Lung Biology Research & Trainee Day
June 7, 2021

Category: Predoc
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Title: Tissue resident memory CD8 T cell subsets exhibit unique metabolic profiles
Abstract: Tissue resident memory T cells (TRM) confer protection against a variety of illnesses ranging from infections to cancers. As demonstrated in the skin, transfer of TRM from immune to naïve hosts is sufficient to prevent herpes simplex virus type 1 (HSV) associated pathology. Comparably, the presence of antigen-specific TRM in a mouse model of melanoma can limit tumor growth. In the lungs, TRM offer critical for protection against influenza, even in the absence of specific antibodies. In the skin, the functions of different CD8 T cell subsets have been linked with distinct metabolic pathways. Skin TRM display a unique metabolic profile compared to other CD8 memory cells subsets. They undergo enhanced fatty acid oxidation and oxidative phosphorylation as compared with circulating memory cells and naïve. However, it is unclear if this programming is universal between all TRM subsets and holds true in the lung. We hypothesize that lung TRM with different integrin profiles will utilize unique metabolic programs. Metabolic profiles of lung CD8 T cells were assessed using a variety of functional metabolic assays including glucose analogue uptake, fatty acid uptake, and oxidative phosphorylation as assessed by fluorescent analogues and dyes measured by flow cytometry. Nonfunctional assays including neutral lipid storage, mitochondrial mass, and mRNA transcript levels of key metabolic genes were also assessed via flow cytometry using fluorescent dyes, while transcripts were quantified with bulk RNAseq. Flux balance analysis was conducted using The COnstraint-Based Reconstruction and Analysis Toolbox (COBRA Toolbox). Lastly, we present for the first time fluximplied: a novel pathway analysis software which integrates rate limiting steps into its analysis to predict differentially regulated metabolic pathways. Our findings indicate that lung TRM show enhanced fatty acid oxidation, more neutral lipid storage, and less glucose uptake than their non-TRM in our influenza mouse model. CD49aposCD103pos exhibit a more traditionally “memory-like” phenotype than their CD49aposCD103neg counterparts, raising questions around functional niches for these two TRM subsets.