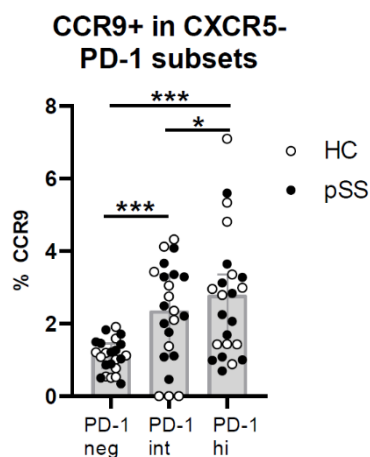


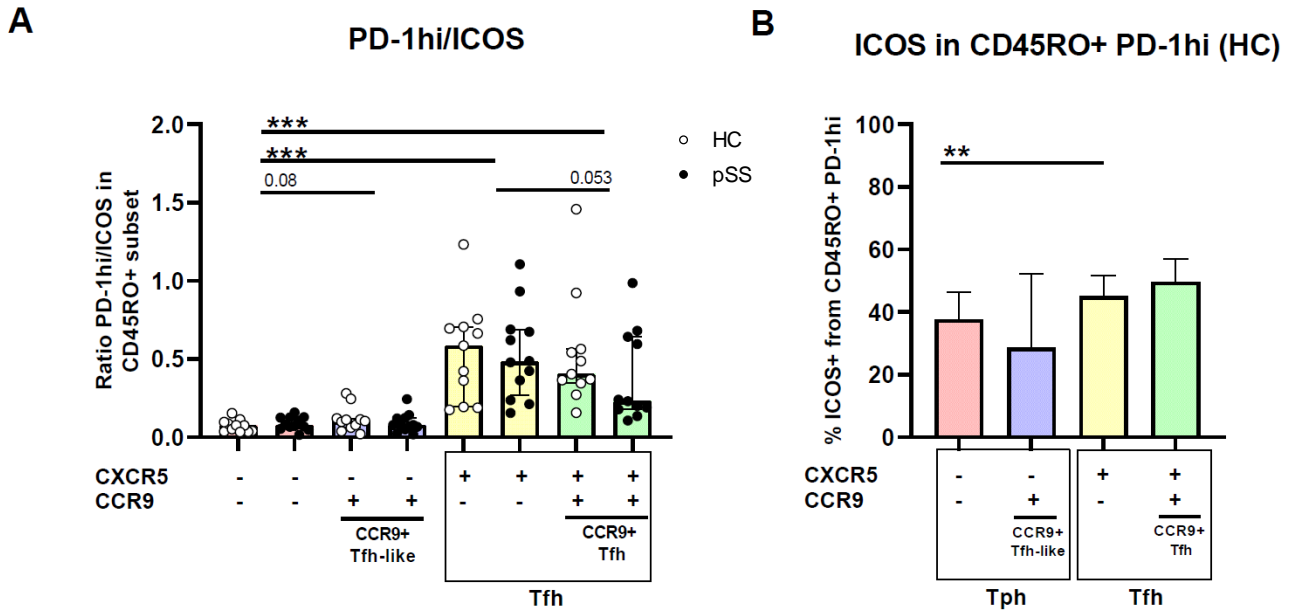
**Supplementary Figure S1. PD-hi staining**

Representative histograms of PD-1 staining in naive and memory (CD45RO+) CD4 T cells from one HC and one pSS patient. Vertical lines in histograms indicate gating of PD-1 negative, PD-1<sup>intermediate</sup>, and PD-1<sup>hi</sup> populations, as can also be seen in representative ICOS/PD-1 dotplot from memory CD4 T cells. HC: healthy control; pSS: primary Sjögren's syndrome; ICOS: inducible T cell co-stimulator; PD-1: programmed death-1.



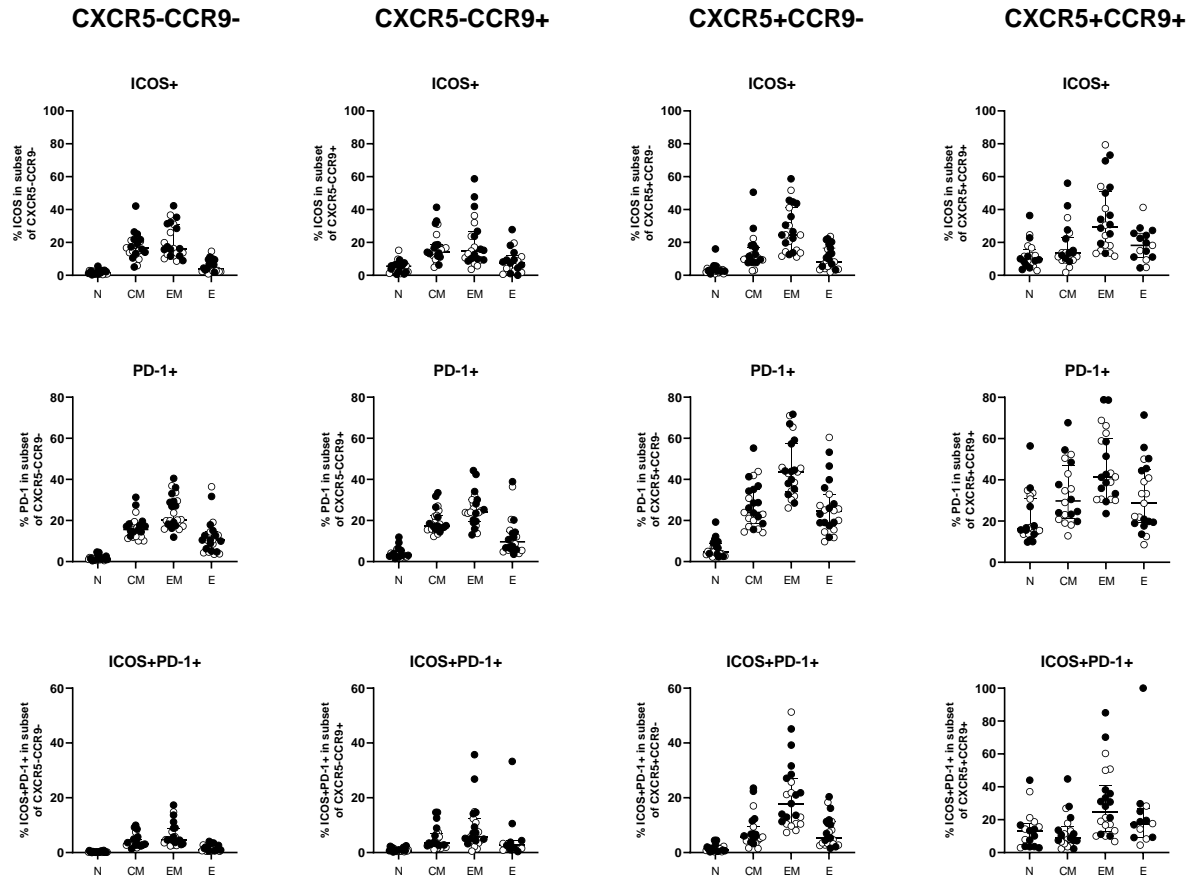
**Supplementary Figure S2. The percentage of CCR9-expressing cells is associated with PD-1 expression**

CCR9 expression is evaluated on total (incl naïve and memory) CXCR5- CD4 T cells with negative, intermediate, and high PD-1 expression. HC: healthy control; pSS: primary Sjögren's syndrome. CCR9: C-C motif chemokine receptor 9; PD-1: programmed death-1; neg: negative; int: intermediate; hi: high. \*, \*\*\* indicates p-value <0.05, 0.001, respectively.



**Supplementary Figure S3. CXCR5-expressing cells have a higher PD-1<sup>hi</sup>/ICOS ratio. Increased ICOS expression in HC was only seen for CXCR5-expressing Tfh cells compared to CXCR5-CCR9<sup>-</sup> cells.**

(A) Ratios of PD-1<sup>hi</sup>/ICOS in memory population of all four CXCR5/CCR9-defined cell subsets in pSS patients and HC. (B) Comparison of ICOS expression between the memory PD-1<sup>hi</sup> CXCR5-CCR9<sup>-</sup> subset compared to the three other subsets in HC. Plots show medians plus interquartile ranges. HC: healthy control; pSS: primary Sjögren's syndrome. Tph: T peripheral helper cell (memory CXCR5-PD-1<sup>hi</sup> CD4 T cell); CCR9<sup>+</sup> Tfh-like: C-C motif chemokine receptor 9-expressing T follicular helper-like cell (CXCR5-CCR9<sup>+</sup> CD4 T cell); ICOS: inducible T cell co-stimulator; PD-1: programmed death-1; \*\*, \*\*\* indicates p-value <0.01, 0.001, respectively.



**Supplementary Figure S4. ICOS+, PD-1+, and ICOS+PD-1+ are significantly lower in naive cells in all CXCR5/CCR9-defined cell subsets.**

Expression of ICOS, PD-1, and ICOS+PD-1+ in naive (N), central memory (CM), effector memory (EM), and effector (E) cells in all four CXCR5/CCR9-defined cell subsets. All comparisons between N cells and CM/EM/E cells are significant within the same CXCR5/CCR9-defined cell subset ( $p < 0.01$ ), except for ICOS expression between N and E in CXCR5-CCR9+ and CXCR5+CCR9+ cells ( $p = 0.19$  and  $p = 0.43$ , respectively), and ICOS+PD-1+ expression between N and E cells in CXCR5+CCR9+ subset ( $p = 0.21$ ). Plots show medians plus interquartile ranges. Naive (N): CD27+CD45RO-; Central memory (CM): CD27+CD45RO+; Effector memory (EM): CD27-CD45RO+; Effector (E): CD27-CD45RO-.

**Supplementary Table S1. Antibodies used for flow cytometry.**

<b>Marker</b>	<b>Fluorochrome</b>	<b>Company</b>	<b>Clone</b>
<b>CD3</b>	AF700	Sony Biotechnology	UCHT1
<b>CD4</b>	BV785	Biolegend	RPA-T4
<b>CD8</b>	PE	Biolegend	RPA-T8
<b>CCR9</b>	APC	Biolegend	L053E8
<b>CXCR5</b>	PerCP-Cy5.5	Biolegend	J252D4
<b>CD27</b>	BV510	BD Biosciences	L128
<b>CD45RO</b>	PE-Cy7	BD Biosciences	UCHL1
<b>ICOS</b>	FITC	Biolegend	C398.4A
<b>PD-1</b>	BV711	BD Biosciences	EH12.1
<b>Fixable Viability Dye</b>	eFluor™ 780	eBioscience	n.a.