



## Renal Cell Carcinoma: Diagnostic and Immunotherapeutic Value of CD248

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### ABSTRACT

The most frequent kind of cancer in the urinary system is Renal Cell Carcinoma (RCC). The survival outcome for advanced RCC remains unsatisfactory despite notable advancements in therapy. Finding novel biomarkers to help with early diagnosis and screen patients for immunotherapy sensitivity would be advantageous. A promising possibility that needs to be looked at is CD248. The dataset from the Cancer Genome Atlas (TCGA) and a clinical sample were used to compare the expression of CD248 in normal and malignant tissues. A CD248-based prognostic signature was created using univariate and multivariate Cox regression analysis to find independent predictive variables. The relationship between the current signature, immune cells that have infiltrated the tumor, the Tumor Mutation Burden (TMB), and immunomodulatory chemicals were assessed. To investigate the underlying mechanism of CD248 in RCC progression, Weighted Gene Coexpression Network Analysis (WGCNA) and enrichment analysis were carried out. A useful biomarker to boost RCC diagnosis and treatment effectiveness is CD248. Co-expressed CD248 genes' immunosuppressive effects could shed light on the current investigation.

**Keywords:** Renal Cell Carcinoma, Immunotherapeutic

### INTRODUCTION

The most fatal malignancy of the urinary system and the sixth most frequent tumor in developed countries is Renal Cell Carcinoma (RCC). According to reports, during the past 50 years, RCC morbidity has more than doubled in North America and Western Europe. In the ensuing decades, it is expected that RCC morbidity will rise quickly in Latin America, Asia, and Africa. In reality, RCC is a sneaky neoplasm with an appallingly low survival rate, with one-third of cases initially identified as metastatic. Targeted therapy has transformed RCC therapies, however, only 12% of patients with advanced or metastatic RCC survive 5 years after diagnosis. Another promising strategy to improve survival outcomes for RCC patients is immunotherapy using immune checkpoint drugs to suppress PD1, CTLA4, and LAG3. However, the treatment efficacy is limited by the poor response rate.

We conducted the present study to examine the prognostic value of CD248 in RCC. The dataset from the Cancer Genome Atlas (TCGA) and clinical samples were used to examine the differences in CD248 expression between normal and malignant tissues. Then, using a variety of clinical factors, we created a CD248-based prognostic signature that improved predicted accuracy. Additionally, assessed was the relationship between the current signature, Tumor-Infiltrating Immune Cells (TIICs), Tumor Mutation Burden (TMB), and immunomodulatory substances. Finally, to investigate the underlying mechanism of CD248 in the development of RCC, Weighted Gene Co-Expression Network Analysis (WGCNA) and enrichment analysis were carried out.

RCC incidence has gradually increased by roughly 1% annually, whereas the high fatality rate has not changed globally. The 5-year survival rate for advanced/metastatic RCC is less than 23%, despite significant advancements in the therapy choices that are currently available. In fact, due to the concealed incidence, between 30% and 50% of RCC patients missed the optimal surgical window. An emerging technique to extend the OS of RCC is immunotherapy. However, a poor clinical outcome is the result of a low response rate. As a result, numerous biomarkers have been proposed to aid in early diagnosis and direct treatment choice. According to Chen et al., miR-30a-3p can prevent RCC invasion and act as a novel prognostic indicator. Additionally demonstrated to play a role in carcinogenesis and RCC formation is miR-142-3p. Along with miRNAs, mRNAs including HHLA2 and syntaxin 6 were linked to shorter lifespans, and their corresponding inhibitors showed potential as a new treatment for RCC. However, the functional impact of a single gene on the development of RCC is minimal. It is still vitally necessary to find sensitive and precise indicators to increase diagnostic and treatment effectiveness.

Immune-Related Proteins (IRPs) and invading immunological cells make up the tumor immune microenvironment, which has become a key factor in the development of tumors. In the current work, we investigated the relationship between the current signature and an

immunologically compromised microenvironment. We discovered that the risk score produced by the current signature significantly increased Treg infiltration in RCC and that high immune scores and high Treg infiltration were associated with poor histological grade, advanced pathological stage, and a higher risk of metastasis, which was consistent with earlier research. Additionally, there was a positive correlation between the risk score and CD8 + Cytotoxic T lymphocytes (CTLs), however, more CTLs had a metastatic effect on RCC rather than a lethal effect. We hypothesize that high immunosuppression of Tregs balances the anti-tumor effects of CTLs, facilitating the survival of cancer cells.

With the help of the WGCNA method and enrichment analysis, potential roles for CD248 in RCC were investigated. According to the findings, CD248 co-expressed genes could be split into five distinct modules, of which the blue and turquoise modules were substantially linked to the development of RCC. Then, using the GO and KEGG algorithms, the discovered prognostic-related modules were examined. As a result, several immunosuppressive GO terms—such as negative regulation of leukocyte activation, migration, adhesion, and differentiation—were considerably enriched, which may shed light on the above-mentioned decrease in CTLs. Additionally, several intramodular hub genes and immunomodulatory signaling pathways were discovered. Novel diagnostic and therapeutic targets may be suggested and validated in vitro or in vivo research.

### **CONCLUSION**

We developed a trustworthy prognostic signature and a valuable biomarker that can accurately forecast the prognosis of RCC patients. Furthermore, the current signature can successfully weed out RCC patients who can benefit from immunotherapy. Possible activities of CD248 and co-expressed genes were discovered by WGCNA and enrichment analysis. These functions may help to explain how CD248 promotes the course of RCC and suggest potential targets for diagnostic and therapeutic procedures.