

**Supplementary Figure 1. Heritability enrichment results for control traits.** (A) Bar graphs display the genetic risk enrichment coefficient (y-axis) and standard error for cell-type specific open chromatin accounting for control peaks and baseline annotations. Open chromatin data were taken from the Calderon *et al.* study. Risk enrichment was assessed using GWAS summary statistics for the positive control traits rheumatoid arthritis, Alzheimer's disease, systemic lupus erythematosus, and the negative control trait height. Bars marked with “\*” indicate  $P < 0.05$ , “\*\*” indicates  $P < 0.01$ , “\*\*\*” indicates  $P < 0.001$ .

**Supplementary Figure 2. Single-cell disease relevant score results for control traits.** (A) Visualization of the Space-Time Gut Cell Atlas using Uniform Manifold Approximation and Projection (UMAP) on the top 20 principal components from 1,997 variable genes from the single-cell RNA-seq expression matrix. Cells are colored based on the coarse cell type annotations from the Space-Time Gut Cell Atlas. (B) Barplots shows the cell type proportions within the whole Space-Time Gut Cell Atlas and within cells with significant disease relevant score (20% FDR) for AS (using IGAS GWAS), Alzheimer's disease (AD) and rheumatoid arthritis (RA). (C) Same UMAP visualization as in A, where cells with significant scDRS score (20% FDR) are colored in red and non-significant cells are colored in gray, for each control trait.

Figure S1

A

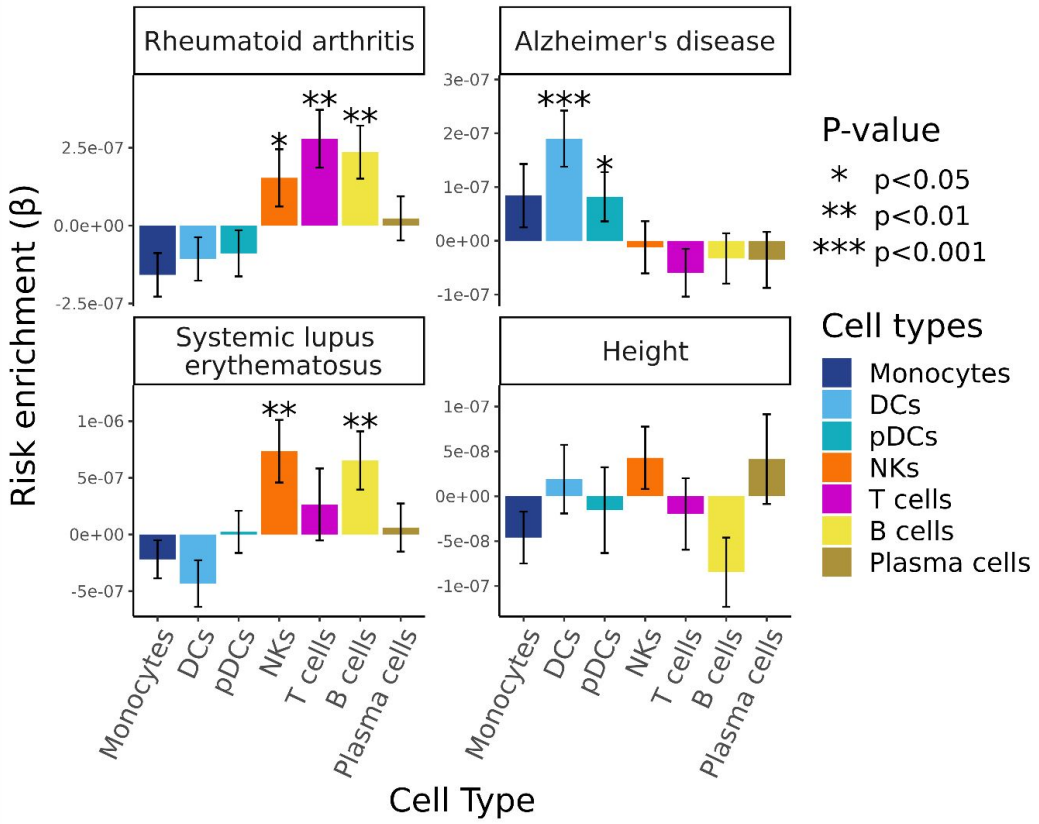
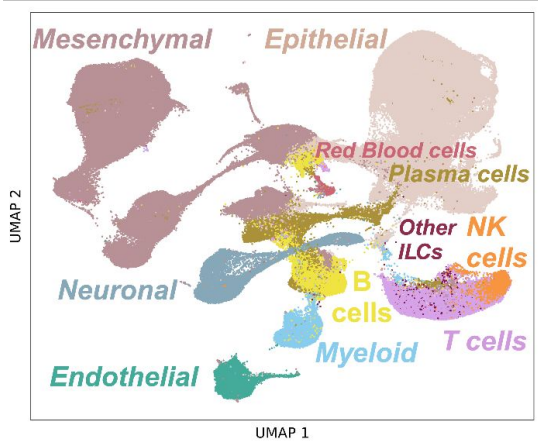
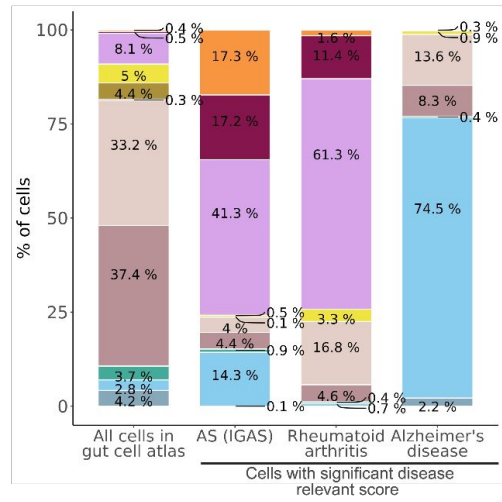


Figure S2

A

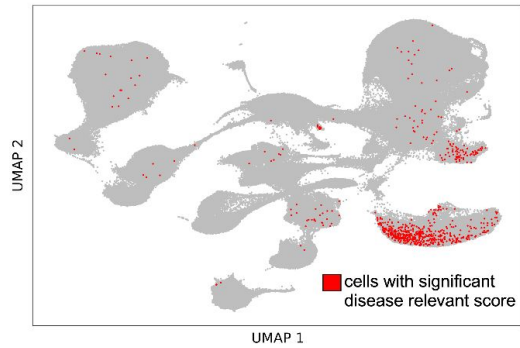


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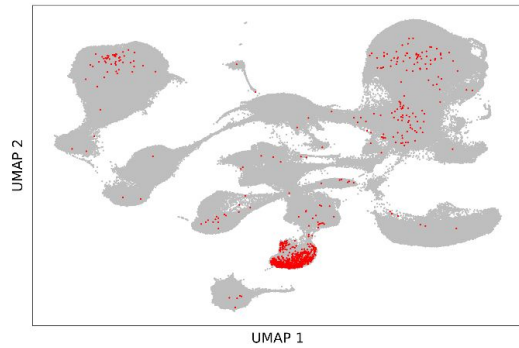


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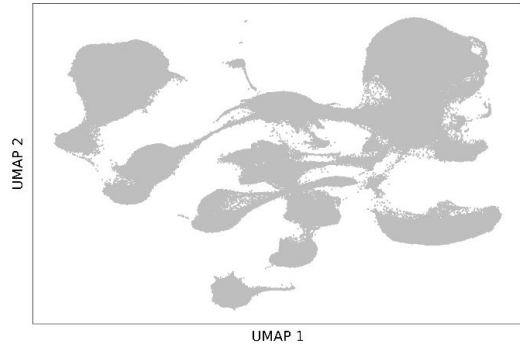
Rheumatoid arthritis



Alzheimer's disease



Systemic lupus erythematosus



Height

