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Mismatch Repair Deficiency as a Predictive and Prognostic Biomarker in Endometrial Cancer

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Introduction

Endometrial cancer represents a significant health concern globally, with its incidence rising steadily in recent years. Mismatch Repair Deficiency (MMRd) has emerged as a crucial biomarker in the diagnosis, prognosis, and treatment of endometrial cancer. This article explores the role of MMRd as a predictive and prognostic biomarker in endometrial cancer, discussing its molecular mechanisms, diagnostic methods, clinical implications, and therapeutic opportunities. Understanding the significance of MMRd in endometrial cancer is essential for optimizing patient management strategies and improving clinical outcomes [1].

Description

Endometrial cancer ranks among the most prevalent gynaecologic malignancies worldwide, with an increasing incidence and mortality rate. While advances in treatment modalities have improved outcomes for many patients, the heterogeneity of endometrial cancer necessitates the identification of reliable biomarkers to guide personalized therapeutic approaches. Mismatch repair deficiency has emerged as a promising biomarker with implications for both prognosis and treatment response in endometrial cancer [2].

Mismatch Repair (MMR) is a highly conserved DNA repair pathway responsible for correcting errors in DNA replication, such as base substitutions, insertions, and deletions. Key components of the MMR pathway include MLH1, MSH2, MSH6, and PMS2 proteins. Deficiencies in these proteins result in impaired MMR function, leading to genomic instability and the accumulation of mutations, a hallmark of cancer development. MMR deficiency can occur through various mechanisms, including germline mutations, somatic mutations, epigenetic silencing, and protein dysfunction, with implications for tumor initiation and progression. Accurate detection of MMR deficiency is essential for guiding clinical decision-making in endometrial cancer patients. Several diagnostic methods are available to assess MMR status, including Immunohistochemistry (IHC) and molecular testing. IHC allows for the visualization of MMR proteins within tumor tissue, facilitating the identification of protein expression abnormalities indicative of MMR deficiency. Molecular testing techniques, such as Microsatellite Instability (MSI) analysis and Next-Generation Sequencing (NGS), provide additional insights into MMR status and associated genomic alterations [3].

MMR deficiency holds significant clinical implications for endometrial cancer patients, influencing prognosis, treatment response, and hereditary cancer risk. MMR-deficient tumors are associated with distinct clinicopathological features, including younger age at diagnosis, higher histological grade, and increased lymphovascular invasion. Importantly, MMR status serves as a prognostic indicator, with MMR-deficient tumors exhibiting favourable outcomes compared to MMR-proficient tumours in certain subsets of patients. The unique molecular characteristics of MMR-deficient endometrial tumors offer potential therapeutic opportunities for targeted interventions. Immunotherapy, particularly immune checkpoint inhibitors targeting programmed cell death protein 1 (PD-1) and programmed death-ligand 1 (PD-L1), has shown promising results in MMR-deficient endometrial cancer patients. Additionally, strategies aimed at exploiting synthetic lethality, such as polypolymerase inhibitors, may provide alternative treatment options for MMR-deficient tumors [4,5].

Conclusion

As our understanding of the role of MMR deficiency in endometrial cancer continues to evolve, future research efforts should focus on elucidating the mechanisms underlying MMR dysfunction, refining diagnostic strategies, and exploring novel therapeutic approaches. Integration of MMR status into clinical practice algorithms will enable more personalized management strategies, ultimately improving outcomes for endometrial cancer patients. In conclusion, MMR deficiency represents a promising predictive and prognostic biomarker in endometrial cancer, offering insights into tumor biology and therapeutic vulnerabilities that can be harnessed to optimize patient care.

Acknowledgement

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Conflict of Interest

None.

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