

Supplemental Figure 1. Histological features of skin TLSs in pemphigus patients from the retrospective study. (A-C) Immunological staining for CD4, CD20, and PNAd in patients with pemphigus vulgaris (n=6) (A), pemphigus foliaceus (n=3) (B), and paraneoplastic pemphigus (n=1) (C). (D) Representative images of immunohistochemical staining for follicular dendritic cells (FDCs), CD11c, D2-40, and lymphotoxin  $\beta$  (LT $\beta$ ).



**Supplemental Figure 2. Expression of gene signatures in TLS-positive and -negative cases.** (A) GSEA of Th1 and B cell related signatures and chemokine gene signatures. (B) Heatmap showing gene expression of chemokine ligands and receptors.



Supplemental Figure 3. Immunofluorescent staining of CXCL13<sup>+</sup> cells in skin TLSs. Immunofluorescence of CXCL13 (green) with CD4, CD8, CD20, CD138, FDC, or HLA-DR (all red). Nuclei were stained with DAPI (light gray). Scale bar =  $100 \mu m$ .





Supplemental Figure 4. scRNA-seq and scTCR-seq of chronic TLS skin lesions to characterize CXCL13<sup>+</sup>CD4<sup>+</sup> T cells. (A) Gating strategy for flow cytometric analysis of live CD45<sup>+</sup> cells in skin. L/D, Live/Dead. (B) Distribution of all expressed gene numbers and expressed genes in each sample. (C and D) UMAP visualization of 2,770 cells with 17 clusters in all patients (C) and TCR $\beta^+$  cells with 10 clusters (D). (E) Visualization of TCR clonality in each patient. Red dots indicate shared TCR clones and blue dots indicate single TCR clones. (F) Trajectory analysis of each cluster. (G) Gating strategy for flow cytometric analysis of CD134<sup>+</sup>CD25<sup>+</sup> (AIM<sup>+</sup>) Tfh cells and non-Tfh memory CD4<sup>+</sup> T cells in PBMCs from a patient with pemphigus vulgars. (H) *CXCL13* expression shown in UMAP. The red dotted line indicates clusters 1 and 5. (I) Expression of *CXCL13* and *IFNG* in clusters 1 and 5. The red dotted line indicates CXCL13<sup>+</sup> cells and the blue dotted line indicates *IFNG*-expressing cells of CXCL13<sup>+</sup> cells. (J) Volcano plot showing DEGs up-regulated (orange dots) and down-regulated (purple dots) in CXCL13<sup>+</sup>CD4<sup>+</sup>T cells compared to CXCL13<sup>-</sup>CD4<sup>+</sup>T cells.



Supplemental Figure 5. Validation of the antibody panel in spatial proteomics. Representative images of a skin TLS stained with 41 different antibodies by CODEX. Scale bar = 100  $\mu$ m.



Supplemental Figure 6. Spatial analysis of CXCL13<sup>+</sup>CD4<sup>+</sup> T cells. (A) Spatial proteomics gating strategy for cell type annotation. (B) Frequencies of marker-positive cells in CD8<sup>+</sup> T cells, HLA-DR<sup>+</sup> cells, and B cells adjacent to CXCL13<sup>+</sup> versus CXCL13<sup>-</sup>CD4<sup>+</sup> T<sub>M</sub> cells (n=9, per image).



**Supplemental Figure 7. mIHC analysis.** (**A**) A representative image of mIHC by Vectra Polaris. Scale bar = 100  $\mu$ m. (**B** and **C**) Densities of Tfh cells, CXCR5<sup>+</sup> B cells (**B**), CXCR5<sup>-</sup> Tregs, and Tfr cells (**C**) based on their distance from the center of CXCL13<sup>+</sup>CD4<sup>+</sup> T cells. Number of ROI = 3. The highlighted blue regions are the location of 10-20  $\mu$ m away from the center of CXCL13<sup>+</sup>CD4<sup>+</sup> T cells.



**Supplemental Figure 8. Functional analysis of CXCL13<sup>+</sup>CD4<sup>+</sup> T cells.** (**A**) Gating strategy for flow cytometric analysis of CXCL13<sup>+</sup>CD4<sup>+</sup> T cells *in vitro*. L/D, Live/Dead. (**B**) Graph showing the frequencies of IFN-γ<sup>+</sup>, TNF-α<sup>+</sup>, and IL-17A<sup>+</sup> cells in the conditions of Treg presence and absence. A upper panel indicates percentage cells of CD4<sup>+</sup> T cells and a lower panel indicates percentage cells of CD4<sup>+</sup> T cells and a lower panel indicates percentage cells of GITR<sup>+</sup>CD4<sup>+</sup> T cells in the conditions of with and without Treg. Paired t tests were used to compare value for 2-variable plots. (**C**) Heatmap showing BiorCarta IL-2 pathway in with versus without Tregs condition. (**D** and **E**) Gating strategy for flow cytometric analysis of *in vitro* differentiation of CXCL13<sup>+</sup>CD4<sup>+</sup> T cells (**D**) and induced Treg (**E**) for co-culture system. (**F**) Dfferentiated CXCL13<sup>+</sup>CD4<sup>+</sup> T cells were co-cultured with induced Tregs in presence or absence recombinant IL-2 protein or TGF-β blocking antibody. Relative frequencies of CXCL13<sup>+</sup> cells in GITR<sup>+</sup>CD25<sup>-/low</sup>CD4<sup>+</sup> T cells (n=8). Paired t tests were used to compare value for 2-variable plots. NS, not significant; \**p* < 0.05.