Identifying Marker Genes to Predict Immune-Related Adverse Events in Patients Receiving Anti-PD-1 Immunotherapy

Nicholas Beatty – Columbia University Vagelos College of Physicians and Surgeons, Class of 2023
Mentor: Syed Bukhari, PhD | Columbia University Mentor: Annette Wu, MD, MPH, PhD
Principal Investigator: Adam Mor, MD, PhD

Research Question: This project aims to identify the different genetic profiles between those who develop immune-related adverse events following cancer treatment anti-PD-1 immunotherapy and those who do not.

BACKGROUND

Anti-PD-1 therapy is an effective cancer treatment that inhibits tumor growth by activating T-cells. However, one in four patients who receive this therapy develop immune-related adverse events (irAEs), or autoimmune reactions manifested as cardiomyopathy, thyroiditis, rheumatoid arthritis, etc. To combat this, we hypothesized that a patient’s irAE risk is genetic, and that gene-expression biomarkers may predict that risk. This project aims to identify those biomarkers.

DESCRIPTION OF LAB

Research was conducted within Dr. Adam Mor’s CUMC immunology lab, which is interested in studying the signaling events associated with T lymphocytes’ function. The lab’s goal is to research strategies to modulate T cell functionality and use that knowledge to develop therapeutic modalities for patients with cancer and autoimmunity.

METHODS

Single cell RNA analysis data was used from the T-cells of eight patients (deemed eligible out of 38 total) who received anti-PD-1 therapy for lung cancer, before they either developed post-therapy rheumatoid arthritis or thyroiditis, or did not. This gene-expression data was then processed using the R package, iCellR, developed at NYU Langone. Single cell analysis data from each condition were mapped according to gene expression profile to cluster cells by T-cell type. Once clustered, specific genes were viewed by expression level in each of the T-cell clusters for each condition and analyzed for differences.

JUND, FOS, SPON2 and CCL4 all showed considerable differences in gene expression between those who went on to develop an immune-related adverse event and those who did not.

FINDINGS

We found multiple T-cell genes that differed in expression between those who developed rheumatoid arthritis or thyroiditis and those who did not, with the most notable differences in apoptotic transcription factors, JUND and FOS. These identified genes may be of significant use in predicting an individual patient’s risk of developing an immune-related adverse event as a result of anti-PD-1 therapy and may inform future healthcare providers deciding between cancer treatment options.

REFERENCES