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Commentary

Integration of Multi-Omics Data to Predict Prognosis in Renal Cell Carcinoma

Michael Thompson*

Department of Urology, Stanford University School of Medicine, Stanford, CA, USA

DESCRIPTION

Renal Cell Carcinoma (RCC) is the most common type of kidney malignancy in adults, accounting for approximately 85% of all kidney cancers. Despite advances in surgical techniques, targeted therapy, and immunotherapy, the prognosis of RCC remains variable, with a significant proportion of patients developing recurrence or metastasis. Conventional prognostic markers, such as TNM stage, tumor grade, and performance status, provide limited predictive accuracy due to the molecular heterogeneity of RCC. To address this challenge, multi-omics approaches, integrating genomic, transcriptomic, epigenomic, proteomic, and metabolomic data, have emerged as a powerful strategy to capture tumor complexity and improve prognostic predictions.

Genomic profiling of RCC has revealed recurrent mutations in genes such as *VHL*, *PBRM1*, *BAP1*, and *SETD2*, which contribute to tumorigenesis and progression. *VHL* mutations, for instance, lead to dysregulated Hypoxia-INDUCIBLE Factor (HIF) signaling, promoting angiogenesis and metabolic reprogramming. However, genomic alterations alone often fail to capture dynamic tumor behavior, as they provide a static view of the mutational landscape. Transcriptomic data, including mRNA and non-coding Ribonucleic Acid (RNA) expression profiles, reflect functional changes in tumor biology and can reveal active pathways associated with aggressive behavior or therapy resistance. Similarly, epigenomic alterations, such as Deoxyribonucleic Acid (DNA) methylation and histone modifications, regulate gene expression and influence tumor progression, while proteomic and metabolomic analyses provide direct insights into the functional and metabolic state of cancer cells. Integration of these layers of information is essential to develop robust prognostic models.

Multi-omics integration allows for comprehensive characterization of RCC tumors, enabling the identification of molecular subtypes with distinct clinical outcomes. For example, studies combining genomic and transcriptomic data have revealed RCC subgroups with differential immune infiltration, angiogenic signatures, and metabolic profiles, which correlate with survival and therapeutic response. Epigenetic markers, including promoter hypermethylation of tumor suppressor genes, have been linked to poor prognosis and can refine risk stratification when combined with other omics layers. Proteomic and metabolomic signatures, such as alterations in lipid metabolism and energy pathways, provide additional functional context, revealing vulnerabilities that may guide treatment decisions. By integrating multi-omics data, researchers can uncover complex interactions

The integration of immune profiling with multi-omics data provides additional prognostic insights. RCC is characterized by significant immune heterogeneity, with variable infiltration of T cells, natural killer cells, and myeloid-derived suppressor cells. Transcriptomic and proteomic analyses can quantify immune signatures, revealing immune-active or immunosuppressive tumor microenvironments. When combined with genomic and epigenomic data, these immune features improve the accuracy of survival predictions and may identify candidates for immune checkpoint inhibitors. Furthermore, metabolic reprogramming in RCC, such as increased glycolysis or lipid metabolism, influences both tumor growth and immune evasion. Multi-omics integration allows for the simultaneous assessment of tumor-intrinsic and immune-related pathways, providing a more holistic understanding of disease progression.

Despite the promise of multi-omics integration, several challenges remain. The high dimensionality and complexity of multi-omics data require advanced computational resources and expertise. Interpreting predictive models can be difficult, particularly when using deep learning approaches, which may act as "black boxes." Integrating clinical, imaging, and multi-omics data further increases complexity but is critical for developing actionable prognostic tools. Additionally, prospective clinical trials are needed to evaluate whether multi-omics-based risk stratification improves patient outcomes, guides therapy selection, and reduces overtreatment. Ethical considerations, including data privacy and sharing, must also be addressed when integrating datasets from multiple institutions.

CONCLUSION

The integration of multi-omics data represents a transformative approach to predict prognosis in renal cell carcinomaIncorporating immune profiling and metabolic

Correspondence to: Michael Thompson, Department of Urology, Stanford University School of Medicine, Stanford, CA, USA, E-mail: Michaelthom789@stanford.edu

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signatures further enhances prognostic power and may inform therapy selection, particularly in the context of immunotherapy and targeted therapy. While challenges related to data complexity, standardization, and clinical translation remain, ongoing multi-institutional collaborations and technological advances are rapidly advancing this field. Ultimately, multi-omics integration has the potential to revolutionize RCC management, enabling personalized, data-driven prognostication and improving patient outcomes.