2023 Annual Research Day Poster Sessions – April 19th, 2023

Session/Poster#	Presenter
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Characterizing Dendritic Cell Subpopulations for Cancer Immunotherapy

Dendritic cells (DCs) are a lineage of hematopoietic stem cells that originate from CD34+ cells in the bone marrow and have been recognized as effective antigen-presenting cells (APCs) in the immune system. Current principles on using DCs for cancer immunotherapy include isolating DC subpopulations from blood, followed by activation and antigen loading, and reinfusion of DCs into patients for antigen-specific T-cell activation. Cancer is a leading cause of death among children; therefore, it can be expected that targeted immunotherapy through DCs will have an important role in pediatric patients. Here, we highlight our efforts to characterize DC subpopulations using umbilical cord blood as a reliable source of DCs in their nascent state. Fluorescence-Activated Cell Sorting (FACS) was performed to sort DCs from umbilical cord blood using cell surface markers for each DC subpopulation. Bulk ATAC-Seq and scRNA-Seq were done for verification of sorted populations and differential expression analysis. We demonstrated that common DC precursors can differentiate into three lineage trajectories: plasmacytoid DCs, classical dendritic cells 1 (cDC1) that activate CD8+ T cells, and cDC2 that activate CD4+ T cells corresponding to unique transcriptional trajectories. Using scRNA-Seq, we further demonstrated differential expression among these three branches that phenotype DC subpopulations, uniquely characterized by the TIM3 marker of T-cell exhaustion. We identified specific DC populations that carry the inhibitory TIM3 and further identified sialic acid-binding immunoglobulin-like lectin (Siglec) receptors. Expression of inhibitory Siglec receptors is a feature of specific DCs from cancer patient samples that can be used to further delineate the complex character of these subpopulations of DCs. Our goal is to further characterize these inhibitory TIM3 and Siglec-expressing subpopulations of DCs in their capacity to generate antigen-specific T cells.