

# Immunohistochemistry

## tumour pathology

### Immunohistochemistry: tumour pathology

Immunohistochemistry has multiple applications in tumour pathology, including elucidation of site of origin and determination of cell type/direction of differentiation. Immunohistochemistry may also help to confirm neoplasia, determine the selection of treatment, refine prognostic predictions and screen for known underlying genetic changes. Numerous immunohistochemical stains help to determine cell type in tumours. Epithelial cells express cytokeratins. Therefore, cytokeratin positivity, though not diagnostic, favours carcinoma (Figure 11.25) over other types of malignancy. Lymphoid markers include the panlymphoid marker CD45, the T-lymphocyte marker CD3 and the B-lymphocyte marker CD20. Markers of melanocytic differentiation include S100, MelanA and HMB45. Chromogranin, synaptophysin

Summary box 11.11 Some immunohistochemical stains used for tumours

typically expresses CD117 (Figure 11.26) and DOG-1. Endothelial cell markers include CD31, which may confirm a diagnosis of vascular neoplasia or highlight vascular invasion by tumours. H&E appearances may indicate or suggest the anatomical site of origin of a metastatic tumour. For example, an adenocarcinoma has several possible sources such as gastrointestinal tract, pancreatobiliary system, bronchus, breast and gynaecology is often of logical tract. A clear cell carcinoma (Figure 11.17) renal origin but could be from the liver, pancreas, parathyroid or endometrium, among other sites. Immunohistochemical stains often provide valuable further information about anatomical origin. Some are highly specific for a particular site, e.g. prostate-specific antigen (PSA) and thyroglobulin. Others are somewhat less specific, e.g. thyroid transcription factor-1 (TTF-1), a marker of bronchogenic or thyroid origin; hepatocyte-specific antigen, suggesting hepatocellular origin; and cytokeratin 20, typically expressed by colorectal epithelium. Several types of Carcinoembryonic antigen (CEA) is present in serous carcinoma (Figure 11.22b). In practice, pathologists encountering a neoplasm of uncertain origin or uncertain phenotype usually request a panel of markers relevant to the clinical setting and to the H&E appearances. Some malignancies, especially poorly differentiated examples, do not conform to the

Cell type/site of origin  
Epithelial (carcinoma): cytokeratins  
Lymphoid (lymphoma): CD45, CD3 (T cells), CD20 (B cells)  
Melanocytic (melanoma): S100, HMB45, Melan A  
Neuroendocrine: synaptophysin, chromogranin  
Vascular: CD31  
Myoid: desmin, actin  
Site of origin/cell type  
Prostate: prostate-specific antigen (PSA)  
Lung: thyroid transcription factor-1 (TTF-1)  
Thyroid: thyroglobulin  
Colorectum: cytokeratin 20 (CK20), CDX2  
Liver: hepatocyte-specific antigen (HSA)  
Gastrointestinal stromal tumour (GIST): CD117, DOG-1  
Prognosis and treatment  
Breast carcinoma and gastric carcinoma: HER-2  
Neuroendocrine tumours: Ki67 proliferation index  
Screening for





Immunohistochemistry: infections and other applications There are antibodies to many infective agents, including cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus, human herpes virus 8 (HHV8), hepatitis B virus and Helicobacter pylori. Some of these organisms, e.g. pylori and CMV, may be obvious or suspected on H&E examination, while others, e.g. EBV and HHV8, always require immunohistochemistry or other techniques for their detection.

Immunohistochemistry can also detect immunoglobulin and complement expression (e.g. in lymphomas or renal biopsies); confirm the abnormal accumulation of various proteins such as alpha-1-antitrypsin (A1AT); and help to characterise amyloid. Newer immunohistochemical markers that detect specific gene mutations are appearing and may become useful in clinical practice in the future. An important example is screening for MMR gene mutations in most gastrointestinal carcinomas Sir Michael Anthony Epstein, b.1921, Professor of Pathology, University of Bristol, Bristol, UK. Yvonne Barr, 1931-2016, Irish born virologist who emigrated to Australia. Epstein and Barr discovered this virus in 1964. BRAF V600E can replace mutational analysis in some settings. The major advantages of immunohistochemistry over other molecular tests for detecting genetic alterations are lower cost and faster turnaround. Summary box 11.12 Uses of immunohistochemistry /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF - /uni25CF /uni25CF - -

Figure 11.27 Immunohistochemistry for Ki67. The proliferative index is approximately 35% in this field. Cell type Neoplasia Direction of differentiation/phenotype Determination of anatomical site of origin Confirmation of neoplasia Grading Selection of treatment Detection of/screening for mutations Prognosis Microorganisms - detection Other Amyloid Immunoglobulins Complement

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Cell type/site of origin Epithelial (carcinoma): cytokeratins Lymphoid (lymphoma): CD45, CD3 (T cells), CD20 (B cells) Melanocytic (melanoma): S100, HMB45, Melan A Neuroendocrine: synaptophysin, chromogranin Vascular: CD31 Myoid: desmin, actin Site of origin/cell type Prostate: prostate-specific antigen (PSA) Lung: thyroid transcription factor-1 (TTF-1) Thyroid: thyroglobulin Colorectum: cytokeratin 20 (CK20), CDX2 Liver: hepatocyte-specific antigen (HSA) Gastrointestinal stromal tumour (GIST): CD117, DOG-1 Prognosis and treatment Breast carcinoma and gastric carcinoma: HER-2 Neuroendocrine tumours: Ki67 proliferation index Screening for mutations Colorectal carcinoma: mismatch repair proteins (MLH1, MSH2, MSH6, PMS2) (a) (b) Figure 11.26 (a) A metastatic tumour composed of spindle cells. The clinical team suspected a diagnosis of gastrointestinal stromal tumour (GIST). (b) Positive immunohistochemistry for CD117, supporting a diagnosis of GIST.

typical immunohistochemical profiles. In all circumstances, interpretation takes place in the light of the clinical picture and imaging findings. Less often, immunohistochemistry helps to confirm malignancy. For example, kappa or lambda light chain restriction (expression of only one immunoglobulin light chain) in lymphoid proliferations suggests clonality and, in turn, neoplasia rather than a reactive process. In general, immunohistochemistry does not distinguish well between benign and malignant. Immunohistochemistry also plays a role in the selection of treatment and in predicting prognosis. For example, assessment of oestrogen receptor (ER) and human epidermal growth factor receptor-2 (HER2) status is routine for carcinomas of the breast (see Immunohistochemistry: tumour pathology while lymphomas are typically subjected to a comprehensive panel of markers that help determine treatment and prognosis. Ki67 proliferative index is an important prognostic factor for neuroendocrine neoplasms ( Figure 11.27 ) .

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Revision #1

Created 2025-12-31 15:08:25 UTC by Omar Ayman

Updated 2025-12-31 15:08:25 UTC by Omar Ayman