## **Supplementary Figure Legends**

**Supplementary Figure S1: Gating strategy. A** Gating strategy using biaxial gating to the isolation of CD45+ cells shown for one representative healthy donor. **B** Leiden clustering of CD45+ cells of the whole dataset. Clustering was used to identify communities of cells that were identified by their respective marker expression (**C**). **D**Final gating result based on the clusters and the marker expression. For further details refer to the Methods section. Healthy controls n=9, IA patients n=7. IA: inflammatory arthritis.

**Supplementary Figure S2: Marker expression of NK cells across tissues.** Marker expressions were plotted as median fluorescence intensity values per sample. Each datapoint represents one sample. The x-axis groups the values by tissue (PB: peripheral blood, SF: synovial fluid). Wilcoxon test was used to compute statistical significance. *p* > 0.05: n.s., p < 0.05: \*, p < 0.01: \*\*, p < 0.001: \*\*\* Healthy controls n=9, IA patients n=7. IA: inflammatory arthritis.

**Supplementary Figure S3: Marker expression of different metaclusters of NK cells in synovial fluid of IA patients**(n=7). Only synovial NK cells were included into this analysis (n=7 patients). Marker expressions were plotted as median fluorescence intensity values per sample. Each datapoint represents one sample. The x-axis groups the values by metacluster as defined in **Figure 2**. Wilcoxon test was used to compute statistical significance. IA: inflammatory arthritis. *p* > 0.05: n.s., p < 0.05: \*, p < 0.01: \*\*, p < 0.001: \*\*\*

**Supplementary Figure S4: Marker expression depending on differentiation rank.** Plotted are the indicated markers in respect to the calculated differentiation rank. While CD56 marks early differentiated cells, CD16 expression is increasing during differentiation. CD57 marks terminally differentiated cells.

**Supplementary Figure S5: Marker expression by differentiation rank.** NK cells have been divided into mature (differentiation rank > 0.3; refer to **Figure 3B** and **Methods section**) and immature cells. Marker expressions are shown as transformed expression values per organ and group and split by the differentiation rank. Healthy controls n=9, IA patients n=7. IA: inflammatory arthritis.

**Supplementary Figure S6: Marker expression of CD8+ T-lymphocytes across tissues.** Marker expressions were plotted as median fluorescence intensity values per sample. Each datapoint represents one sample. The x-axis groups the values by tissue (PB: peripheral blood, SF: synovial fluid). Wilcoxon test was used to compute statistical significance. *p* > 0.05: n.s., p < 0.05: \*, p < 0.01: \*\*, p < 0.001: \*\*\* Healthy controls n=9, IA patients n=7. IA: inflammatory arthritis.

**Supplementary Figure S7: Phenotypic heterogeneities of T helper lymphocytes in PB and SF of patients with IA.** **A**Sample correlation analysis. Samples were correlated as described in the Methods section. Hierarchical clustering revealed three subgroups which correspond to cells of different tissue and patient cohort. **B** Sample-wise principal component analysis. Samples were grouped by PCA and coloured by tissue and patient cohort (left) and the metaclusters (right) as calculated in C. **C**Differential expression analysis. Fold-changes (x-axis, asinh\_fc) were calculated as described in the Methods section. Notably, CD4+T-cells analysed from PB show significant phenotypic differences comparing healthy controls and patients with IA, including expression changes of CD16, TIGIT and KLRG1. Comparison of cells extracted from PB and SF show a differential phenotype with the elevation of activation markers such as PD-1, CD69 and HLA-DR and the corresponding downregulation of CD27.Corresponding boxplot representations are shown in **Supplementary Figure S8**. **D and E** UMAP representation of CD4+ T lymphocytes. Colouring by tissue and patient cohort suggests substantial differences of cells obtained from the different conditions. Marker expression showed that SF CD8+T-cells were characterized by lower expression of CD27 while elevating activation markers such as PD1, HLA-DR, TIGIT and CD69. PB: peripheral blood, SF: synovial fluid, IA: inflammatory arthritis. P-values were calculated as described in the Methods section (Kruskal) where p-values above 0.05 were considered not significant (n.s.). Corresponding boxplot representations are shown in **Supplementary Figure S8**. Healthy controls n=9, IA patients n=7. IA: inflammatory arthritis.

**Supplementary Figure S8: Marker expression of CD4+ T-lymphocytes across tissues.** Marker expressions were plotted as median fluorescence intensity values per sample. Each datapoint represents one sample. The x-axis groups the values by tissue (PB: peripheral blood, SF: synovial fluid). Wilcoxon test was used to compute statistical significance. *p* > 0.05: n.s., p < 0.05: \*, p < 0.01: \*\*, p < 0.001: \*\*\* Healthy controls n=9, IA patients n=7. IA: inflammatory arthritis.