Machine Learning to Predict Response to Anti-PD1 in Melanoma Using Genetic Biomarkers

Barksdale, Sarah (School: Episcopal School of Jacksonville)

Programmed cell death-1 (PD-1) is an inhibitory receptor that provides a checkpoint against autoimmunity. The PD-1:PD-L1 signalling pathway inhibits T cell function, which allows cancer cells to evade attack. Anti-PD1 treatment uses antibodies to inhibit this pathway and has increased the five-year survival rate of metastatic melanoma from 5% to 40-60%. However, treatment is extremely costly and 30% of patients experience immune-related adverse events. The goal of this project was to develop an algorithm to predict patient response to anti-PD1 in melanoma to aid physicians in treatment prescriptions, highlighting those likely to respond well to treatment and preventing large costs and high toxicity for those who may not. The dataset includes the gene expression, mutation load, demographic factors, clinical response, and survival of melanoma patients treated with Pembrolizumab or Nivolumab. Synthetic Minority Oversampling Technique was performed to augment the number of patients with a complete response (the minority label) to prevent model bias. Logistic regression, random forest regression, and support vector machines prediction models with recursive feature elimination were created and tested with 10-fold cross validation. Initial models failed to accurately predict patient survival; however, each model had above a 70% accuracy rate when predicting tumor response. The Random Forest model has been the most successful, with a 93% accuracy rate. Recursive Feature Elimination indicated the four most significant genes in the prediction model (PTEN, WNT, BRAF, PD-1) that can be used as biomarkers for patient response. This prediction model and novel biomarkers could aid doctors in treating melanoma by highlighting patients who will respond well to anti-PD1.

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