Data Mining to Identify Therapeutic Targets for Transplant Rejection

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Despite major advances in immunosuppression, thousands of transplanted organs are still rejected, endangering the lives of many patients. Traditional approaches to understanding transplant rejection rely on testing one mechanism or gene at a time. A big data-mining approach is advantageous because it narrows down the countless possibilities to the most probable mechanisms that can then be tested in a laboratory setting. Last year, I attempted to identify genes responsible for the formation of tissue-resident memory T lymphocytes (TRM) that cause rejection by studying an idealized model in which the lymphocytes were genetically homogeneous. This year, I extended my analysis to a physiologically realistic model in which the T lymphocytes were heterogeneous (polyclonal). By applying multidimensional statistical and machine learning algorithms (PCA, UMAP, pseudotime, and differential gene expression) to single-cell RNA sequencing data, I determined whether the gene expression trends present in my original homogenous data set were also apparent in the polyclonal data set, revealing relationships between a specific gene (Pa2g4) and formation of TRM. I validated my gene discovery by analyzing a flow cytometry experiment detecting higher expression of this transcription factor in TRM. Future studies will test in animals whether targeting the Pa2g4 gene or its protein product protects against rejection of transplanted grafts.

Awards Won:
Third Award of $1,000