Role of Immunohistochemistry in Diagnosis of Cancer

Immunohistochemistry (IHC) was originally described by Coons *et al.*, in 1941 and developed an immunofluorescence technique to detect corresponding antigens in frozen tissue sections.[1] This method became popular in surgical pathology in the 1990s.[2] IHC is a method performed in the laboratory to identify specific antigens or analytes in a tissue sample using monoclonal or polyclonal antibodies.[3] (Figure 1). Immunohistochemistry in cancer diagnosis is used to look at the specific antigens that are unique or over-expressed, also known as analytes, to answer a number of research and clinical questions including

(a) distinguish a tissue as being cancerous,
(b) assess whether a patient should receive or is responding to therapy or
(c) evaluate the immune response at the site of a tumor.

To perform immunohistochemistry, a tissue biopsy is formalin-fixed and paraffin embedded before being processed into sections and fixed onto slide. The slides are incubated with an antibody that will bind to the antigen of interest. The sites of antibody and antigen binding in the tissue are visualized using fluorescent or light microscopes, depending on the type of antibody used.[4]

An antibody is a molecule that has the property of combining specifically with a second molecule, termed the *antigen*. Antibodies are immunoglobulin molecules consisting of two basic units: a pair of light chains (either a kappaor a lambda pair) and a pair of heavy chains (gamma,alpha, mu, delta, or epsilon). An antigen is any moleculethat is sufficiently complex that it maintains a relatively rigid three-dimensional profile and is foreign to the animal into which it is introduced. Good antigens are proteins and carbohydrates that are sufficiently complex to possess a unique three-dimensional "charge-shape"profile. In fact, such molecules may bear more than one unique three-dimensional structure capable of inducing antibody formation. Each of these individual sites on a molecule may be termed an *antigenic determinant* (or *epitope*), being the exact site on the molecule with which the antibody combines. For a protein, the term *epitope* corresponds to a cluster of amino acid residues that binds specifically to the paratope of an antibody. [5]

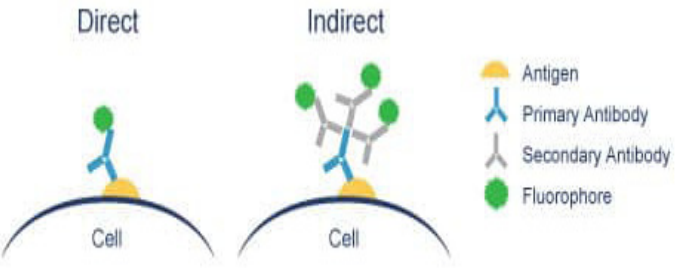

Figure 1

Applications of IHC: [6,7]

IHC involves specific antigen–antibody reactions, it has apparent advantage over traditionally used special enzyme staining techniques that identify only a limited number of proteins, enzymes, and tissue structures. IHC has become a crucial technique and is widely used in many medical research laboratories as well as clinical diagnostics.

1. Diagnosis of Tumors

A. **Classification of poorly differentiated neoplasm**

a. Carcinoma (cytokeratin +) vs
b. Lymphoma (CD45+) vs
c. Melanoma (S100+, Melan-A+, HMB45+)

B. **Diagnosis of carcinoma of unknown primary**

a. Colon (CDX2+) vs
b. Lung (TTF1+) vs
c. Prostate (PSA+ve)

C. **Diagnosis of invasion**

a. Loss of myoepithelial cells (breast cancer)
b. Loss of basal cell (prostate cancer)
c. Loss of basement membrane/collagen type IV (various carcinomas, rarely used)

2. Assessment of markers reflecting prognosis (Prognostic markers)

a. Ki67/MIB1 (general proliferation markers)
b. p53 (general markers of apoptosis)

c. HER2 (adverse prognosis in breast cancer)
d. CD38 (adverse prognosis in chronic lymphocytic leukemia)

3. Assessment of markers reflecting a therapeutic response (Predictive or Theranostic markers)

a. ER/PR (Tamoxifen for breast cancer)
b. HER2 (Herceptin for breast cancer)
c. c-kit (Gleevec for GIST, CML, other, mutation more predictive than IHC)

4. Detection of micrometastasis

a. Melanoma (melanocytic markers)
b. Breast cancer (cytokeratins)

5. Identification of infectious organism

a. Viruses (HSV, CMV)
b. Other organism (Toxoplasma, pneumocystis)

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