Sphingosine-1-phosphate receptor 2 is required for retention of follicular helper T cells in germinal centers

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ABSTRACT
Follicular helper T (Tfh) cells access the B cell follicle to promote antibody responses, and are particularly important for germinal center reactions. However, the molecular mechanisms of how Tfh cells are physically associated with GCs are incompletely understood. Here we report that sphingosine-1-phosphate receptor 2 (S1PR2), which has recently been shown to play a role in GC B cell localization, is also important for GC-association of Tfh cells. Analysis using an S1pr2-reporter mouse strain suggested that S1PR2 is expressed at varied levels in Tfh cells, and that S1PR2-high Tfh cells are localized in GCs whereas S1PR2-low Tfh cells are scattered throughout the B cell follicle. S1PR2-deficient Tfh cells exhibited reduced accumulation in GCs, which was attributed to impaired retention in GCs based on two-photon imaging analysis. Expression of Bcl6, Il4, and Il21 in Tfh cells was positively correlated with S1pr2 expression. These results suggest that S1PR2-high Tfh cells are GC-resident Tfh cells bearing the advanced capability to promote long-term B cell responses.