The dynamics of Gγ4 during CD4 T cell activation

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In untreated HIV, provirus is preferentially found in CD4+ T follicular helper cells (Tfh). In health, Tfh are essential to generate antibody mediated protection against pathogens and promote memory during vaccination. How Tfh differentiate and function, especially in humans, is incompletely understood. In our recent single cell sequencing work, we identified the G protein γ subunit Gγ4 (Gene name: GNG4) as highly expressed and preferentially accessible in tonsil germinal center like Tfh. Within intact tonsil tissue, we found that *GNG4* is spatially restricted to the germinal center and is the most distinguishing feature of GC-positioned Tfh compared to other known GC Tfh markers like *BCL6*. Gγ4 is part of the G protein γ subunit family and predominantly expressed in neuronal and endocrines tissues. Its presence in T cells has only been recently described and its function in CD4 T cells is still unknown. Interestingly, Gγ4 protein is also inducible in CD4 T cells in response to TCR dependent stimulation. However, once TCR stimulus is removed, Gγ4 protein expression drops dramatically within 24 hrs. This contrasts with other T cell activation markers like ICOS and CD38 that increase when stimulus is removed. We found this to be true in tonsil tissue where *GNG4* expression in Tfh was dependent on proximity to light zone GC B cells. In summary, Gγ4 is highly specific to cells residing in the germinal center that are actively engaging with germinal center B cells and in vitro, removal of TCR stimulus causes a loss in expression of Gγ4. In future studies, we will focus on the requirement for functionality via deleting and overexpressing *GNG4* in human CD4 T cells.