraffin section.**

Polymer Ancillaries

**Peroxidase Block**

**Blocking Reagent**

25 mL RE7101

Novocastra Peroxidase Block, RE7101, is intended for use in the peroxidase based immunohistochemical (IHC) staining procedures. The presence of pseudoperoxidase (erythrocytes) and endogenous peroxidase in paraffin sections to be stained by immunoperoxidase procedures, can result in non-specific staining. A method for the blocking of pseudoperoxidase was described (Streefkerk J G, Journal of Histochemistry and Cytochemistry. 20: 829 (1972)). This product is used in a peroxidase based IHC procedure. Incubating sections with Novocastra Peroxidase Block, RE7101, can neutralize endogenous peroxidase activity. 25 mL of reagent is supplied.

**Protein Block**

**Blocking Reagent**

25 mL RE7102

Novocastra Protein Block, RE7102, is intended for use in immunohistochemical (IHC) staining procedures. In immunohistochemistry, diffuse non-specific staining (background) may occur as a result of hydrophobic and ionic interactions between antibodies and tissue components. Novocastra Protein Block, RE7102, is a serum-free, protein blocker. 25 mL of reagent is supplied.

**Novolink Polymer**

1,250 Tests kit Novolink Max Polymer RE7260-K

250 Tests kit Novolink Polymer RE7200-K

Novolink (Polymer), RE7200-K, is a two part ready-to-use kit comprising 25 mL of Novocastra Post Primary Block, RE7111, and 25 mL of Novolink Polymer, RE7112, sufficient to perform approximately 250 tests. The larger format Novolink Max (Polymer), RE7260-K, is a two-part ready-to-use kit comprising 125 mL of Novocastra Post Primary Block, RE7159, and 125 mL of Novolink Polymer, RE7161, sufficient to perform approximately 1,250 tests.

**Novolink DAB (Polymer)**

1,250 Tests kit Novolink Max DAB (Polymer) RE7270-K

250 Tests kit Novolink DAB (Polymer) RE7230-K

Novolink Max DAB (Polymer) RE7270-K is a two part DAB kit comprising 150 mL of Novolink Substrate Buffer (Polymer), RE7143, and 8mL of Novocastra DAB Chromogen, RE7162, sufficient to perform approximately 1,250 tests. Novolink DAB (Polymer), RE7230-K, is a two part DAB kit comprising 30 mL of Novolink DAB Substrate Buffer, RE7143, and 3 mL of Novocastra DAB Chromogen, RE7105, sufficient to perform approximately 250 tests.
DAB Enhancer

25 mL RE7125

Novocastra DAB Enhancer, RE7125, is used to enhance the staining of the Novocastra Peroxidase Detection Systems RE7110-K/RE7120-K, Novocastra Concentrated Peroxidase System, Novolink Polymer Detection Systems and the Peroxidase Detection System for Novocastra RTU Primary Antibodies, RE7100-K. This product is used in peroxidase-based immunohistochemical (IHC) procedures to allow the qualitative identification by light microscopy of antigens in sections of formalin-fixed, paraffin-embedded tissue. It intensifies the staining of the chromogen, 3, 3’ diaminobenzidine (DAB). 25 mL of DAB Enhancer is supplied.

Hematoxylin

25 mL RE7107

Novocastra Hematoxylin, RE7107, is intended for use in immunohistochemical (IHC) staining procedures. Hematoxylin stains cell nuclei and has many uses in histology, the most common of which is the Hematoxylin and Eosin stain. In IHC procedures, hematoxylin can be used as a counterstain to aid the visualization and localization of the colored end product. 25 mL of the reagent is supplied.

Peroxidase ABC

Concentrated Peroxidase Detection System

500 Tests kit Concentrated Peroxidase Detection System RE7130-K

Novocastra Concentrated Peroxidase Detection System (500 tests), RE7130-K, is for the visualization of mouse IgG, mouse IgM and rabbit IgG primary antibodies. The detection system contains Novocastra Concentrated Biotinylated Secondary Antibody, RE7108, Novocastra Concentrated Streptavidin-HRP, RE7109, Novocastra DAB Chromogen, RE7105, and Novocastra DAB Substrate Buffer, RE7106. The components in this kit are concentrated and require dilution prior to use.

Peroxidase Detection Systems (Ready-to-Use)

250 Tests kit Peroxidase Detection System RE7110-K

500 Tests kit Peroxidase Detection System RE7120-K

Novocastra Peroxidase Detection Systems (250 tests), RE7110-K, and (500 tests), RE7120-K, are for the visualization of mouse IgG, mouse IgM and rabbit IgG primary antibodies. Each detection system contains Novocastra Peroxidase Block, RE7101, Novocastra Protein Block, RE7102, Novocastra Biotinylated Secondary Antibody, RE7103, Novocastra Streptavidin-HRP, RE7104, Novocastra DAB Chromogen, RE7105, Novocastra DAB Substrate Buffer, RE7106, and Novocastra Hematoxylin, RE7107. The components in these kits are pre-diluted, ready-to-use reagents in color coded bottles for ease of use and ultimate convenience. Components of these Detection Systems are also available, separately.

Peroxidase Detection System for Novocastra RTU Primary Antibodies

500 Tests kit Peroxidase Detection System RE7100-K

Product Specific Information

Novocastra Peroxidase Detection System for Novocastra RTU Primary Antibodies, RE7100-K is a system titered for the optimum visualization of Novocastra ready-to-use (RTU) mouse IgG, mouse IgM and rabbit IgG primary antibodies. The kit consists of Novocastra Biotinylated Secondary Antibody, RE7144, Novocastra Streptavidin-HRP, RE7145, Novocastra DAB Chromogen, RE7105, and Novocastra DAB Substrate Buffer, RE7146. The components in this kits are pre-diluted, ready-to-use reagents in color coded bottles for ease of use and ultimate convenience.

Streptavidin-HRP

25 mL RE7104

Streptavidin-HRP is a streptavidin-conjugated horseradish peroxidase reagent. It is supplied ready-to-use in a volume of 25 mL.
ABC Ancillaries

Avidin/Biotin Blocking System

2 × 18 mL kit RE7170-K  F P W

Some tissues may bind avidin, biotinylated horseradish peroxidase, biotinylated alkaline phosphatase or other Biotin/Avidin System components without prior addition of biotinylated antibody. This binding may be due to endogenous biotin or biotin-binding proteins, lectins or non-specific binding substances present in the section. If high background is present using Avidin Biotin Complex (ABC) reagents, or other avidin conjugates in the absence of biotinylated secondary antibody, the use of the Novocastra Avidin/Biotin Blocking System RE7170-K may be of benefit. 18 mL of each reagent is supplied.

Biotinylated Secondary Antibody

25 mL RE7103 P  IVD

Biotinylated secondary antibody is for the detection of mouse IgG, mouse IgM and rabbit IgG primary antibodies. It is supplied ready-to-use in a volume of 25 mL.

Chromogens

3,3’ Diaminobenzidine Tetrahydrochloride

10 tablets NCL-DAB  F P W

3,3’ diaminobenzidine tetrahydrochloride (DAB) is a substrate for horseradish peroxidase, suitable for use in immunohistochemical staining and Western blotting techniques. 10 DAB tablets are provided in individually sealed foil packs. Each tablet is sufficient to produce 10 mL of working strength DAB solution.

DAB (250 tests)

250 Tests kit RE7190-K  P  IVD

DAB (250 tests) is a two part DAB kit comprising 30 mL Novocastra DAB Substrate Buffer, RE7106, and 3 mL of Novocastra DAB Chromogen, RE7105, and is sufficient to perform approximately 250 tests.
Hapten Antibodies

Clone Hyb-8
1 mL lyophilized Biotin NCL-BIOTIN F P W O

Clone PAK
1 mL lyophilized Dinitrophenyl NCL-DNP F P W O

NCL-BIOTIN is an antibody of high affinity, suitable for the localisation of biotinylated antibodies or oligonucleotide probes. NCL-BIOTIN may also be used in ELISA techniques. NCL-DNP may be used for the detection of dinitrophenyl-labeled antibodies. NCL-DNP may also be used for the detection of dinitrophenyl-labeled probes in Southern and Northern blotting techniques.

Goat Anti-Mouse Peroxidase-Conjugated Immunoglobulin

1 mL NCL-GAMP F P W O

NCL-GAMP is an affinity-purified polyclonal anti-mouse immunoglobulin conjugated to horseradish peroxidase. NCL-GAMP is a useful reagent for immunohistochemistry, Western blotting and ELISA techniques.

NovoPen

1 reagent pen NCL-PEN F P

NovoPen is designed to minimize wastage of reagents by allowing the user to ring the tissue(s) or cells to be stained thereby localizing the staining reagents. The pen contains a light blue hydrophobic reagent which is soluble in commonly used clearing agents, eg xylene and xylene substitutes. It can be used in immunostaining techniques on paraffin sections, frozen sections and on cytology preparations and is insoluble in alcohol and acetone. NovoPen is compatible with enzyme or fluorescent-based detection systems. The pen is supplied as a single item together with a product datasheet.
Manual Detection Systems

Products in this catalog are subject to regulatory approval.
This catalog is not for use in the USA.

For detailed information on all products please visit our website:
www.leica-microsystems.com
Buffers

Frozen Immunofluorescence Electron microscopy
Paraffin Flow cytometry Other applications
Western blotting

NOVOCASTRA™

EPITOPE RETRIEVAL REAGENTS AND BUFFERS
COMPLETE CONFIDENCE

Don’t compromise – always rely on Novocastra diluent, retrieval solutions and ancillary reagents. Novocastra antibodies are proven with Novocastra primary antibody diluent, don’t trust your important stains to unproven substitutes.

• Novocastra diluent – the proven performer
• Novocastra retrieval solutions – a range of pH levels lets you optimize your retrieval
• Novocastra ancillaries – completing the total IHC/ISH staining solution

NOVOCASTRA™ EPITOPE RETRIEVAL REAGENTS AND BUFFERS
Buffers

Antibody Diluent

500 mL RE7133 F P O VWD

Novocastra IHC Diluent is intended for use as a diluent for Novocastra primary antibodies, Novocastra Concentrated Biotinylated Secondary Antibody, RE7108, and Novocastra Concentrated Streptavidin-HRP, RE7109, in immunohistochemical (IHC) procedures. Novocastra IHC Diluent is not intended for the reconstitution of lyophilized reagents. Volume supplied is 500 mL.

Normal Serum Reagents

Blocking Reagent

10 mL Normal Goat Serum NCL-G-SERUM F P VWD
10 mL Normal Horse Serum NCL-H-SERUM F P VWD
10 mL Normal Rabbit Serum NCL-R-SERUM F P VWD

Normal serum is often used as a negative control or as a blocking reagent in immunoaassays. These may be of use as ‘no primary’ controls and as a diluent for primary and secondary antibody reagents. Novocastra offers these animal sera in a convenient 10 mL pack size. 200 mL of working strength diluent can be prepared, sufficient for up to 2000 slides.

Epitope Retrieval Solutions

Epitope Retrieval Solutions pH6

1 L pH6 (x10 Concentrate) RE7113 P (HIER) VWD
500 mL pH6 (x10 Concentrate) RE7114 P (HIER) VWD

Novocastra Epitope Retrieval Solutions are intended for Heat Induced Epitope Retrieval (HIER) on formalin-fixed, paraffin-embedded tissue sections as part of an immunohistochemical procedure. HIER using an appropriate pH solution improves the staining of some antibodies by exposing epitopes within tissue that has been masked during fixation. The development of Epitope Retrieval using heat was first reported in 1991 by Shi S-R et al., Journal of Histochemistry and Cytochemistry 39: 741-748 (1991). Since then numerous studies have been published looking at the effects of molarity, pH and heating methods on epitope retrieval. A universal HIER technique suitable for all epitopes does not exist. A combination of different heating methods and epitope retrieval solutions may be used to optimize unmasking of antigens where this technique is recommended. HIER is not recommended for all antibodies. Optimum conditions for epitope retrieval should be validated by the user, as these are dependant upon tissue, fixation and/or primary antibody. RE7113 is supplied as a 1 L volume, sufficient to prepare 10 L of working solution. RE7114 is supplied as a 500 mL volume, sufficient to prepare 5 L of working solution.

Epitope Retrieval Solutions pH8

1 L pH8 (x10 Concentrate) RE7116 P (HIER) VWD

Novocastra Epitope Retrieval Solutions are intended for Heat Induced Epitope Retrieval (HIER) on formalin-fixed, paraffin-embedded tissue sections as part of an immunohistochemical procedure. HIER using an appropriate pH solution improves the staining of some antibodies by exposing epitopes within tissue that has been masked during fixation. The development of Epitope Retrieval using heat was first reported in 1991 by Shi S-R et al., Journal of Histochemistry and Cytochemistry 39: 741-748 (1991). Since then numerous studies have been published looking at the effects of molarity, pH and heating methods on epitope retrieval. A universal HIER technique suitable for all epitopes does not exist. A combination of different heating methods and epitope retrieval solutions may be used to optimize unmasking of antigens where this technique is recommended. HIER is not recommended for all antibodies. Optimum conditions for epitope retrieval should be validated by the user, as these are dependant upon tissue, fixation and/or primary antibody. RE7116 is supplied as a 1 L volume, sufficient to prepare 10 L of working solution.
Epitope Retrieval Solution pH9

1 L pH9 (x10 Concentrate) RE7119 P (HIER) [IVD]

Novocastra Epitope Retrieval Solutions are intended for Heat Induced Epitope Retrieval (HIER) on formalin-fixed, paraffin-embedded tissue sections as part of an immunohistochemical procedure. HIER using an appropriate pH solution improves the staining of some antibodies by exposing epitopes within tissue that has been masked during fixation. The development of Epitope Retrieval using heat was first reported in 1991 by Shi S-R et al. Journal of Histochemistry and Cytochemistry 39: 741-748 (1991). Since then numerous studies have been published looking at the effects of molarity, pH and heating methods on epitope retrieval. A universal HIER technique suitable for all epitopes does not exist. A combination of different heating methods and epitope retrieval solutions may be used to optimize unmasking of antigens where this technique is recommended. HIER is not recommended for all antibodies. Optimum conditions for epitope retrieval should be validated by the user, as these are dependant upon tissue, fixation and/or primary antibody. RE7119 and RE7224 are supplied as a 1 L volume, sufficient to prepare 10 L of working solution.


Enzyme Proteinase K (IHC)

100 mL kit RE7160-K P (Enzyme) [IVD]

Enzyme pretreatment of formalin-fixed, paraffin-embedded tissue sections improves the staining of some antibodies by exposing epitopes within tissue that have been masked during fixation. The first proteolytic enzyme employed for epitope retrieval was trypsin. More recently, proteinase K which is commonly used in in situ hybridization techniques has been reported to be of use.

Product Specific Information

Novocastra Enzyme Proteinase K (IHC), RE7160-K, is intended for the enzymatic pretreatment of formalin-fixed, paraffin-embedded tissue sections prior to incubation with a primary antibody in an immunohistochemical (IHC) procedure. This product can be used for epitope retrieval with Novocastra antibodies for which trypsin is recommended, known exceptions to this are NCL-C-JEJUNI, NCL-BrdU, NCL-CYCLIN D1, NCL-COLL-Iip, and NCL-CYCLIN D1-GM. This two part kit comprises 0.75 mL of Enzyme Proteinase K Concentrate, RE7126, and 100 mL of Enzyme Proteinase K Buffer, RE7127, sufficient to produce 100 mL of working strength enzyme solution. This product is used in an IHC procedure, which allows the qualitative identification by light microscopy. Epitope retrieval by enzymatic pretreatment is recommended for a limited number of antibodies. Optimum conditions for epitope retrieval should be validated by the user as these are dependent upon tissue, fixation and/or primary antibody.

Liver pre-treated with Enzyme Proteinase K (RE7160-K). Staining for Cytokeratin 8/18 using NCL-L-S03. Paraffin section.
The Novocastra ISH probe range includes Fluorescein-Conjugated Oligonucleotide probes for the qualitative detection of RNA transcripts.
Control Probe (Fluorescein-Conjugated)

50 Tests, 10 Tests liquid probe NCL-CONTROL

Product Specific Information

NCL-CONTROL has been produced by labeling randomly generated oligonucleotide sequences with fluorescein using the same procedures as applied to the mRNA specific oligonucleotide probes from Leica Microsystems. Therefore, NCL-CONTROL is ideally suited for use as a negative control alongside RNA specific probes providing confirmation of the staining pattern obtained by these specific oligonucleotide probes.

Cytomegalovirus Probe (Fluorescein-Conjugated)

50 Tests liquid probe NCL-CMV

Cytomegalovirus (CMV) infection may occur in lung, kidney, gut and other organs of individuals who are immunologically immature, such as the fetus and neonate. CMV infection also occurs in situations of immunosuppression such as transplant recipients, individuals undergoing chemotherapy and those with HIV infection.

Product Specific Information

NCL-CMV detects an early gene RNA transcript which is expressed in permissive infection.

Epstein-Barr virus Probe (Fluorescein-Conjugated)

50 Tests, 10 Tests liquid probe NCL-EBV

EBV infection is associated with a variety of pathological conditions. The virus has been reported to be demonstrated in infectious mononucleosis, Burkitt’s lymphoma, the Reed Sternberg cells of Hodgkin’s disease and in nasopharyngeal carcinoma. In HIV infection, EBV has also been reported to be demonstrated in primary CNS lymphomas and oral hairy leukoplakia lesions.

Product Specific Information

NCL-EBV is a fluorescein-labelled oligonucleotide cocktail designed to demonstrate cells latently-infected with EBV. The probe hybridizes to abundantly expressed Epstein-Barr virus-encoded RNA (EBER) transcripts which are concentrated in the nuclei of latently-infected cells. These transcripts are thought to block the activation of dsRNA-dependent eukaryotic initiation factor 2a (eIF-2a) protein kinase DAI. In the absence of EBER, eIF-2a inhibits cellular protein synthesis.

Epstein-Barr virus Probe ISH Kit

50 Tests kit NCL-EBV-K

Epstein-Barr virus encoded RNA (EBER) is reported to be present in both latent and lytic EBV infection. These transcripts are thought to block the activation of dsRNA-dependent eukaryotic initiation factor 2a (eIF-2a) protein kinase DAI.

Product Specific Information

NCL-EBV-K contains a fluorescein-labelled oligonucleotide cocktail for the detection of mRNA sequences contained in 1 mL of hybridization solution sufficient to stain 50 preparations. A control probe is a fluorescein-labelled random oligonucleotide cocktail contained in 1 mL of hybridization solution which is also included. The control probe is ideally suited for use as a negative control alongside the EBV probe. Other reagents include 500 µg of lyophilized Proteinase K, anti-fluorescein isothiocyanate conjugated to alkaline phosphatase, 5-bromo-4-chloro-3-indolyl phosphate (BCIP) and nitro blue tetrazolium (NBT) in dimethylformamide solution, levamisole hydrochloride and 3-aminopropyltriethoxysilane (APES)-coated slides.

Histone Probe (Fluorescein-Conjugated)

50 Tests liquid probe NCL-HISTONE-513

The synthesis of histone mRNA is closely coupled with DNA replication. During the S phase of the cell cycle the level of histone mRNA increases over fifty fold then rapidly disappears at the start of the G2 phase. These changes are produced by rapid mRNA degradation as well as modulation of transcription. The presence, therefore, of abundant quantities of histone mRNA provides an indicator of cycling cells which can be easily detected.

Product Specific Information

NCL-HISTONE-513 is a fluorescein-labelled oligonucleotide cocktail for the detection of histone, H2b, H3 and H4 mRNA sequences contained in 1 mL of hybridization solution sufficient for in situ hybridization.

Histone Probe ISH Kit

50 Tests kit NCL-HISTONE-513

Histone mRNA is associated with a variety of pathological conditions. The virus has been reported to be demonstrated in infectious mononucleosis, Burkitt’s lymphoma, the Reed Sternberg cells of Hodgkin’s disease and in nasopharyngeal carcinoma. In HIV infection, EBV has also been reported to be demonstrated in primary CNS lymphomas and oral hairy leukoplakia lesions.

Product Specific Information

NCL-HISTONE-513 is a fluorescein-labelled oligonucleotide cocktail for the detection of histone, H2b, H3 and H4 mRNA sequences contained in 1 mL of hybridization solution sufficient for in situ hybridization.

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For detailed information on all products please visit our website: www.leica-microsystems.com

Products in this catalog are subject to regulatory approval. This catalog is not for use in the USA.
Human Herpesvirus (type 8) Probe (Fluorescein-Conjugated)

50 Tests, 10 Tests liquid probe NCL-HHV8

Human herpesvirus 8 (HHV-8), also known as Kaposi’s sarcoma associated herpesvirus, is one of the eight known human herpes viruses and belongs to the Gammaherpesvirinae, the same subfamily as Epstein-Barr virus. HHV8 has a large double strand DNA genome that carries a complement of over 85 open reading frames.

**Product Specific Information**

NCL-HHV8 is a cocktail of fluorescein-labelled oligonucleotide probes contained in 1 mL of hybridization solution, designed to hybridize with a small transcript, designated T1.1 mRNA, which accumulates in the nuclei of infected cells.

Poly d(T) Probe (Fluorescein-Conjugated)

50 Tests liquid probe NCL-POLYd(T)

The precursors of mRNA are transcribed from DNA by RNA polymerase II and are known as heterogeneous nuclear RNA (hnRNA). Enhanced stability is conferred to 70 to 90 percent of these transcriptions by the addition of 5’ methyl caps and 3’ tails of approximately 200 adenyl residues. Following these reactions, most hnRNA is spliced to remove non-coding intron sequences to produce mRNA. Due to the destruction of RNases by formalin fixation, polyadenylated mRNA sequences are conserved in routine paraffin wax preparations, only when they have been fixed promptly. This can be readily demonstrated using labelled polythymidine (poly d(T)) probes. Detection of poly A tails provides a way of monitoring the translational activity of cells and assessing the relative preservation of mRNA in tissue preparations.

**Product Specific Information**

NCL-POLYd(T) consists of fluorescein-labelled oligonucleotide for the detection of polyadenylated mRNA sequences contained in 1 mL of hybridization solution.

Proteinase K

500 μg lyophilized enzyme NCL-PK

**Product Specific Information**

NCL-PK is effective for the digestion of proteins on tissue sections, as a pre-treatment, to aid in the preparation of mRNA and its detection by in situ hybridization methods using oligonucleotide probes from Leica Microsystems.

Kappa/Lambda Probes (Fluorescein-Conjugated)

2 × 25 Tests, 2 x 5 Tests liquid probes NCL-KAP/LAM

Immunoglobulins are polypeptides that consist of heavy and light protein chains. There are two classes of light chain: kappa and lambda. The ratio of kappa chains to lambda chains varies in a species-specific fashion. In humans about 60 percent of light chains are kappa. However, in any individual immunoglobulin molecule the light chains will be either kappa or lambda, never a mixture. B cells contain kappa or lambda mRNA.

**Product Specific Information**

NCL-KAP/LAM consists of two sets of fluorescein-conjugated kappa and lambda oligonucleotide probes provided in two separate vials, each containing 0.5 mL of hybridization solution, sufficient for the in situ hybridization staining of 25 kappa and 25 lambda preparations, respectively.

Universal ISH Detection Kit

100 Tests kit NCL-ISH-D

**Product Specific Information**

The Universal ISH Detection Kit from Leica Microsystems is intended for the detection of bound fluorescein-conjugated oligonucleotide probes. The ISH Detection Kit comprises affinity-purified rabbit F(ab’) anti-fluorescein isothiocyanate conjugated to alkaline phosphatase, 5-bromo-4-chloro-3-indolyl phosphate (BCIP) and nitroblue tetrazolium (NBT) and levamisole hydrochloride.
PRIMER SETS - ADVANCED REAGENTS FOR DETECTION

Inhibitors of the polymerase chain reaction (PCR) are common leading to considerable blunting of the potentially exquisite sensitivity of this method. Such false-negative results pass unrecognized unless an internal (amplification) control is routinely included in the test. Primer Sets from Novocastra normally consist of a pair of oligonucleotide primers and an internal control template. The target DNA and internal control DNA co-amplify with the same primers but yield products of a different size. The PCR products may be resolved on an agarose gel, giving a rapid, sensitive test at low cost. Each primer set has been tested in conventional heated block instruments, as well as capillary air thermal cyclers and comes with detailed instructions and sample preparation advice.

NOVOCASTRA PRIMER SETS

A schematic diagram illustrating the use of a Primer Set for the amplification and detection of microbial, or viral DNA by the PCR process. Lane A, DNA ladder. Lane B, sample.
Corynebacterium diphtheriae

100 Tests primer set NCL-CD-PS

Large outbreaks of diphtheria in eastern Europe and modern travel have led to an increased awareness of Corynebacterium diphtheriae. Most western isolates are still non-toxigenic, but toxin tests require experience and expertise.

**Product Specific Information**

The Corynebacterium diphtheriae primer set, NCL-CD-PS, consists of a pair of oligonucleotide primers (CD-1 and CD-2) which amplify a 246bp region of the toxin gene alpha subunit. Also provided is an internal control DNA for aiding in the detection of false-negative PCR results. The internal control DNA may be added to the test PCR, where it will amplify with the same primers but yield a product of different size.

![Agarose gel: electrophoresis of PCR products using NCL-CD-PS. Lane A, 100bp ladder (Promega). Lane B, Reagent blank. Lanes C-F and H, five toxigenic Corynebacterium diphtheriae isolates. Lane G, non-toxigenic Corynebacterium diphtheriae isolate. The polymerase chain reaction (PCR) process is covered by patents owned by Hoffman La-Roche Inc. and Hoffman La-Roche Ltd. Purchase of these products does not carry a licence to perform the PCR process.](image)

Mycobacterium tuberculosis

100 Tests primer set NCL-MT-PS

There is a rising incidence of tuberculosis, an emergence of drug-resistant strains of Mycobacterium tuberculosis and an overlap with AIDS. Direct detection and identification of Mycobacterium tuberculosis in sputum is possible by PCR. Some low level infections may be missed (but later detected by culture), but it is reported that PCR will certainly identify all strains of Mycobacterium tuberculosis detected by conventional microscopy (60 to 80 percent).

**Product Specific Information**

The Mycobacterium tuberculosis primer set, NCL-MT-PS, consists of a pair of oligonucleotide primers (MT-1 and MT-2) which amplify the 123bp insertion sequence IS6110. The sequence is unique to members of the Mycobacterium tuberculosis complex (MTBC) and is present as a sequence in multiple copies in many common isolates. Also provided is an internal control DNA for aiding in the detection of false-negative PCR results.

![Agarose gel: electrophoresis of PCR products using NCL-MT-PS. Lane A, 123bp ladder (Sigma). Lane B, internal control only. Lanes C, D and E, Mycobacterium tuberculosis, Mycobacterium avium and Mycobacterium intracellulare isolates, respectively. Lanes F and G, Mycobacterium tuberculosis-positive human sputa. Lane H, Mycobacterium tuberculosis-positive, formalin-fixed, paraffin-embedded human lung. The polymerase chain reaction (PCR) process is covered by patents owned by Hoffman La-Roche Inc. and Hoffman La-Roche Ltd. Purchase of these products does not carry a licence to perform the PCR process.](image)
Familiar and trusted Novocastra clones for use on Ventana Medical Systems’ NexES® and BenchMark™ Series immunohistochemistry staining platforms. Each antibody has been independently proven to pass a lot-to-lot verification test with equivalent Ventana Medical Systems products.
bcl-2 Oncoprotein

Clone bcl-2/100/D5
50 Tests ORG-8714

Bcl-2 antigen is a member of a family of proteins that are involved in apoptosis. The antigen is an integral inner mitochondrial membrane protein of 25 kD and has wide tissue distribution. It is considered to act as an inhibitor of apoptosis. For this reason bcl-2 expression is inhibited in germinal centers where apoptosis forms part of the B cell production pathway. In 90 percent of follicular lymphomas a translocation occurs which juxtaposes the bcl-2 gene at 18q21, to an immunoglobulin gene, with subsequent deregulation of gene expression and cell proliferation.

Product Specific Information
Origin bcl-2 (Clone bcl-2/100/D5) is recommended for use in the differentiation of lymphomas from reactive lymph nodes.

Refer to page 60 for further information about Clone bcl-2/100/D5.

CD3

Clone PS1
50 Tests ORG-8982

The CD3 antigen is a marker of T cell differentiation, expressed in normal and neoplastic T cells. The CD3 antigen is first detected in early thymocytes and its appearance probably represents one of the earliest indicators of commitment to the T cell lineage.

Product Specific Information
T cell phenotype in lymphoproliferative disorders may be indicated using Origin CD3 (Clone PS1) as part of a panel of antibodies.

Refer to page 70 for further information about Clone PS1.

CD4

Clone 1F6
50 Tests ORG-8756

The CD4 antigen is expressed on a T cell subset (helper/inducer) representing 45 percent of peripheral blood lymphocytes and at a lower level on monocytes. Most cases of cutaneous T cell lymphoma, including mycosis fungoides, express the CD4 antigen. HTLV-1 associated adult T cell leukemia/lymphoma is also generally CD4 positive.

Origin CD4 (Clone 1F6) on tonsil.
**CD5**

Clone 4C7  
50 Tests ORG-8919  

CD5 is a protein of 67 kD, expressed on 95 percent of thymocytes and 72 percent of peripheral blood lymphocytes. In lymph nodes, the main reactivity is observed on T cells. CD5 antigen is expressed by many T cell lymphomas, activated T cells and on a subset of B cells. CD5 antigen expression is reported in T cell acute lymphocytic leukemias (T-ALL), some B cell chronic lymphocytic leukemias (B-CLL) as well as B and T cell lymphomas. CD5 antigen is not expressed in follicular cell lymphomas.

Product Specific Information  
Origin CD5 (Clone 4C7) can be used in the differential diagnosis of lymphomas, including mantle cell lymphomas.  
Refer to page 71 for further information about Clone 4C7.

**CD8**

Clone 1A5  
50 Tests ORG-8936  

The CD8 molecule is composed of two chains and has a molecular weight of 32 kD. It has been found on a subset of normal cytotoxic/suppressor cells which make up approximately 20-35 percent of human peripheral blood lymphocytes. The CD8 molecule is reported to be detected on natural killer cells, 80 percent of thymocytes, on a sub-population of 30 percent of peripheral blood null cells and 16-30 percent of bone marrow cells.

Product Specific Information  
T cell disorders may be characterized using Origin CD8 (Clone 1A5) as part of a panel of antibodies.  
Refer to page 72 for further information about Clone 1A5.

**CD10**

Clone 56C6  
50 Tests ORG-8941  

CD10 antigen is also known as neprilysin and common acute lymphoblastic leukemia antigen (CALLA). CD10 antigen is expressed on a wide variety of normal and neoplastic cells.

Product Specific Information  
CD10 expression is reported on cells of lymphoblastic, Burkitts’ and follicular lymphomas and on B cells from patients with chronic myelocytic leukemia, as such, Origin CD10 (Clone 56C6) may be used in the differential diagnosis of small B cell lymphoma and the subtyping of lymphoblastic leukemia.  
Refer to page 73 for further information about Clone 56C6.

**CD23**

Clone 1B12  
50 Tests ORG-8826  

The CD23 antigen, a membrane glycoprotein of 45 kD, is reportedly found on a subpopulation of peripheral blood cells, B lymphocytes and on EBV-transformed B lymphoblastoid cell lines. The CD23 molecule is also known as the low affinity IgE receptor found on B cells. Expression has been reported on neoplastic cells from B cell chronic lymphocytic leukemias and centrocytic/centroblastic lymphomas.

Product Specific Information  
Origin CD23 (Clone 1B12) is recommended for use in the differential diagnosis of small B cell lymphomas.  
Refer to page 76 for further information about Clone 1B12.
CD79a

Clone 11E3
50 Tests ORG-8975

CD79a is a cytoplasmic domain, disulfide linked heterodimer protein. This protein is noncovalently associated with the membrane bound immunoglobulins on B cells. This complex of polypeptides and immunoglobulin constitutes the B cell receptor. The two components of this complex are designated CD79a and CD79b. The CD79a antigen is reported to first appear at the pre-B cell stage where it is found as an intracellular component. The CD79a antigen is reported in the majority of acute leukemias of precursor B cell types, B cell lines, B cell lymphomas and in some myelomas. It is not present in myeloid or T cell lines.

Product Specific Information
An antibody panel including Origin CD79a (Clone 11E3) may be used in the characterization of B cell disorders.

Refer to page 84 for further information about Clone 11E3.

Origin CD79a (Clone 11E3) on tonsil. Paraffin section.

Cytokeratin

Clone 34βE12
50 Tests ORG-8735

The expression of different cytokeratins in epithelial-derived tumors and the general tendency towards maintenance of cytokeratin polypeptide patterns during malignant growth and metastasis serves as a basis for approaching the characterization of tumors, using cytokeratins as differentiation markers.

Product Specific Information
Origin Cytokeratin (Clone 34βE12) is recommended for the characterization of squamous and ductal carcinomas arising from complex epithelia and is of value in the differentiation of benign and malignant small-acinar lesions of the prostate gland.

Refer to page 137 for further information about Clone 34βE12.

Origin Cytokeratin (Clone 34βE12) on squamous cell carcinoma. Paraffin section.

Desmin

Clone DE-R-11
50 Tests ORG-8889

Human desmin is a 53 kD cytoplasmic intermediate filament protein in striated and smooth muscle cells. It is confined to the Z bands in skeletal and cardiac muscle giving a characteristic striated appearance when immunohistochemically stained.

Product Specific Information
Origin Desmin (Clone DE-R-11) is recommended as an aid in the determination of tumors of myogenic origin, such as those arising from smooth muscle, leiomyomas and those derived from striated muscle. The antibody does not recognize other intermediate filament proteins.

Refer to page 101 for further information about Clone DE-R-11.

Origin Desmin (Clone DE-R-11) on bowel. Paraffin section.

Estrogen Receptor

Clone 6F11
50 Tests ORG-8871

Estrogen receptor (ER) expression in breast cancer tissue is an important parameter in the prediction and response to endocrine therapy. Monoclonal antibodies to ER have allowed the determination of ER status to be carried out in routine histopathology laboratories quantitatively and qualitatively.

Product Specific Information
Origin Estrogen Receptor (Clone 6F11) is indicated as an aid in prognosis and prediction of therapy in breast cancer, it binds specifically to the ER alpha antigen in the nuclei of normal and neoplastic tissues.

Refer to page 106 for further information about Clone 6F11.

Origin Estrogen Receptor (Clone 6F11) on breast carcinoma. Paraffin section.
**Ki67**

Clone MM1  
50 Tests ORG-8772

Ki67 is a nuclear cell cycle associated protein, which is expressed in all active parts of the cell cycle (G1, S, G2 and mitosis) but not in resting cells (G0). In contrast to many other cell cycle associated proteins the Ki67 antigen is consistently absent in quiescent cells and is not detectable during DNA repair processes. Thus, the presence of Ki67 is strictly associated with the cell cycle and confined to the nucleus.

**Product Specific Information**

Origin Ki67 (Clone MM1) can be utilized in the assessment of cell proliferation in normal and neoplastic tissues.

Refer to page 126 for further information about Clone MM1.

**Melanosome**

Clone HMB45  
50 Tests ORG-8854

The melanosome antigen has been identified in retinal pigment epithelium (RPE) but is reported to be reactive only with transient prenatal and infantile RPE. Tumor cells of epithelial, lymphoid, glial and mesenchymal origin are reported to be negative.

**Product Specific Information**

Origin Melanosome (Clone HMB45) is recommended for use as part of a panel of antibodies for the diagnosis of melanoma.

Refer to page 120 for further information about Clone HMB45.

**Melan A**

Clone A103  
50 Tests ORG-8953

Melan A, a product of the MART-1 gene, is a melanocyte differentiation marker recognized by autologous cytotoxic T lymphocytes. Other melanoma-associated markers recognized by autologous cytotoxic T cells are reported to include MAGE-1, MAGE-3, tyrosinase, gp100, gp75, BAGE-1 and GAGE-1. The analysis of these different molecules and their expression in individual melanomas may be of help in the study of their particular roles in tumorigenesis.

**Product Specific Information**

Origin Melan A (Clone A103) is recommended for the assessment of Melan A in melanocytic lesions.

Refer to page 132 for further information about Clone A103.

**Progesterone Receptor**

Clone 16  
50 Tests ORG-8721

The human progesterone receptor (PR) is expressed as two isoforms, PRA (94 kD) and PRB (114 kD), which function as ligand-activated transcription factors. The PRA form is a truncated version of the PRB form, lacking the first 164 N-terminal amino acids. In humans, PRA activity acts as a transdominant repressor of the transcriptional of PRB, glucocorticoid receptor, ER, androgen receptor and mineralocorticoid receptor.

**Product Specific Information**

Origin Progesterone Receptor (Clone 16) binds specifically to the PRA antigen in the nuclei of normal and neoplastic tissues, as such it is recommended for determining the progesterone receptor alpha status of breast cancer tissue.

Refer to page 152 for further information about Clone 16.
Synaptophysin

Clone 27G12
50 Tests ORG-8848

The Synaptophysin antigen is an integral membrane glycoprotein present in many human normal and neoplastic neuroendocrine cells. It is reported to occur in presynaptic vesicles of the neurons in the brain, spinal cord and retina and in similar vesicles in the adrenal medulla and as well as neuromuscular junctions. The synaptophysin antigen may be involved in synaptic vesicle formation and exocytosis.

Product Specific Information

Synaptophysin (Clone 27G12) is recommended for the identification of tumors of neuroendocrine origin and differentiation.

Refer to page 160 for further information about clone 27G12.

Origin Synaptophysin (Clone 27G12) on carcinoid tumor. Paraffin section.

Terminal Deoxynucleotidyl Transferase

Clone SEN28
50 Tests ORG-8865

Human TdT, a nuclear DNA polymerase with a molecular weight of 58 kD, is reported to be expressed in primitive B and T cells of the normal thymus and bone marrow, acute lymphoblastic lymphomas and leukemias.

Product Specific Information

The determination of TdT expression is reported to be most valuable when it is difficult to differentiate histologically between lymphoblastic lymphoma and Burkitts’ lymphoma, as such, Origin TdT (Clone SEN28) is recommended for use in the diagnosis and differentiation of acute lymphoblastic leukemia/lymphoma from other lymphomas.

Refer to page 162 for further information about Clone SEN28.

Origin TdT (Clone SEN28) on lymphoid leukemia. Paraffin section.
### Bond

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Product Name Index

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Paraffin
Western blotting
Immunofluorescence
Flow cytometry
Electron microscopy
Other applications
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<td>Human Spasmolytic Polypeptide</td>
<td>NCL-HSP</td>
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<td>Human von Willebrand Factor (Factor VIII-related antigen)</td>
<td>NCL-L-vWF</td>
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<td>Human von Willebrand Factor (Factor VIII-related antigen) Bond ready-to-use</td>
<td>PA0400</td>
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<td>Hypoxia Inducible Gene 2 Protein</td>
<td>NCL-L-HIG2</td>
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<td>ICAM-1 (CD54)</td>
<td>NCL-CD54-307</td>
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<td>IHC Diluent</td>
<td>RE7133</td>
<td>181</td>
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<td>Immunoglobulin A</td>
<td>NCL-L-IgA</td>
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<td>Immunoglobulin D</td>
<td>NCL-L-IgD</td>
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<td>Immunoglobulin G</td>
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<td>Immunoglobulin M</td>
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<td>InhibinA</td>
<td>NCL-L-InhibinA</td>
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<td>Insulin</td>
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<td>Interleukin 6</td>
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<td>Involucrin</td>
<td>NCL-INV</td>
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<td>Kappa/Lambda Probes (Fluorescein-Conjugated)</td>
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<td>Kappa Light Chain</td>
<td>NCL-KAP-L1C1</td>
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<td>Ki67 Antigen</td>
<td>NCL-Ki67p</td>
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<td>Lambda Light Chain</td>
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<td>NCL-LAMp</td>
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<td>Lamin A/C</td>
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<td>Linker for Activation of T Cells</td>
<td>NCL-L-LAT</td>
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<td>Linker for Activation of T Cells</td>
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<td>LMP-1 (Epstein-Barr virus)</td>
<td>NCL-EBV-CS1-4</td>
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<td>L-selectin (CD62L)</td>
<td>NCL-C62L-489</td>
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<td>Lung Resistance-Related Protein (110 kD)</td>
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<td>Mac-1 (CD11b)</td>
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<td>Matrix Metalloproteinase 2</td>
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<td>Matrix Metalloproteinase 9</td>
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W Western blotting
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E Electron microscopy
O Other applications
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