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Immunohistochemistry in Diagnostic Pathology

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Description

Immunohistochemistry is an interdisciplinary set of scientific techniques used for the visualization of tissue level and cellular architecture. It exists at the intersection of the fields of immunology, histology and chemistry. Immunohistochemical staining plays a critical role in clinical diagnostic pathology. Seeing the dispersion of various proteins and other cellular components in a tissue sample allows pathologists to render or corroborate a clinical diagnosis. In order to visualize the localization of cellular components, the field exploits the natural ability of antibody proteins from the immune system to bind to a specific antigen. A parallel field, immunocytochemistry, involves the same set of techniques applied to cells, not full tissue sections. However, the two terms are sometimes used interchangeably by researchers.

In the early 1940s, scientists demonstrated that antibodies that were labeled with a florescent tag maintained specificity for their antigen. Building on this discovery, scientists then incubated tissues with these fluorescently labeled antibodies and examined the tissues for the signal under fluorescence microscopy. The localization of antibodies and thus their tags to the antigens allowed them to directly determine the presence and location of antigens within these samples.

Over the last few decades, the techniques used in immunohistochemical staining have become exponentially more complex. Several milestones have accelerated the growth of the field of immunohistochemistry with the first one being the introduction of enzyme-labeled antibodies that allow visualization of targeted antigens by bright-field microscopy. The production of monoclonal antibodies with greater specificity has resulted in countless types of antibodies, tags and reagents available for use. Signal strength can be improved with antigen retrieval methods that enhance the ability of antibodies to bind to epitopes in formalin-fixed paraffin-embedded tissues. Archival tissue samples can be stained, allowing for potential retrospective research. Other recent developments include sensitive secondary detection systems, automated staining systems and digital imaging analysis. The strength of the signal can be further amplified using indirect epitope detection in which tagged secondary antibodies that are specific against the untagged primary antibody are applied to the tissue. Improvements in consistency, reproducibility and stain quality made possible with automated system and image analysis technologies allow for accurate quantification of staining in tissue samples. All of these developments in turn advance clinical diagnosis and propel research.

As the complexity of immunohistochemical techniques has progressed so has their utility. The exploitation of the specificity of these interactions enables us to detect particular molecules of interest in tissue samples through immunohistochemical methods. In addition to being adjunct diagnostic tolls discussed in subsequent research, immunohistochemical markers can now be used as screening tests for hereditary syndromes. In the era of personalized medicine, biomarker expression can guide risk stratification and therapeutic decision. The association of these molecules with certain disease presentation allows us to use information gathered through staining as biomarkers for diseases. Thus an entire line of study within the field of immunohistochemistry involves the discovery of these biomarkers and their clinical relevance. Currently, several biomarkers are approved by Food and Drug Administration for diagnostic use in cancer, including HER2, estrogen receptor and epidermal growth factor receptor. An ever-growing body of literature catalogues the relationships between expressions of various proteins and diseases. Presence of these biomarkers within a tumor can be used by the medical team to guide and personalize treatment.

Immunohistochemical techniques are growing progressively more sensitive and specific. Our understanding and manipulation of antibody-epitope interactions have allowed immunohistochemistry and other related technologies to grow into fields of their own, including immunofluorescence and *insitu* hybridization using DNA and RNA probes. Antibodies have grown into powerful clinical and research tools. Further research should include the conceptual framework of immunohistochemistry, outline technical mechanisms and explain its clinical relevance.