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Molecular pathology vs traditional histology: Bridging the diagnostic gap.

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Introduction

The fields of molecular pathology and traditional histology represent two essential pillars in disease diagnosis, particularly in oncology and genetic disorders. While traditional histology focuses on the microscopic anatomy of tissues and cells, molecular pathology delves into the genetic and molecular mechanisms underlying disease. The integration of these two methodologies is transforming the landscape of diagnostic medicine, offering more precise and personalized patient care.[1].

Traditional histology has long been the cornerstone of pathological diagnosis. It involves examining tissue architecture, cell morphology, and staining characteristics to identify abnormalities. Hematoxylin and eosin (H&E) staining remains a widely used technique that enables pathologists to evaluate cell size, shape, and organization, crucial for diagnosing cancers and inflammatory diseases. However, histology is limited in its ability to detect early molecular changes that precede morphological alterations..[2].

Molecular pathology, on the other hand, utilizes techniques such as polymerase chain reaction (PCR), fluorescence in situ hybridization (FISH), and next-generation sequencing (NGS) to analyze DNA, RNA, and protein profiles in tissue samples . These methods can detect genetic mutations, chromosomal abnormalities, gene expression levels, and epigenetic changes with high sensitivity and specificity . For instance, the detection of HER2 gene amplification in breast cancer or EGFR

mutations in non-small cell lung cancer (NSCLC) has direct implications for targeted therapy.[3]

The diagnostic gap between histology and molecular pathology becomes evident in ambiguous cases where histological features alone cannot provide a definitive diagnosis. In such cases, molecular tests can identify biomarkers that not only confirm the diagnosis but also guide therapeutic decisions. For example, in colorectal cancer, microsatellite instability (MSI) testing complements histological evaluation and helps identify patients who may benefit from immunotherapy. [4].

Furthermore, integrating molecular pathology with histological analysis has improved the accuracy of prognostic assessments. Molecular subtyping of tumors, such as in gliomas (IDH mutation and 1p/19q co-deletion), allows for a more nuanced classification beyond histological grade, impacting treatment strategies and patient outcomes Despite its advantages, molecular pathology is not without limitations. It requires specialized equipment, technical expertise, and is often more expensive and time-consuming than histology. Additionally, not all molecular changes are clinically actionable, and over-reliance on molecular data can overlook the broader tissue context provided by histology [5].

Conclusion

The future of pathology lies in the integration of both approaches. Digital pathology and artificial intelligence (AI)-driven platforms are enabling simultaneous analysis of histological images and molecular data, paving the way for more

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comprehensive diagnostic models. By bridging the gap between morphology and molecular alterations, pathologists can offer a more complete and precise diagnosis, enhancing patient care in the era of precision medicine.

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