Aquaporin 9 expression predicts outcomes and immune infiltrations in clear cell renal cell carcinoma

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Objectives:
Growing evidence has demonstrated immune reactivity as a confirmed important carcinogenesis and therapy efficacy for clear cell renal cell carcinoma (ccRCC). Aquaporin 9 (AQP9) is involved in many immune-related signals; however, its role in ccRCC remains to be elucidated. This study investigated AQP9 expression in tumor tissues and defined the prognostic value in ccRCC patients.

Methods:
A total of 913 ccRCC patients with available RNA-sequence data from the Cancer Genome Atlas (TCGA) database and Fudan University Shanghai Cancer Center (FUSCC) were consecutively recruited in analyses. Differential transcriptional and proteome expression profiles were obtained and validated using multiple datasets. A partial likelihood test from Cox regression analysis was developed to address the influence of independent factors on progression-free survival (PFS) and overall survival (OS). The Kaplan–Meier method and log-rank test were performed to assess survival. Receiver operating characteristic (ROC) curves were used to describe binary classifier value of AQP9 using area under the curve (AUC) score. Functional enrichment analyses and immune infiltration analysis were used to describe significantly involved hallmark pathways of hub genes.

Results:
Significantly elevated transcriptional and proteomic AQP9 expressions were found in ccRCC samples. Increased AQP9 mRNA expression was significantly associated with advanced clinicopathological parameters and poor survival outcomes in ccRCC patients from TCGA cohort. A total of 913 ccRCC patients were enrolled in analyses. Differential transcriptome and proteome expression profiles were evaluated and validated using multiple datasets. A partial likelihood test from Cox regression analysis was developed to address the influence of independent factors on progression-free survival (PFS) and overall survival (OS). The Kaplan–Meier method and log-rank test were performed to assess survival. Receiver operating characteristic (ROC) curves were used to describe binary classifier value of AQP9 using area under the curve (AUC) score. Functional enrichment analyses and immune infiltration analysis were used to describe significantly involved hallmark pathways of hub genes.

Conclusions:
Our study revealed that elevated AQP9 expression was significantly correlated with aggressive progression, poor survival and immune infiltrations in ccRCC patients, and we validated its prognostic value in a real-world cohort. These data suggest that AQP9 may act as an oncogene and a promising prognostic marker in ccRCC.