[BIOINFO 2023]

Identifying microRNAs associated with tumor immunotherapy response using an interpretable machine learning model

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Predicting clinical responses to tumor immunotherapy is essential to reduce side effects and the potential for sustained clinical responses. Nevertheless, preselecting patients who are likely to respond to such treatments remains highly challenging. Here, we explored the potential of microRNAs (miRNAs) as predictors of immune checkpoint blockade(ICB) responses using a machine learning approach. First, we constructed random forest models to predict the response to tumor ICB therapy using miRNA expression profiles across 19 cancer types. The contribution of individual miRNAs to each prediction process was determined by employing SHapley Additive exPlanations (SHAP) for model interpretation. Remarkably, the predictive performance achieved by using a small number of miRNAs with high feature importance was similar to that achieved by using the entire miRNA set. Additionally, the genes targeted by these miRNAs were closely associated with tumor- and immune-related pathways. In conclusion, this study demonstrates the potential of miRNA expression data for assessing tumor immunotherapy responses. Furthermore, we confirmed the potential of informative miRNAs as biomarkers for the prediction of immunotherapy response, which will advance our understanding of tumor immunotherapy mechanisms.