Genetics Day Poster Submission

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Title: TRANSCIPTION FACTOR NFIL3 REGULATES THE CD8 T CELL IMMUNE RESPONSE IN INFLUENZA

Abstract: After an acute respiratory infection is cleared, most T cells that controlled the infection die off. Tissue resident memory CD8 T cells (TRM) remain in the lung, poised to fight off a recurrent infection. These TRM have large impacts on the survival and morbidity of subsequent infection. While many have studied this subset to understand what causes differentiation into this essential T cell subset, a master regulator of this phenotype remains elusive. To these ends, RNA and ATAC sequencing experiments of TRM were conducted after viral clearance to investigate the existence of a master regulator. Transcription factor Nfil3 became a likely candidate after integrated omics analyses. Flow cytometry to fully characterize the levels of Nfil3 in all T cell subsets of the lung, spleen, and draining lymph node was conducted 7, 14, and 43 days post infection (dpi). At days 7 and 14 dpi, Nfil3 correlated with pre-TRM markers. At 43 dpi, Nfil3 was highest in TRM and lowest in central memory T cells. Finally, experiments were performed to investigate if Nfil3 played a causal role in TRM development or maintenance. T cells were transduced with Nfil3 overexpression constructs and adoptively transferred into mice, which were then infected. Notable changes in differentiation were observed between treatment and control. T cell proliferation and motility were also affected ex vivo in a proliferation dye assay and video assay respectively, implying that Nfil3 plays a role in the acute response. Finally, using a CD8-specific inducible floxout system, Nfil3 was floxed out during acute infection and 3 weeks after during the memory phase to appreciate the effect on T cell differentiation. Overall, we argue Nfil3 plays a role in CD8 T cell differentiation in respiratory infections.