



The Use of Molecular Histology in the Investigation of Solid Tumors

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Received date: March 12, 2021; Accepted date: March 19, 2021; Published date: March 23, 2021

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In human cancer, dominant oncogenes and tumor suppressor gene mutations are critical occurrences. Many molecular methods, including single-strand conformational polymorphism, polymerase chain reaction, cloning, and sequencing, are employed to detect these anomalies, however, the biological significance of these alterations is not always obvious. Immunohistochemistry (ICH) or western blotting of aberrant gene products can reveal information about their cellular localization and expression in neoplastic vs normal cells, as well as a hint regarding their function. For example, ICH has demonstrated that deletion of the intercellular adhesion molecule E-cadherin, or aberrant localization from the cell membrane to the cytoplasm, is associated with a widespread tumor phenotype and a poor clinical prognosis. Similarly, in a variety of human malignancies, ICH of β -catenin (a protein that binds E-cadherin and is essential for its function) has shown 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. Such research demonstrates how morphological analysis may occasionally give insight into molecular activity and malfunction in human cancer.

Because cancer is fundamentally a genetic illness, most cancer research has focused on understanding how numerous oncogenes and tumor suppressor genes become defective in human malignancy. The variety of approaches for investigating these anomalies has recently expanded, with several new and sophisticated molecular techniques being accessible. These include utilizing polymerase chain reaction and DNA sequencing to identify mutations, as well as comparative genomic hybridization on genomic microarrays to detect gene

amplifications and deletions on a genome-wide scale. However, for a variety of reasons, these novel methods have yet to find a place in the normal work of the diagnostic histopathology laboratory. They might be costly to set up and run, or they can yield unsatisfactory results from standard formalin-fixed paraffin wax embedded specimens, necessitating specimen processing changes. Furthermore, while these methods may frequently properly detect the presence or absence of mutations, establishing their specific biological significance from such data is not always straightforward.

However, a variety of alternative methods have already found a place in the work of many histopathology laboratories, either as diagnostic or research tools. These methods, which include immunohistochemistry, western blotting, and in situ hybridization to assess mRNA expression, allow for direct visualization of aberrant gene products. Immunohistochemistry is a popular diagnostic technique for determining the presence or absence of certain proteins in regularly fixed and embedded materials. It is cheap, simple to conduct, and can aid in the visualization of cell types in vivo that may have abnormalities.

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.