



The Application of Molecular Histology to the Study of Solid Tumors

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Mutations in dominant oncogenes and tumour suppressor genes are common in human cancer. Many molecular approaches are used to discover these aberrations, including single-strand conformational polymorphism, polymerase chain reaction, cloning, and sequencing. However, the biological significance of these changes is not always clear. In neoplastic vs. normal cells, immunohistochemistry (ICH) or western blotting of aberrant gene products can offer information about their cellular localization and expression, as well as a suggestion about their function. For example, ICH has found that loss of the intercellular adhesion molecule E-cadherin, or abnormal location of E-cadherin from the cell membrane to the cytoplasm, is linked to a wide range of tumour phenotypes and a poor prognosis. Similarly, ICH of β -catenin (a protein that binds E-cadherin and is required for its function) has been observed in a variety of human cancers, with abnormal cellular localization in the nucleus; in particular, colorectal carcinomas, where abnormal forms of the adenomatous polyposis coli gene product cause nuclear and cytoplasmic sequestration of β -catenin. This type of research shows how morphological examination can sometimes reveal molecular activity and dysfunction in human cancer. Because cancer is essentially a genetic disease, most cancer research has centred on figuring out how a variety of oncogenes and tumour suppressor genes malfunction in human cancer. With the availability of various new and advanced molecular tools, the number of approaches for analysing these anomalies has recently increased. To discover mutations, researchers use polymerase chain reaction and DNA sequencing, as well as comparative genomic hybridization using genomic microarrays to detect gene amplifications and deletions on a genome-wide scale. These novel technologies, however, have yet to find a place in the diagnostic histopathology laboratory's routine work for a variety of reasons. They can be expensive to set up and run, or they can produce disappointing results from typical formalin-fixed paraffin wax embedded specimens, requiring adjustments in specimen processing.

Furthermore, while these approaches can often correctly detect the presence or absence of mutations, determining their biological significance from such data is not always simple. Alternative approaches, on the other hand, have already found a place in many histopathology laboratories' work, whether as diagnostic or research tools. These techniques, which include immunohistochemistry, western blotting, and in situ hybridization to measure mRNA expression, provide direct detection of abnormal gene products. Immunohistochemistry is a widely used diagnostic method for identifying the presence or absence of certain proteins in fixed and embedding materials. It is inexpensive, simple to do, and can aid in the imaging of aberrant cell types in vivo.

In general, approaches like these can:

- Offer valuable information on the location of aberrant gene products (either between different cell types or within subcellular compartments)
- Offer data on the amount of gene expression of such products in tumor cells versus normal cells
- In certain cases, give insights into the function of specific changed genes and their products.

This method elegantly connects the molecular biology of every tumor under investigation to its histological features and behaviour.