INTERPRETATION

FLEX Ready-to-Use Atlas of Stains - 4<sup>th</sup> Edition



# FLEX Ready-to-Use Atlas of Stains





#### Committed to raising the bar for higher quality

During the last decades, organizations such as CAP, UK NEQAS and NordiQC have successfully implemented many initiatives to improve standardization in immunohistochemistry. At the same time, laboratories are striving to deliver accurate clinical diagnostic results while facing and adapting to the increasing number of challenges. It is vital for pathology laboratories to make continuous improvements to maintain the quality of diagnoses, and to be a professional counterpart and key resource to oncologists, and other clinicians.

#### Pathology laboratories face an increasing number of challenges today

- Escalating workload due to higher number of immunohistochemistry tests per patient case
- Time-consuming procedures
- Lack of qualified staff
- Healthcare costs
  - aging population with a corresponding rise in cancer cases
  - higher number of immunohistochemistry tests per patient case
- Low reproducibility and quality issues
- Inadequate workflow optimization
- Multiple steps of information transcription in various systems

While overcoming these challenges, a pathology laboratory must also improve time to diagnosis and reduce error rates, while delivering correct diagnostic results with a high level of certainty that the physician can rely on.

At Dako, we are committed to supporting pathology laboratories to overcome these challenges. We strive to deliver scientific advancements through leading-edge products and services to facilitate better, more informed decision making in diagnostics.

Dako is the first company in the industry, to embed high-quality control concepts into ready-touse procedures. The Dako FLEX Ready-to-Use (RTU) primary antibodies work on formalin-fixed, paraffin-embedded, tissue sections as a set of dedicated reagents for clinical routine diagnostics.

The FLEX RTU concept is unique, since it focuses on delivering the correct diagnostic end-result while improving time to diagnosis, reducing manual error rates, and simplifying information retrieval through bar-coded labeling. Equally important, it maintains and delivers reliable staining performance.

The Dako FLEX RTU antibody selection, together with the easy-to-use Dako EnVision™ FLEX/ FLEX+ visualization systems provide:

- Consistently high diagnostic certainty
- Efficient workflow with predictable speed and high capacity
- Service and support you can rely on for maximum uptime

This guide is the product of collaboration with a panel of distinguished experts in the field of pathology. At Dako we work to build lasting partnerships with leading experts to ensure that we optimize the staining performance of our products in line with your demands.

Our aim is that this guide will support you on a better path in cancer diagnostics.

For further information on antibody panels and staining performance, we recommend the following references:

- Jasani B. and Schmid K.W, Immunocytochemistry in Diagnostic Histopathology, W.B. Saunders Company, 1993
- The UK NEQAS home page for immunocytochemistry: http://www.ukneqasicc.ucl.ac.uk/
- The NordiQC home page: http://www.nordiqc.org

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<sup>-</sup> Dabbs D et. al., Diagnostic Immunohistochemistry, 3rd Edition, Elsevier, 2006

<sup>-</sup> Taylor C. R. et. al. Immunomicroscopy, 3rd edition, vol. 19, 2007

#### Ensuring desired staining performance with the help of an expert panel

The FLEX RTU concept was launched in 2008, and the staining performance of the products was developed in collaboration with leading pathologists and their laboratory managers. In the process of ensuring desired staining performance, a panel of these distinguished anatomic pathology experts specified the relevant criteria and reviewed the staining results obtained during development of all the antibodies.

During a year-long process, the expert panel specified the required staining performance for each individual antibody.

In acknowledging the many contributions we have received, we wish to thank the members of our expert panel and their laboratory managers for sharing their knowledge and insight:



From left: Mr. Andrew Dodson, Royal Liverpool University Hospital, UK Prof. Dr. Alvin Martin University of Louisville School of Medicine Department of Pathology, USA Mr. Søren Nielsen Aalborg Hospital , Department of Pathology, Denmark Prof. Dr. Robert Osamura, Tokai University School of Medicine, Japan Dr. Clive Taylor, Keck School of Medicine of USC, USA Ms. Sheron Lear University of Louisville School of Medicine Department of Pathology, USA Dr. David Dabbs, Magee Women's Hospital, USA Dr. Miguel Piris Centro Nacional de Investigaciones Oncologicas Carlos III, Spain Dr. Kengo Takeuchi, Japanese Foundation for Cancer Research, Japan Prof. Dr. Bharat Jasani, Cardiff University, UK Mrs. Lydia Sánchez Verde Centro Nacional de Investigaciones Oncologicas Carlos III, Spain Dr. Assia Bassarova Radiumhospitalet, Oslo, Norway Dr. John Gosney Royal Liverpool University Hospital, UK Mrs. Kim Mcmanus Magee Women's Hospital, USA Dr. Jahn Nesland Radiumhospitalet, Oslo, Norway (not in the photo)

Based on these guidelines, Dako has developed a standard procedure for all FLEX Ready-to-Use (RTU) primary antibodies that increases productivity without compromising the staining performance accepted by the expert panel. Using the guidelines, this Atlas of Stains provides examples of the staining performance which the panel accepted. The accompanying descriptions are summaries of the written input initially submitted by the expert panel for the guidelines.

We also thank Cooperative Human Tissue Network (funded by the National Cancer Institute) for providing valuable human tissues for our studies.

Dako will continuously launch new FLEX RTU antibodies, which are directly suited to the needs of pathologist laboratory. The performance and staining of these products have been reviewed and accepted by Dr. Clive Taylor, Keck School of Medicine of USC, USA, Biomedical Scientist Søren Nielsen, Scheme Organizer at NordiQC, Denmark, and Associate Professor Mogens Vyberg, Aarhus University Hospital, Denmark. The new clones will be marked in Atlas of Stains with "NEW".

This Atlas of Stains is by no means intended to override the professional judgment of a certified pathologist. The contents are provided as information only, and Dako neither claims nor warrants the universal validity of the information provided concerning Differential Diagnosis, as there are national and professional differences in the acceptance of the relevance of various markers.

#### FLEX Ready-to-Use

During the past 40 years, immunohistochemistry has become increasingly important in diagnostic pathology, and is now an essential daily tool for cancer diagnosis in most laboratories worldwide.

This has led to intense focus on utilizing and expanding IHC for purposes such as implementation of new markers, use of established markers in new areas, and optimization of immunohistochemical techniques. However, IHC is technically complex, and determining what to choose in order to deliver the right results is a major challenge for laboratories. The fact is that there are more than 1 million options when a pathologist sets up a protocol to analyze and report on merely one single antibody!

This is why it is so encouraging that Dako has developed the FLEX Ready-to-Use Immunohistochemical System. Dako's reagents have been set up for use in optimized and streamlined protocols, as a robust backbone for a wide range of diagnostic markers.

The system has been designed on the basis of input from IHC experts in surgical pathology who have long and widely acknowledged experience in both general pathology and hematopathology. Input from this large number of IHC experts have been used to align the system and the antibodies to obtain the quality necessary for meeting the demands of routine diagnostic procedures. To obtain appropriate sensitivity and specificity in developing the Ready-to-Use Immunohistochemical System, the performance of each primary antibody has been tested on a wide range of cancers which reflect the diagnostic applications of the specific antibody. Each primary antibody has also been tested on various benign tissues to identify positive controls that could be recommended.

Identification of benign tissue for recommended control and the precise description and photographs of microscopic reaction patterns in the Atlas of Stains are truly unique, and will greatly facilitate final quality evaluation of the antibody markers in laboratories.

By providing access to a photo gallery and library of detailed information on appropriate controls in the use of antibodies – and how to interpret control and reaction patterns – the Atlas of Stains is destined to become a valuable tool for all laboratories that perform IHC from local clinics and hospitals to large university laboratories.

Always remember: There is no Ready-to-Use antibody! There is a Ready-to-Use Immunohistochemical System. To obtain the performance accepted by the surgical experts and portrayed in the Atlas of Stains, the new series of FLEX Ready-to-Use antibodies must be used within the system frames established by Dako.



Scheme Coordinator, NordiQC Aalborg University Hospital, Denmark

### How to read the Atlas of Stains

The diagnostic staining performance delivered by the Dako FLEX Ready-to Use (RTU) system has been accepted by leading experts in the field and worked out in collaboration with Søren Nielsen, Scheme Organizer at NordiQC. The Dako FLEX RTU procedure makes it possible to deliver a high quality staining performance in all relevant clinical tissues.

Information on the antibodies has been organized under the following four headings:

- Clinical Application
- Reaction Location
- Recommended Control
- Differential Diagnosis

The Atlas of Stains illustrates the staining performance of each antibody in the FLEX RTU system and provides examples of:

- Staining performance in relevant clinical tissues (See below examples in Figure 1A and 1B and Figure 2A and 2B)
- Staining performance in the recommended control tissue (See below examples in Figure 1C and Figure 2C)

#### Table 1. Quality indicators

Quality indicator	IHC staining intensity
High-expression (HE) structures	Moderate to strong
Low-expression (LE) structures	Weak to moderate

**Figure 1.** FLEX RTU Monoclonal Mouse Anti-Human CD79α, Clone JCB117, Code IR621 or IS621.



**Figure 1A.** Precursor B-lymphoblastic leukemia/lymphoma disseminated to testis stained with Anti- $CD79\alpha$ . The majority of the neoplastic cells show a weak to moderate membraneous and cytoplasmic staining reaction.

Figure 2. FLEX RTU Monoclonal Mouse Anti-Human Calretinin, Clone DAK-Calret 1, Code IR627 or IS627.



Figure 2A. Granulosa cell tumor stained with Anti-Calretinin. The majority of the neoplastic cells show a weak to moderate nuclear and cytoplasmic staining reaction.

The code IR/IS refers to:

IR = FLEX ready-to-use antibodies for Autostainer Link instruments

IS = FLEX ready-to-use antibodies for Dako Autostainer/Autostainer Plus instruments

The basis for evaluating the quality of IHC performance is the use of proper controls. Benign tissue that is easily accessible and interpretable is recommended as control for most antibodies in the FLEX RTU system. Accompanying photos illustrate the reaction pattern of the cell types and/or cellular structures which should be identified in the control tissue. These cell types and/or cellular structures should be considered as quality indicators which it is critical to identify in order to monitor appropriate FLEX RTU performance.

The quality indicators are divided into high-expression (HE, moderate to strong) and low-expression (LE, weak to moderate) structures. When using the FLEX RTU system on control tissue, it will be normal to find a strong staining in some structures (HE structures) along with a less strong staining in other structures (LE structures). During development, it has been verified that the antigen expression in the vast majority of clinical samples lies within the antigen expression range defined by the HE and LE structures. Please note that for some antibodies only HE structures are identified, and for some antibodies no benign control tissue exists.

Because it is calibrated to give optimal staining of HE and LE control structures (Figure 1C and Figure 2C), the FLEX RTU system provides optimal staining in clinical samples with antigen expression ranging from low to high (Figure 1A-1B and Figure 2A-2B). This is why the FLEX RTU system provides highly sensitive IHC performance in a wide range of relevant cancers, and yields IHC results with a high signal-to-noise ratio that facilitates interpretation.



Figure 1B. Plasmacytoma stained with Anti-CD79 $\alpha$ . The majority of the neoplastic cells show a strong cytoplasmic staining reaction.



**Figure 1C.** Tonsil stained with Anti-CD79 $\alpha$ . The mantle/marginal zone B cells are HE structures showing a moderate to strong membraneous and cytoplasmic staining reaction, while the germinal center B cells are LE structures showing a moderate, but distinct staining reaction. Plasma cells show a strong cytoplasmic staining reaction. The encircled cells/ cellelular structures are representatives of the HE and LE structures.



**Figure 2B.** Epithelial mesothelioma stained with Anti-Calretinin. The majority of the neoplastic cells show a strong nuclear and cytoplasmic staining reaction.



Figure 2C. Colon stained with Anti-Calretinin. The peripheral nerves show a distinct nuclear and cytoplasmic staining reaction. The ganglion cells are HE structures with a moderate to strong staining reaction, whereas the axons are LE structures that are weak to moderately stained. The encircled cells/cellelular structures are representatives of the HE and LE structures.

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▲ Currently unavailable in the US.

▲ Not available in the US.

Antibody:	Monoclonal Mouse Anti-Human
	Actin (Muscle)
Clone:	HHF35
Code:	IR700 or IS700
Clinical Application	For identification of soft tissue tumors with muscle differentiation, i.e. leiomyoma, leiomyo- sarcoma (Fig. A) and rhabdomyosarcoma (Fig. B).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> All the smooth muscle cells in vessel walls, muscle layers and lamina muscularis mucosa should show a moderate to strong cytoplasmic staining reaction. The fine layer of myoepithelial cells delineating the surface epithelial cells should be demonstrated.
	No staining reaction should be seen in the epithelial cells (Fig. C).
	<b>Tongue:</b> Myoepithelial cells of the mucous/salivary glands should show a weak to moderate staining reaction <b>(Fig. D)</b> . No staining should be seen in the epithelial cells.
Differential Diagnosis*	1. Leiomyosarcoma vs. carcinoma. 2. Rhabdomyosarcoma vs. other malignant mesenchymal tumors.



Figure A. Leiomyosarcoma. The majority of the neoplastic cells show a moderate to strong staining reaction.



Figure B. Rhabdomyosarcoma. The majority of the neoplastic cells show a weak to moderate staining reaction.



**Figure C.** Colon. All the smooth muscle cells in vessel walls, lamina muscularis mucosa and myoepithelial cells around colonic crypts show a moderate to strong staining reaction.



Figure D. Tongue. The myoepithelial cells of the mucous/salivary glands show a weak to moderate staining reaction.

Antibody:	Polyclonal Rabbit Anti-Human Alpha-1-Antitrypsin
Code:	IR505 or IS505
Clinical Application	Primarily for identification of alpha-1-antitrypsin (A1AT) accumulation in the hepatocytes of A1AT deficient liver (Fig. A).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Tonsil:</b> The germinal center macrophages of the secondary follicles should show a moderate to strong staining reaction and neutrophil granulocytes should show a weak to moderate distinct coarse granular cytoplasmic staining reaction <b>(Fig. B)</b> .
	<b>Liver:</b> The Kupffer cells should show a moderate to strong distinct granular staining reaction, while the hepatocytes should be negative or show a weaker granular cytoplasmic staining reaction <b>(Fig. C).</b>
Differential Diagnosis*	Granular cell tumor vs. histiocytic skin reaction.



Figure A. A1AT deficient liver. The hepatocytes with alpha-1-antitrypsin deficiency show a strong granular cytoplasmic staining reaction (seen in a standard HE stained slide as an accumulation of eosinophilic lysosomes), while normal hepatocytes show a weak staining reaction.



**Figure B.** Tonsil. The germinal center macrophages show a moderate to strong and the neutrophils a weak to moderate staining reaction.



**Figure C.** Liver. The Kupffer cells show a moderate to strong distinct granular staining reaction, while the hepatocytes show a weak and diffuse cytoplasmic staining reaction.

## Antibody: Polyclonal Rabbit Anti-Human Alpha-1-Fetoprotein

Code:	IR500 or IS500
Clinical Application	Primarily for identification of hepatocellular carcinoma, hepatoid tumor, and germ cell tumors of the testis and ovary such as yolk sac tumor (Fig. A) and embryonal carcinoma (Fig. B and Fig. C).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Embryonal carcinoma:</b> Focally, the neoplastic cells should show a moderate to strong cytoplasmic staining reaction with minimal background staining (Fig. B and Fig. C).
Differential Diagnosis*	<ol> <li>Yolk sac tumor vs. clear cell carcinoma.</li> <li>Embryonal carcinoma vs. testicular seminoma.</li> </ol>



Figure A. Yolk sac tumor. The neoplastic cells show a focal and distinct cytoplasmic staining reaction.



Figure B. Embryonal carcinoma. The neoplastic cells show a focal and distinct cytoplasmic staining reaction.



Figure C. Embryonal carcinoma. The neoplastic cells show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Rabbit Anti-Human AMACR (P504S)
Clone:	13H4
Code:	IR060 or IS060
<b>Clinical Application</b>	For identification of prostate adenocarcinoma. The majority of the prostatic adenocarcinoma cells should show a granular cytoplasmic staining reaction (Fig. A and Fig. B).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Prostate adenocarcinoma:</b> The majority of the carcinoma cells should show a moderate to strong granular cytoplasmic staining reaction.
	Benign prostatic hyperplasia: The epithelial cells of the hyperplastic prostate glands should be negative or only focally show a weak granular cytoplasmic staining reaction (Fig. C).
Differential Diagnosis*	Prostatic adenocarcinoma vs. benign prostatic lesion.



Figure A. Prostate adenocarcinoma. The majority of the carcinoma cells show a distinct granular cytoplasmic staining reaction and the benign glands are mostly negative.



**Figure B.** Prostate adenocarcinoma. The majority of the carcinoma cells show a distinct granular cytoplasmic staining reaction. A spotty granular cytoplasmic staining is also seen in a few cells of the benign glands.



Figure C. Prostate. The hyperplastic glands show a weak granular cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human Amyloid A
Clone:	mc1
Code:	IR605 or IS605
<b>Clinical Application</b>	For identification and classification of AA-amyloidosis (Fig. A to Fig. C).
<b>Reaction Location</b>	Extracellular and cytoplasm.
Recommended Control	<b>Kidney with amyloidosis:</b> The smooth muscle cells in the vessels and in the glomerular cap- illary network should show a moderate to strong cytoplasmic staining reaction, while the basal membrane of the renal glomeruli should show a weak to moderate staining reaction ( <b>Fig. C</b> ).
Differential Diagnosis*	AA-amyloidosis vs. other types of amyloidosis or inflammatory disease.



Figure A. Colon with amyloidosis. The smooth muscle cells in the vessels show a weak staining reaction.



Figure B. Appendix with amyloidosis. The smooth muscle cells in the vessels show a strong staining reaction.



Figure C. Kidney with amyloidosis. The smooth muscle cells in the vessels and in the glomerular capillary network show a moderate to strong cytoplasmic staining reaction, while the basal membrane of the renal glomeruli show a weak to moderate staining reaction.

Antibody: Clone: Code:	Monoclonal Mouse Anti-Human B-Cell-Specific Activator Protein DAK-Pax5 IR650 or IS650
<b>Clinical Application</b>	For identification of pro/pre B cells, mature B cells and in the classification of lymphomas (Fig. A and Fig. B).
<b>Reaction Location</b>	Nuclear.
Recommended Control	<ul><li>Tonsil: Virtually all B cells should show a moderate to strong nuclear staining reaction.</li><li>A weak to moderate cytoplasmic staining reaction can be seen in germinal center B cells (Fig. C).</li><li>No staining reaction should be seen in plasma cells or in the squamous epithelial cells.</li></ul>
Differential Diagnosis*	<ol> <li>B-cell lymphoma vs. T-cell lymphoma.</li> <li>Identification of Reed-Sternberg cells in classic Hodgkin lymphoma.</li> </ol>



Figure A. Hodgkin lymphoma. The Reed-Sternberg cells show a weak to moderate nuclear staining reaction.



**Figure B.** *B*-cell chronic lymphatic leukemia/small lymphocytic lymphoma. The majority of the neoplastic cells show a moderate to strong nuclear staining reaction.



**Figure C.** Tonsil. The B cells in the mantle zone and in the germinal center show a moderate to strong nuclear staining reaction. The germinal center B cells also show a weak cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human BCL2 Oncoprotein
Clone:	124
Code:	IR614 or IS614
Clinical Application	Primarily for identification of follicular lymphoma (Fig. A). Various B- and T-cell lymphoprolifer- ative diseases and some diffuse large B-cell lymphomas are BCL-2 positive. Burkitt lymphoma /leukemia is generally negative for BCL-2 (Fig. B).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Tonsil:</b> The scattered T cells in the germinal centers and the mantle zone B cells should show a moderate to strong cytoplasmic staining reaction. The germinal center B cells should be negative ( <b>Fig. C</b> ). The basal epithelial cells should show a weak to moderate staining reaction ( <b>Fig. D</b> ).
Differential Diagnosis*	<ol> <li>Follicular lymphoma vs. Burkitt lymphoma/leukemia.</li> <li>Follicular lymphoma vs. reactive germinal center.</li> <li>Diffuse large B-cell lymphoma mimicking Burkitt lymphoma/leukemia vs. Burkitt lymphoma/ leukemia.</li> </ol>



Figure A. Follicular lymphoma. The majority of the neoplastic cells show a distinct cytoplasmic staining reaction.



**Figure B.** Burkitt lymphoma/leukemia. The neoplastic cells are negative for BCL2 and only benign T cells are stained.



**Figure C.** Tonsil. The scattered T cells in the germinal centers and the mantle zone B cells show a moderate to strong cytoplasmic staining reaction. The germinal center B cells are negative.



Figure. D. Tonsil. The basal epithelial cells show a weak to moderate staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	BCL6 Protein
Clone:	PG-B6p
Code:	IR625 or IS625
<b>Clinical Application</b>	For classification of diffuse large B-cell lymphomas (Fig. A), follicular lymphomas (Fig. B) and Burkitt lymphoma/leukemia.
<b>Reaction Location</b>	Nucleus.
Recommended Control	<b>Tonsil:</b> The majority of the germinal center B cells should show a moderate to strong nuclear staining reaction ( <b>Fig. C</b> ). The squamous epithelial cells should show a weak to moderate nuclear staining reaction ( <b>Fig. D</b> ).
Differential Diagnosis*	Diffuse large B-cell lymphoma/follicular lymphoma vs. mantle cell lymphoma/MALT lymphoma.



Figure A. Diffuse large B-cell lymphoma (germinal center subtype). The majority of the neoplastic cells show a distinct nuclear staining reaction.



Figure B. Follicular lymphoma. The majority of the neoplastic cells show a distinct nuclear staining reaction.



**Figure C.** Tonsil. The majority of the germinal center B cells show a moderate to strong nuclear staining reaction.



Figure. D. Tonsil. The squamous epithelial cells show a weak to moderate nuclear staining reaction.

Antibody:	Monoclonal Mouse Anti-Human Beta-Catenin
Clone: Code:	β-Catenin-1 IR702 or IS702
Clinical Application	For identification of desmoid tumors, colorectal cancer <b>(Fig. A)</b> and colon adenoma <b>(Fig. B)</b> .
<b>Reaction Location</b>	Membrane, cytoplasm and/or nuclear.
Recommended Control	<b>Appendix/Colon:</b> The epithelial cells should show a moderate to strong predominantly membranous staining reaction (a weak cytoplasmic reaction is accepted) ( <b>Fig. C</b> ). A weak membranous reaction can be seen in scattered endothelial cells, satellite cells in peripheral nerves and in the follicular dendritic network in the germinal centers of lymph nodes.
	Liver: The hepatocytes should show a weak to moderate predominantly membranous staining reaction (Fig. D).
Differential Diagnosis*	<ol> <li>Desmoid tumor vs. gastrointestinal stromal tumor.</li> <li>Normal colon vs. colon adenoma and adenocarcinoma.</li> </ol>



**Figure A.** Colon adenocarcinoma. Many of the neoplastic cells show a moderate to strong nuclear staining reaction, while the normal epithelial cells show a membranous staining reaction.



Figure B. Colon adenoma. The majority of the dysplastic cells show a moderate to strong nuclear staining reaction with weaker costaining of cytoplasm.



Figure C. Colon. The epithelial cells show a moderate to strong predominantly membranous staining reaction.



Figure D. Liver. The hepatocytes show a weak to moderate predominantly membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	GA 125
Clone:	M11
Code:	IR701 or IS701
<b>Clinical Application</b>	For identification of serous ovarian carcinoma (Fig. A) and mesothelioma (Fig. B).
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Fallopian tube:</b> The apical brush border of the majority of the epithelial cells should show a moderate to strong predominantly membranous staining reaction <b>(Fig. C)</b> .
Differential Diagnosis*	<ol> <li>Ovarian adenocarcinoma vs. other adenocarcinoma.</li> <li>Mesothelioma vs.other tumor, e.g. melanoma and lung adenocarcinoma.</li> </ol>



Figure A. Serous ovarian carcinoma. The majority of the neoplastic cells show a moderate to strong predominantly membranous staining reaction.



Figure B. Mesothelioma. A significant porportion of the neoplastic cells show a moderate to strong predominantly membranous staining reaction.



Figure C. Fallopian tube. The apical brush border of the epithelial cells shows a moderate to strong predominantly membranous staining reaction.

## Antibody: Polyclonal Rabbit Anti-Human Calcitonin

- - -

Code:	IR515 or IS515
<b>Clinical Application</b>	For identification of thyroid medullary carcinoma (Fig. A and Fig. B) and thyroid C cells (Fig. C).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Thyroid:</b> Scattered as single cells among normal thyroid follicles, the parafollicular C cells should show a moderate to strong distinct granular cytoplasmic staining reaction <b>(Fig. C).</b>
Differential Diagnosis*	Thyroid medullary carcinoma vs. thyroid follicular carcinoma.



Figure A. Thyroid medullary carcinoma. The neoplastic cells show a strong staining reaction for calcitonin.



**Figure B.** Thyroid medullary carcinoma. The neoplastic cells show a strong cytoplasmic staining reaction.



**Figure C.** Thyroid. A thyroid C cell showing a strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Caldesmon
Clone:	h-CD
Code:	IR054 or IS054
<b>Clinical Application</b>	For identification of smooth muscle and tumors with smooth muscle origin such as leiomyo- sarcoma (Fig. A), leiomyoma (Fig. B), angioleiomyoma and glomus tumor.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> The smooth muscle cells in the blood vessels, muscularis mucosa and lamina muscularis propria should show a moderate to strong distinct cytoplasmic staining reaction ( <b>Fig. C</b> ).
	<b>Normal breast or breast with hyperplasia:</b> The myoepithelial cells around the ducts and lobules should show a moderate to strong cytoplasmic staining reaction and no reaction of epithelial cells. Muscle cells in blood vessels should show a strong cytoplasmic staining reaction.
Differential Diagnosis*	1. Uterine leiomyosarcoma vs. carcinoma. 2. Uterine leiomyosarcoma vs. endometrial stromal sarcoma.



Figure A. Leiomyosarcoma. The neoplastic cells show a strong cytoplasmic staining reaction - the intensity can vary from weak to strong.



Figure B. Leiomyoma. The neoplastic cells and smooth muscle cells of small blood vessel wall (lower right corner) show a strong cytoplasmic staining reaction.



Figure C. Appendix. The smooth muscle cells show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Cairetinin
Clone:	DAK-Calret 1
Code:	IR627 or IS627
Clinical Application	Primarily for identification of mesothelial cells and malignant mesothelioma of the epithelial type (Fig. A) and in the differential diagnosis of mesothelioma vs. primary/metastatic lung or ovarian adenocarcinoma. Other tumors such as granulosa cell tumor also express calretinin (Fig. B).
<b>Reaction Location</b>	Nucleus and cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> The peripheral nerves should show a distinct nuclear and cytoplasmic staining reaction. The staining reaction in ganglion cells should be moderate to strong, whereas the axons should be weakly to moderately stained (Fig. C). Peripheral macrophages should also show a nuclear and cytoplasmic staining reaction. No staining should be seen in the epithelial cells.
Differential Diagnosis*	<ol> <li>Mesothelioma vs. carcinoma.</li> <li>Adenomatoid tumor vs. hemangioma.</li> <li>Sex cord stromal tumor vs. ovarian epithelial tumor.</li> </ol>



Figure A. Epithelial mesothelioma. The majority of the neoplastic cells show a distinct nuclear and cytoplasmic staining reaction.



**Figure B.** Granulosa cell tumor. The majority of the neoplastic cells show a distinct nuclear and cytoplasmic staining reaction.



**Figure C.** Colon. The ganglion cells show a strong staining reaction and the axons show a weak to moderate staining reaction.

Monoclonal Mouse Anti-Human
Carcinoembryonic Antigen
11-7
IR622 or IS622
For identification of carcinoembryonic antigen (CEA)-positive glycocalyx surface of gastrointes- tinal cells and colon carcinoma <b>(Fig. A).</b> CEA is expressed by various tumors such as lung adenocarcinoma, meningioma and medullary carcinoma of the thyroid <b>(Fig. B).</b>
Membrane and cytoplasm.
<b>Appendix/Colon:</b> The epithelial cells of the appendical mucosa should show a moderate to strong cytoplasmic staining reaction. At the luminal surface and the glycocalyx, the staining is stronger than cells in the basal layer. Both compartments should be demonstrated <b>(Fig. C)</b> .
<b>Tonsil:</b> The squamous epithelial cells should, focally, show a weak to moderate cytoplasmic staining reaction. If well preserved, 2/3 of the upper layer should be demonstrated <b>(Fig. D).</b>
<ol> <li>Colorectal carcinoma vs. ovarian carcinoma.</li> <li>Colorectal carcinoma vs. prostatic carcinoma.</li> <li>Thyroid medullary carcinoma vs. thyroid follicular carcinoma.</li> <li>Urothelial carcinoma vs. renal cell carcinoma.</li> <li>Pancreatic ductal carcinoma vs. acinic cell carcinoma.</li> <li>(For hepatocellular carcinoma, polyclonal CEA should be used).</li> </ol>



Figure A. Colon adenocarcinoma. The majority of the neoplastic cells show a distinct and predominantly cytoplasmic staining reaction.



Figure B. Medullary carcinoma of thyroid. The neoplastic cells show a strong membranous and cytoplasmic staining reaction.



**Figure C.** Colon. The epithelial cells of the appendical mucosa show a moderate to strong cytoplasmic staining reaction. At the luminal surface and the glycocalyx, the staining is stronger than in cells in the basal layer.



Figure D. Tonsil. Focally, the squamous epithelial cells show a weak to moderate cytoplasmic staining reaction.

Antibody:	Polyclonal Rabbit Anti-Human Carcinoembryonic Antigen (CEA)
Code.	IR320 01 18320
<b>Clinical Application</b>	For identification of the histogenesis of epithelial tumors in several morphological categories (Fig. A and Fig. B).
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Liver:</b> The bile canaliculi should show a moderate to strong membranous staining reaction <b>(Fig. C)</b> . No staining reaction should be seen in hepatocytes or only a weak, diffuse cytoplasmic staining reaction.
	<b>Pancreas:</b> Intercalated ducts/acinar ducts should show a weak to moderate membranous staining reaction ( <b>Fig. D</b> ).
Differential Diagnosis*	<ol> <li>Hepatocellular carcinoma vs. cholangiocarcinoma.</li> <li>Hepatocellular carcinoma vs. metastatic carcinoma spread to the liver.</li> </ol>



Figure A. Hepatocellular carcinoma. The bile canaliculi show a distinct moderate staining reaction.



Figure B. Secondary adenocarcinoma spread to the liver. The neoplasic cells show a moderate to strong staining reaction, and in the surrounding liver tissue the bile canaliculi show a distinct staining reaction.



Figure C. Liver. The bile canaliculi show a moderate to strong membranous staining reaction.



**Figure D.** Pancreas. The acinar ducts show a weak membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD1a
Clone:	O10
Code:	IR069 or IS069
Clinical Application	For identification of thymoma (Fig. A), precursor T-lymphoblastic leukemia/lymphoma and Langerhans' cell histiocytosis.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Tonsil or skin:</b> The Langerhans' cells in the squamous epithelium should show a moderate to strong predominantly membranous staining reaction <b>(Fig. B).</b> The epithelial cells should be negative.
	<b>Thymus:</b> The cortical thymocytes should show a moderate to strong predominantly mem- branous staining reaction <b>(Fig. C).</b>
Differential Diagnosis*	T-cell lymphoblastic lymphoma vs. mature T-cell lymphoma or B-cell neoplasm.



Figure A. Thymoma. Lymphoblasts intermingled with negative epithelial cells of the thymoma show a strong predominantly membranous staining reaction.



**Figure B.** Skin. The Langerhans' cells in the squamous epithelium show a moderate to strong predominantly membranous staining.



Figure C. Thymus. The cortical thymocytes show a strong predominantly membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD2
Clone:	AB75
Code:	IR651 or IS651
Clinical Application	For identification of normal T cells and related neoplasms such as precursor T-lymphoblastic leukemia/lymphoma (Fig. A), peripheral T-cell lymphoma (Fig. B) and anaplastic large cell lymphoma.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Tonsil:</b> Virtually all T cells and NK cells should show a predominantly membranous and cy- toplasmic staining reaction. The crowded T cells in the T-zone should show a moderate to strong continuous membranous staining reaction. The scattered T cells in the germinal center should show a strong continuous membranous staining reaction ( <b>Fig. C and D</b> ).
	<b>Appendix/Colon:</b> Intraepithelial T cells in the epithelium should show a moderate to strong staining reaction.
Differential Diagnosis*	T-cell lymphoma vs. B-cell lymphoma.



Figure A. Precursor T-lymphoblastic leukemia/lymphoma. The majority of the neoplastic cells show a distinct predominantly membranous staining reaction.



**Figure B.** Peripheral T-cell lymphoma. The majority of the neoplastic cells show a distinct predominantly membranous staining reaction.



**Figure C.** Tonsil. The crowded T cells in the T-zone show a moderate to strong membranous staining reaction, and the scattered T cells in the germinal center show a strong continuous membranous staining reaction.



**Figure D.** Tonsil. The crowded T cells in the T-zone show a moderate to strong membranous staining reaction, and the scattered T cells in the germinal center show a strong continuous membranous staining reaction.

Antibody: Polyclonal Rabbit Anti-Human CD3

Code:	IR503 or IS503
<b>Clinical Application</b>	For identification of T cells and their neoplasms such as T- and/or NK-cell lymphomas (Fig. A and Fig. B) and mycosis fungoides.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Tonsil:</b> Virtually all T cells should show a predominantly membranous and weaker cytoplasmic staining reaction. Both the crowded T cells in the T-zone and the scattered T cells in the germinal center should show a moderate to strong staining reaction ( <b>Fig. C</b> ).
Differential Diagnosis*	T- or NK-cell neoplasms vs. other neoplasms.



Figure A. Peripheral T-cell lymphoma. The majority of the neoplastic cells show a distinct membranous and cytoplasmic staining reaction.



Figure B. Precursor T-lymphoblastic leukemia/lymphoma. The majority of the neoplastic cells show a distinct staining reaction - predominantly membranous, but may be cytoplasmic.



**Figure C.** Tonsil. The crowded T cells in the T-zone and the scattered T cells in the germinal center show a moderate to strong staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD4
Clone:	4B12
Code:	IR649 or IS649
Clinical Application	For identification of thymocytes, T-helper cells and related tumors such as peripheral T-cell lymphoma (unspecified) (Fig. A), anaplastic large cell lymphoma (Fig. B) and mycosis fungoides.
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Tonsil:</b> The T-helper cells should show a moderate to strong distinct membranous staining reaction. Both the crowded T-helper cells in the T-zone and the scattered T-helper cells in the germinal center should be demonstrated <b>(Fig. C).</b>
	<b>Liver:</b> Kupffer cells and the endothelial cells of the liver sinusoids should show a weak to moderate staining reaction, while the hepatocytes should be negative <b>(Fig. D).</b>
Differential Diagnosis*	1. T-cell lymphoma vs. B-cell lymphoma. 2. Subtyping of T-cell lymphoma.



Figure A. Peripheral T-cell lymphoma. The majority of the neoplastic cells show a strong distinct membranous staining reaction.



Figure B. Anaplastic large cell lymphoma. The majority of the neoplastic cells show a strong distinct membranous staining reaction.



**Figure C.** Tonsil. The crowded T-helper cells in the T-zone and the scattered T-helper cells in the germinal center show a moderate to strong staining reaction.



Figure D. Liver. Kupffer cells and the endothelial cells of the liver sinusoids show a weak to moderate staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD5
Clone:	4C7
Code:	IR082 or IS082
Clinical Application	For identification of B-and T-cell malignancies including B-cell chronic lymphoid leukemia/ small lymphocytic lymphoma, mantle cell lymphoma <b>(Fig. A)</b> and T-cell lymphoma and leuke- mia.
<b>Reaction Location</b>	Membrane and/or cytoplasmic.
Recommended Control	<b>Tonsil:</b> Virtually all T cells should show a moderate to strong membranous, but also cyto- plasmic reaction ( <b>Fig. B</b> ). The crowded T cells in the T-zone and the scattered T cells in the germinal center should be distinctively demonstrated and show a continuous membranous staining reaction. In the mantle zone, a weak membranous staining reaction should be seen in scattered B cells, but these B cells may be difficult to distinguish from more strongly stained T cells that also are present.
Differential Diagnosis*	B-cell chronic lymphocytic leukemia / small lymphocytic lymphoma and mantle cell lymphoma vs. follicular cell lymphoma.



**Figure A.** Mantle cell lymphoma. The neoplastic cells show a moderate to strong membraneous staining reaction.



Figure B. Tonsil. The crowded T cells in the T-zone and the scattered T cells in the germinal center should show a moderate to strong staining reaction.

Antibody:	Monoclonal Mouse Anti-Human CD7
Clone:	CBC.37
Code:	IR643 or IS643
<b>Clinical Application</b>	For identification of T-cell lymphoma (Fig. A and Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Tonsil:</b> Virtually all T cells should show a predominantly membranous staining reaction. The crowded T cells in the T- zone should show a strong continuous membranous reaction and the scattered T cells in the germinal center should show a moderate to strong staining reaction <b>(Fig. C)</b> .
	<b>Appendix/Colon:</b> The intraepithelial T cells should show a moderate to strong distinct staining reaction, while the epithelial cells should be negative <b>(Fig. D).</b>
Differential Diagnosis*	1. T-cell lymphoma vs. B-cell lymphoma.



Figure A. Precursor T-lymphoblastic leukemia/lymphoma. The majority of the neoplastic cells show a strong membranous staining reaction.



**Figure B.** Peripheral T-cell lymphoma. The majority of the neoplastic cells show a strong membranous staining reaction.



**Figure C.** Tonsil. The crowded T cells in the T- zone show a strong continuous membranous staining reaction and the scattered T cells in the germinal center show a moderate to strong staining reaction.



Figure D. Appendix. The intraepithelial T cells show a moderate to strong distinct staining reaction, while the epithelial cells are negative.

Antibody:	Monoclonal Mouse Anti-Human
	CD8
Clone:	C8/144B
Code:	IR623 or IS623
<b>Clinical Application</b>	For identification of cytotoxic/suppressor T cells and their neoplastic counterparts (Fig. A).
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Tonsil:</b> In the interfollicular zone, approximately 30-40% of the T cells should show a moderate to strong predominantly membranous staining reaction ( <b>Fig. B</b> ).
	<b>Spleen:</b> The sinusoidal lining cells should show a weak to moderate staining reaction. <b>(Fig. C).</b>
Differential Diagnosis*	1. T-cell lymphoma vs. B-cell lymphoma. 2. Subtyping of T-cell lymphoma.



Figure A. Peripheral T-cell lymphoma. Focally, the neoplastic cells show a moderate to strong cytoplasmic and membraneous staining reaction.



**Figure B.** Tonsil. T cells in the interfollicular zone show a moderate to strong predominantly membranous staining reaction.



Figure C. Spleen. The sinusoidal lining cells show a weak to moderate staining reaction, and scattered T cells show a strong staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD10
Clone:	56C6
Code:	IR648 or IS648
Clinical Application	For identification of Burkitt lymphoma/leukemia, follicular lymphoma (except grade III), precursor B-cell lymphoblastic leukemia/lymphoma (Fig. A) and renal cell carcinoma of the clear cell type (Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	Liver: The bile canaliculi should show a moderate to strong distinct staining reaction with minimal staining reaction in the hepatocytes (Fig. C).
	<b>Tonsil:</b> Virtually all the germinal center cells should show a weak to moderate predominantly membranous staining reaction. The neutrophils should show a membranous staining reaction, while all the peripheral lymphocytes should be negative <b>(Fig. D)</b> .
Differential Diagnosis*	<ol> <li>Follicular lymphoma vs. other low grade/small to medium-sized B-cell lymphomas such as mantle cell lymphoma and MALT lymphoma.</li> <li>Renal cell carcinoma (clear cell type) vs. other clear cell type neoplasms.</li> <li>Endometrial stromal sarcoma vs. uterine leiomyosarcoma.</li> </ol>



Figure A. Precursor B-cell lymphoblastic leukemia/lymphoma. The neoplastic cells show a strong membranous staining reaction.



Figure B. Renal cell carcinoma (clear cell type). Focally, the neoplastic cells show a moderate membranous staining reaction.



**Figure C.** Liver. The bile canaliculi should show a moderate to strong distinct staining reaction with minimal staining reaction in the hepatocytes.



**Figure D.** Tonsil. The germinal center cells show a weak to moderate predominantly membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD15
Clone:	Carb-3
Code:	IR062 or IS062
Clinical Application	For identification of mononuclear Hodgkin cells and Reed-Sternberg cells in Hodgkin lymphoma (Fig. A). This antibody also labels lung adenocarcinoma (Fig. B).
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	Lymph node with Hodgkin lymphoma: Hodgkin cells and the Reed-Sternberg cells show a distinct membranous and cytoplasmic staining reaction (Fig. A).
	<b>Kidney:</b> Both the proximal and distal tubules should show a weak to strong distinct and pre- dominantly membranous and cytoplasmic staining reaction ( <b>Fig. C</b> ).
	<b>Tonsil:</b> The neutrophils, eosinophils and macrophages should show a moderate to strong granular cytoplasmic staining reaction <b>(Fig. D).</b>
Differential Diagnosis*	1. Hodgkin lymphoma vs. thymoma. 2. Hodgkin lymphoma vs. T-cell-rich B-cell lymphoma.



Figure A. Hodgkin lymphoma. The majority of the Hodgkin cells and the Reed-Sternberg cells show a distinct membranous staining reaction and cytoplasmic staining.



Figure B. Lung adenocarcinoma. The neoplastic cells of the adenocarcinoma show a strong cytoplasmic staining reaction.



Figure C. Kidney. The proximal and distal tubules show a weak to strong distinct and predominantly membranous and cytoplasmic staining reaction.



**Figure D.** Tonsil. The neutrophiles, eosinophiles and germinal center macrophages show a strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD19
Clone:	LE-CD19
Code:	IR656 or IS656
<b>Clinical Application</b>	For identification of B cells in normal and neoplastic tissue (Fig. A and Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Tonsil:</b> Virtually all B cells both in the mantle zone and within the germinal centers should show a moderate to strong membranous staining reaction <b>(Fig. C)</b> . No staining should be seen in the epithelial cells.
	<b>Appendix/Colon:</b> In the lamina propria, scattered plasma cells should show a weak to moderate membranous staining reaction <b>(Fig. D)</b> .
Differential Diagnosis*	1. B-cell lymphoma vs. T-cell lymphoma. 2. B-cell lymphoma relapse after MabThera (or similar anti-CD20) treatment.



Figure A. Precursor B-cell lymphoblastic leukemia/lymphoma. The majority of the neoplastic cells show a moderate to strong predominantly membranous staining reaction.



Figure B. B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma. The majority of the neoplastic cells show a moderate to strong predominantly membranous staining reaction.



**Figure C.** Tonsil. The B cells in the mantle zone and in the germinal center show a moderate to strong membranous staining reaction.



Figure D. Colon. The plasma cells in the lamina propria show a weak to moderate membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD20cy
Clone:	L26
Code:	IR604 or IS604
<b>Clinical Application</b>	For identification of the B-cell lineage and different types of B-cell lymphoma (Fig. A) like man- tle cell lymphoma (Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Tonsil:</b> Virtually all mantle zone and germinal center B cells should show a moderate to strong, crisp and continuous membranous staining reaction. The germinal center cells show a stronger staining reaction compared to mantle zone B cells ( <b>Fig. C</b> ). Scattered B cells in the squamous epithelial surface should show a weak to moderate staining reaction. The squamous epithelial cells should be negative.
Differential Diagnosis*	<ol> <li>Gastrointestinal lymphoma vs. carcinoma.</li> <li>B-cell lymphoma vs. T-cell lymphoma.</li> <li>Large B-cell lymphoma vs. melanoma.</li> </ol>



Figure A. B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma. The majority of the neoplastic cells show a distinct membranous staining reaction.



Figure B. Mantle cell lymphoma. The majority of the neoplastic cells show a distinct membranous staining reaction.



Figure C. Tonsil. The mantle zone and germinal center B cells show a moderate to strong, crisp and continuous membrane staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
Clone: Code:	1F8 IR608 or IS608
Clinical Application	For identification of follicular dendritic cells, mature B cells and structural alterations in the meshwork of follicular dendritic cells in some malignant lymphomas like follicular lymphoma <b>(Fig. A and Fig. B)</b> and angioimmunoblastic T-cell lymphoma.
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Tonsil:</b> The follicular dendritic cells in the germinal centers should show a moderate to strong membranous staining reaction demonstrating the follicular dendritic network. In the mantle zone a few activated B cells may show a weak to moderate membranous staining reaction <b>(Fig. C).</b>
Differential Diagnosis*	<ol> <li>Follicular dendritic cell tumor vs. other spindle cell tumors.</li> <li>Angioimmunoblastic T-cell lymphoma vs. other T-cell lymphomas.</li> </ol>



Figure A. Follicular lymphoma (grade I). The follicular dendritic cell network is distinctively stained.



Figure B. Follicular lymphoma (grade III). The follicular dendritic cell network is distinctively stained.



**Figure C.** Tonsil. The follicular dendritic cells in the germinal center show a moderate to strong staining reaction, and the activated B cells in the mantle zone show a weak to moderate membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD23
Clone:	DAK-CD23
Code:	IR781 or IS781
Clinical Application	For identification of both normal B lymphocytes and malignant lymphomas such as B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (Fig.A). Mantle cell lymphoma is generally negative for CD23 (Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Tonsil:</b> The follicular dendritic cells in the germinal centers should show a moderate to strong membranous staining reaction, and a subpopulation of B cells in the mantle zone should show a weak to moderate membranous staining reaction (Fig. C).
Differential Diagnosis*	B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma vs. mantle cell lymphoma.



Figure A. B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma. The majority of the neoplastic cells show a distinct membranous staining reaction.



Figure B. Mantle cell lymphoma. The neoplastic cells are negative and only remnants of entrapped follicular dendritic cells show a positive staining reaction.



**Figure C.** Tonsil. Follicular dendritic cells in the germinal centers show a moderate to strong staining reaction, and a subpopulation of B cells in the mantle zone show a weak to moderate staining reaction.
Antibody:	Monoclonal Mouse Anti-Human
	CD30
Clone:	Ber-H2
Code:	IR602 or IS602
<b>Clinical Application</b>	For identification of Reed-Sternberg cells in Hodgkin lymphoma (Fig. A) and anaplastic large cell lymphoma (Fig. B).
<b>Reaction Location</b>	Membrane and cytoplasm (paranucleus).
Recommended Control	<b>Tonsil:</b> At the edge of the germinal centers, a few activated cells should show a moderate to strong membranous staining reaction with a focal paranuclear dot-like staining. Plasma cells may show a focal cytoplasmic staining reaction <b>(Fig. C).</b>
Differential Diagnosis*	<ol> <li>Hodgkin lymphoma vs. thymoma.</li> <li>Hodgkin lymphoma vs. T-cell-rich B-cell lymphoma.</li> <li>Embryonal carcinoma vs. testicular seminoma.</li> </ol>



Figure A. Classic Hodgkin lymphoma. The majority of the Reed-Sternberg cells show a distinct membranous staining reaction and a paranuclear dot-like reaction.



**Figure B.** Anaplastic large cell lymphoma. The majority of the neoplastic cells show a distinct membranous staining reaction.



Figure C. Tonsil. Activated lymphocytes and plasma cells show a moderate to strong staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD31, Endothelial Cell
Clone:	JC70A
Code:	IR610 or IS610
Clinical Application	For identification of endothelial cells, and benign and malignant vascular disorders such as hemangiosarcoma <b>(Fig. A),</b> kaposi sarcoma <b>(Fig. B)</b> and angiosarcomas.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> A moderate to strong and predominantly membranous, but also cytoplasmic staining reaction should be seen in the normal blood and lymphatic vascular endothelial cells ( <b>Fig. C</b> ). Activated B and T cells should show a weak to moderate staining reaction.
	<b>Tonsil:</b> Endothelial cells in vascular and lymphatic spaces should show a moderate to strong cytoplasmic staining reaction, while the mantle zone B cells should show a weak to moderate membranous staining reaction ( <b>Fig. D</b> ).
Differential Diagnosis*	1. Hemangiosarcoma vs. hemangiopericytoma. 2. Hemangioma vs. adenomatoid tumor.



Figure A. Hemangiosarcoma. The majority of the neoplastic cells show a distinct membranous and cytoplasmic staining reaction. Normal blood vessel endothelium and lymphatic endothelium are strongly stained.



Figure B. Kaposi sarcoma. An intense membranous and cytoplasmic staining is seen predominantly in the angiomatoid areas.



Figure C. Colon. The normal blood and lymphatic vascular endothelial cells show a moderate to strong staining reaction.



Figure D. Tonsil. The mantle zone B cells show a weak to moderate membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD34 Class II
Clone:	QBEnd 10
Code:	IR632 or IS632
<b>Clinical Application</b>	For identification of vascular and lymphatic vessels (Fig. A) and tumors of vascular origin (Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Appendix:</b> The endothelial cells of all vessels should show a distinct predominantly membra- nous staining reaction. Especially, the endothelial cells of the small submucosal vessels should be demonstrated. Lymphoid and epithelial cells should be negative, focally, stromal cells can be positive.
	Liver: The endothelial cells of the portal vessels and the periportal sinusoids should show a distinct moderate to strong staining reaction. Hepatocytes should be negative (Fig. C).
Differential Diagnosis*	<ol> <li>Dermatofibrosarcoma vs. dermatofibroma.</li> <li>Solitary fibrous tumor vs. sarcomatoid mesothelioma.</li> <li>Gastrointestinal stromal tumor vs. gastrointestinal carcinoma.</li> <li>Malignant phyllode tumors vs. spindle cell carcinoma of the breast.</li> </ol>



Figure A. Lymphoma. The endothelial cells of vascular and lymphatic vessels show a strong predominantly membranous staining reaction.



**Figure B.** Angiosarcoma. The neoplastic cells show a moderate to strong and predominantly membranous staining reaction.



Figure C. Liver. The endothelial cells of the portal vessels and the periportal sinusoids show a moderate to strong distinct staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD43
Clone:	DF-T1
Code:	IR636 or IS636
<b>Clinical Application</b>	For identification of low-grade B-cell lymphoma (Fig. A), peripheral T-cell lymphoma (Fig. B) and myeloid disorders.
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Tonsil:</b> Virtually all T cells should show a predominantly membranous staining reaction. The crowded T cells in the T-zone should show a strong staining reaction. The scattered T cells and macrophages in the germinal center should show a moderate to strong staining reaction <b>(Fig. C).</b>
	<b>Appendix/Colon:</b> The T cells and plasma cells in lamina propria should show a moderate to strong membranous staining reaction. The macrophages should show a weak to moderate staining reaction, while the epithelial cells should be negative <b>(Fig. D)</b> .
Differential Diagnosis*	<ol> <li>Mantle cell lymphoma/B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma vs. follicular lymphoma.</li> <li>Reactive B cells vs. neoplastic B cells.</li> </ol>



Figure A. B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma. The neoplastic cells show a moderate distinct staining reaction, and normal T cells show a strong distinct staining reaction.



**Figure B.** Peripheral T-cell lymphoma. The majority of the neoplastic cells show a distinct membranous staining reaction.



**Figure C.** Tonsil. The crowded T cells in the T-zone show a strong staining reaction, whereas the scattered T cells and macrophages in the germinal center show a moderate to strong staining reaction.



**Figure D.** Appendix. The T cells and plasma cells in lamina propria show a moderate to strong staining reaction, and the macrophages show a weak to moderate staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD45, Leucocyte Common Antigen
Clone:	2B11 + PD7/26
Code:	IR751 or IS751
<b>Clinical Application</b>	For identifying tumors of lymphoid origin (Fig. A and Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Tonsil:</b> All lymphocytes should show a moderate to strong membranous staining reaction. Histiocytes and macrophages should at least show a weak membranous staining reaction. Surface epithelial cells should be negative <b>(Fig. C).</b>
	<b>Brain:</b> The microglial cells should show a weak to moderate and predominantly membranous staining reaction ( <b>Fig. D</b> ).
	Bone marrow: All lymphoid cells should be strongly stained in a crisp cell membrane pattern.
Differential Diagnosis*	<ol> <li>Lymphoma vs. seminoma.</li> <li>Lymphoma vs. carcinoma.</li> <li>Lymphoma vs. sarcoma.</li> <li>Lymphoma vs. melanoma.</li> </ol>



Figure A. B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma. The majority of the neoplastic cells show a strong membranous staining reaction.



Figure B. Acute myeloid leukemia. The neoplastic cells show a strong membranous staining reaction.



**Figure C.** Tonsil. Lymphocytes show a strong membranous staining reaction, whereas histiocytes and macrophages show a weak to moderate membranous staining reaction.



Figure D. Cerebellum. The microglial cells show a weak to moderate and predominantly membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD56
Clone:	123C3
Code:	IR628 or IS628
Clinical Application	For identification of natural killer (NK) cells, NK-like T cells, neural/neuroendocrine tissues and their neoplasms such as small cell carcinoma of the lung (Fig. A) and carcinoid tumor (Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Colon:</b> A moderate to strong and predominantly membranous staining reaction should be seen in the peripheral nerves in tunica muscularis - both the axons and the ganglion cells should be stained <b>(Fig. C).</b>
	Tonsil: The NK cells should show a weak to moderate membranous staining reaction (Fig. D).
Differential Diagnosis*	Small cell carcinoma of lung vs. Ewing's sarcoma/primitive neuroectodesmal tumor.



**Figure A.** Small cell carcinoma of the lung. The majority of the neoplastic cells show a strong predominantly membranous staining reaction.



**Figure B.** Carcinoid tumor. The majority of the neoplastic cells show a predominantly membranous staining reaction.



**Figure C.** Colon. The peripheral nerves in tunica muscularis - both the axons and the ganglion cells – show a moderate to strong and predominantly membranous staining reaction.



Figure D. Tonsil. The NK cells show a weak to moderate membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD57
Clone:	TB01
Code:	IR647 or IS647
Clinical Application	For identification of Hodgkin lymphoma (lymphocyte-predominant subtype) <b>(Fig. A and Fig. B),</b> T-cell large granular lymphocyte disorder, oligodendroglioma and neuroendocrine tumor.
<b>Reaction Location</b>	Membrane and/or cytoplasmic.
Recommended Control	<b>Tonsil:</b> Scattered activated T cells predominantly located in the germinal center as well as NK cells in the T-zone of the tonsil and at the edge of the germinal center should show a moderate to strong staining reaction <b>(Fig. C).</b>
	<b>Appendix/Colon:</b> Schwann cells of the post-ganglionic neurons and their cell bodies should show a weak to moderate staining reaction ( <b>Fig. D</b> ). Neuroendocrine cells in the epithelial surface should show a distinct staining reaction, whereas the epithelial cells should be negative.
Differential Diagnosis*	T-cell large granular lymphocyte disorders vs. malignant fibrous histiocytoma and fibrosar- coma.



Figure A. Hodgkin lymphoma (LP subtype). T cells surrounding the L&H cells show a distinct membranous staining reaction.



Figure B. Hodgkin lymphoma (LP subtype). T cells surrounding the L&H cells show a distinct membranous staining reaction.



Figure C. Tonsil. Scattered activated T cells as well as NK cells located in the germinal center show a moderate to strong staining reaction.



**Figure D.** Appendix. Schwann cells of the post-ganglionic neurons and their cell bodies show a weak to moderate staining reaction. The neuroendocrine cells in the epithelial surface show a strong staining reaction, whereas the epithelial cells are negative.

Antibody:	Monoclonal Mouse Anti-Human
	CD68
Clone:	KP1
Code:	IR609 or IS609
<b>Clinical Application</b>	For identification of macrophages, other members of the mononuclear phagocyte lineage, and neoplasm of myeloid (Fig. A and Fig. B) and macrophage/monocyte origin.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Tonsil:</b> In the germinal centers of the secondary follicles, the macrophages should show a moderate to strong cytoplasmic staining reaction. In the interfollicular areas, the granulocytes and macrophages should show a granular cytoplasmic staining reaction (Fig. C).
	<b>Normal brain:</b> The microglial cells should show a weak to moderate cytoplasmic staining reaction while the other cell types should be negative <b>(Fig. D).</b>
Differential Diagnosis*	<ol> <li>Histiocytosis vs. T-cell lymphoma.</li> <li>Myeloid neoplasms vs. lymphoid neoplasms.</li> <li>Acute myeloid leukemia vs. acute lymphoblastic leukemia.</li> </ol>



Figure A. Acute myeloid leukemia (FAB type M1). The neoplastic cells show a distinct granular cytoplasmic staining reaction.



**Figure B.** Acute myeloid leukemia (FAB type M5). The neoplastic cells show a distinct granular cytoplasmic staining reaction.



**Figure C.***Tonsil.* In the germinal center, the macrophages show a moderate to strong cytoplasmic staining reaction.



Figure D. Cerebellum. The microglial cells show a weak to moderate cytoplasmic staining reaction, while the other cell types are negative.

Antibody:	Monoclonal Mouse Anti-Human
	CD68
Clone:	PG-M1
Code:	IR613 or IS613
Clinical Application	For identification of macrophages, M4 (myelomonocytic) and M5 (monocytic) types of acute myeloid leukemia <b>(Fig. A and Fig. B),</b> and histiocytic sarcoma. Acute myeloid leukemia (FAB type M1) is negative for this protein.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Tonsil:</b> In the germinal centers of the secondary follicles, the macrophages should show a moderate to strong cytoplasmic staining reaction. In the interfollicular areas, the granulocytes and macrophages should show a granular cytoplasmic staining reaction <b>(Fig. C)</b> .
	<b>Normal brain:</b> The microglial cells should show a weak to moderate cytoplasmic staining reaction, while the other cell types should be negative <b>(Fig. D).</b>
Differential Diagnosis*	<ol> <li>Acute myeloid leukemia (FAB type M4 and M5) vs. acute myeloid leukemia (FAB type M1, M2 and M3).</li> </ol>

2. Histiocytosis vs. T-cell lymphoma.



Figure A. Acute myeloid leukemia (FAB type M1). The neoplastic cells of subtype M1 are negative (expect a few normal myelocytes). Monocytes and cells with monocytic differentiation show a cytoplasmic staining reaction.



**Figure C.** Tonsil. In the germinal center, the macrophages show a moderate to strong cytoplasmic staining reaction.



Figure B. Acute myeloid leukemia (FAB type M5). The neoplastic cells of subtype M5 show a distinct cytoplasmic staining reaction. Monocytes and cells with monocytic differentiation show a cytoplasmic staining reaction.



Figure D. Cerebellum. The microglial cells show a weak to moderate cytoplasmic staining reaction, while the other cell types are negative.

Antibody:	Monoclonal Mouse Anti-Human
	CD79α
Clone:	JCB117
Code:	IR621 or IS621
Clinical Application	For identification of B cells during all stages of differentiation and of B-cell neoplasm (Fig. A and Fig. B).
<b>Reaction Location</b>	Cytoplasm and membrane.
Recommended Control	<b>Tonsil:</b> The mantle zone B cells should show a moderate to strong membranous and cy- toplasmic staining reaction, while the germinal center B cells should show a moderate, but distinct staining reaction. Plasma cells should show a strong cytoplasmic staining reaction (Fig. C).
Differential Diagnosis*	B-cell lymphoma vs. T-cell lymphoma, except for T-lymphoblastic lymphoma.



Figure A. Plasmacytoma. The majority of the neoplastic cells show a moderate to strong cytoplasmic staining reaction.



Figure B. Precursor B-lymphoblastic leukemia/lymphoma disseminated to the testis. The majority of the neoplastic cells show a weak to moderate staining reaction.



Figure C. Tonsil. The mantle zone B cells show a strong staining reaction, while the germinal center B cells show a moderate staining reaction. Plasma cells show a strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human CD99, MIC2 Gene Products, Ewing's Sarcoma Marker
Clone:	12E7
Code:	IR057 or IS057
Clinical Application	For identification of glioblastomas and ependymomas of the CNS, certain islet cell tumors of the pancreas, Ewing's sarcoma <b>(Fig. A)</b> , granulosa cell tumor <b>(Fig. B)</b> and primitive peripheral neuroectodermal tumors.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	Pancreas: Islet cells should show a moderate to strong cytoplasmic staining reaction (Fig. C).
	<b>Tonsil:</b> The lymphocytes should a show a weak to moderate and predominantly membranous staining reaction. The squamous epithelial cells should show a weak to moderate membranous staining reaction <b>(Fig. D).</b>
	<b>Thymus:</b> A moderate to strong membranous staining reaction should be seen in the cortical thymocytes.
Differential Diagnosis*	<ol> <li>Synovial sarcoma vs. spindle cell carcinoma vs. sarcomatoid mesothelioma vs. biphasic mesothelioma.</li> <li>Ewing's sarcoma/primitive neuroectodesmal vs. small cell carcinoma.</li> <li>Ewing's sarcoma/primitive neuroectodesmal vs. rhabdomyosarcoma.</li> </ol>

4. Granulosa cell tumor vs. carcinoma.

\* Differential diagnosis is aided by the results from a panel of antibodies.



Figure A. Ewing's sarcoma. Most tumor cells show a strong membranous and cytoplasmic staining reaction.



**Figure B.** Granulosa cell tumor. The neoplastic cells show a weak to moderate membranous and cytoplasmic staining reaction.



**Figure C.** Pancreas. The pancreatic islet cells show a moderate to strong cytoplasmic staining reaction.



Figure D. Tonsil. The squamous epithelial cells show a weak to moderate membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD138
Clone:	MI15
Code:	IR642 or IS642
<b>Clinical Application</b>	For identification of malignancies involving terminally differentiated plasma cells and multiple myeloma (Fig. A), and for subclassification of diffuse large B-cell lymphoma (Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Tonsil:</b> The majority of the plasma cells should show a moderate to strong predominantly membranous staining reaction. In the germinal center, scattered stimulated immunoblasts should show a weak to moderate staining reaction, while the majority of the germinal center cells and peripheral lymphocytes should be negative. The epithelial cells should show a weak to moderate staining reaction ( <b>Fig. C</b> ).
	<b>Appendix/Colon:</b> The majority of the plasma cells in lamina propria should show a moderate to strong membranous staining reaction. The luminal and basal epithelial cells should be demonstrated <b>(Fig D).</b>
Differential Diagnosis*	<ol> <li>Subtyping of diffuse large B-cell lymphoma.</li> <li>Carcinoma vs. mesothelioma.</li> </ol>



Figure A. Myeloma. The majority of the neoplastic cells show a strong and distinct membranous staining reaction.



**Figure B.** Diffuse large B-cell lymphoma. The neoplastic cells show a distinct membranous staining reaction.



Figure C. Tonsil. The majority of the plasma cells show a moderate to strong predominantly membranous staining reaction. In the germinal center, scattered stimulated immunoblasts show a moderate to strong staining reaction. The epithelial cells show a moderate staining reaction.



**Figure D.** Appendix. The plasma cells in lamina propria and the epithelial cells show a moderate to strong predominantly membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CD246, ALK Protein
Clone:	ALK1
Code:	IR641 or IS641
<b>Clinical Application</b>	For identification of ALK-positive anaplastic large cell lymphoma (Fig. A and Fig. B).
<b>Reaction Location</b>	Nucleus and/or cytoplasm.
Recommended Control	Anaplastic large cell lymphoma (t (2;5) translocation): Scattered neoplastic cells should show a strong nuclear and cytoplasmic staining reaction (Fig. A and Fig. B).
Differential Diagnosis*	ALK-positive anaplastic large cell lymphomas vs. classical Hodgkin lymphoma.



Figure A. Anaplastic large cell lymphoma (t(2;5) translocation). Scattered neoplastic cells show a strong nuclear and cytoplasmic staining reaction.



**Figure B.** Anaplastic large cell lymphoma (t(2;5) translocation). Scattered neoplastic cells show a strong nuclear and cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	CDX-2
Clone:	DAK-CDX-2
Code:	IR080 or IS080
Clinical Application	For identification of adenocarcinoma (Fig. A) and carcinoids (Fig. B) of the gastrointestinal tract.
<b>Reaction Location</b>	Nucleus.
Recommended Control	<b>Appendix:</b> Virtually all the enterocytes of the appendiceal mucosa should show a moderate to strong nuclear reaction ( <b>Fig. C</b> ). The basal cells should show a strong staining reaction, whereas the luminal cells should show a moderate staining reaction. The cytoplasmic compartment should be negative or show only a weak staining reaction.
	<b>Pancreas:</b> The ductal and scattered intercalated/central acinar epithelial cells should show a distinct weak to moderate nuclear staining reaction (Fig. D). No cytoplasmic staining reaction should be seen.
Differential Diagnosis*	Metastatic adenocarcinoma of the intestinal tract vs. other organs.



Figure A. Colon adenocarcinoma. The neoplastic cells show a strong nuclear staining reaction.



Figure B. Carcinoids. The tumor cells of a gastrointestinal carcinoid tumor show a strong nuclear staining reaction.



Figure C. Appendix. Mucosal epithelial cells show a strong nuclear staining reaction.



Figure D. Pancreas. The intercalated epithelial cells show a weak to moderate nuclear staining reaction.

## Antibody: Polyclonal Rabbit Anti-Human Chorionic Gonadotropin

## Code: IR508 or IS508

**Clinical Application** For identification of human chorionic gonadotropin-containing trophoblastic elements in germ cell tumors, choriocarcinoma (**Fig. A**), granulosa cell tumor, hydatiform mole and seminoma with syncytiotrophoblastic giant cells (**Fig. B**).

Reaction Location Cytoplasm.

**Recommended Control Placenta:** The syncytiotrophoblasts and trophoblasts should show a moderate to strong and distinct predominantly cytoplasmic reaction. The stroma should be negative, and only a weak reaction should be seen in macrophages and serum (Fig. C).

Differential Diagnosis\*

Choriocarcinoma vs. epithelial trophoblastic tumors.
 Testicular seminoma vs. embryonal carcinoma.
 Complete hydatidiform mole vs. partial hydatidiform mole.



Figure A. Chorionic carcinoma. The neoplastic syncytiotrophoblasts show a moderate to strong cytoplasmic staining reaction with minimal background staining.



**Figure B.** Seminoma. The neoplastic syncytiotrophoblast cells show a moderate to strong cytoplasmic staining reaction.



Figure C. Placenta. The trophoblasts and syncytiotrophoblasts show a strong and distinct predominantly cytoplasmic staining reaction.

## Antibody: Polyclonal Rabbit Anti-Human Chromogranin A

Code:	IR502 or IS502
Clinical Application	For identification of neuroendocrine cells and tumors with neuroendocrine differentiation. For example, small cell lung carcinoma (Fig. A), medullary carcinoma of thyroid (Fig. B), parathyroid tumors, paraganglioma and carcinoid tumors are positive for this antibody.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> The neuroendocrine cells in the epithelial surface should show a moderate to strong coarse cytoplasmic staining reaction, whereas the epithelial cells should be negative. The axons and perikarya of the neurons and ganglion cells in the submucosa and in the tunica muscularis (Auerbach's plexus) should show a weak to moderate granular cytoplasmic staining reaction and no staining of the surrounding muscle cells ( <b>Fig. C and D</b> ).
	Brain: The cortical neurons and axons should show a distinct granular staining reaction.
Differential Diagnosis*	<ol> <li>Pheochromocytoma vs. adrenocortical tumor.</li> <li>Carcinoids vs. carcinoma.</li> <li>Thyroid medullary carcinoma vs. thyroid follicular carcinoma.</li> </ol>

4. Islet cell tumor vs. acinic cell carcinoma.



Figure A. Small cell lung carcinoma. The majority of the neoplastic cells show a finely granular, distinct cytoplasmic and focally dot-like staining reaction.



**Figure B.** Medullary thyroid carcinoma. The majority of the neoplastic cells show a distinct cytoplasmic staining reaction.



**Figure C.** Colon. The neuroendocrine cells in the epithelial surface show a moderate to strong coarse cytoplasmic staining reaction, whereas the epithelial cells are negative.



Figure D. Colon. The axons and perikarya of the neurons and ganglion cells in the submucosa and in the tunica muscularis show a weak to moderate granular cytoplasmic staining reaction

Antibody:	Monoclonal Rabbit Anti-Human
	Cyclin D1
Clone:	EP12
Code:	IR083 or IS083
Clinical Application	For identification of mantle cell lymphoma (Fig. A). Most B-cell chronic lymphocytic leukemia/ small lymphocytic lymphomas should be negative.
<b>Reaction Location</b>	Nucleus.
Recommended Control	<b>Tonsil:</b> The suprabasel layer of the squamous epithelium should show a moderate to strong nuclear staining reaction (Fig. B), while the lymphoid tissue should show no staining reaction.
Differential Diagnosis*	Mantle cell lymphoma vs. chronic lymphocytic leukemia/lymphoma and follicular lymphoma.



Figure A. Mantle cell lymphoma. The neoplastic cells show a moderate to strong nuclear staining reaction.



**Figure B.** Tonsil. The suprabasel layer of the squamous epithelium shows a moderate to strong staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Cytokeratin
Clone:	AE1/AE3
Code:	IR053 or IS053
Clinical Application	For identification of tumors of epithelial origin such as squamous cell carcinoma, seminoma (Fig. A) and Merkel cell tumor (Fig. B).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Tonsil:</b> The squamous mucosa should show a strong and diffuse cytoplasmic staining reaction in all cell layers. The interdigitating reticulum cells of the lymphoid tissue can be positive <b>(Fig. C).</b>
	Liver: The majority of the hepatocytes should show a weak to moderate and predominantly membranous reaction, and the bile duct epithelial cells should show a moderate to strong cytoplasmic staining reaction (Fig.D).
Differential Diagnosis*	<ol> <li>Carcinoma vs. sarcoma.</li> <li>Carcinoma vs. melanoma.</li> <li>Carcinoma vs. lymphoma.</li> </ol>



Figure A. Seminoma. Focally, some neoplastic cells show a moderate cytoplasmic staining reaction, while the vast majorities are entirely negative.



**Figure B.** Merkel cell tumor. Some neoplastic cells show a focal and dot-like cytoplasmic staining reaction for cytokeratin.



Figure C. Tonsil. The squamous mucosa show a strong and diffuse cytoplasmic staining reaction in all cell layers.



**Figure D.** Liver. The majority of the liver cells show a moderate predominantly membranous staining reaction, and the bile duct epithelial cells show a strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Cytokeratin 5/6
Clone:	D5/16 B4
Code:	IR780 or IS780
Clinical Application	For differential diagnosis of poorly differentiated squamous cell carcinoma <b>(Fig. A)</b> vs. adenocarcinoma, epithelioid mesothelioma vs. lung carcinoma, usual/atypical ductal hyperplasia vs. ductal carcinoma in situ of the breast, and prostate carcinoma vs. its benign mimics <b>(Fig. B)</b> .
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Tonsil:</b> The squamous epithelial cells should show a moderate to strong cytoplasmic staining reaction. The staining should be seen in all cell layers in the epithelial surface <b>(Fig. C)</b> .
	<b>Prostate:</b> The basal cells should show a weak to moderate cytoplasmic staining reaction with no or only focal staining of the secretory cells ( <b>Fig. D</b> ).
Differential Diagnosis*	<ol> <li>Mesothelioma vs. adenocarcinoma.</li> <li>Benign prostatic glands vs. prostatic adenocarcinoma.</li> </ol>



Figure A. Squamous cell carcinoma of lung. The majority of the neoplastic cells show a strong cytoplasmic staining reaction.



Figure B. Prostate hyperplasia and prostate carcinoma. The normal and benign glands show a distinct cytoplasmic staining reaction in the basal cells. Normal secretory cells and the neoplastic cells are negative or show only a focal staining reaction.



**Figure C.** Tonsil. The squamous epithelial cells show a moderate to strong cytoplasmic staining reaction. The staining reaction is seen in all cell layers.



**Figure D.** Prostate. The basal cells show a moderate cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Cytokeratin 7
Clone:	OV-TL12/30
Code:	IR619 or IS619
Clinical Application	For identification of tumors of unknown origins and for staining of cytokeratin 7 (CK 7) in glan- dular and transitional epithelial cells appearing in various tumors such as adenocarcinoma of the lung, breast <b>(Fig. A</b> ), endometrium, thyroid gland, ovary <b>(Fig. B)</b> and chromophobe renal cell carcinoma.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Pancreas:</b> The epithelial cells of the large, intermediate and intercalating ducts should show a distinct cytoplasmic staining reaction. The epithelial cells of the large acinar ducts should show a moderate to strong staining reaction, whereas the epithelial cells of the intercalating pancreatic ducts should show a weak to moderate staining reaction. The pancreatic acinar cells should be negative ( <b>Fig. C</b> ).
	Breast: The breast epithelial cells should show a strong cytoplasmic staining reaction.
Differential Diagnosis*	<ol> <li>Carcinoma of the urinary bladder vs. prostatic carcinoma.</li> <li>Ovarian carcinoma vs. colonic carcinoma.</li> <li>Lung carcinoma vs. breast carcinoma.</li> </ol>

- 4. Cholangiocarcinoma vs. hepatoma.
- 5. Paget's disease vs. Bowen's disease.



\* Differential diagnosis is

aided by the results from a panel of antibodies.

Figure A. Breast lobular carcinoma. The majority of the neoplastic cells show a distinct and predominantly cytoplasmic, but also membrane accentuated staining reaction.



Figure B. Serous ovarian carcinoma. A strong cytoplasmic staining reaction is seen in the neoplastic cells.



**Figure C.** Pancreas. The epithelial cells of the large acinar ducts show a moderate to strong staining reaction, whereas the epithelial cells of the intercalating pancreatic ducts show a weak to moderate staining reaction. The pancreatic acinar cells are negative.

Antibody:	Monoclonal Mouse Anti- Cytokeratin 17
Clone:	E3
Code:	IR620 or IS620
Clinical Application	For staining of cytokeratin (CK 17) in myoepithelial cells of human complex epithelia found in various carcinomas such as pancreatic adenocarcinoma (Fig. A) and squamous cell carcinoma of the lung (Fig. B).
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Skin:</b> A moderate to strong cytoplasmic staining reaction should be seen in the squamous, granular and cornified layer of the hair follicles, whereas the basal layer should be negative. The apocrine glands should be at least focally stained in cytoplasm/membrane. Myoepithelial cells <b>(Fig. C)</b> of the sweat glands should show a moderate to strong cytoplasmic staining reaction. The normal gland epithelial cells and the squamous epithelium should be negative.
	<b>Breast hyperplasia:</b> The myoepithelial cells of the epithelial acini should show a strong and distinct cytoplasmic staining reaction with no staining in the epithelial cells.
Differential Diagnosis*	Pancreatic adenocarcinoma vs. gastric adenocarcinoma.



Figure A. Pancreatic adenocarcinoma. A moderate to strong cytoplasmic staining reaction is seen in a large proportion of the neoplastic cells.



Figure B. Lung squamous cell carcinoma. The neoplastic cells show a moderate to strong membranous and cytoplasmic staining reaction.



**Figure C.** Skin. The myoepithelial cells of the sweat glands show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human Cytokeratin 18
Clone: Code:	DC 10 IR618 or IS618
<b>Clinical Application</b>	For identification of some epithelial tumors like Merkel cell carcinoma (Fig. A), seminoma (Fig. B) and epithelioid hemangioendothelioma.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Liver:</b> The bile duct epithelial cells should show a moderate to strong cytoplasmic staining reaction, whereas the liver cells should show a weak to moderate and predominantly membranous staining reaction. The staining reaction can be heterogeneous with the strongest staining in the periportal zones. Kupffer cells should be negative (Fig. C).
Differential Diagnosis*	1. Merkel cell carcinoma vs. basal cell carcinoma. 2. Seminoma vs. melanoma.



Figure A. Merkel cell carcinoma. The majority of the neoplastic cells show a distinct cytoplasmic and focally dot-like staining reaction.



Figure B. Seminoma. Several neoplastic cells show a focal and distinct cytoplasmic staining reaction - in some areas the staining may be more dot-like. The majority of the neoplastic cells are negative.



**Figure C.** Liver. The bile duct epithelial cells show a moderate to strong cytoplasmic staining reaction, whereas the liver cells show a weak to moderate staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Cytokeratin 19
Clone:	RCK108
Code:	IR615 or IS615
<b>Clinical Application</b>	For identification of epithelial tumors with cytokeration 19 (CK 19)-expression such as breast carcinoma (Fig. A), thyroid papillary carcinoma (Fig. B) and cholangiocarcinoma.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	Liver: The bile duct epithelial cells should show a moderate to strong cytoplasmic staining reaction, whereas the liver cells should be negative (Fig. C).
	<b>Tonsil:</b> The squamous epithelial cells should focally show a weak to moderate cytoplasmic staining reaction with the strongest staining in the basal layer <b>(Fig. D).</b>
	<b>Esophageal or vaginal mucosa:</b> The basal cells of the mucosa should show a strong cytoplasmic staining reaction.
Differential Diagnosis*	<ol> <li>Cholangiocarcinoma vs. hepatocellular carcinoma.</li> <li>Thyroid papillary carcinoma vs. hyalinizing trabecular tumor of thyroid.</li> </ol>



Figure A. Breast carcinoma. The majority of the neoplastic cells show a strong cytoplasmic staining reaction.



Figure B. Thyroid papillary carcinoma. The neoplastic cells show a strong cytoplasmic staining reaction, whereas the adjacent normal thyroid is negative.



**Figure C.** Liver. The bile duct epithelial cells show a moderate to strong cytoplasmic staining reaction, whereas the liver cells are negative.



**Figure D.** Tonsil. Focally, the squamous epithelial cells show a weak to moderate cytoplasmic staining reaction with the strongest staining in the basal layer.

Antibody:	Monoclonal Mouse Anti-Human
	Cytokeratin 20
Clone:	K <sub>s</sub> 20.8
Code:	IR777 or IS777
Clinical Application	Primarily for identification of gastrointestinal tumors (Fig. A), mucinous ovarian tumors and Merkel cell carcinoma (Fig. B). Anti-Cytokeratin 20 stains the normal gastrointestinal epithe- lium and urothelium.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> The columnar epithelial cells should show a distinct cytoplasmic staining reaction. The luminal cells will typically show a moderate to strong staining reaction, whereas the epithelial cells of the basal crypts will only show a weak to moderate staining reaction, except for endocrine cells that should show a moderate to strong staining reaction ( <b>Fig. C</b> ).
Differential Diagnosis*	<ol> <li>Merkel cell carcinoma vs. basal cell carcinoma.</li> <li>Colonic carcinoma vs. ovarian carcinoma vs. colon carcinoid.</li> <li>Cholangiocarcinoma vs. hepatoma vs. fibrolamellar hepatoma.</li> </ol>



Figure A. Colon adenocarcinoma. The majority of the neoplastic cells show a strong cytoplasmic staining reaction.



Figure B. Merkel cell carcinoma. The majority of the neoplastic cells show a perinuclear cytoplasmic and dot-like staining reaction.



Figure C. Colon. The luminal cells show a moderate to strong staining reaction, whereas the epithelial cells of the basal crypts show a weak to moderate staining reaction. Endocrine cells of the basal crypt show a moderate to strong staining reaction.

Antibody: Clone: Code:	Monoclonal Mouse Anti-Human Cytokeratin, High Molecular Weight 34βE12 IR051 or IS051
Clinical Application	For differential diagnosis between prostatic adenocarcinoma and prostatic intraepithelial neoplasia (PIN) or its benign mimics such as atypical hyperplasia. The demonstration of cytokeratin high molecular weight (CK HMW) in the basal cells is indicative of benign lesion, whereas the absence is indicative of malignancy (Fig. A and Fig. B). Anti-CK HMW should be used with antibodies to other markers such as AMACR for a more precise diagnosis. Anti-CK HMW is also used in the demonstration of squamous cell carcinoma of lung, epithelioid mesothelioma, transitional cell carcinoma and nasopharyngeal carcinoma.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Tonsil:</b> The squamous epithelial cells should show a moderate to strong distinct cytoplasmic staining reaction. The staining reaction should be seen in all cell layers in the epithelial surface <b>(Fig. C).</b>
	<b>Prostate:</b> The basal cells should show a strong cytoplasmic staining reaction with no or only focal reaction of the secretory cells.

### **Differential Diagnosis\***

Prostatic intraepithelial neoplasia vs. prostatic adenocarcinoma.
 Breast ductal adenosis vs. breast tubular carcinoma.



Figure A. Prostate adenocarcinoma. The basal cells show a strong cytoplasmic staining reaction with a continuous pattern in a normal gland (center). The staining reaction is absent in the adjacent carcinoma cells.



Figure B. Prostate adenocarcinoma. Various staining reaction patterns are seen: Continuous cytoplasmic staining in normal gland, discontinuous pattern in PIN and no staining in invasive cancer cells.



**Figure C**.*Tonsil.* The squamous epithelial cells show a strong distinct cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-
	Cytomegalovirus
Clone:	CCH2 + DDG9
Code:	IR752 or IS752**
<b>Clinical Application</b>	For identification of cytomegalovirus infection in human tissues (Fig. A and Fig. B).
<b>Reaction Location</b>	Nucleus and cytoplasm.
Recommended Control	Lesion with cytomegalovirus infection: Cells infected with cytomegalovirus should show a moderate to strong nuclear and cytoplasmic staining reaction (Fig. A and Fig. B). No back-ground staining should be seen.
Differential Diagnosis*	Cytomelogavirus infection vs. other infections.

\*\* Not available in the US.



Figure A. Lung tissue with cytomegalovirus infection. The lung lesion shows a strong nuclear and cytoplasmic staining reaction of cytomegalovirus.



Figure B. Lung tissue with cytomegalovirus infection. Infected cells show a strong nuclear and cytoplasmic staining reaction of cytomegalovirus in the alveoli.

Antibody:	Monoclonal Mouse Anti-Human
	D2-40
Clone:	D2-40
Code:	IR072 or IS072
Clinical Application	For identification of lymphatic invasion in a variety of cancers and the differential diagnosis between epithelioid mesothelioma (Fig. A) and lung adenocarcinoma. Seminoma often shows a positive staining reaction (Fig. B).
<b>Reaction Location</b>	Cytoplasm and membrane
Recommended Control	<b>Appendix:</b> The lymphatic endothelial cells should show a moderate to strong predominantly cytoplasmic staining reaction and the Cajal cells of the muscularis propria should show a weak to moderate predominantly membranous staining reaction (Fig. C). Endothelial cells should be negative.
	<b>Tonsil:</b> The lymphatic endothelial cells, follicular dendritic cells and basal squamous endothe- lial cells should show a moderate to strong staining reaction <b>(Fig. D).</b>
Differential Diagnosis*	<ol> <li>Mesothelioma vs. adenocarcinoma.</li> <li>Lymphatic endothelium vs. blood vessel endothelium.</li> </ol>



Figure A. Mesothelioma. The majority of the neoplastic cells show a moderate to strong membranous and cytoplasmic staining reaction.



Figure B. Seminoma. The neoplastic cells and lymphatic endothelial cells show a strong membranous and cytoplasmic staining reaction.



**Figure C.** Appendix. Cajal cells (lower left corner) show a moderate to strong cytoplasmic staining reaction.



Figure D. Tonsil. The lymphatic endothelial cells and basal epithelial cells show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Desmin
Clone:	D33
Code:	IR606 or IS606
<b>Clinical Application</b>	For identification of smooth and striated muscle cells and reactive mesothelial cells, tumors of muscle origin like leiomyoma (Fig. A) and rhabdomyosarcoma (Fig. B).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> The smooth muscle cells in muscularis mucosa and muscularis propria as well as along the crypts in lamina propria should show a moderate to strong cytoplasmic staining reaction. In lamina propria, the majority of the smooth muscle cells in the small vessels should show a weak to moderate occasionally dot-like staining reaction ( <b>Fig. C</b> ).
	<b>Striated muscle:</b> An intense cytoplasmic staining reaction concentrated in the Z-bands should be seen in the muscle cells.
Differential Diagnosis*	<ol> <li>Sarcoma vs. lymphoma.</li> <li>Sarcoma vs. carcinoma vs. malignant mesothelioma.</li> <li>Sarcoma vs. melanoma.</li> <li>Rhabdomyosarcoma vs. Ewing's sarcoma/primitive neuroectodesmal tumor.</li> </ol>



Figure A. Uterine leiomyoma. The majority of the neoplastic cells show a moderate to strong cytoplasmic staining reaction.



Figure B. Rhabdomyosarcoma. The majority of the neoplastic cells show a moderate to strong cytoplasmic staining reaction.



**Figure C.** Colon. The smooth muscle cells along the crypts in lamina propria show a moderate to strong cytoplasmic staining reaction. The smooth muscle cells in the small vessels show a weak to moderate staining reaction.

Antibody:	Monoclonal Mouse Anti-Human <mark>E-Cadherin</mark>
Clone:	NCH-38
Code:	IR059 or IS059
Clinical Application	For differential diagnosis between ductal and lobular carcinoma of the breast. E-cadherin is positive in breast ductal carcinoma (Fig. A) and negative in lobular carcinoma (Fig. B). E-cadherin also stains normal breast duct and various tumors such as esophageal adenocarcinoma and squamous carcinoma, and transitional cell carcinoma of the bladder.
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Appendix/Colon:</b> Virtually all the epithelial cells should show a moderate to strong distinct membranous staining reaction <b>(Fig. C).</b>
	Liver: Both the hepatocytes and the ductal cells should show a weak to moderate distinct membranous staining reaction (Fig. D).
Differential Diagnosis*	Breast ductal carcinoma vs. breast lobular carcinoma.



Figure A. Breast ductal carcinoma. All the tumor cells show a strong membranous staining reaction.



Figure B. Breast lobular carcinoma. The breast lobular carcinoma cells stain negative.



**Figure C.** Appendix. Virtually all the epithelial cells show a strong membranous staining reaction.



Figure D. Liver. The hepatocytes show a weak to moderate staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Epithelial Antigen
Clone:	Ber-EP4
Code:	IR637 or IS637
<b>Clinical Application</b>	For differential diagnosis of adenocarcinoma (Fig. A) vs. malignant mesothelioma (Fig B.) and basal cell carcinoma vs. squamous cell carcinoma of the skin.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> The epithelial cells should show a moderate to strong predominantly mem- branous staining reaction ( <b>Fig. C</b> ). No staining reaction should be seen in lymphocytes apart from a cytoplasmic staining reaction in macrophages in lamina propria.
	<b>Kidney:</b> The epithelial cells lining the Bowman's capsule should show a weak to moderate staining reaction. Epithelial cells in the tubule should show a moderate to strong distinct staining reaction <b>(Fig. D).</b>
Differential Diagnosis*	<b>Liver:</b> The bile duct epithelial cells should show a distinct predominantly membranous staining reaction, while hepatocytes should be negative.
	<ol> <li>Adenocarcinoma vs. malignant mesothelioma.</li> <li>Basal cell carcinoma vs. squamous cell carcinoma of the skin.</li> </ol>



Figure A. Lung adenocarcinoma. The majority of the neoplastic cells show a distinct predominantly membranous staining reaction.



Figure B. Mesothelioma. The majority of the neoplastic cells are negative. Only a few cells show a positive staining reaction.



Figure C. Colon. The columnar epithelial cells should show a moderate to strong staining reaction.



**Figure D.** Kidney. The epithelial cells lining the Bowman's capsule show a weak to moderate staining reaction, whereas epithelial cells in the collecting tubule show a moderate to strong staining reaction.

# Antibody: Monoclonal Mouse Anti-Human Epithelial Membrane Antigen

Clone: E29 Code: IR62

IR629 or IS629

Clinical ApplicationFor identification of tumors of epithelial origin in a wide variety of tissues (Fig. A and Fig. B).Reaction LocationMembrane and cytoplasm.Recommended ControlBreast: The epithelial cells should show a moderate to strong membranous staining reaction<br/>on the apical part of the cell membrane and, occasionally, on the entire circumference of the<br/>cell membrane (Fig. C). A granular cytoplasmic staining reaction can also be observed.Tonsil: The reactive squamous epithelial cells should show a moderate to distinct cytoplasmic<br/>staining reaction - mainly in the superficial cell layers. The plasma cells should show a weak to<br/>moderate predominantly membranous staining reaction (Fig. D).

**Differential Diagnosis\*** 

- 1. Meningioma vs. schwannoma.
- 2. Chordoma vs. chondrosarcoma.
  - 3. Metastatic carcinoma vs. adrenocortical tumor.
  - 4. Metastatic renal cell carcinoma vs. hepatocellular carcinoma.
- 5. Paget's disease vs. Bowen's disease.



Figure A. Breast ductal carcinoma. The majority of the neoplastic cells show a moderate to strong membranous and cytoplasmic staining reaction.



**Figure B.** The mesothelioma. The malignant mesothelioma cells show a strong staining reaction in membrane and cytoplasm.



Figure C. Breast. Epithelial cells show a strong staining reaction.



**Figure D.** Tonsil. The squamous epithelial cells show a moderate to strong distinct cytoplasmic staining reaction, and the plasma cells show a weak to moderate predominantly membranous staining reaction.

Antibody:	Monoclonal Mouse Anti- Epstein-Barr Virus, IMP-1
Clone:	CS.1-4
Code:	IR753 or IS753 <sup>▲</sup>
Clinical Application	For identification of Epstein-Barr virus-infected cells expressing the latent membrane protein (LMP-1) such as in Hodgkin lymphoma (Fig. A), Burkitt lymphoma/leukemia (Fig. B) and nasopharyngeal carcinoma.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	Hodgkin lymphoma (classical and mixed cellularity): At least focally, the Reed-Sternberg cells should show a moderate to strong predominantly membranous, but also cytoplasmic staining reaction, occasionally in a dot-like pattern (Fig. A).
	<b>Epstein-Barr virus-positive Burkitt lymphoma/leukemia:</b> At least focally, the neoplastic cells should show a moderate to strong predominantly membranous, but also cytoplasmic staining reaction, occasionally in a dot-like pattern <b>(Fig. B).</b>
Differential Diagnosis*	Epstein-Barr virus infection vs. other infection.

- \* Differential diagnosis is aided by the results from a panel of antibodies.
- ▲ Not available in the US.



**Figure A.** Hodgkin lymphoma. Reed-Sternberg cells show a moderate to strong staining reaction for Epstein-Barr virus.



Figure B. Burkitt lymphoma/leukemia. Burkitt lymphoma/leukemia cells show a strong membranous and cytoplasmic staining reaction for Epstein-Barr virus.

Antibody:	Monoclonal Rabbit Anti-Human Ets-Related Gene (ERG)
Clone:	EP111
Code:	IR659
Clinical Application	For identification of prostate adenocarcinoma (Fig. A and Fig. B). Overexpression of the ERG gene products is associated with prostate cancer.
<b>Reaction Location</b>	Nuclear.
Recommended Control	Vascular system in all tissues. Endothelial cells should show a moderate to strong nuclear staining (Fig. C).
Differential Diagnosis*	Prostate adenocarcinoma vs. benign prostate tissue.



**Figure A.** Prostate adenocarcinoma. The majority of neoplastic cells show a moderate to strong nuclear staining reaction.



**Figure B.** Prostate adenocarcinoma. The majority of neoplastic cells show a moderate to strong nuclear staining reaction.



**Figure C.** Endothelial cells of the vascular system. Endothelial cells show a moderate to strong nuclear staining in virtually all tissues.

Antibody:	Monoclonal Mouse Anti-Human
	Estrogen Receptor $\alpha$
Clone:	1D5
Code:	IR657 or IS657
<b>Clinical Application</b>	For assessment of estrogen receptor status in breast carcinomas (Fig. A and Fig. B).
<b>Reaction Location</b>	Nucleus.
Recommended Control	Breast carcinoma with moderate estrogen receptor expression: The neoplastic cells should show a moderate staining reaction (Fig. B).
	<b>Cervix:</b> Virtually all the columnar and basal squamous epithelial cells as well as the stromal cells (with the exception of endothelial cells and smooth muscle cells) should show a moderate to strong nuclear staining reaction. The intermediate and superficial squamous epithelial cells should show a weak to moderate nuclear staining reaction ( <b>Fig. C</b> ).
Differential Diagnosis*	<ol> <li>Hormone receptor status in breast carcinoma.</li> <li>Metastatic carcinoma of the breast vs. other organs.</li> </ol>



Figure A. Breast ductal carcinoma. The majority of the neoplastic cells show a distinct nuclear staining reaction.



Figure B. Breast ductal carcinoma. The majority of the neoplastic cells show a modrate staining reaction.



**Figure C.** Cervix. The columnar and basal squamous epithelial cells as well as the stromal cells show a moderate to strong and distinct nuclear staining reaction. The intermediate and superficial squamous epithelial cells show a weak to moderate nuclear staining reaction.

Antibody:	Monoclonal Rabbit Anti-Human
	Estrogen Receptor a
Clone:	EP1
Code:	IR084 or IS084
<b>Clinical Application</b>	For assessment of estrogen receptor status in breast cancer (Fig. A and B).
<b>Reaction Location</b>	Nucleus.
Recommended Control	Breast carcinoma with moderate ER expression: The neoplastic cells should show a moderate staining reaction (Fig. B).
Differential Diagnosis*	<ol> <li>Hormone receptor status in breast carcinoma.</li> <li>Metastatic cancer of the breast vs. other organs.</li> </ol>



Figure A. Breast ductal carcinoma with positive estrogen receptor expression. Neoplastic cells show a strong nuclear staining reaction.



**Figure B.** Breast ductal carcinoma with positive estrogen receptor expression. Neoplastic cells show a moderate staining reaction.

## Antibody: Polyclonal Rabbit Anti-Human Gastrin

Code:	IR519 or IS519
<b>Clinical Application</b>	For identification of gastrin-secreting neuroendocrine tumors (Fig. A and Fig. B).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Antral mucosa of the stomach:</b> The G cells should show a moderate to strong cytoplasmic staining reaction ( <b>Fig. C</b> ). Occasionally, a slightly diffuse staining reaction from the G cells may be appreciated as the state of the
	be seen. The epimelial cells should be negative.



Figure A. Gastrin-producing tumor spread to the liver. The majority of the neoplastic cells show a moderate granular staining reaction.



Figure B. Gastrin-producing tumor spread to the lymph node. The majority of the neoplastic cells show a strong and distinct cytoplasmic staining reaction.



Figure C. Antral mucosa of the stomach. The G cells show a moderate to strong cytoplasmic staining reaction with a slight diffusion in the vicinity of the reaction.
Antibody:	Monoclonal Mouse Anti-Human GCDFP-15
Clone:	23A3
Code:	IR077 or IS077
<b>Clinical Application</b>	For identification of metastases from breast carcinoma. (Fig. A).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Breast hyperplasia:</b> At least focally, the ductal epithelial cells should show a moderate to strong cytoplasmic reaction <b>(Fig. B).</b>
	Skin: At least focally, the epithelial cells of the sweat glands should show a moderate to strong cytoplasmic staining reaction (Fig. C). Squamous epithelial cells should be negative.
Differential Diagnosis*	Metastatic cancer of the breast vs. metastases from other organs.



**Figure A.** Breast ductal carcinoma. The neoplastic cells show a moderate to strong cytoplasmic staining reaction.



**Figure B.** Breast hyperplasia. The ductal epithelial cells show a moderate to strong staining reaction.



Figure C. Skin. Focally, the epithelial cells of the sweat glands show a moderate to strong staining reaction.

## Antibody: Polyclonal Rabbit Anti-Glial Fibrillary Acidic Protein

Code:	IR524 or IS524
<b>Clinical Application</b>	For identification of astrocytes in the central nervous system and related tumors (Fig. A and Fig. B).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	Brain: The astrocytes should show a moderate to strong cytoplasmic staining reaction (Fig. C).
	<b>Appendix/Colon:</b> Ganglion cells, e.g. in Auerbach's and Meissner's plexus, should show a weak to moderate staining reaction <b>(Fig. D).</b>
Differential Diagnosis*	Glioma vs. metastatic carcinoma.



Figure A. Astrocytoma. The majority of the neoplastic cells show a strong cytoplasmic staining reaction.



**Figure B.** *Glioblastoma. The majority of the neoplastic cells show a strong cytoplasmic staining reaction.* 



Figure C. Brain. The astrocytes show a moderate to strong cytoplasmic staining reaction.



Figure D. Colon. The ganglion cells in Meissner's plexus show a weak to moderate staining reaction.

# Antibody: Polyclonal Rabbit Anti-Helicobacter Pylori

## Code: IR523 or IS523\*\*

Clinical Application	For identification of helicobacter pylori infection in gastritis <b>(Fig. A and Fig. B)</b> and primary gastric lymphomas.
<b>Reaction Location</b>	Helicobacter pylori bacteria.
Recommended Control	<b>Gastric mucosa infected with helicobacter pylori:</b> The bacteria lining the gastric mucosa should show a moderate to strong staining reaction. No staining reaction should be seen in the epithelial cells. In the lamina propria, scattered macrophages can show a positive staining reaction (Fig. A and Fig. B).
Differential Diagnosis*	Gastritis (helicobacter pylori infection vs. other causes).

\* Differential diagnosis is aided by the results from a panel of antibodies.

 Not currently available in the US.



Figure A. Gastric mucosa infected with helicobacter pylori. Helicobacter pylori in the gastric mucosa lining show a moderate to strong staining reaction.



Figure B. Gastric mucosa infected with helicobacter pylori. Helicobacter pylori in the gastric mucosa lining show a moderate to strong staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
Clone: Code:	OCH1E5 IR624 or IS624
Clinical Application	For differential diagnosis of hepatocellular tumors <b>(Fig. A and Fig. B)</b> , clear cell hepatocellular carcinomas from other clear cell malignancies, and for the distinction of hepatoblastoma, especially, the embryonal type from other small, round cell tumors of childhood.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	Liver: The hepatocytes should show a moderate to strong granular cytoplasmic staining reaction, while the bile duct epithelial cells should be negative (Fig. C).
Differential Diagnosis*	<ol> <li>Hepatocellular carcinoma vs. cholangiocarcinoma.</li> <li>Hepatocellular carcinoma vs. renal cell carcinoma.</li> </ol>



Figure A. Hepatocellular carcinoma. The neoplastic cells show a strong, homogeneous and granular cytoplasmic staining reaction.



Figure B. Hepatocellular carcinoma. The neoplastic cells show a strong and homogeneous granular cytoplasmic staining reaction.



Figure C. Liver. The hepatocytes show a moderate to strong granular cytoplasmic staining reaction. The bile duct epithelial cells are negative.

# Antibody:Polyclonal Rabbit Anti-<br/>Herpes Simplex Virus Type 1Code:IR521 or IS521Clinical ApplicationFor identification of herpes simplex virus infection in human tissue (Fig. A to C).Reaction LocationIntranucleus.Recommended ControlLesion with herpes simplex virus infection: T cells infected with herpes simplex virus (type 1 or type 2) should show a weak to strong and occasionally diffuse intranuclear staining reaction (Fig. A to C).Differential Diagnosis\*Herpes simplex virus infection vs. other infection.



Figure A. Liver. Cells infected with herpes simplex virus show a weak to strong and occasionally diffuse intranuclear staining reaction.



Figure B. Placenta. Cells infected with herpes simplex virus show a weak to strong and occasionally diffuse intranuclear staining reaction.



Figure C. Brain. Cells infected with herpes simplex virus show a moderate to strong and occasionally diffuse intranuclear staining reaction.

Antibody:	Polyclonal Rabbit Anti-Human IgD
Code:	IR517 or IS517
Clinical Application	For identification of human IgD (delta-chains) in splenic marginal zone lymphoma (Fig. A), mantle cell lymphoma (Fig. B), B-cell chronic lymphocytic/leukemia/small lymphocytic lymphoma and rare subsets of multiple myeloma.
<b>Reaction Location</b>	Membrane and cytoplasm
Recommended Control	<b>Tonsil:</b> The majority of the mantle zone B cells should show a moderate to strong predominantly membranous reaction <b>(Fig. C).</b> The background should be negative or show only a minimal staining reaction.
Differential Diagnosis*	IgD vs. other subtypes of lymphomas.



**Figure A.** Splenic marginal zone lymphoma. The neoplastic cells show a strong membranous and cytoplasmic staining reaction.



**Figure B.** Mantle cell lymphoma. The neoplastic cells show a moderate predominantly membranous staining reaction.



Figure C. Tonsil. Mantle zone B cells show a moderate to strong staining reaction.

Antibody:	Polyclonal Rabbit Anti-Human IgG
Code:	IR512 or IS512
Clinical Application	For identification of plasma cells and related lymphoid cells containing IgG, and for IgG plasma cell neoplasia <b>(Fig. A).</b> Additionally, the antibody may be used for distinguishing neoplastic monoclonal proliferation from reactive hyperplasia of plasma cells.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Tonsil:</b> 60-70% of the plasma cells should show a moderate to strong cytoplasmic staining reaction. Immunoblasts in the germinal center should also show a moderate to strong staining reaction. <b>(Fig. B).</b>
	<b>Bone marrow:</b> 60-70% of the plasma cells should show a strong cytoplasmic staining reaction.
Differential Diagnosis*	Subtyping for B-cell neoplasm: IgG subtype vs. IgM subtype vs. IgA subtype.



**Figure A.** Plasmacytoma IgG subtype. Atypical plasma cells of plasmacytoma show a weak to strong staining reaction.



Figure B. Tonsil. Plasma cells and immunoblasts show a moderate to strong cytoplasmic staining reaction.

Antibody:	Polyclonal Rabbit Anti-Human IgM
Code:	IR513 or IS513
Clinical Application	For identification of plasma cells and lymphoid cells containing IgM. It is also used for the clas- sification of IgM subtype for B-cell neoplasia <b>(Fig. A).</b> Additionally, the antibody may be used for distinguishing neoplastic monoclonal proliferation from reactive plasma cell hyperplasia.
<b>Reaction Location</b>	Cytoplasm and membrane.
Recommended Control	<b>Tonsil:</b> Virtually all mantle zone B cells should show a weak to moderate distinct membranous staining reaction, while immunoblasts and plasma cells in the germinal center should show a moderate to strong cytoplasmic staining reaction <b>(Fig. B)</b> .
	Bone marrow: About 10% of the plasma cells should be stained.
Differential Diagnosis*	Subtyping for B-cell neoplasm: IgM subtype vs. IgG subtype vs. IgA subtype.



**Figure A.** *CLL IgM* subtype. A strong IgM staining is seen in the neoplas-tic cells.



Figure B. Tonsil. The mantle zone B cells show a moderate staining reaction, whereas immunoblasts and plasma cells in the germinal center show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human Inhibin-α
Clone:	R1
Code:	IR058 or IS058
Clinical Application	For identification of ovarian sex cord and stromal tumors such as granulosa cell tumor <b>(Fig. A).</b> Other positive tumors include complete hydatiform mole, gynandroblastoma and adrenal cortical adenocarcinoma.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Placenta:</b> The trophoblasts and syncytiotrophoblasts should show a moderate to strong heterogeneous and granular cytoplasmic staining reaction (Fig. B).
	<b>Testis:</b> Both Leydig cells and Sertoli cells should show a moderate to strong, distinct granular cytoplasmic staining reaction ( <b>Fig. C</b> ).
Differential Diagnosis*	<ol> <li>Granulosa cell tumor vs. carcinoma.</li> <li>Adrenocortical tumor vs. renal cell carcinoma.</li> <li>Adrenocortical tumor vs. pheochromocytoma.</li> </ol>



Figure A. Granulosa cell tumor. The tumor cells show a moderate to strong granular cytoplasmic staining reaction.



**Figure B.** *Placenta. The trophoblasts and the syncytiotrophoblasts show a heterogeneous cytoplasmic staining reaction.* 



**Figure C.** Testis. Leydig cells and Sertoli cells show a moderate to strong staining reaction.

# Antibody: Polyclonal Guinea Pig Anti-Insulin

Code:	IR002 or IS002
<b>Clinical Application</b>	For identification of insulin-producing cells in normal and neoplastic tissue (Fig. A).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Pancreas:</b> The B cells in the islets of Langerhans <b>(Fig. B)</b> should show a moderate to strong cytoplasmic staining reaction. The acinar epithelial cells of the pancreas should be negative.
Differential Diagnosis*	Insulinoma vs. other endocrine tumors of the pancreas.



Figure A. Insulinoma. Focally, the neoplastic cells show a moderate to strong granular cytoplasmic staining reaction.



Figure B. Pancreas. The B cells in the islets of Langerhans show a moderate to strong cytoplasmic staining reaction.

Antibody:	Polyclonal Rabbit Anti-Human Kappa Light Chains
Code:	IR506 or IS506
Clinical Application	For identification of plasma cells and lymphoid cells containing kappa light chains, and for classification of kappa light chain restriction <b>(Fig. A and Fig. B)</b> for monoclonal gammopa-thies and amyloidosis.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Tonsil:</b> Approximately 40-60 % of the B cells in the mantle zone should show a weak to moderate membranous staining reaction, while the B lymphocytes in the germinal center should be negative or only weakly demonstrated. Plasma cells and immunoblasts in the germinal center should show a moderate to strong cytoplasmic staining reaction. Some background reaction in serum, connective tissue and epithelial cells is accepted ( <b>Fig. C</b> ).
	<b>Bone marrow:</b> Approximately 40-60 % of the plasma cells should show a strong cytoplasmic staining reaction.
Differential Diagnosis*	IgK subtype vs. IgL subtype for B-cell neoplasm.



Figure A. B-cell lymphoma. Most neoplastic cells show a distinct membranous and cytoplasmic staining reaction.



Figure B. Plasmacytoma. The tumor cells show a strong cytoplasmic staining reaction.



Figure C. Tonsil. B cells in the mantle zone show a weak to moderate membranous staining reaction, while the B lymphocytes in the germinal center are weakly demonstrated. Plasma cells and immunoblasts in the germinal center show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Ki-67 Antigen
Clone:	MIB-1
Code:	IR626 or IS626
Clinical Application	For identification of proliferating cells in normal and neoplastic tissues such as Burkitt lymphoma/leukemia (Fig. A), colon adenocarcinoma (Fig. B), soft-tissue sarcoma, prostatic adenocarcinoma and breast carcinoma.
<b>Reaction Location</b>	Nucleus and perinucleus.
Recommended Control	<b>Tonsil:</b> In the secondary follicles, virtually all the germinal center B cells should show a moderate to strong nuclear staining reaction - the staining is the strongest in the dark zone and the weakest in the light zone below the mantle zone ( <b>Fig. C</b> ). The parabasal squamous epithelial cells should show a weak to moderate nuclear staining reaction ( <b>Fig. D</b> ).
	<b>Esophagus:</b> The basal and parabasal epithelial cells should show a distinct nuclear staining reaction.
Differential Diagnosis*	<ol> <li>High grade non-Hodgkin lymphoma vs. low grade non-Hodgkin lymphoma.</li> <li>Burkitt lymphoma/leukemia vs. other lymphoma.</li> <li>Anal intraepithelial neoplasm vs. hyperplasia or dysplasia.</li> </ol>



Figure A. Burkitt lymphoma/leukemia. Virtually all the neoplastic cells show a distinct nuclear staining reaction.



Figure B. Colon adenocarcinoma. The neoplastic cells show a distinct nuclear staining reaction, while only a few normal basal epithelial cells are stained.



**Figure C.** Tonsil. The germinal center B cells show a moderate to strong nuclear staining reaction.



Figure D. Tonsil. The parabasal squamous epithelial cells show a weak to moderate nuclear staining reaction.

Antibody:	Polyclonal Rabbit Anti-Human Lambda Light Chains
Code:	IR507 or IS507
Clinical Application	For identification of plasma cells and lymphoid cells containing lambda light chains, and for classification of lambda light chain restriction <b>(Fig. A)</b> for monoclonal gammopathies and amyloidosis.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Tonsil:</b> The mantle zone B cells should show a moderate to strong membranous staining reaction, while immunoblasts and plasma cells in the germinal center should show a moderate to strong cytoplasmic staining reaction <b>(Fig. B).</b>
	<b>Bone marrow:</b> Approximately 40-50% of the plasma cells should show a strong cytoplasmic staining reaction.
Differential Diagnosis*	IgL subtype vs. IgK subtype for B-cell neoplasm.



**Figure A.** *Plasmacytoma lambda subtype. The plasmacytoma cells show a strong cytoplasmic staining reaction.* 



**Figure B.** Tonsil. The B cells and plasma cells show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human Mammaglobin
Clone: Code:	304-1A5 IR074 or IS074
<b>Clinical Application</b>	For identification of breast ductal carcinoma (Fig. A).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	Breast hyperplasia: At least focally, the ductal epithelial cells should show a moderate to strong cytoplasmic staining reaction (Fig. B).
	Skin: At least focally, the epithelial cells of the sweat glands should show a moderate to strong cytoplasmic staining reaction. The squamous epithelial cells should be negative (Fig. C).
Differential Diagnosis*	Metastatic breast carcinoma vs. other primary/metastatic tumors.



**Figure A.** Breast ductal carcinoma. Neoplastic cells show a moderate to strong cytoplasmic staining reaction.



**Figure B.** Breast hyperplasia. The ductal epithelial cells show a moderate to strong cytoplasmic staining reaction.



**Figure C.** Skin. The epithelial cells of the sweat glands show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human Mast Cell Tryptase
Clone:	AA1
Code:	IR640 or IS640
<b>Clinical Application</b>	For identification of atypical or immature mast cells in mast cell leukemia and small mast cell infiltrates in cutaneous mastocytosis <b>(Fig. A and Fig. B).</b>
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Tonsil:</b> The interfollicular mast cells should show a moderate to strong cytoplasmic staining reaction <b>(Fig. C).</b> Occasionally, a weak and diffuse staining pattern in the vicinity of the labeled cells may be seen. Lymphocytes should be negative.
	<b>Appendix/Colon:</b> Mast cells in the lamina propria should show a moderate to strong distinct cytoplasmic staining reaction, while the epithelial cells should be negative <b>(Fig. D).</b> Occasionally, a weak and diffuse staining pattern in the vicinity of the labeled cells may be seen.
Differential Diagnosis*	Mast cell disease vs. other inflammatory cell infiltrates.



Figure A. Mastocytosis in the bone marrow. The majority of the mast cells show a strong cytoplasmic staining reaction.



Figure B. Mastocytosis in the subcutis. The majority of the mast cells show a strong cytoplasmic staining reaction.



**Figure C.** Tonsil. The interfollicular mast cells show a strong cytoplasmic staining reaction. A weak and diffuse staining pattern in the vicinity of the labeled cells is seen.



Figure D. Colon. Mast cells in the lamina propria show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Melan-A
Clone:	A103
Code:	IR633 or IS633
<b>Clinical Application</b>	For identification of melanoma (Fig. A). Melan-A is also expressed by various tumors such as granulosa cell tumor (Fig. B), adrenocortical carcinoma and angiomyolipoma.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Skin:</b> The melanocytes in the basal layer of the epidermis and nevus cells should show a strong distinct cytoplasmic staining reaction and squamous epithelial cells should be negative <b>(Fig. C).</b>
	<b>Adrenal gland:</b> Virtually all the adrenal cortical cells should show a weak to moderate distinct granular staining reaction throughout all zones of the gland <b>(Fig. D).</b>
Differential Diagnosis*	<ol> <li>Spindle cell melanoma vs. spindle cell carcinoma.</li> <li>Melanoma vs. lymphoma.</li> </ol>



Figure A. Melanoma. The metastatic melanoma cells show a strong cytoplasmic staining reaction for melan-A.



**Figure B.** Granulosa cell tumor. The majority of the neoplastic cells show a strong granular cytoplasmic staining reaction.



Figure C. Skin. The melanocytes in the basal layer of the epidermis show a moderate to strong cytoplasmic staining reaction.



Figure D. The adrenal cortical cells show a weak to moderate staining reaction.

Antibody:	Monoclonal Mouse Anti-Human Melanosome
Clone:	HMB45
Code:	IR052 or IS052
<b>Clinical Application</b>	For identification of melanocytes with immature melanosome formation in normal skin, nevus and melanoma tissue.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	Melanoma: The majority of the melanoma cells should show a moderate to strong, distinct and granular cytoplasmic staining reaction (Fig. A and Fig. B).
	<b>Nevus:</b> The nevus cells in the dermis should show a moderate to strong distinct cytoplasmic staining reaction. <b>(Fig. C).</b>
Differential Diagnosis*	<ol> <li>Melanoma vs. carcinoma.</li> <li>Angiomyolipoma vs. sarcomatoid renal cell carcinoma.</li> </ol>



Figure A. Melanoma. The skin melanoma cells show a moderate to strong cytoplasmic staining reaction.



**Figure B.** Metastatic melanoma. The metastatic melanoma cells show a strong cytoplasmic staining reaction.



**Figure C.** Skin nevus. The nevus cells in the dermis and the melanocytes in the basal layer of the epidermis show a moderate to strong granular cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	MUC2
Clone:	CCP58
Code:	IR658
Clinical Application	For identification of mucinous adenocarcinoma of gastrointestinal origin (Fig. A) and intestinal metaplasia in Barrett's esophagus (Fig. B).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	Colon: Goblet cells should show a moderate to strong cytoplasmic staining reaction (Fig. C).
Differential Diagnosis*	Colon adenocarcinoma metastatic to the ovary vs. primary mucinous ovary tumor.



Figure A. Colon adenocarcinoma metastatic to the ovary. The neoplastic cells show a moderate to strong cytoplasmic staining reaction.



**Figure B.** Barrett's esophagus. The neoplastic cells show a moderate to strong cytoplasmic staining reaction.



Figure C. Colon. Goblet cells in the tubular glands show a moderate to strong cytoplasmic staining reaction

Antibody:	Monoclonal Mouse Anti-Human MUM1 Protein
Clone:	MUM1p
Code:	IR644 or IS644
<b>Clinical Application</b>	For subclassification of lymphoid malignancies (Fig. A and Fig. B).
<b>Reaction Location</b>	Nucleus and cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> Plasma cells in the lamina propria should show a moderate to strong nuclear staining reaction <b>(Fig. C).</b> The epithelial cells should be negative.
	<b>Tonsil:</b> In the germinal center, activated B cells should show a weak to moderate nuclear staining reaction ( <b>Fig. D</b> ). The interfollicular plasma cells should show a moderate to strong nuclear staining reaction. Only a minimal cytoplasmic staining reaction should be seen. The squamous epithelial cells should be negative.
Differential Diagnosis*	Subtyping of diffuse large B-cell lymphoma.



**Figure A.** Myeloma. The majority of the neoplastic cells show a strong nuclear staining reaction.



Figure B. Classic Hodgkin lymphoma. Reed-Sternberg cells show a nuclear staining reaction.



Figure C. Appendix. Plasma cells in lamina propria show a moderate to strong nuclear staining reaction. Only a minimal cytoplasmic staining reaction is seen.



**Figure D.** Tonsil. Activated B cells in the germinal center show a weak to moderate nuclear staining reaction, and interfollicular plasma cells show a moderate to strong nuclear staining reaction. Only a minimal cytoplasmic staining reaction is seen.

Antibody:	Monoclonal Mouse Anti-Human MutL Protein Homolog 1 (MLH1)
Clone:	ES05
Code:	IR079 or IS079
Clinical Application	For differential identification of colorectal carcinoma. When deficient, the MutL Protein Homolog 1 (MLH1) is associated with the onset of hereditary non-polyposis colorectal cancer (HNPCC) (Fig. A and Fig. B).
<b>Reaction Location</b>	Nucleus.
Recommended Control	<b>Appendix/Colon:</b> Virtually all cells should show a distinct nuclear staining reaction. The basal epithelial cells should show a moderate to strong staining reaction, whereas the luminal epithelial cells and smooth muscle cells at least should show a weak to moderate staining reaction ( <b>Fig. C</b> ).
	<b>Tonsil:</b> Virtually all cells should show a distinct nuclear reaction. Germinal center cells should show a moderate to strong staining reaction, whereas the mantle zone B and T cells should at least show a weak to moderate staining reaction <b>(Fig. D)</b> .
Differential Diagnosis*	<ol> <li>HNPCC vs. other sporadic colorectal cancer.</li> <li>Microsatellite instability evaluation in various cancer types such as e.g. endometrial and prostate adenocarcinoma.</li> </ol>



Figure A. Colon adenocarcinoma with loss of MLH1 protein. The neoplastic cells show no nuclear staining reaction, while entrapped stromal cells show a moderate to strong nuclear staining reaction.



**Figure B.** Colon adenocarcinoma with intact MLH1 gene function. Both the neoplastic cells, stromal cells and remnants of benign epithelial cells show a moderate to strong nuclear staining reaction.



Figure C. Appendix. Virtually all of the epithelial cells and stromal cells show a moderate to strong nuclear staining reaction.



**Figure D.** Tonsil. The majority of the cells show a moderate to strong nuclear staining reaction.

Antibody: Clone: Code:	Monoclonal Mouse Anti-Human MutS Protein Homolog 2 (MSH2) FE11 IR085
Clinical Application	For the evaluation of colorectal carcinoma. MSH2 protein deficiency, as indicated by a loss of staining in tumor cells, identifies colorectal cancers with defects in DNA mismatch repair. This usually results from germline mutations in the <i>MSH2</i> gene that confer a hereditary predisposition to colorectal and to a lesser degree other cancers, known collectively as Lynch syndrome <b>(Fig. A and B).</b>
<b>Reaction Location</b>	Nucleus.
Recommended Control	Appendix/Colon: Virtually all cells should show a distinct nuclear staining reaction. The basal epithelial cells should show a moderate to strong staining reaction whereas the luminal epithelial cells and smooth muscle cells at least should show a weak to moderate staining reaction (Fig. C). Delayed fixation or long term storage of cut sections may reduce staining intensity which may impact interpretation.
Differential Diagnosis*	Cancers associated with MSH2 mutation or loss of expression vs. MSH2 intact cancers.



**Figure A.** Colon adenocarcinoma with loss of MSH2 protein. The neoplastic cells show no nuclear staining reaction, adjacent normal stromal cells show a moderate to strong nuclear staining reaction.



Figure B. Colon adenocarcinoma with intact MSH2 expression. The neoplastic cells, stromal cells and remnants of benign epithelial cells show a moderate to strong nuclear staining reaction.



Figure C. Appendix. Virtually all of the epithelial cells and stromal cells show a moderate to strong nuclear staining reaction.

Antibody:	Monoclonal Rabbit Anti-Human MutS Protein Homolog 6 (MSH6)
Clone:	EP49
Code:	IR086
Clinical Application	For the evaluation of colorectal carcinoma. Loss of MSH6 protein in colorectal cancers identi- fies tumors with defects in DNA mismatch repair. This is most often a consequence of loss of expression of its heterodimeric partner MSH2, but also rarely results from germline mutations in the <i>MSH6</i> gene that confer a hereditary predisposition to colorectal and to a lesser degree other cancers, known collectively as Lynch syndrome <b>(Fig. A and B)</b> .
<b>Reaction Location</b>	Nucleus.
Recommended Control	<b>Appendix/Colon:</b> Virtually all cells should show a distinct nuclear staining reaction. The basal epithelial cells should show a moderate to strong staining reaction whereas the luminal epithelial cells and stromal cells at least should show a weak to moderate staining reaction ( <b>Fig. C</b> ). Delayed fixation or long term storage of cut sections may reduce staining intensity which may impact interpretation.
Differential Diagnosis*	Cancers associated with MSH6 mutation or loss of expression vs. MSH6 intact cancers.



Figure A. Colon adenocarcinoma with loss of MSH6 protein. The neoplastic cells show no nuclear staining reaction, while entrapped stromal cells show a moderate to strong nuclear staining reaction.



Figure B. Colon adenocarcinoma with intact MSH6 expression. The neoplastic cells, stromal cells and remnants of benign epithelial cells show a moderate to strong nuclear staining reaction.



Figure C. Appendix. Virtually all of the epithelial cells, stromal cells, and smooth muscle cells show a moderate to strong nuclear staining reaction.

Antibody:	Polyclonal Rabbit Anti-Human Myeloperoxidase
Code:	IR511 or IS511
Clinical Application	For differential diagnosis between lymphoid and myeloid tumors as myeloid tumors are generally positive and lymphoid tumors negative. For example, myeloblasts and immature myeloid cells of acute myelogenous leukemia (Fig. A), monomyelocytic leukemia and erythroleukemia are positive for myeloperoxidase.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Liver:</b> The neutrophils and Kupffer cells should show a strong granular cytoplasmic staining reaction and hepatocytes should be negative or show a weak staining reaction <b>(Fig. B).</b>
	<b>Tonsil:</b> The neutrophils and eosinophils in the interfollicular zones and the germinal center macrophages should show a moderate to strong granular cytoplasmic staining reaction <b>(Fig. C).</b>
Differential Diagnosis*	Leukemia vs. lymphoma.



**Figure A.** Acute myeloid leukemia (M4). A strong granular cytoplasmic staining reaction is seen in part of the neoplastic cells, and a weak or absent staining is observed in the monocytes.



Figure B. Liver. The neutrophils and Kupffer cells show a moderate to strong staining reaction.



Figure C. Tonsil. The neutrophils and eosinophils show a moderate to strong granular cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-
	Myogenin
Clone:	F5D
Code:	IR067 or IS067
<b>Clinical Application</b>	For identification of rhabdomyosarcoma (Fig. A) and Wilms' tumor (Fig. B).
<b>Reaction Location</b>	Nucleus.
Recommended Control	<b>Rhabdomyosarcoma:</b> At least focally, the neoplastic cells should show a moderate to strong nuclear reaction and no, or only a minimal, cytoplasmic reaction. No background staining should be seen (Fig. A).
	Leiomyosarcoma: No staining should be seen in the neoplastic cells (Fig. C).
Differential Diagnosis*	<ol> <li>Rhabdomyosarcoma vs. leiomyosarcoma.</li> <li>Rhabdomysosarcoma vs. other small round cell tumors.</li> </ol>



Figure A. Rhabdomyosarcoma. Tumor cells show a moderate to strong nuclear staining reaction.



Figure B. Wilms' tumor. Some tumor cells show a strong nuclear staining reaction.



Figure C. Leiomyosarcoma. Tumor cells are negative for myogenin.

Antibody:	Monoclonal Mouse Anti-Human Neurofilament Protein
Clone:	2F11
Code:	IR607 or IS607
<b>Clinical Application</b>	For identification of neurons (axons) of the central and peripheral nervous system, and for identification of tumors with neuronal differentiation as well as Merkel cell carcinoma (Fig. A).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> The ganglion cells and the large axons in the plexus of Auerbach should show a moderate to strong cytoplasmic staining reaction, whereas the axons in the muscularis externa should show a weak to moderate staining reaction. Smooth muscle cells and epithelium should be negative <b>(Fig. B)</b> .
	Brain: All neurons and axonal processes should show a moderate to strong fibrillar cytoplas- mic staining reaction (Fig. C).
Differential Diagnosis*	1. Neuroblastoma vs. Wilms' tumor. 2. Merkel cell carcinoma vs. lymphoma.



Figure A. Merkel cell carcinoma. A strong heterogeneous, cytoplasmic and dot-like staining reaction is seen in the neoplastic cells.



**Figure B.** Colon. The ganglion cells and the large axons in the Auerbach's plexus show a moderate to strong cytoplasmic staining reaction, whereas the axons in the muscularis externa show a weak to moderate staining reaction.



Figure C. Cerebellum. All neurons and axonal processes show a moderate to strong fibrillar cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Neuron-Specific Enolase
Clone:	BBS/NC/VI-H14
Code:	IR612 or IS612
Clinical Application	For identification of both normal neuronal and neuroendocrine cells and corresponding tumors such as schwannoma (Fig. A) and carcinoid tumors (Fig. B).
<b>Reaction Location</b>	Nucleus and cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> A moderate to strong granular cytoplasmic and nuclear staining reaction should be seen in the neuroendocrine cells of the mucosa and in the ganglion cells. The axons should show a weak to moderate granular cytoplasmic staining reaction. The epithelial cells should be negative <b>(Fig. C)</b> .
	<b>Pancreas:</b> The Langerhans' islets and single neuroendocrine cells in the pancreatic ducts should show a strong granular cytoplasmic and nuclear staining reaction.
Differential Diagnosis*	<ol> <li>Schwannoma vs. meningioma.</li> <li>Carcinoid tumor vs. carcinoma.</li> </ol>



Figure A. Schwannoma. The neoplastic cells show a weak to moderate staining reaction.



Figure B. Carcinoid tumor. The neoplastic cells show a moderate to strong granular cytoplasmic staining reaction.



**Figure C.** Colon. The neuroendocrine cells of the mucosa and the ganglion cells show a moderate to strong granular cytoplasmic and nuclear staining reaction. The axons show a weak to moderate granular cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Nucleophosmin
Clone:	376
Code:	IR652 or IS652
Clinical Application	For identification of both wild-type nucleophosmin (NPM) (Fig. A) and the mutated counter- part NPMc+ (Fig. B). It is useful for the identification of leukemic blasts in a subgroup of acute myeloid leukemia cases with a normal karyotype.
<b>Reaction Location</b>	Nucleus and cytoplasm.
Recommended Control	<b>Liver:</b> The majority of the normal hepatocytes should show a distinct or reticulated moderate to strong nuclear staining reaction, while some nuclei are negative. Mitotic and post-mitotic cells should show a weak to moderate cytoplasmic staining reaction (Fig. C).
	<b>Cerebellum:</b> The majority of the normal neurons should show a moderate to strong distinct nuclear staining reaction, whereas some nuclei are negative. Large Purkinje neurons and some small granular neurons should show a weak to moderate cytoplasmic staining reaction <b>(Fig. D).</b>
Differential Diagnosis*	Acute myeloid leukemia with normal karyotype vs. acute myeloid leukemia with abnormal karyotype.



Figure A. Acute myeloid leukemia (NPM1 Exon 12 normal; NPMc-). The majority of the leukemic blasts show a distinct nuclear staining reaction and no cytoplasmic staining reaction.



Figure B. Acute myeloid leukemia (NPM1 Exon 12 mutant; NPMc+). The majority of the leukemic blasts show a distinct nuclear staining reaction and a moderate to strong cytoplasmic staining reaction.



Figure C. Liver. The majority of the normal hepatocytes show a moderate to strong nuclear staining reaction, while some nuclei are negative. Mitotic and post-mitotic cells show a weak to moderate cytoplasmic staining



**Figure D.** Brain. The majority of the normal neurons show a distinct nuclear staining reaction. Large Purkinje neurons and some small granular neurons show a weak to moderate cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	p53 Protein
Clone:	DO-7
Code:	IR616 or IS616
Clinical Application	For identification of wild-type and mutant-type p53 protein and accumulation in human neo- plasia such as serous ovarian carcinoma ( <b>Fig. A</b> ), transitional cell carcinoma of the bladder ( <b>Fig. B</b> ), carcinoma of breast, lung and endometrium, follicular lymphoma and mantle cell lymphoma.
<b>Reaction Location</b>	Nucleus.
Recommended Control	<b>Colon adenocarcinoma with normal colon tissue:</b> The majority of the neoplastic cells should show a moderate to strong distinct nuclear staining reaction. The normal epithelial cells should be negative, except for the basal cells that may show a weak to moderate nuclear staining reaction (Fig. C).
	<b>Esophagus:</b> The parabasal layer of the epithelial cells should show a distinct nuclear staining reaction.
Differential Diagnosis*	<ol> <li>Malignant mesothelioma or carcinoma of pleural effusion vs. reactive mesothelium.</li> <li>Uterine serous carcinoma vs. endometrioid carcinoma.</li> </ol>

3. Lung sarcoma vs. lung inflammatory pseudotumor.



Figure A. Serous ovarian carcinoma. Virtually all the neoplastic cells show a moderate to strong nuclear staining reaction.



**Figure B.** Transitional cell carcinoma of the bladder. The neoplastic cells show a focal moderate to strong nuclear staining reaction.



Figure C. Colon adenocarcinoma. The neoplastic cells show a moderate to strong nuclear staining reaction, while normal colon epithelial cells are negative, except for a few scattered basal cells that show a weak to moderate nuclear staining reaction.

Antibody:	Monoclonal Mouse Anti-Human Placental Alkaline Phosphatase
Clone:	8A9
Code:	IR779 or IS779
Clinical Application	For identification of malignant germ cell tumors (Fig. A and Fig. B) such as dysgerminoma and embryonal carcinoma.
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Placenta:</b> The brush border of the syncytio- and cytotrophoblasts should show a moderate to strong and predominantly membranous staining reaction. The cytoplasmic compartment of the syncytiotrophoblasts and trophoblasts should show a weak to moderate cytoplasmic staining reaction. Some cytoplasmic staining in the smooth muscle cells and myofibroblasts is also acceptable <b>(Fig. C)</b> .
Differential Diagnosis*	1. Seminoma vs. carcinoma. 2. Seminoma vs. melanoma vs. lymphoma.



Figure A. Seminoma. The majority of the neoplastic cells show a moderate to strong predominantly membranous, but also cytoplasmic staining reaction.



Figure B. Testis with intratubular germ cell neoplasia. The neoplastic cells show a moderate to strong predominantly membranous, but also cytoplasmic staining reaction. Normal germ cells are negative.



Figure C. Placenta. The brush border of the syncytio- and cytotrophoblasts show a moderate to strong membranous staining reaction, whereas the cytoplasmic compartment of the syncytio- and cytotropho-

Antibody:	Monoclonal Mouse Anti-
	Pneumocystis Jiroveci
Clone:	3F6
Code:	IR635 or IS635
Clinical Application	For identification of <i>Pneumocystis jiroveci,</i> previously known as <i>P. carinii</i> (P. jiroveci) (Fig. A and Fig. B).
<b>Reaction Location</b>	Membrane.
Recommended Control	<b>Lesion with Pneumocystis jiroveci infection (lung):</b> The cyst walls of the <i>Pneumocystis jiroveci</i> should show a moderate to strong staining reaction, while the trophozites should show a weak to moderate, diffuse and granular reaction. No reaction should be seen in epithelial or lymphatic cells ( <b>Fig. A and Fig. B</b> ).
Differential Diagnosis*	Pneumocystis jiroveci infection vs. other infection.



Figure A. Lung infected with Pneumocystis jiroveci. The cyst walls of the Pneumocystis Jiroveci show a moderate to strong staining reaction, while the trophozites show a weak to moderate, diffuse and granular staining reaction.



Figure B. Lung infected with Pneumocystis jiroveci. The cyst walls of the Pneumocystis Jiroveci show a moderate to strong staining reaction, while the trophozites show a weak to moderate, diffuse and granular staining reaction.

Antibody:	Monoclonal Rabbit Anti-Human Postmeiotic Segregation Increased 2 (PMS2)
Clone:	EP51
Code:	IR087
Clinical Application	For the evaluation of colorectal carcinoma. Loss of PMS2 protein in colorectal cancers identi- fies tumors with defects in DNA mismatch repair. This is most often a consequence of loss of expression of its heterodimeric partner MLH1 via either MLH1 hypermethylation or less often a germline mutation in <i>MLH1</i> both associated with hereditary predisposition to colorectal and to a lesser degree other cancers, known collectively as Lynch syndrome (Fig. A and B).
<b>Reaction Location</b>	Nucleus.
Recommended Control	<b>Appendix/Colon:</b> Virtually all cells should show a distinct nuclear staining reaction. The basal epithelial cells should show a moderate to strong staining reaction whereas the luminal epithelial cells and stromal cells at least should show a weak to moderate staining reaction ( <b>Fig. C</b> ). Delayed fixation or long term storage of cut sections may reduce staining intensity which may impact interpretation.
Differential Diagnosis*	Cancers associated with <i>PMS2</i> mutation or loss of expression vs. PMS2 intact cancers.



Figure A. Colon adenocarcinoma with loss of PMS2 protein. The neoplastic cells show no nuclear staining reaction, while stromal cells, lymphocytes and residual normal epithelial cells show a moderate to strong nuclear staining reaction.



Figure B. Colon adenocarcinoma with intact PMS2 expression. Virtually all of the neoplastic cells, stromal cells and remnants of benign epithelial cells show a moderate to strong nuclear staining reaction.



Figure C. Appendix. Virtually all of the epithelial cells and stromal cells show a moderate to strong nuclear staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Progesterone Receptor
Clone:	PgR 636
Code:	IR068 or IS068
Clinical Application	For measuring of the relative level of expression for progesterone receptor in breast cancer tissue (Fig A). It also labels meningioma cells (Fig. B).
<b>Reaction Location</b>	Nucleus.
Recommended Control	<b>Cervix:</b> A strong and distinct nuclear staining reaction should be seen in the columnar epithe- lial cells, the basal squamous epithelial cells and the stromal cells in the uterine cervix <b>(Fig. C).</b>
	<b>Breast (female 15-45 yrs):</b> Normal epithelial cells in ducts and lobules should show a moderate to strong nuclear staining reaction. Some cytoplasmic staining is acceptable.
Differential Diagnosis*	1. Meningioma vs. schwannoma. 2. Endometrial stromal sarcoma vs. monophasic synovial sarcoma.



Figure A. Breast ductal carcinoma. The neoplastic cells show a strong nuclear staining reaction.



Figure B. Meningioma. Most neoplastic cells show a distinct nuclear staining reaction.



Figure C. Uterine cervix. Epithelial cells and stromal cells show a strong staining reaction.



Figure D. Breast. Ductal epithelial cells show a moderate to strong nuclear staining reaction.

Antibody:	Polyclonal Rabbit Anti-Human Prostate-Specific Antigen
Code:	IR514 or IS514
Clinical Application	For identification of tumors of prostatic origin (Fig. A and Fig. B). Except for prostate glands and prostatic epithelial neoplasia, bladder urothelium, urethra, periurethral glands and seminal vesicles are also stained positive for prostate-specific antigen.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Normal prostate and benign prostatic hyperplasia:</b> The majority of the prostate luminal epithelial cells should show a moderate to strong cytoplasmic staining reaction. A weak staining of the stromal compartment is accepted <b>(Fig. C).</b>
Differential Diagnosis*	Metastatic prostatic carcinoma vs. metastatic tumors of non-prostatic origin.



Figure A. Prostatic adenocarcinoma. The neoplastic cells and the hyperplastic glands show a moderate to strong and diffuse cytoplasmic staining reaction.



Figure B. Prostatic adenocarcinoma. The neoplastic cells show a heterogeneous staining reaction.



**Figure C.** Prostate. The prostate luminal epithelial cells show a strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Renal Cell Carcinoma Marker
Clone:	SPM314
Code:	IR075 or IS075
<b>Clinical Application</b>	For identification of renal cell carcinoma vs. non-renal cell tumors (Fig. A).
<b>Reaction Location</b>	Membrane and cytoplasm.
Recommended Control	<b>Kidney:</b> The epithelial cells of the proximal tubules should show a moderate to strong predominantly membranous staining reaction (Fig. B).
Differential Diagnosis*	<ol> <li>Renal cell carcinoma vs. hepatocellular carcinoma.</li> <li>Renal cell carcinoma vs. urothelial carcinoma.</li> </ol>



Figure A. Renal cell carcinoma (clear cell type). The majority of the neoplastic cells show a moderate to strong predominantly membranous staining reaction.



Figure B. Kidney. The epithelial cells of the proximal tubules show a moderate to strong membranous and cytoplasmic staining reaction.

Antibody: Polyclonal Rabbit Anti-S100

### Code: IR504 or IS504

**Clinical Application** Primarily for initial screening of melanoma (**Fig. A**). S100 protein is found in many tumors with neuroectodermal origin such as schwannoma (**Fig. B**) and neurofibromas. It is also found in Langerhans' cell histiocytosis and chondroblastoma.

**Reaction Location** Nucleus and cytoplasm.

Recommended Control Appendix/Colon: The satellite cells and the Schwann cells of the peripheral nerves should show a moderate to strong cytoplasmic and nuclear staining reaction. Adipocytes should show a weak to moderate staining reaction. Macrophages should also be positive. No staining should be seen in the epithelial and smooth muscle cells (Fig. C and D).

**Skin:** Nerves and melanocytes in the basal layer of the epidermis should show a strong cytoplasmic and nuclear staining reaction.

**Differential Diagnosis\*** 

- Melanoma vs. lymphoma.
   Melanoma vs. leiomyosarcoma.
- 3. Spindle cell melanoma vs. spindle cell carcinoma.



Figure A. Malignant melanoma. The neoplastic cells show a diffuse nuclear and cytoplasmic staining reaction.



Figure B. Schwannoma. Most neoplastic cells show a strong nuclear and cytoplasmic staining reaction.



Figure C. Colon. The satellite cells and the Schwann cells of the peripheral nerves show a strong cytoplasmic and nuclear staining reaction.



Figure D. Colon. The adipocytes show a weak to moderate staining reaction.

Antibody:	Monoclonal Mouse Anti-Human
	Smooth Muscle Actin
Clone:	1A4
Code:	IR611 or IS611
<b>Clinical Application</b>	For identification of smooth muscle cells, myofibroblasts, and myoepithelial cells and their tumors such as leiomyoma (Fig. A) and leiomyosarcoma (Fig. B).
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Appendix/Colon:</b> All the smooth muscle cells in vessel walls, muscle layers and lamina muscularis mucosa should show a moderate to strong cytoplasmic staining reaction. The smooth muscle cells lining the epithelial surface should be demonstrated. No staining reaction should be seen in the epithelial cells ( <b>Fig. C</b> ).
	Liver: The smooth muscle cells lining the sinusoids should show a weak to moderate cytoplasmic staining reaction (Fig. D).
	<b>Breast:</b> A strong cytoplasmic staining of the myoepithelial cells around the ducts and lobules as well as a strong staining reaction of the smooth muscle cells in the vessel walls should be seen.
Differential Diagnosis*	<ol> <li>Leiomyosarcoma vs. giant gastrointestinal stromal tumor.</li> <li>Breast ductal carcinoma in situ vs. breast microinvasive carcinoma or adenocarcinoma.</li> </ol>



**Figure A.** Uterine leiomyoma. The majority of the neoplastic cells show a moderate to strong cytoplasmic staining reaction.



Figure B. Leiomyosarcoma. The majority of the neoplastic cells show a moderate to strong cytoplasmic staining reaction.



**Figure C.** Colon. The smooth muscle cells show a moderate to strong cytoplasmic staining reaction.



Figure D. Liver. The smooth muscle cells lining the sinusoids show a weak to moderate cytoplasmic staining reaction.
Antibody: Clone: Code:	Monoclonal Mouse Anti-Human Smooth Muscle Myosin Heavy Chain SMMS-1 IR066 or IS066			
Clinical Application	For identification of myoepithelial cells in the breast, and for identification of smooth muscle neoplasm. Myoepithelial cells are generally present in breast hyperplasia and ductal carcinoma in situ, and absent in invasive breast carcinoma <b>(Fig. A and Fig. B).</b>			
<b>Reaction Location</b>	Cytoplasm.			
Recommended Control	Uterus: The smooth muscle cells of the myometrium should be demonstrated (Fig. C).			
	<b>Appendix:</b> The smooth muscle cells in the muscle layers should show a moderate to strong cytoplasmic staining reaction, and the smooth muscle cells of small vessels should show a weak to moderate staining reaction (Fig. D). The epithelial cells should be negative.			
Differential Diagnosis*	Ductal carcinoma in situ vs. microinvasion vs. invasive carcinoma of the breast.			



**Figure A.** Breast hyperplasia. The myoepithelial cells around the ducts and the smooth muscle cells in the vessel walls show a strong staining reaction.



Figure B. Breast invasive ductal carcinoma with ductal carcinoma in situ. The myoepithelial cells in the ductal carcinoma in situ show decreased expression of smooth muscle heavy chain myosin, while the staining is absent or disrupted in the invasive areas.



**Figure C.** Uterus. Smooth muscle cells of the myometrium show a moderate to strong staining reaction.



Figure D. Appendix. Smooth muscle cells in muscle layers and blood vessels show a moderate to strong cytoplasmic staining reaction.

Antibody:	Monoclonal Mouse Anti-				
	Synaptophysin				
Clone:	SY38				
Code:	IR776 or IS776				
Clinical Application	For identification of a wide spectrum of neuroendocrine neoplasms and tumors with neuroen- docrine differentiation. These include the neural tumors (neuroblastoma, ganglioneuroblas- toma, ganglioneuroma, pheochromocytoma and paraganglioma), the epithelial tumors (pan- creatic islet cell neoplasm, medullary thyroid carcinoma, pituitary and parathyroid adenoma, and carcinoids of bronchopulmonary and gastrointestinal tract), and tumors with neuroendo- crine differentiation (small ( <b>Fig. A</b> ) and non-small cell cancer of lung, Merkel cell carcinoma ( <b>Fig. B</b> ) and extrapulmonary small cell cancer).				
<b>Reaction Location</b>	Cytoplasm.				
Recommended Control	<b>Appendix/Colon:</b> The neuroendocrine cells in the epithelial surface should show a moder- ate to strong cytoplasmic staining reaction, while the epithelial cells should be negative. The axons of the peripheral nerves in the mucosa, submucosa and the muscularis propria should show a weak to moderate granular cytoplasmic staining reaction ( <b>Fig. C</b> ).				
Differential Diagnosis*	<ol> <li>Carcinoid tumor vs. carcinoma.</li> <li>Merkel cell carcinoma vs. basal cell carcinoma.</li> <li>Small cell carcinoma of lung vs. lymphoma.</li> </ol>				
* Differential diagnosis is					



Figure A. Small cell lung carcinoma. The majority of the neoplastic cells show a strong distinct cytoplasmic and focally dot-like staining reaction.



Figure B. Merkel cell carcinoma. The majority of the neoplastic cells show a strong distinct cytoplasmic and focally dot-like staining reaction.



**Figure C.** Colon. The neuroendocrine cells in the epithelial surface show a moderate to strong cytoplasmic staining reaction. The axons of the peripheral nerves in the mucosa, submucosa and the muscularis propria show a weak to moderate granular cytoplasmic staining reaction.

Antibody:	Polyclonal Rabbit Anti- Terminal Deoxynucleotidyl Transferase (TdT)				
Code:	IR001 or IS001				
<b>Clinical Application</b>	For identification of precursor B- and T-cell lymphoblastic lymphoma/leukemia, and for identification of thymoma (Fig. A and Fig. B).				
<b>Reaction Location</b>	Nucleus.				
Recommended Control	<b>Thymus:</b> The subcapsular and cortical thymocytes should show a moderate to strong distinct nuclear staining reaction, whereas the medullar thymocytes should be negative <b>(Fig. C)</b> .				
	<b>Tonsil:</b> In the interfollicular zone, a few perisinusoidal cells can show a distinct nuclear staining reaction. All other cells in the tonsil should be negative.				
Differential Diagnosis*	Lymphoblastic lymphoma/leukemia vs. myeloid leukemia/sarcoma.				



Figure A. Thymoma. The thymocytes (T lymphoblasts) show a strong nuclear staining reaction.



**Figure B.** Thymoma. The thymocytes (*T* lymphoblasts) show a strong nuclear staining reaction.



Figure C. Adult thymus. The subcapsular and cortical thymocytes show a strong distinct nuclear staining reaction.

## Antibody: Polyclonal Rabbit Anti-Human Thyroglobulin

Code:	IR509 or IS509
Clinical Application	For identification of tumors of thyroid origin such as thyroid follicular carcinoma <b>(Fig. A),</b> papillary thyroid carcinoma <b>(Fig. B),</b> Hürthle cell tumor of thyroid, and anaplastic carcinoma of thyroid.
<b>Reaction Location</b>	Cytoplasm.
Recommended Control	<b>Thyroid:</b> The cuboidal to columnar follicular epithelial cells should show a weak to moderate cytoplasmic staining reaction, while the extracellular colloids should show a moderate to strong staining reaction ( <b>Fig. C</b> ).
Differential Diagnosis*	<ol> <li>Thyroid follicular carcinoma vs. thyroid medullary carcinoma.</li> <li>Thyroid carcinoma vs. metastatic renal cell carcinoma.</li> </ol>



Figure A. Thyroid follicular carcinoma. The neoplastic cells show a strong cytoplasmic staining reaction.



**Figure B.** *Papillary thyroid carcinoma. The neoplastic cells show a strong cytoplasmic staining reaction.* 



Figure C. Thyroid. The cuboidal to columnar follicular epithelial cells show a weak to moderate cytoplasmic staining reaction. The extracellular colloids show a moderate to strong staining reaction.

Antibody:	Monoclonal Mouse Anti- Thyroid Transcription Factor (TTF-1)					
Clone:	8G7G3/1					
Code:	IR056 or IS056					
Clinical Application	For differential diagnosis of primary vs. metastatic tumors in the lung and thyroid. The antibody labels normal cells of thyroid and lung as well as corresponding tumors like thyroid papillary carcinoma (Fig. A) and lung adenocarcinoma (Fig. B). Mesothelioma is negative with this marker.					
<b>Reaction Location</b>	Nucleus.					
Recommended Control	<b>Thyroid:</b> Virtually all thyroid follicular epithelial cells should show a moderate to strong distinct nuclear staining reaction with no, or only a minimal, cytoplasmic or background staining reaction ( <b>Fig. C</b> ).					
	Lung: The type II pneumocyte cells and the Clara cells lining the alveolar walls should show a moderate to strong distinct nuclear staining reaction. If present, the columnar epithelial cells of the respiratory ducts should be negative or show a weak nuclear staining reaction (Fig. D).					
Differential Diagnosis*	<ol> <li>Thyroid carcinoma vs. metastatic renal cell carcinoma.</li> <li>Lung small cell carcinoma vs. Merkel cell carcinoma. With this particular antibody TTF-1 immunoreactivity was demonstrated in the majority of pulmonary atypical carcinoids but was rare in typical carcinoids.</li> </ol>					



Figure A. Lung small cell carcinoma. The neoplastic cells show a moderate to strong nuclear staining reaction.



**Figure B.** Thyroid follicular carcinoma. The tumor cells show a moderate to strong nuclear staining reaction.



Figure C. Thyroid. The thyroid follicular epithelial cells show a moderate to strong distinct nuclear staining reaction with no, or only a minimal, cytoplasmic or background staining reaction.



Figure D. Lung. The type II pneumocytes lining the alveolar walls show a moderate to strong nuclear staining reaction. The epithelial cells of the respiratory ducts are negative or show a weak nuclear staining reaction.

Antibody:	Monoclonal Mouse Anti-Human					
	Tyrosinase					
Clone:	T311					
Code:	IR061 or IS061					
<b>Clinical Application</b>	For identification of melanocytic lesions and melanoma (Fig. A and Fig. B).					
<b>Reaction Location</b>	Cytoplasm.					
Recommended Control	<b>Skin:</b> The melanocytes in the basal layer of the epidermis should show a weak to moder distinct cytoplasmic staining reaction, and no staining should be seen in the squamous epithelial cells and eccrine glands ( <b>Fig. C</b> ).					
	<b>Nevus:</b> A moderate to strong distinct granular cytoplasmic staining reaction should be seen in the nevus cells of the dermis and the melanocytes in the basal layer of the epidermis ( <b>Fig. D</b> ).					
Differential Diagnosis*	Melanoma vs. carcinoma.					



**Figure A.** Melanoma. The neoplastic cells show a strong granular cytoplasmic staining reaction.



Figure B. Melanoma. The neoplastic cells show a moderate to strong cytoplasmic staining reaction.



Figure C. Skin. The melanocytes in the basal layer of the epidermis show a weak to moderate distinct cytoplasmic staining reaction.



**Figure D.** Nevus. The nevus cells of the dermis and the melanocytes in the basal layer of the epidermis show a moderate to strong granular cytoplasmic staining.

Antibody:	Monoclonal Mouse Anti- Villin				
Clone:	1D2 C3				
Code:	IR076 or IS076				
<b>Clinical Application</b>	For identification of colon adenocarcinomas (Fig. A) and renal cell carcinoma (Fig. B).				
<b>Reaction Location</b>	Membrane and cytoplasm.				
Recommended Control	<b>Appendix:</b> The appendiceal enterocytes should show a moderate to strong predominantl membranous staining reaction <b>(Fig. C).</b> The cytoplasm will typically show a diffuse and we staining reaction.				
	Liver: The majority of the hepatocytes should show a weak to moderate membranous stain- ing reaction with no, or only a minimal, cytoplasmic staining reaction (Fig. D).				
Differential Diagnosis*	Adenocarcinoma especially gastrointestinal tract vs. mesothelioma or non-epithelial tumors.				



Figure A. Colon adenocarcinoma. The neoplastic cells show a strong membranous and cytoplasmic staining reaction.



**Figure B.** Renal cell carcinoma. The majority of the neoplastic cells show a strong predominantly membranous staining reaction.



**Figure C.** Appendix. The appendiceal enterocytes show a strong membranous and cytoplasmic staining reaction.



**Figure D.** Liver. Hepatocytes show a weak to moderate membranous staining reaction.

Antibody:	Monoclonal Mouse Anti-				
	Vimentin				
Clone:	V9				
Code:	IR630 or IS630				
Clinical Application	For identification of cells of mesenchymal origin in normal and neoplastic tissues such as B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (Fig. A).				
<b>Reaction Location</b>	Cytoplasm.				
Recommended Control	<b>ol Tonsil:</b> All peripheral cells should show a distinct cytoplasmic staining reaction. The cells ir the capsule/mantle zone of the secondary follicles should show a moderate to strong stain reaction. Stromal cells and endothelial cells should be demonstrated <b>(Fig. B)</b> .				
	Liver: Sinusoid smooth muscle cells in the liver should show a weak to moderate cytoplasmic staining reaction (Fig. C).				
	<b>Appendix/Colon:</b> The interepithelial cells should show a moderate to strong distinct cyto- plasmic staining with no reaction in the epithelial cells. Smooth muscle cells in the lamina pro- pria should show a moderate to strong focal cytoplasmic staining reaction.				



Figure A. B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma. The majority of the neoplastic cells show a distinct cytoplasmic staining reaction.



Figure B. Tonsil. Lymphocytes and endotehelial cells show a strong cytoplasmic staining reaction.



**Figure C.** Liver. The macrophages and lymphocytes show a weak to moderate staining reaction, while the hepatocytes are negative.

## Antibody: Polyclonal Rabbit Anti-Human Von Willebrand Factor

Code:	IR527 or IS527					
Clinical Application	For identification of acute myeloid leukemia FAB type M7 <b>(Fig. A)</b> and angiosarcoma <b>(Fig. B)</b> .					
<b>Reaction Location</b>	Cytoplasm.					
Recommended Control	<b>Appendix/Colon:</b> The endothelial cells of both blood and lymphatic vessels in lamina propria should show a moderate to strong staining reaction, while the epithelial cells should be negative <b>(Fig. C)</b> .					
	<b>Liver:</b> The endothelial cells lining the sinusoids should show a weak to moderate staining reaction, while the liver cells should be negative or only focally positive ( <b>Fig. D</b> ). The endothelial cells in the vessels in the portal areas should be distinctively demonstrated.					
Differential Diagnosis*	<ol> <li>Angiosarcoma vs. carcinoma.</li> <li>Subtyping of acute myeloid leukemia.</li> </ol>					



Figure A. Acute myeloid leukemia (FAB type M7). The neoplastic cells show a strong predominantly cytoplasmic staining reaction.



**Figure B.** Hemangiosarcoma. The majority of the neoplastic cells show a moderate to strong predominantly cytoplasmic staining reaction.



Figure C. Colon. The endothelial cells of both blood and lymphatic vessels in lamina propria show a moderate to strong staining reaction.



**Figure D.** Liver. The endothelial cells lining the sinusoids show a weak to moderate staining reaction.

Antibody:	Monoclonal Mouse Anti-Human Wilms' Tumor 1 (WT1) Protein					
Clone:	6F-H2					
Code:	IR055 or IS055					
<b>Clinical Application</b>	For identification of Wilms' tumor, malignant mesothelioma <b>(Fig. A)</b> and serous ovarian adenocarcinoma <b>(Fig. B).</b>					
<b>Reaction Location</b>	Nucleus.					
Recommended Control	<b>Fallopian tube:</b> Epithelial cells and the majority of the smooth muscle cells should show a moderate to strong nuclear staining reaction. A weak cytoplasmic background staining in these cells is accepted. Endothelial cells will typically show a moderate to strong cytoplasmic staining reaction <b>(Fig. C)</b> .					
Differential Diagnosis*	1. Wilms' tumor vs. neuroblastoma. 2. Peritoneal mesothelioma vs. serous carcinoma.					



Figure A. Mesothelioma. The majority of the tumor cells show a strong nuclear staining reaction with no, or only a minimal, cytoplasmic or background staining reaction.



**Figure B.** Ovarian serous adenocarcinoma. The majority of the neoplastic cells show a distinct nuclear staining reaction. A weak cytoplasmic staining reaction can also be seen in some cells.



Figure C. Fallopian tube. The columnar epithelial cells and the muscle cells show a strong nuclear staining reaction.

Antibody:	Monoclonal Mouse Anti-Human				
	ZAP-70				
Clone:	2F3.2				
Code:	IR653 or IS653				
<b>Clinical Application</b>	For identification of ZAP-70 in a subset of B-cell chronic lymphocytic leukemias/small lympho- cytic lymphoma (Fig. A and Fig. B).				
<b>Reaction Location</b>	Nucleus and cytoplasm.				
Recommended Control	<b>Tonsil:</b> The isolated T cells in the germinal center should show a moderate to strong stain- ing reaction, and the T cells in the T-zone should show a weak to moderate staining reaction <b>(Fig. C).</b> The germinal center B cells should be negative.				
Differential Diagnosis*	B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma with unmutated immuno- globulin gene vs. B-chronic lymphocytic leukemia/small lymphocytic lymphoma with mutation.				



Figure A. B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma with reaction associated with unmutated Ig heavy chain status. The majority of the neoplastic cells show a moderate to strong nuclear and cytoplasmic staining reaction.



Figure B. B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma with reaction associated with mutated Ig heavy chain status. The neoplastic cells are negative, and only the T cells show a strong nuclear and cytoplasmic staining reaction.



**Figure C.** Tonsil. The scattered T cells in the germinal center show a strong staining reaction, and the T cells in the T-zone show a moderate staining reaction.

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