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Genomic Alterations in Rare Cancers: A Comprehensive Pathological Review.

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Introduction

Rare cancers, defined as malignancies with an incidence of fewer than six cases per 100,000 individuals annually, collectively account for approximately 20% of all cancer diagnoses worldwide. While their low prevalence poses challenges for clinical trials and therapeutic development, advances in high-throughput genomic technologies have revolutionized our understanding of their molecular underpinnings. Genomic alterations—including point mutations, copy number variations, chromosomal rearrangements, and epigenetic modifications—play a pivotal role in tumor initiation, progression, and therapeutic resistance in these uncommon malignancies [1, 2, 3, 4, 5].

The pathological assessment of rare cancers, when complemented with genomic profiling, not only aids in accurate diagnosis but also uncovers targetable molecular pathways. For instance, alterations in KIT and PDGFRA genes are characteristic of gastrointestinal stromal tumors (GIST), while SMARCB1 loss is a defining feature of malignant rhabdoid tumors. In recent years, integrative approaches combining histopathology, immunohistochemistry, and next-generation sequencing (NGS) have facilitated precision medicine applications for rare cancer patients. This review aims to provide a comprehensive pathological perspective on the spectrum of genomic alterations in rare cancers, highlighting their diagnostic, prognostic, and therapeutic implications.

Conclusion

Genomic alterations in rare cancers present both challenges and opportunities in the realm of diagnostic pathology and therapeutic oncology. Although their infrequency complicates large-scale clinical research, the molecular signatures identified through genomic profiling have opened avenues for targeted interventions, individualized treatment regimens, and improved patient prognoses. The integration of pathology with genomic science is critical, ensuring that even the rarest malignancies are approached with evidence-based precision. Continued international collaborations, data-sharing platforms, and inclusion of rare cancers in genomic research initiatives will be essential to translate these molecular insights into tangible clinical benefits.

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