Basics of Hematology and Patho-histology

Practical Course in Molecular Pathology

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www.mfpl.ac.at/mfpl-group/group/muellner.html
(Müllner homepage / research)
E. coli + macrophages

<table>
<thead>
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</thead>
<tbody>
<tr>
<td>Neutrophil</td>
<td></td>
<td><img src="image" alt="Image" /></td>
<td>54–62%[^5]</td>
<td>10–12</td>
<td>- bacteria&lt;br&gt; - fungi</td>
<td>multilobed (H&amp;E Stain)</td>
<td>full of pink-orange (H&amp;E Stain)</td>
<td>6 hours–few days (days in spleen and other tissue)</td>
</tr>
<tr>
<td>Eosinophil</td>
<td></td>
<td><img src="image" alt="Image" /></td>
<td>1–6%</td>
<td>10–12</td>
<td>- parasites&lt;br&gt; - in allergic reactions</td>
<td>bi-lobed</td>
<td>- full of pink-orange (H&amp;E Stain)</td>
<td>8–12 days (circulate for 4–5 hours)</td>
</tr>
<tr>
<td>Basophil</td>
<td></td>
<td><img src="image" alt="Image" /></td>
<td>&lt;1%</td>
<td>12–15</td>
<td>- in allergic reactions</td>
<td>bi-lobed or tri-lobed</td>
<td>large blue</td>
<td>?</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td></td>
<td><img src="image" alt="Image" /></td>
<td>25–33%</td>
<td>7–8</td>
<td>- B cells: various pathogens&lt;br&gt; - T cells:&lt;br&gt; - CD4+ (helper): extracellular bacteria broken down into peptides presented by MHC class 2 molecule.&lt;br&gt; - CD8+ cytotoxic T cells: virus-infected and tumor cells.&lt;br&gt; - γδ T cells:&lt;br&gt; - Natural killer cells: virus-infected and tumor cells.</td>
<td>deeply staining, eccentric</td>
<td>NK-cells and Cytotoxic (CD8+) T-cells[^7]</td>
<td>weeks to years</td>
</tr>
<tr>
<td>Monocyte</td>
<td></td>
<td><img src="image" alt="Image" /></td>
<td>2–8%</td>
<td>14–17</td>
<td>Monocytes migrate from the bloodstream to other tissues and differentiate into tissue resident macrophages or dendritic cells.</td>
<td>kidney shaped</td>
<td></td>
<td>hours to days</td>
</tr>
<tr>
<td>Macrophage</td>
<td></td>
<td><img src="image" alt="Image" /></td>
<td>21 (human)[^8]</td>
<td></td>
<td>Phagocytosis (engulfment and digestion) of cellular debris and pathogens, and stimulation of lymphocytes and other immune cells that respond to the pathogen.</td>
<td>none</td>
<td></td>
<td>activated: days immature: months to years</td>
</tr>
<tr>
<td>Dendritic cells</td>
<td></td>
<td><img src="image" alt="Image" /></td>
<td></td>
<td></td>
<td>Main function is as an antigen-presenting cell (APC) that activates T lymphocytes.</td>
<td></td>
<td></td>
<td>similar to macrophages</td>
</tr>
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</table>
Mature white blood cell types I

White Blood cells (WBCs) are frequently also referred to as peripheral blood mononuclear cells (PBMCs).

Granulocytes in general are part of the innate immune system. Names derive from staining with hematoxylin and eosin. Whereas basophils stain dark blue and eosinophils are bright red, neutrophils stain neutral to pink.

**Basophil granulocytes**  
Least common granulocyte type (0.01- 0.3% of WBCs). Large cytoplasmic granules obscure the nucleus under the microscope. When unstained, the nucleus is visible and usually has 2 lobes. Basophils appear in inflammatory reactions, particularly those causing allergies, mainly via the vasodilator histamine (antihistamines!). They also contain the anticoagulant heparin, which prevents blood from clotting too quickly.

**Eosinophil granulocytes**  
About 1-6% of WBCs; component of innate immune system to combat parasites and certain infections; also associated with allergy and asthma. Following activation, eosinophils effector functions include production and release (degranulation) of cytotoxic substances (granule proteins, reactive oxygen species …) and production of lymphokines etc. stimulating e.g. the adaptive immune system (TGFβ, IL-2, IL-6, TNFα …).

**Neutrophil granulocytes**  
Most abundant WBC type (40-75%) and essential part of the innate immune system. A pathogen is likely to first encounter a neutrophil. Normally contain a nucleus of 2-5 lobes. Neutrophils quickly congregate at a infection site, attracted by cytokines from activated endothelium, mast cells, or macrophages. Besides cytotoxic granule content, neutrophils also release cytokines, which in turn amplify inflammatory reactions by several other cell types.
Mature white blood cell types II

Neutrophil granulocytes; most abundant PBMC type

Neutrophils 1800x; 9-14 µm in diameter, 40-75% of WBCs in a blood smear; segmented or lobed nucleus; cytoplasm has granules (0.1-0.4 µm) that stain variably and weakly from light blue to azure to violet.

Granules in general contain a wide variety of cytotoxic proteins that can be released in a process termed degranulation.
Eosinophils: Wright's stain; 1800x; 10-14 µm in diameter, 1-6% of WBCs in a blood smear; usually have bi-lobed nuclei like spectacles; reddish granules are relatively uniform in size, 0.6 µm in diameter and refractile.
Mature white blood cell types IV

Basophil granulocytes

**Basophils** – Wright's stain; magnification 1800x; 8-14 µm in diameter and <1% of WBCs in a blood smear. Cytoplasmic granules are of variable size and stain intensely with methylene blue, obscuring the nucleus.

**Wright's stain** (James Homer Wright) facilitates the differentiation of blood cell types. It is used primarily to stain blood smears examined under a light microscope. In cytogenetics it stains chromosomes to facilitate diagnosis of aberrations. Because it distinguishes easily between blood cells, it became widely used for performing differential white blood cell counts, which are routinely ordered when infections are expected. There are variants known as **buffered Wright stain** or **Wright-Giemsa stain**.
**Mature WBC types V granulocytes**

**Left:** electron micrograph of various (electron-dense) cytoplasmic granules of a resting neutrophil. Peroxidase-positive granules are azurophil granules (or primary granules, *pg*), which appear large and dark. Specific granules (or secondary granules, *sg*) are smaller in size. Nucleus (*N*); centriole (*ce*); mitochondria (*m*).

Dr Elizabeth Cramer, INSERM U474 Cochin Hospital, Paris.

**Right:** One almost ideal picture showing once more all three types of granulocytes next to each other. Top right, Eosinophil; middle, Neutrophil; bottom right, Basophil.
Scanning electron micrograph of a neutrophil (yellow; false color), engulfing anthrax bacteria (orange). Note that a phagocytosing macrophage would appear similar (see below).

modified from Wikipedia
Mature white blood cell types VI

Monocytes and macrophages

**Monocytes**: 1800x; 12-15 µm in diameter; 2-10% of WBCs in a blood smear; kidney shaped nuclei, no real granules. Volume ratio cytosol / nucleus smaller than with granulocytes but larger than with lymphocytes. Half of them are stored in spleen. Monocytes have two main functions: (1) replenish resident macrophages and dendritic cells under normal states, and (2) as part of the innate immune system move quickly (8-12 hours) to infection sites in response to inflammation signals, and divide / differentiate there into macrophages and dendritic cells.
Mature white blood cell types VII

Monocytes and macrophages

**Macrophages:** ~ 21 µm in diameter, irregular shape; granules and nucleus similar to monocytes; usually not observable in blood smears; reside in tissue and bone marrow, ingesting cell debris (e.g. aged erythrocytes) and after immune stimulation also bacteria etc.

**Top:** Macrophages ingesting bacteria; **right:** Simplified diagram of phagocytosis and destruction of a bacterial cell. Note that also neutrophils are capable of phagocytosis.
Lymphocytes (human). Wright's stain. 1800x; B- and T cells are 7-8 µm in diameter, i.e. not much larger than erythrocytes and consist almost entirely of nuclei; 10-40% of WBCs in a blood smear; round nuclei stain intensely; cytoplasm may stain light blue and contain a few azurophilic granules. There are also larger (~ 12 µm) granular lymphocytes, better known as natural killer cells (NK cells).
Blood Smear + Cytospins

Exp Gen III Course, 2012-12
Cytospins: contrast, colour, and saturation enhancement

Exp Gen III Course, 2012-12
Sample preparation for histology (general)

**Fixation** aims to preserve the shape of the cells or tissue involved by increasing their rigidity. Chemical fixatives generate chemical bonds between proteins and other substances within the sample (formaldehyde). Other common fixatives like ethanol, methanol, acetic acid and combinations thereof denature proteins.

**Larger pieces of tissue** e.g. from human biopsies are mostly fixed with para-formaldehyde solutions (formalin) and then dehydrated / permeabilized by an ascending series of alcohol baths. Subsequently specimens are treated with xylol (attention, toxic) to remove the ethanol and infiltrated with liquid (xylol-soluble) paraffin at 56°C*. Next the samples are cooled to -10°C** and thin slices of ~ 2µm produced using a microtome and put unto slides. There they are stably attached – fixed – to the glass by heating to 65°C***. Paraffin is removed again by xylol in a descending series of ethanol baths. These tissue samples are then stained appropriately, covered with sealant and coverslips, and inspected. Such slides are usually stable for years.

With a **blood smear** the sample can be directly applied to a slide and air dried instead of fixation. **PBMC** preparations can be collected as cytopsins.

*** For immunohistochemistry this and following steps have to be omitted.

** This facilitates cutting of lipid-rich tissues; this is no cryo-micromotome (cryostat)

* In professional labs this step is massively accelerated by a ‘vacuum infiltration processor’.
Hematoxylin / Eosin stain

**Hematoxylin** – Upon spontaneous oxidation hematoxylin forms haematein, a compound that forms strongly colored complexes with certain metal ions, notably Fe(III) and Al(III) salts. Metal-haematein (also ‘Hämalaun’ or ‘Hämatoxylin-Lack’, mostly with Al^{3+}) complexes are used to stain cell nuclei of histological samples prior to microscopic examination. It is a permanent stain.

Eosin – most often used as a counterstain to hematoxylin, imparting a pink or red color to cytoplasm, cell membranes, and some extracellular structures like connective tissue. It also imparts a strong red color to red blood cells. In skillfully made preparations collagen and cytoplasm (especially muscle) acquire different shades of pink. Eosin actually refers to two very closely related compounds. Most often used is eosin Y (slight yellowish cast). Eosin B has a faint bluish cast. The two dyes are interchangeable.

Eosinophilic granulocytes → stain easily with eosin
Principle of colon (= large intestine) adenoma + carcinoma

The large intestine is subdivided into the ascending colon, the transverse colon, the descending colon, and the sigmoid colon. The small intestine is ‘above’ and starting from the stomach consists of duodenum, jejunum and ileum.
Box 1 | Histopathology of colorectal cancer

Intestinal epithelial crypts → Aberrant crypt focus → Adenoma → Carcinoma

- APC
- KRAS Other oncogenes?
- SMAD2/SMAD4 Chromosome 18q LOH
- TP53 Chromosome 17p LOH

Nuclear β-catenin levels and chromosomal instability

Fodde et al., NatRevCancer 1, 55-67, (2001)
Throughout the large intestine, a monolayer of epithelial cells lines tubular glands or crypts. These are invaginations of the epithelium that effectively increase the surface area of the colon and rectum. The small number of stem cells located at the base of each crypt give rise, by asymmetric division, to four cellular types: columnar absorptive cells, goblet cells (mucus-secreting), and neuroepithelial cells, and paneth cells which are occasionally present at the base of crypts in the caecum and ascending colon. Dividing cells are located in the lower third of the crypt, whereas the differentiated types are found in the upper two-thirds. The cells continuously migrate upwards and are eventually exfoliated into the lumen by an apoptotic mechanism. The process of epithelial renewal takes 3–6 days. Cell mitotic rates in the colonic epithelium equal loss rates. Intestinal tumors are the result of an increase in this gain:loss ratio. The earliest manifestations of colorectal neoplasia are the aberrant crypt foci or ACF only visible by methylene blue staining or by microscopy. ACF usually encompass few crypts and can be composed either of cells of normal morphology (nondysplastic), or dysplastic cells (see figure). The latter are more likely to progress to become a polyp - a benign tumor mass that protrudes into the lumen from the intestinal epithelium1 (see figure). Polyps, like their ACF counterparts, can be of two types: hyperplastic (nondysplastic) and adenomatous dysplastic). Hyperplastic polyps preserve normal architecture and cellular morphology, whereas adenomatous polyps are characterized by abnormalities in both inter- and intracellular organization. The epithelium is organized in multiple layers, nuclei are enlarged, and their alignment at the basal membrane is lost (see figure). (Figures courtesy Edward C. Klatt M.D., Florida State University College of Medicine.)
normal colon (large intestine)
Peyer's Patches are visible with the naked eye. Notice the germinal center where B-cells proliferate. These are a major source of antibody production.
Bar = 250 Microns

www.kumc.edu/instruction/medicine/anatomy/histoweb/lymphoid/lymph07.htm

eugraph.com/histology/digest/ileum.html
normal colon (large intestine)
colon adenoma – high resolution
colon adenoma – medium resolution

adenoma

normal colon
colorectal adenocarcinoma metastasis to a lymph node. The cancerous cells are at the top center-left of the image, in glands (circular/ovoid structures) and eosinophilic (bright pink). H&E stain; Wikipedia
colon carcinoma – high resolution

Histopathologic image of colonic carcinoid stained by hematoxylin and eosin; Wikipedia
Lung
Details of alveoli, bronchiole and blood circulation

picture: Wikipedia german
large surface area, many capillaries (black arrows) filled with erythrocytes, many small air spaces (alveoli).
Slide: Lung HJ I-22, 40x

vp = visceral pleura
br = bronchiole
bv = blood vessel
* = alveolus

Slide: Lung HJ I-22, 400x

sm = smooth muscle
ep = epithelium

eugraph.com/histology/resp/lung.html
lung cancer

Subtypes (Wikipedia, modified)

Adenocarcinoma: originating in the epithelial cells of glandular tissue and forming glandular structures; 30-40% of all lung carcinomas. It is found peripherally, arising from goblet cells or type II pneumocytes.

Squamous cell carcinoma due to squamous metaplasia; accounts for 20-30% of lung tumors and is usually hilar in origin.

Small cell carcinoma is almost certainly due to smoking; metastasize early, and may secrete ADH, lowering patient’s sodium concentration; 10-15% of lung neoplasms; aggressive and difficult to recognize due to undifferentiated nature; most commonly central in the lung.

Figure: small cell lung carcinoma; microscopic view of a needle biopsy (HE-stain?); note nuclei of various size
Figure 1  Lung Cancer Cell Types, how the pathologist classifies the cancer

Adenocarcinoma

Large Cell Carcinoma

Squamous Cell Carcinoma

Small Cell Carcinoma

lung cancer schematically
**lung cancer**

Immunohistochemical stained lung normal bronchiolar tissue (A) and normal alveolar tissue (C) with matched adjacent squamous cell carcinoma tissue section (B) and matched adjacent adenocarcinoma section (D) respectively. Original magnification x100.
SCLC (top right) + squamous cell carcinoma
Lung cancer derived from mucus-producing cells. It contains bizarre nuclei and areas where mucus has accumulated ("mucus lakes") because the glands no longer know where to send it. The mucus will be pale-pink as it contains some protein.
normal liver

The liver develops as an outgrowth of the gut. The principle cells are **hepatocytes**. To maximise their contact with blood, hepatocytes are arranged into roughly hexagonal **lobules**. Blood within the portal vein and hepatic artery enters at the corners of these hexagonal lobules, and percolates through a network of **sinusoids** past the hepatocytes to reach a **central vein** in the centre of each lobule. At the corners of the lobules a portal vein branch, hepatic artery branch and bile duct branch run together surrounded by connective tissue and this is called a **portal triad**.
normal liver
fatty liver – following e.g. chronic alcohol abuse
liver cancer

right third: normal liver tissue

left part: adenocarcinoma metastasis from distant organ
liver cancer – hepatocellular carcinoma in situ
The kidney is composed of two regions, the **renal cortex and medulla**. The cortex lies between capsule and medulla and contains renal corpuscles, proximal tubules, and distal tubules. The medulla is home to the loop of Henle, vasa recta, and collecting tubules. Urine from the various collecting ducts drains into the renal pelvis, urethra, and bladder.

The rather infrequently occurring **kidney cancer** is also known as **renal cell carcinoma**. It is an abnormal growth of the cells lining the tubules of the kidney.
renal medulla

In these images, all tubules are cut in cross section, indicating that they are parallel and arranged perpendicular to the plane of section.
The larger tubules in this image are collecting ducts. The smaller tubules are ascending thick segments of loops of Henle. Descending thin segments are also present but not as conspicuous. ts: thin segment, loop of Henle, dt = distal tubule (ascending thick segment, loop of Henle), cd = collecting duct
The cortex of the kidney is distinguished by characteristic renal corpuscles, each of which consists of a glomerulus surrounded by Bowman's capsule.
The cortex of the kidney is distinguished by characteristic renal corpuscles, each of which consists of an outer envelope of simple squamous epithelium (Bowman's capsule surrounding a fluid-filled space (Bowman's space) within which is suspended a glomerulus (glom).
The bulk of the cortex consists of convoluted tubules. Cells comprising proximal tubules stain more intensely eosinophilic than those comprising distal tubules, and have nuclei spaced somewhat farther apart. The lumens of distal tubules (\textit{d}) commonly appear more open and clear than those of proximal tubules (\textit{p}).
renal cell carcinoma

most common type of renal cell carcinoma, i.e. **clear cell carcinoma** on right half of the image; non-tumour kidney is seen on the left. Nephrectomy specimen, H&E stain.
Typical appearance of clear cell renal cell carcinoma (H&E stain): nests of epithelial cells with clear cytoplasm and a distinct cell membrane, separated by a delicate branching network of vascular tissue.
β-Catenin is part of a complex of proteins that constitute adherens junctions (AJs). AJs are necessary for the creation and maintenance of epithelial cell layers by regulating cell growth and adhesion between cells. β-Catenin also anchors the actin cytoskeleton and may be responsible for transmitting the contact inhibition signal that causes cells to stop dividing once the epithelial sheet is complete. β-catenin also plays an important role in the Wnt-signalling pathway. When Wnt is not present, GSK-3 (a kinase) constitutively phosphorylates the β-catenin protein. β-catenin is associated with axin (scaffolding protein) complexed with GSK3 and APC (adenomatosis polyposis coli). The creation of said complex acts to substantially increase the phosphorylation of β-catenin by facilitating the action of GSK3. When β-catenin is phosphorylated, it is degraded and, thus, will not build up in the cell to a significant level. When Wnt binds to frizzled (Fz), its receptor, dishevelled (Dsh), is recruited to the membrane. GSK3 is inhibited by the activation of Dsh by Fz. Because of this, β-catenin is permitted to build up in the cytosol and can be subsequently translocated into the nucleus to perform a variety of functions. It can act in conjunction with TCF and LEF to activate specific target genes involved in different processes.

Clinical Significance: An increase in β-catenin production has been noted in basal cell carcinoma and leads to the increase in proliferation of related tumors. Mutations in this gene are a cause of colorectal cancer (CRC), medulloblastoma (MDB), and ovarian cancer. Also, β-catenin binds to the product of the APC gene, which is mutated in adenomatous polyposis of the colon.
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IHC stain for β-catenin
mainly at plasma membrane
normal colon 1
IHC stain for β-catenin
normal colon 2
IHC stain for β-catenin colon carcinoma 1
nuclear + cytoplasmic localization
IHC stain for β-catenin colon carcinoma 2
IgG control
hematoxylin counterstain
normal colon 2
‘Six1’ activates TGF-β signaling and induces EMT in vivo

Paraffin-embedded tissue sections from MCF7 tumors in nude mice were immunostained E-cadherin. Six1 induced redistribution of E-cadherin from a membranous pattern in the control tumors to a cytoplasmic pattern. Original magnification ×400; Scale bar 100 μm.

*Figure 4 from: Micalizzi et al., J Clin Invest. 2009; 119(9):2678 doi:10.1172/JCI37815*
Epithelial–mesenchymal transitions in tumour progression
Jean Paul Thiery, Nature Reviews Cancer 2, 442-454 (June 2002) doi:10.1038/nrc822
Detailed immunocytochemical analysis of adenomas and adenocarcinomas of the colon has revealed interesting distributions of E-cadherin, β-catenin, laminin-5 and fibronectin at sites of tumour remodelling. Adenomas branch by the budding and branching of pre-existing tubes, without the dissociation of single cells. A strong positive signal for nuclear β-catenin is detected predominantly at sites of budding epithelial cells during the branching process. The branching process increases with the size of the adenoma, enabling the tumor to expand rapidly into the stroma - a mechanism that is observed in transgenic mice producing β-catenin in intestinal epithelial cells. In adenocarcinoma, invasion also involves the release of single cells by a process that involves epithelial–mesenchymal transition (EMT) in the zone of the tumor that is progressing within the stroma. These solitary cells originate from budding sites that are positive for β-catenin. The figure shows branched epithelial structures in the centre of a colon carcinoma producing E-cadherin in cell–cell contacts (a), whereas β-catenin is mostly present in adherens junctions that are proximal to the apical domain (b). The E-cadherin-negative solitary cells (c), which often still produce nuclear β-catenin (arrows) (d), subsequently form tumor-cell plates and new branching tubules, gradually relocalizing β-catenin at the cell surface. These solitary cells produce large amounts of cytoplasmic fibronectin and laminin-5 – highly potent inducers of motility. The production of large amounts of nuclear β-catenin seems to make cells receptive to different environmental signals, which can either lead to EMT, resulting in these cells becoming solitary invasive cells, or can cause them to reassemble into epithelial structures. These E-cadherin-negative cells have lost their polarity and remain quiescent, in contrast to the highly polarized cells in the branched structures. Very similar structures (fully differentiated branched tubules in the centre of the tumor, with tumor-cell plates and single cells at the invasive front) are also seen in the corresponding metastases. … (Images courtesy of Thomas Brabletz, University of Erlangen–Nurnberg, Germany.)

Epithelial–mesenchymal transitions in tumour progression
Jean Paul Thiery, Nature Reviews Cancer 2, 442-454 (June 2002) doi:10.1038/nrc822
left panels: Ras-transformed mammary epithelial cells (NMuMG-Ras) in collagen gel cultures (3D) form hollow, alveolar structures of polarized epithelial cells expressing E-cadherin and a cortical actin ring but no mesenchymal markers (vimentin).

right panels: Addition of TGFβ (6 days) induces these cells to undergo epithelial-mesenchymal transition (EMT), characterized by unorganized structures of fibroblastoid cells expressing no E-cadherin but cytoplasmic actin and vimentin.
RESIDUAL MATERIAL
Proliferating Cell Nuclear Antigen

The protein encoded by this gene is found in the nucleus and is a cofactor of DNA polymerase delta. Proliferating Cell Nuclear Antigen is commonly known as PCNA. It acts as a processivity factor for DNA polymerase δ in eukaryotic cells. It achieves this processivity by encircling the DNA, thus creating a topological link to the genome. It is an example of a DNA clamp. PCNA is clamped to DNA through the action of replication factor C,5 (RFC; a heteropentameric member of the AAA+ class of ATPases). PCNA itself acts as a homotrimer and helps increase the processivity of leading strand synthesis during DNA replication. In response to DNA damage, the protein is ubiquitinated and is involved in the RAD6-dependent DNA repair pathway.

PCNA was originally identified as an antigen that is expressed in the nuclei of cells during the DNA synthesis phase of the cell cycle.2 Expression of PCNA is under the control of E2F transcription factor-containing complexes.6 Two transcript variants encoding the same protein have been found for this gene.1

Antibodies against proliferating cell nuclear antigen (PCNA) or monoclonal antibody termed Ki-67 can be used for grading of different neoplasms, e.g. astrocytoma. They can be of diagnostic and prognostic value.
PCNA-Expression als Marker zur Charakterisierung der Proliferationsaktivität beim Mammakarzinom

C. Minguillon I, Schönborn, R. Braun, W. Lichtenegger
Universitäts-Frauenklinik U.K.R.V., Standort Charlottenburg, Pulsstr. 4-14, D-14059 Berlin

Zusammenfassung

Die Wertigkeit des neuen monoklonalen Antikörpers (MAk) Anti-PCNA (Proliferating Cell Nuclear Antigen) zur Bestimmung der Proliferationsaktivität wurde anhand von 275 histologisch gesicherten Mammakarzinomen untersucht. Etablierte Prognosefaktoren (Histologie, Grading, Tumorgröße, Nodalstatus, Hormonrezeptorstatus) und die Wachstumsfraktion-KI67 wurden mit der PCNA-Expression korreliert.

PCNA erweist sich als zuverlässiger Marker zur Bestimmung der Proliferationsaktivität. Der Vorteil dieser Bestimmung liegt in der unkomplizierten Methodik und Reproduzierbarkeit durch die mögliche Anwendung an formalinfixierten und paraffineingebetteten Material.

Einleitung

Die zelluläre Proliferation von Tumoren hat als prognostischer Faktor in der letzten Zeit zunehmend an Bedeutung gewonnen. Bisherige Untersuchungsmethoden wie das Zählen von Mitose, die Bestimmung des Thymidian-Labeling-Index, die Flow-Zytometrie und die Beurteilung der Wachstumsfraktion durch Ki67 haben sich als zuverlässige Indikatoren zur Einschätzung des Tumorverhaltens erwiesen (1, 2).
Immunohistochemistry with anti-PCNA Monoclonal Antibody


Formalin-fixed, paraffin-embedded rat breast cancer stained with PCNA antibody using peroxidase-conjugate and AEC chromogen. Note nuclear staining of tumor cells.

Immunohistochemistry of paraffin-embedded Breast cancer using PCNA Antibody 60097-1-Ig (under 10x lens); http://www.ptglab.com/PView/PCNA-Antibody-60097-1-Ig-PVIEW.htm
Immunohistochemistry of paraffin-embedded Breast cancer using PCNA Antibody 60097-1-Ig (under 10x lens); http://www.ptglab.com/PView/PCNA-Antibody-60097-1-Ig-PVIEW.htm
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