

# Artificial Intelligence & Machine Learning

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## Gene signature for response prediction to immunotherapy in metastatic Renal Cell Carcinoma

To date, immune checkpoint inhibitors (ICIs) have emerged as a leading treatment for metastatic cancer, significantly improving patient survival while causing relatively few side effects. However, the objective response rate for ICIs remains low—approximately 20-25% in renal cell carcinoma (RCC), underscoring the urgent need for predictive response biomarkers. Several state-of-the-art signatures have been revealed in top-tier journals, highlighting the importance of this field. As the number of genes (~20,000) far exceeds the sample sizes of typical training sets (generally  $\leq 300$ ), we first developed feature selection procedures to reduce the number of features to a few hundred. We then trained multiple machine learning classifiers using the selected genes and the IMmotion150 dataset, which includes RNA-seq and clinical data from 77 patients with metastatic RCC (mRCC). Notably, our predictor LogitDA, using the identified 27-gene signature, achieved a prediction AUC of 0.72 in an independent dataset PCD4989g(mRCC). Our signature for mRCC was second to T exhaust in prediction AUC but surpassed the six established signatures in prediction accuracy. Finally, from our signature, we identified we uncovered two prognostic biomarkers FLNC and NIPAL1 for progression-free survival with BH-adjusted  $P < 0.02$  (log-rank test; adjusted  $P < 0.0025$ ) in the IMmotion150 dataset.

### Keywords

biomarker, cancer, immunotherapy, machine learning, regression, prediction

### Biography

Prof. Grace S. Shieh received her PhD in Statistics from Dept. Of Statistics, University of Wisconsin, and is currently a Full research fellow at Inst. Of Statistical Science, Academia Sinica, and is an adjunct professor at National Taiwan University. She is an Associate editor of STAT and Frontiers in Genetics, Statistical Genetics and Methodology Section. She has been working on computational oncology since 2010, and recently her team focuses on precision medicine, esp. prediction of response of cancer patients to immunotherapy.