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Individualized immune-related gene signature predicts immune status and oncologic outcomes in clear cell renal call carcinoma patients

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Xiong Y. , Liu L. , Bai Q. , Xia Y. , Wang J. , Guo J.

Zhognshan Hospital, Fudan University, Dept. of Urology, Shanghai, China

Introduction & Objectives: To develop an individualized immune-related gene signature that predicts oncologic outcomes and immune status of ccRCC.

Materials & Methods: Our study retrospectively analyzed expression profile of ccRCC including 1 microarray data set and 1 RNA-Seq data set. The immune related gene pair (IGP) index was constructed and validated based on pairwise comparison in 634ccRCC patients. Association with overall survival (OS), progression-free interval (PFI) and disease specific survival (DSS) was evaluated by Kaplan-Meier analysis, univariate and multivariate cox regression survival analysis. Prognostic values of different risk models were compared using Harrel's C-index.

Results: The IGP index of 17 gene pairs was an adverse independent risk factor in multivariate analyses for OS (HR, 1.718; P=0.001), PFI (HR, 1.550; P=0.006) and DSS (HR, 2.201; P=0.001) in ccRCC patients. It showed comparable prognostic accuracy with ccA/ccB signature (C-index for OS, 0.657 vs 0.640; P=0.686) and better intra tumor homogeneity. Immunosuppressive immune cell, markers and pathways referring to immune suppression were all enriched in high immune risk tumors. The integrated immune-clinical prognostic score outperformed ccA/ccB signature and UISS risk model in terms of C-index for estimation of OS (P<0.001), PFI (P<0.001) and DSS (P<0.001).

Conclusions: The proposed IGP index is a robust and promising biomarker for estimating oncologic outcomes in ccRCC. High immune risk tumors are highly immunosuppressive.