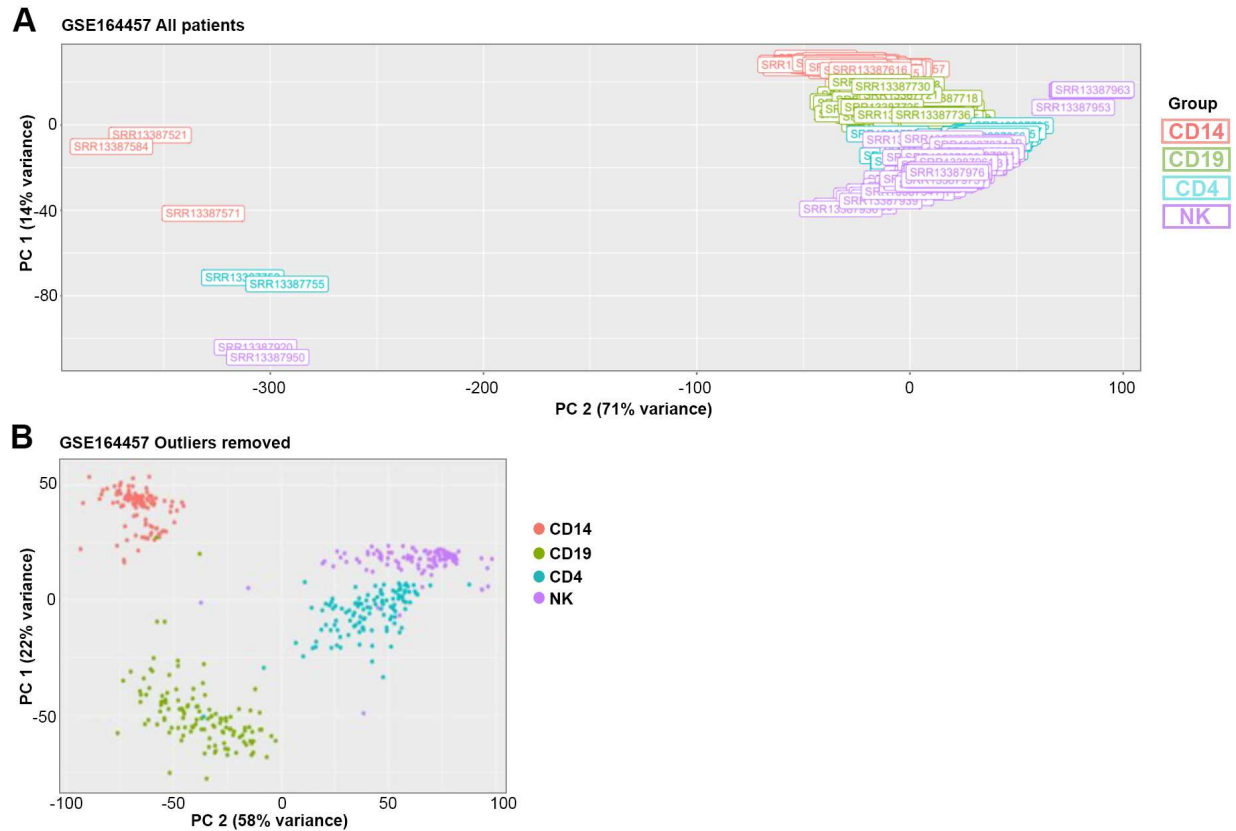


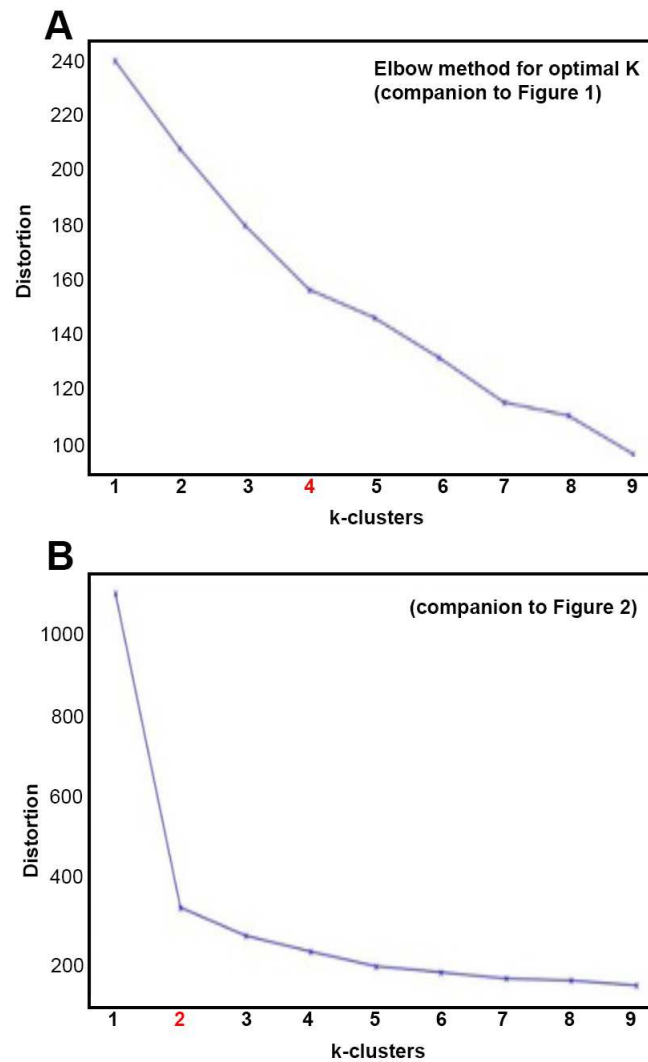
## Supplementary Figures and Legends

## Figure S1



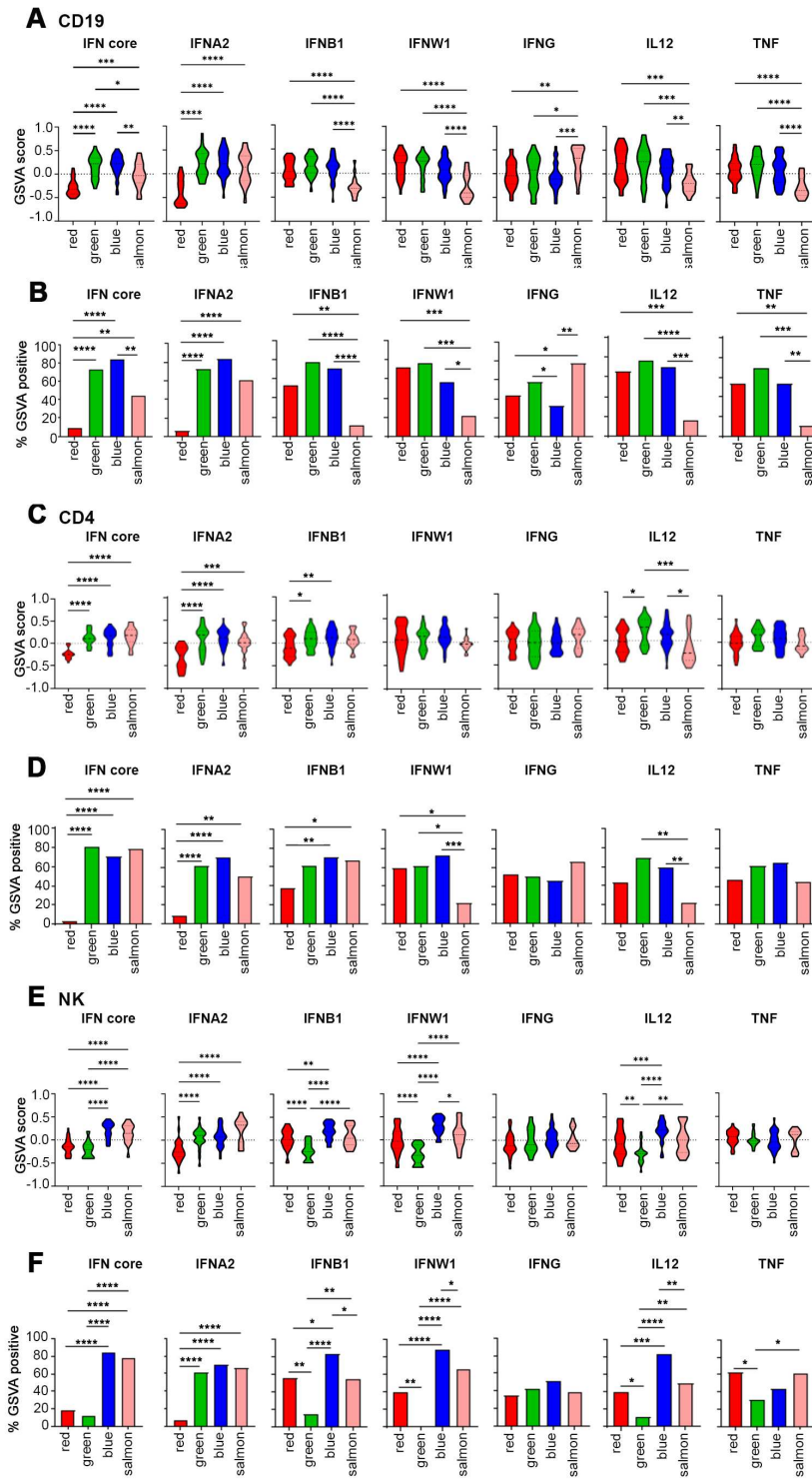
**Supplementary Figure S1: A.** PCA plot of log<sub>2</sub> normalized counts in the four cell types (CD14+ monocytes, CD19+ B cells, CD4+ T cells and NK cells) without outliers removed. **B:** PCA plot of log<sub>2</sub> normalized counts in the four cell types with outliers removed.

## Figure S2



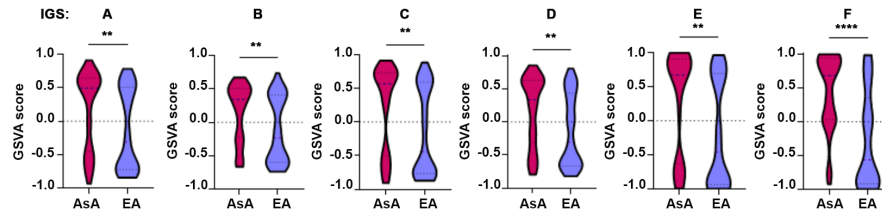
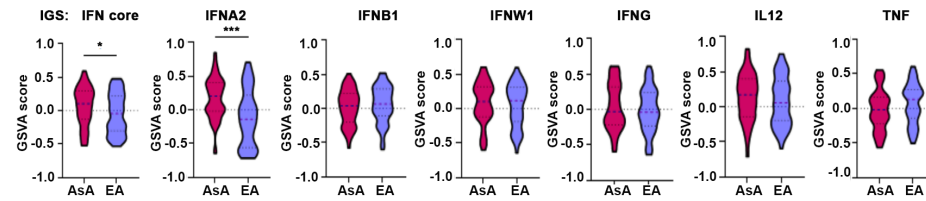
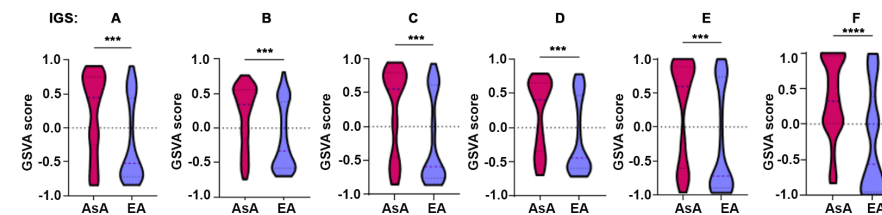
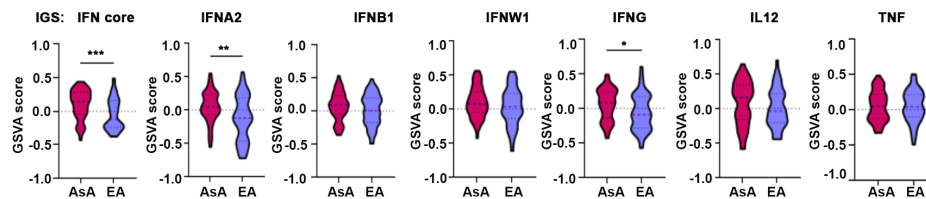
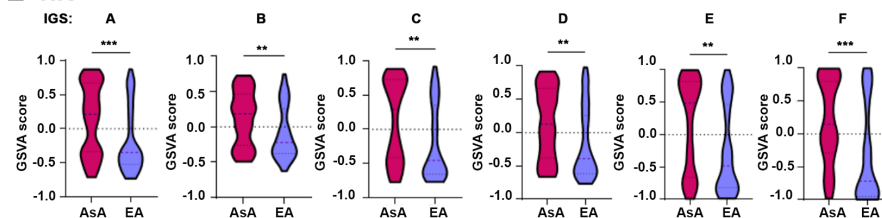
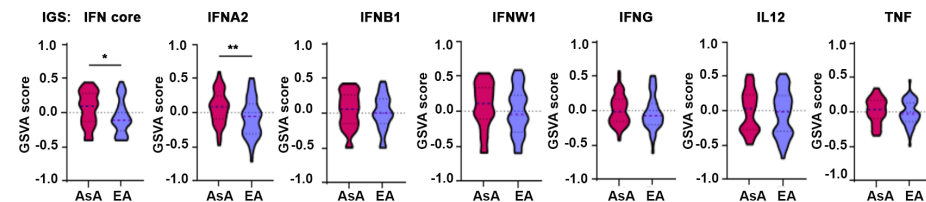
**Supplementary Figure S2: A.** Elbow plot for the k-means clustering in **Figure 1A**. The optimal number of subsets was set at 4 based on the plot. **B.** Elbow plot for the k-means clustering in **Figure 2**. The optimal number of subsets was set at 2 based on the plot.

Figure S3



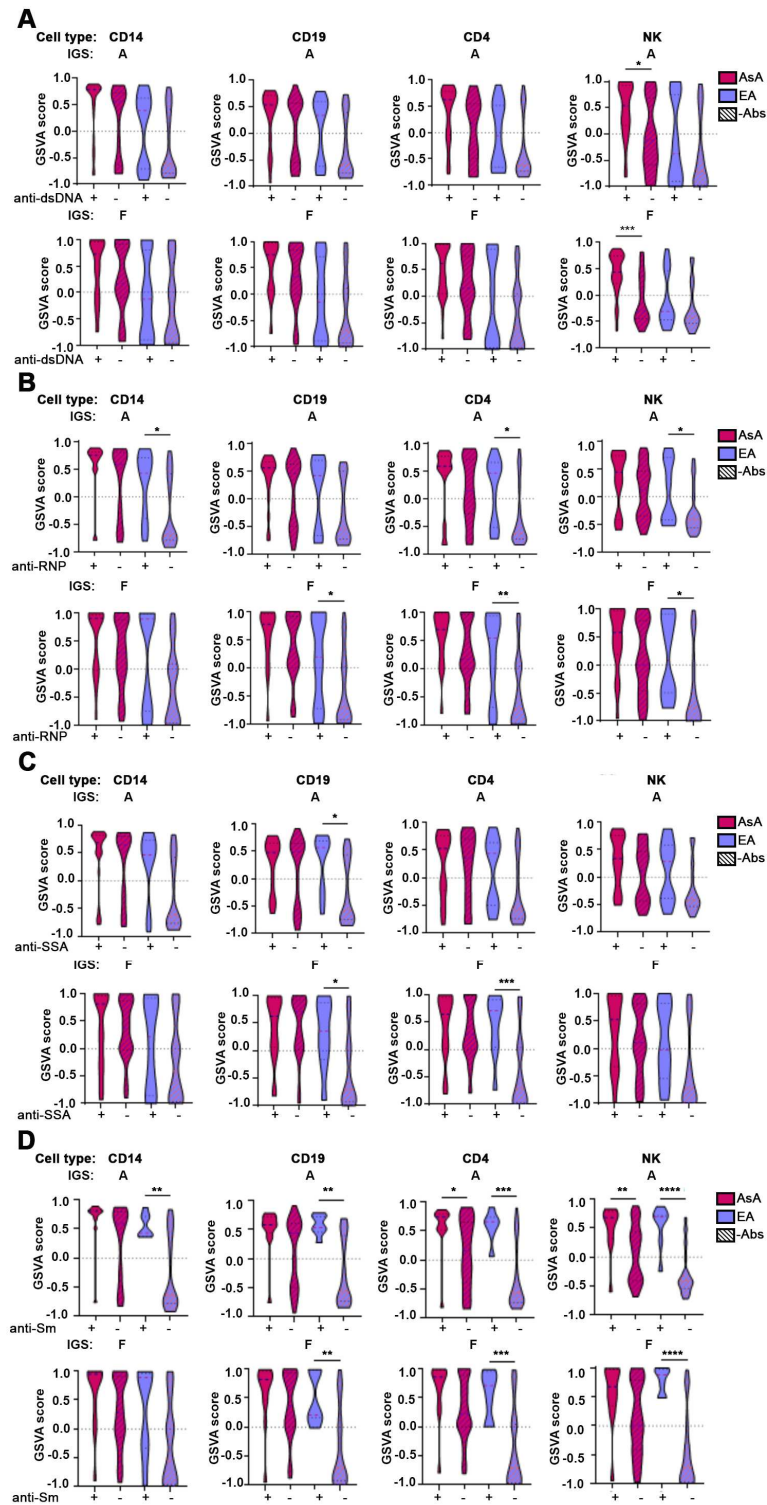
**Supplementary Figure S3: A.** Violin plots of GSVA scores of the original 5 interferon modules (IFN Core, IFNA2, IFNB1, IFNW1, IFNG) as well as IL-12 and TNF in each of the four patient subsets within B cells. Significance measures are:  $*=p<0.05$ ,  $**=p<0.01$ ,  $***=p<0.001$ ,  $****=p<0.0001$  and determined by Welch's t-test. The red subset contains 32 patients, the green subset contains 26 patients, the blue subset contains 37 patients and the salmon subset contains 18 patients. **B.** Bar plots showing the percentage of patients in each subset that are GSVA positive for the various IGSs within B cells. Statistical significance is shown using a Chi-Square test of proportion. **C.** Violin plots of GSVA scores of the original 5 interferon modules as well as IL-12 and TNF in each of the four patient subsets within T cells. **D.** Bar plots showing the percentage of patients in each subset that are GSVA positive for the various IGSs within T cells. **E.** Violin plots of GSVA scores of the original 5 interferon modules as well as IL-12 and TNF in each of the four patient subsets within NK cells. **F.** Bar plots showing the percentage of patients in each subset that are GSVA positive for the various IGSs within NK cells.

Figure S4

**A CD19****B CD19****C CD4****D CD4****E NK****F NK**

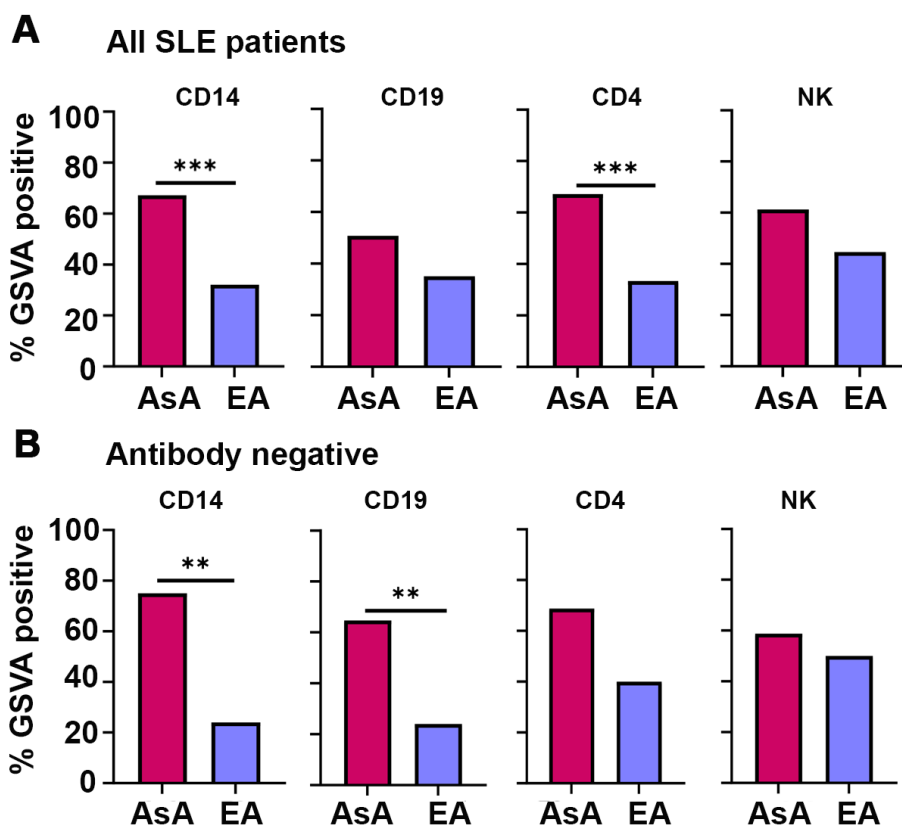
**Supplemental Figure S4: A.** Violin plots showing GSVA scores in AsA and EA patients derived using the 6 new IGS modules in B cells. Significance measures are:  $*=p<0.05$ ,  $**=p<0.01$ ,  $***=p<0.001$ ,  $****=p<0.0001$  determined using Welch's t-test. **B.** Violin plots of GSVA scores in AsA and EA patients using the original 5 IGS modules (IFN Core, IFNA2, IFNB1, IFNW1, IFNG) as well as IL12 and TNF in B cells. For **A-B**, AsA 63 patients, EA 57 patients. **C.** Violin plots showing GSVA scores in AsA and EA patients derived using 6 new IGS modules in T cells. **D.** Violin plots of GSVA scores in AsA and EA patients using the original 5 IGS modules as well as IL12 and TNF in T cells. For **C-D** the AsA group consists of 61 patients and the EA group consists of 57 EA patients. **E.** Violin plots showing GSVA scores in AsA and EA patients derived using 6 new IGS modules in NK cells. **F.** Violin plots of GSVA scores in AsA and EA patients using the original 5 IGS modules as well as IL12 and TNF in NK cells. For **E-F**, the AsA group contains 62 patients and the EA group contains 56 patients.

Figure S5



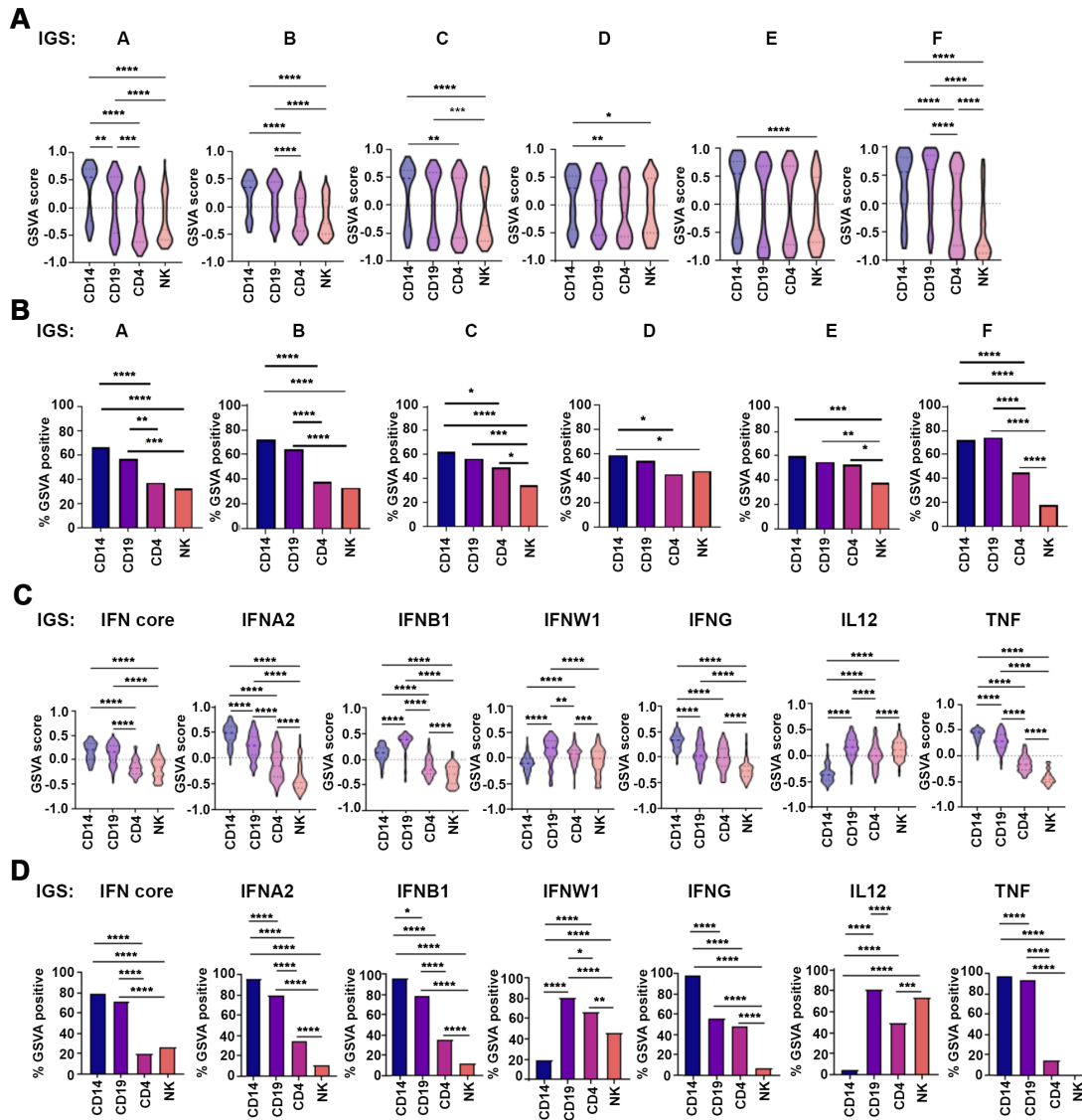
**Supplementary Figure S5: A-D** Violin plots of GSVA expression in the presence (+) and absence (-) of anti-dsDNA antibodies (**A**), in the presence (+) and absence (-) of anti-RNP antibodies (**B**), in the presence (+) and absence (-) of anti-SSA antibodies (**C**) and in the presence (+) and absence (-) of anti-Smith antibodies (**D**) across all cell types using the original 6 new IFN signatures (A-F). In **A**, the AsA+ group contains 32 patients, the AsA- group contains 31 patients, the EA+ group contains 20 patients and the EA- group contains 37 patients. In **B**, the AsA+ group contains 20 patients, the AsA- group contains 43 patients, the EA+ group contains 14 patients and the EA- group contains 43 patients. In **C**, the AsA+ group contains 28 patients, the AsA- group contains 35 patients, the EA+ group contains 9 patients and the EA- group contains 48 patients. In **D**, the AsA+ group contains 13 patients, the AsA- group contains 50 patients, the EA+ group contains 7 patients and the EA- group contains 50 patients. The Significance is only shown within the same ancestry for clarity. For all violin plots, significance measures are: \*=p<0.05, \*\*=p<0.01, \*\*\*=p<0.001, \*\*\*\*=p<0.0001 determined using Dunnett t-test.



**Figure S6**

**Supplementary Figure S6: A.** Bar plots showing the percentage of GSVA positive patients for the upstream IGS in all cell types. significance measures are:  $*=p<0.05$ ,  $**=p<0.01$ ,  $***=p<0.001$ ,  $****=p<0.0001$  determined using a Chi-square test of proportion.

**B.** Bar plots showing the percentage of GSVA positive and autoantibody negative patients for the upstream IGS in all cell types.

**Figure S7**

**Supplementary Figure S7: A.** Violin plots of GSVa expression of each of the six new signatures by cell type. For all violin plots, significance measures are:  $*=p<0.05$ ,  $**=p<0.01$ ,  $***=p<0.001$ ,  $****=p<0.0001$  determined using Dunning t-test. The monocyte group consists of 117 patients, the B cell group consists of 120 patients, and the T and NK cell groups consists of 118 patients. **B.** Bar plots of the percent of GSVa positive

patients by each of the select signatures by cell type. Significance was determined using a Chi-square test of proportion. **C.** Violin plots of GSVA expression of each of the original signatures by cell type. **D.** Bar plots of the percent of GSVA positive patients by each of the original signatures by cell type.