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**“The Tetraspanin CD9 regulates CD4⁺ T follicular helper
cell function during acute viral infection”**

by
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Thursday, March 17th, 2022
10:30 A.M.

Join Zoom Presentation

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ABSTRACT

T follicular helper (Tfh) cells comprise a subset of CD4⁺ T helper (Th) cells phenotypically and functionally distinct from other Th cells, such as the classical Th1, Th2 and Th17 subsets. Tfh cells are located within in the B-cell follicles and germinal centers (GCs), where they secrete the cytokines IL-21 and interferon- γ (IFN- γ) or IL-4 to aid B cell proliferation and survival, immunoglobulin affinity selection, and differentiation into memory B and long-lived plasma cells. Throughout the course of the GC response, Tfh cells have been shown to progressively differentiate in terms of their localization, surface ligand expression and cytokine production to 'fine tune' the GC reaction. However, a way to phenotypically identify the different stages of Tfh cell differentiation remains unknown.

In this dissertation, we identified that CD9, a tetraspanin protein, is temporally upregulated on a subset of Tfh cells (CD9^{hi}) following acute LCMV infection. The upregulation of CD9 occurred after Tfh cell differentiation and its expression was not influenced by TCR affinity. We show that CD9^{hi} Tfh cells exhibited enhanced migration to CXCL12 and CXCL13 compared to CD9^{lo} Tfh cells. Transcriptional analysis demonstrated that CD9^{hi} and CD9^{lo} Tfh cells are distinct subsets characterized by enhanced expression of cell cycling and PI3K activated genes in the CD9^{hi} fraction. The CD9^{hi} Tfh cells had increased proliferation compared to the CD9^{lo} Tfh cells corroborating our transcriptional data. Furthermore, we found that the CD9^{hi} Tfh cell subsets were the primary producers of IL-21 and IFN- γ , downstream of PI3K signaling. Thus, CD9 identifies a transcriptionally distinct subset of Tfh cells primarily comprised of the cytokine producers responsible for promoting GC responses during viral infections.