Characteristics of the tumor microenvironment and potential immunotherapy strategies in renal cell carcinoma: a supplementary report

Olivier Dubois, Sanjay Sharma, Margot Dubois

Renal cell carcinoma (RCC) is a highly vascularized and immunogenic malignancy with a complex tumor microenvironment (TME) that shapes disease progression and therapeutic resistance. Despite advances in immune checkpoint inhibitors (ICIs) and targeted therapies, clinical responses remain heterogeneous, underscoring the need for a deeper understanding of RCC immunobiology. This review comprehensively examines the immunosuppressive TME of RCC, emphasizing the roles of cytotoxic and immunosuppressive immune cells, carcinoma-associated fibroblasts (CAFs), abnormal vasculature, and extracellular matrix (ECM) remodeling in fostering immune evasion. This review summarized emerging biomarkers-including PD-L1 expression, tumor mutational burden (TMB), gene mutations, and immune-based subtypes-that may predict ICI response. Furthermore, we evaluate current immunotherapeutic strategies, such as ICIs, combination therapies, and novel approaches targeting immunosuppressive cells and metabolic pathways. While combination therapies have improved outcomes, challenges like toxicity and resistance persist, necessitating biomarker-driven patient stratification and optimized treatment sequencing. Future directions should focus on deciphering TME heterogeneity and developing precision immunotherapy strategies to enhance clinical efficacy in RCC.

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