The American Journal of Human Genetics, Volume *107*

Supplemental Data

Analysis of Trans-Ancestral SLE Risk Loci Identifies Unique Biologic Networks and Drug Targets in African and European Ancestries

Katherine A. Owen, Andrew Price, Hannah Ainsworth, Bryce N. Aidukaitis, Prathyusha Bachali, Michelle D. Catalina, James M. Dittman, Timothy D. Howard, Kathryn M. Kingsmore, Adam C. Labonte, Miranda C. Marion, Robert D. Robl, Kip D. Zimmerman, Carl D. Langefeld, Amrie C. Grammer, and Peter E. Lipsky

Supplemental Figures

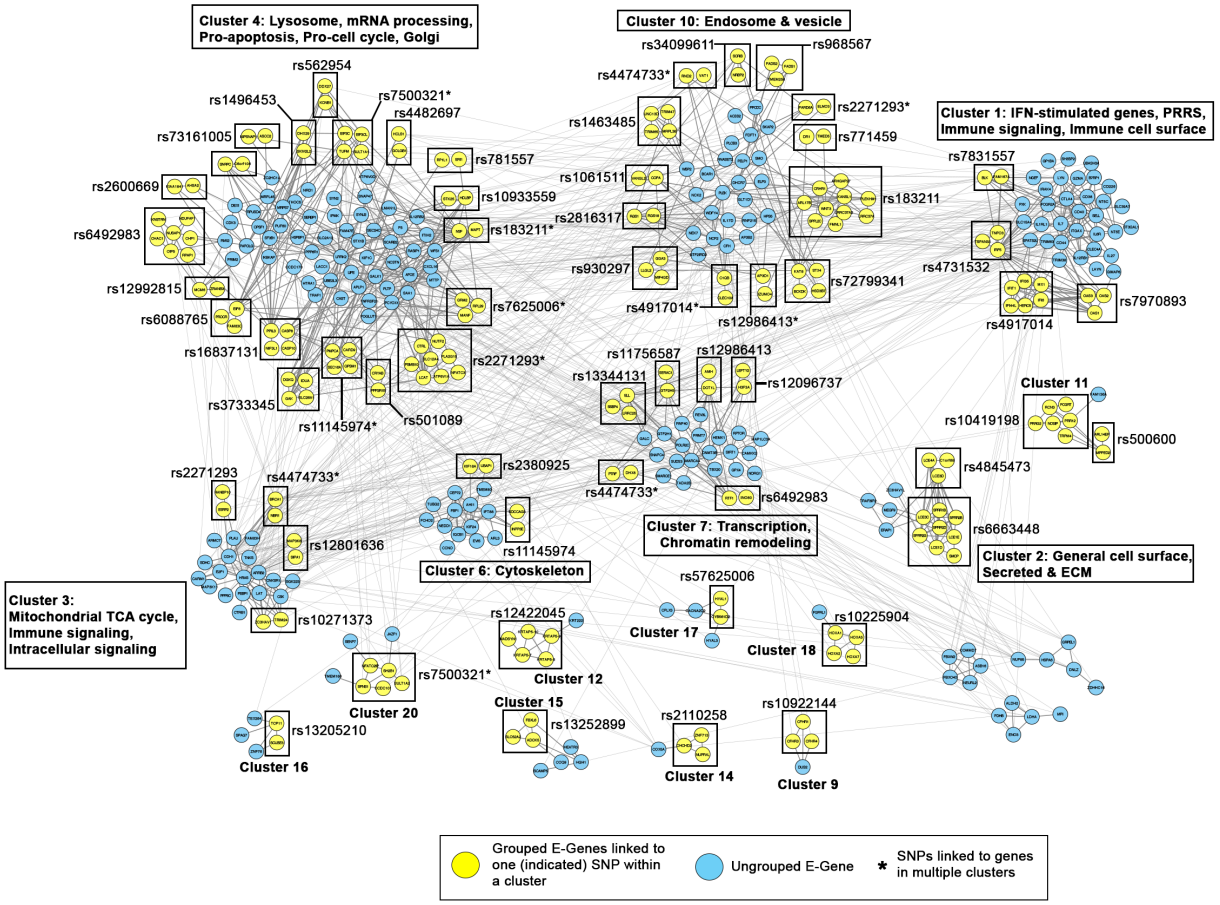

Figure S1. SNPs impact multiple E-Genes within a functional protein-protein interaction-based molecular network. Protein-protein interaction networks consisting of E-Genes were generated using STRING, clustered using MCODE and visualized using Cytoscape. Grouped E-Genes linked to a SNP are indicated with boxing. SNPs linked to groups of genes in multiple clusters are indicated with an asterisk. Functional BIG-C category annotation is provided for select clusters.

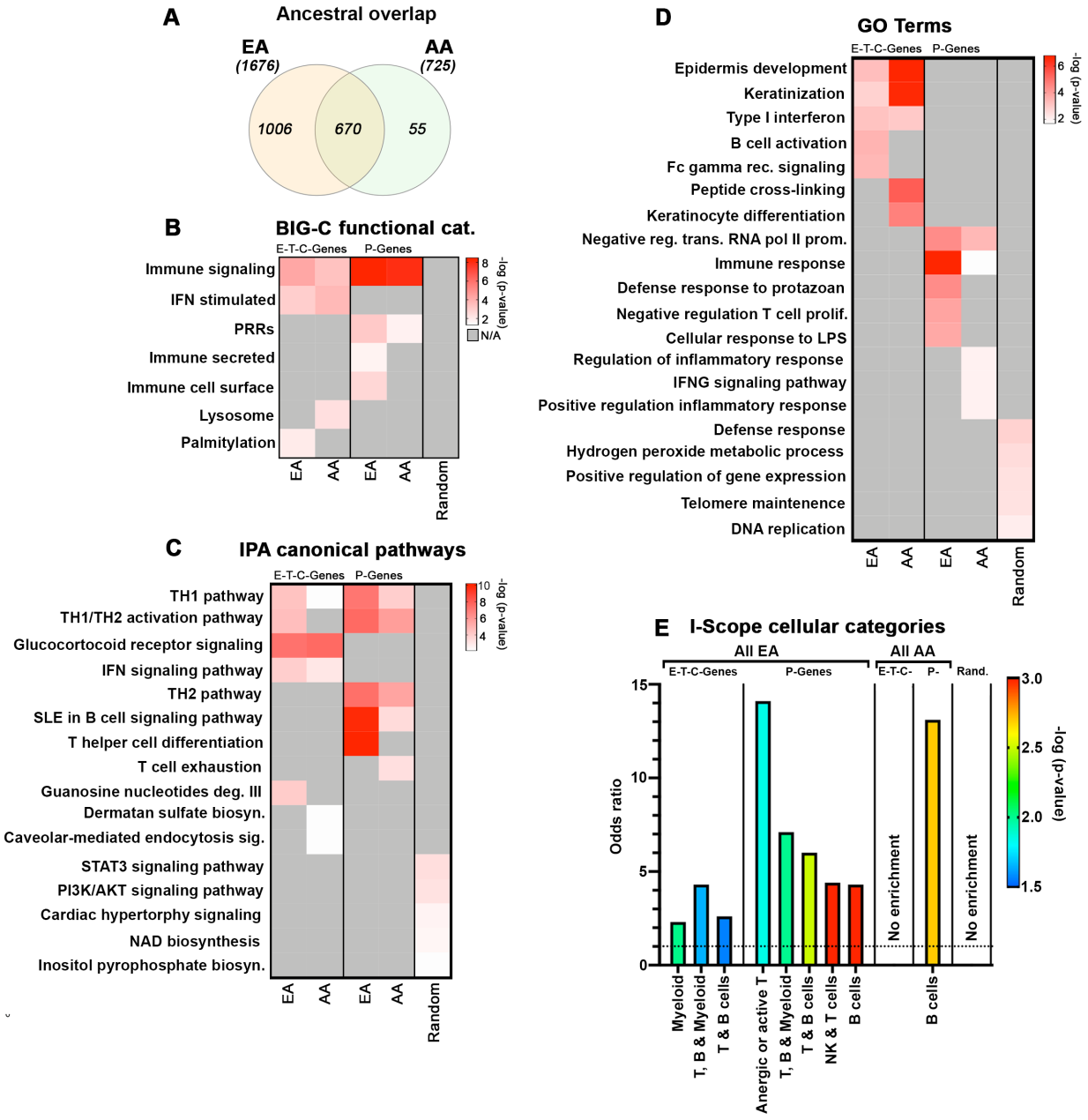

Figure S2. Overlap and functional characterization of all EA and AA-associated genes. (**A**) Venn diagram showing the overlap between the full cohort of EA (EA + shared; 1676) and AA genes (AA + shared; 725). (**B-D**) EA, AA and a cohort of random (499 genes) SNP-predicted genes were analyzed to determine enrichment using functional definitions from the BIG-C annotation library, IPA canonical pathways and GO terms. E-T- and C-Genes were analyzed together; P-Genes were examined separately. Enrichment was defined as any category with an odds ratio (OR) >1 and –log10(p-value) >1.33. (**E**) I-Scope hematopoietic cell enrichment defined as any category with an OR >1, indicated by the dotted line, and –log10(p-value) >1.33.

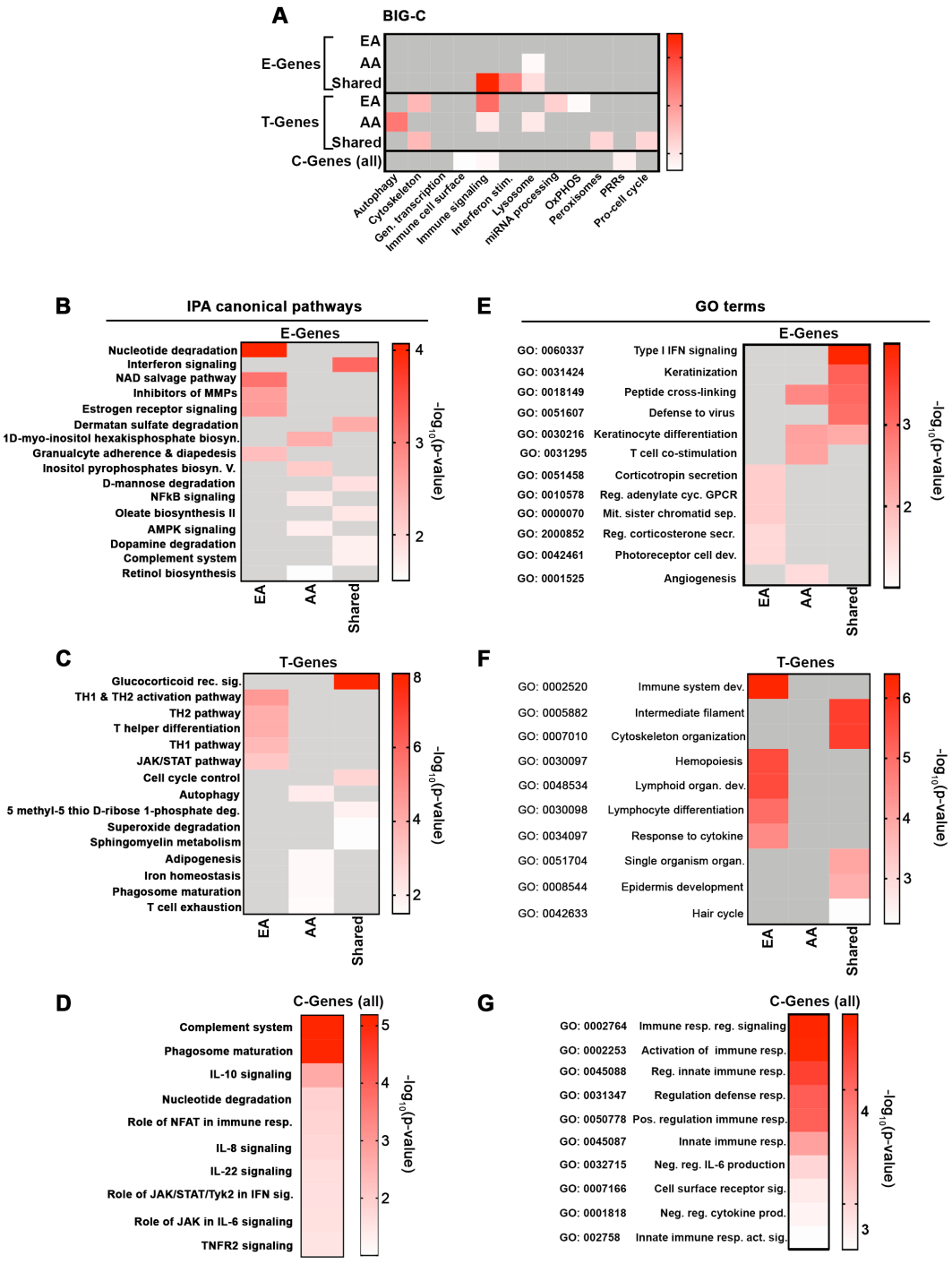

Figure S3. Functional characterization of predicted genes by discovery method. (**A**) Ancestry-dependent and independent E-, T- and C-Genes were independently analyzed by discovery method (source) to determine enrichment using functional definitions from the BIG-C annotation library. Enrichment was defined as any category with an odds ratio (OR) >1 and –log10(p-value) >1.33. (**B-F**) Heatmap visualization of the top five significant IPA canonical pathways (B-D) and the top five significant gene ontogeny (GO) terms (D-F) for E- and T-Genes organized by ancestry. Due to the smaller number of C-Genes, this gene set was analyzed together. Top pathways with –log10(p-value) >1.33 are listed.

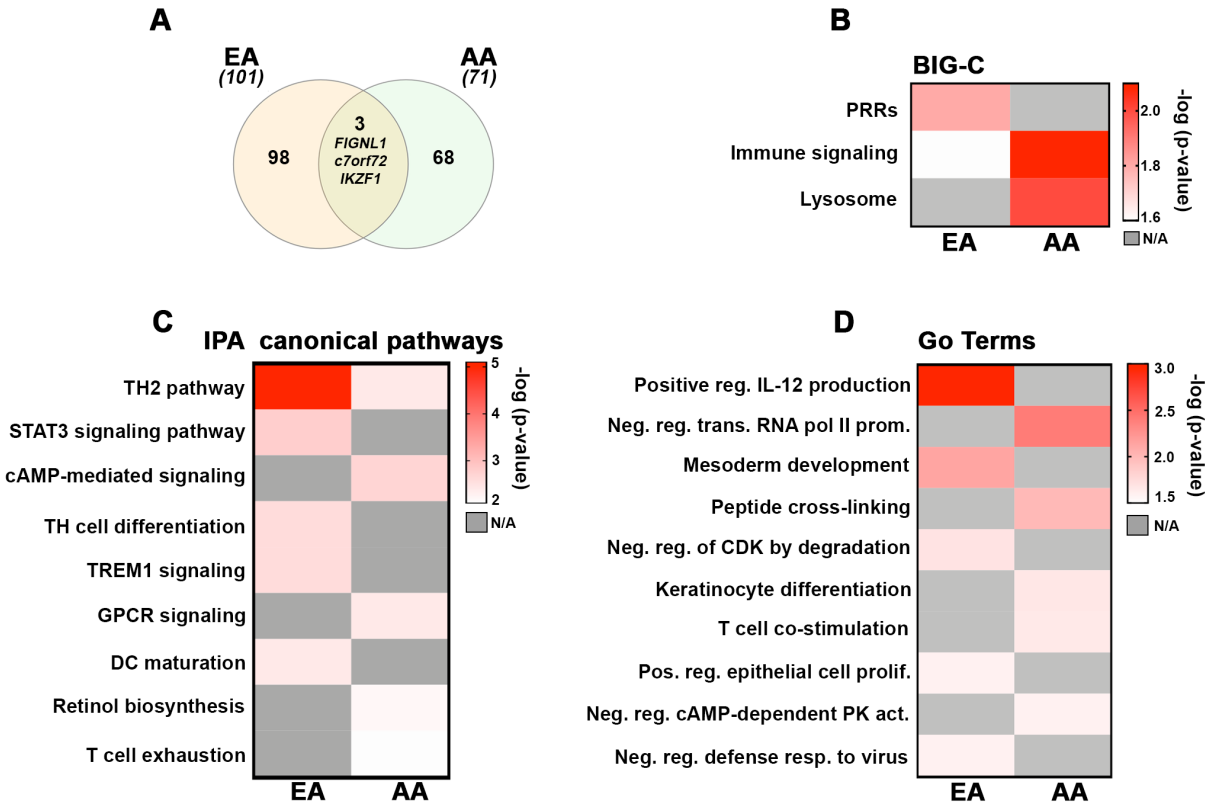

Figure S4. Overlap and functional characterization of 101 EA and 71 AA SNP-predicted genes. (**A**) 77 of the most significantly associated SLE-EA SNPs were used to predict 101 EA (E-T-C-P) genes. These genes were directly compared to the 71 genes predicted by 77 AA SLE SNPs. Venn diagram depicts the overlap between the gene sets. (**B-D**) Heatmap visualization of EA and AA functional categories, the top five significant IPA canonical pathways and GO terms for each gene list. Top pathways with –log10(p-value) >1.33 are listed.

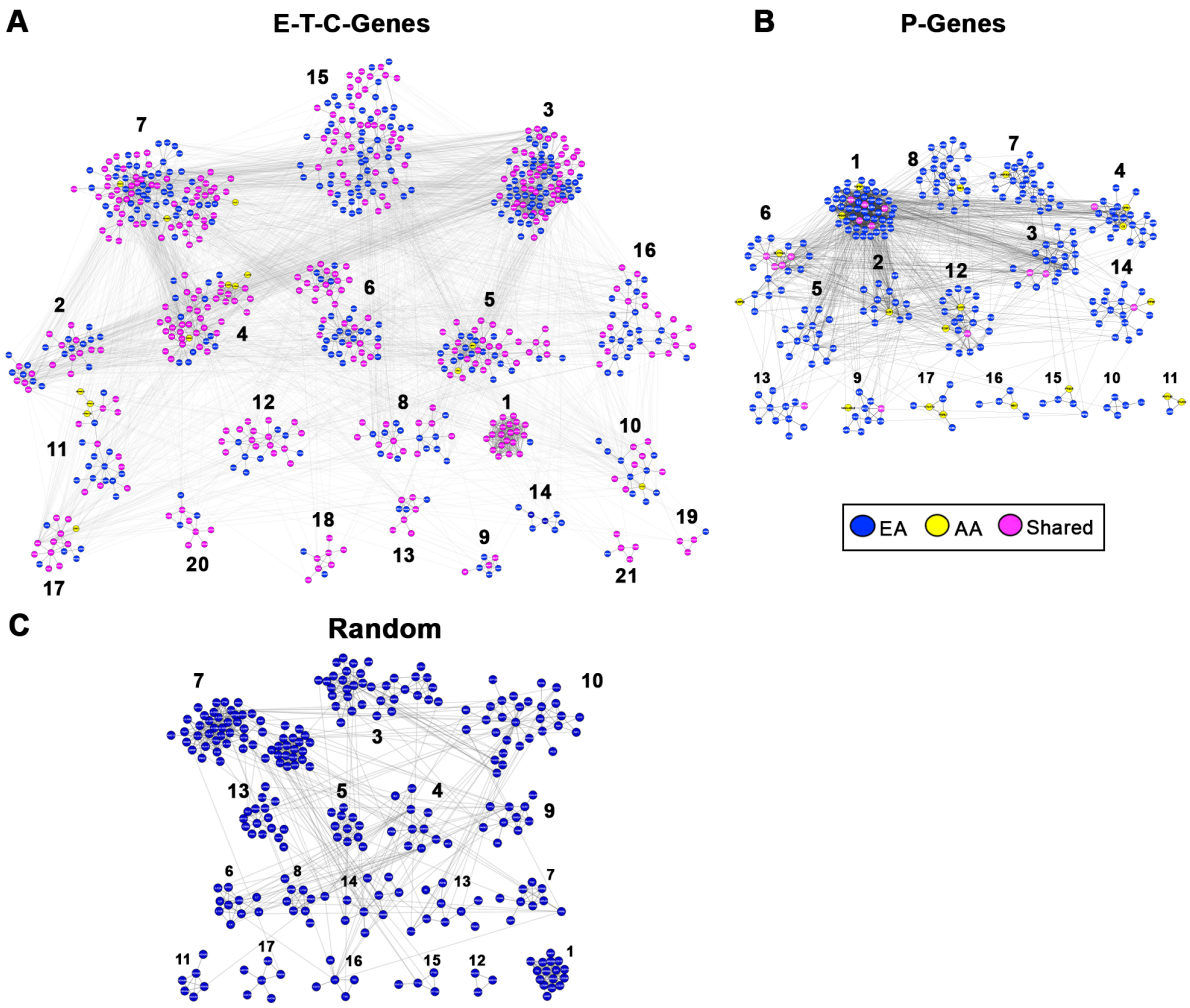

Figure S5. Protein-protein interaction-based clustering of predicted and random genes. PPIs and clusters were generated via CytoScape using the STRING and MCODE plugins. Clusters are determined by the strength of protein-protein interactions, calculated by pooling information from publicly available literature. (**A-C**) Numbered clusters composed of individual predicted genes; ancestry indicated by node color in legend.

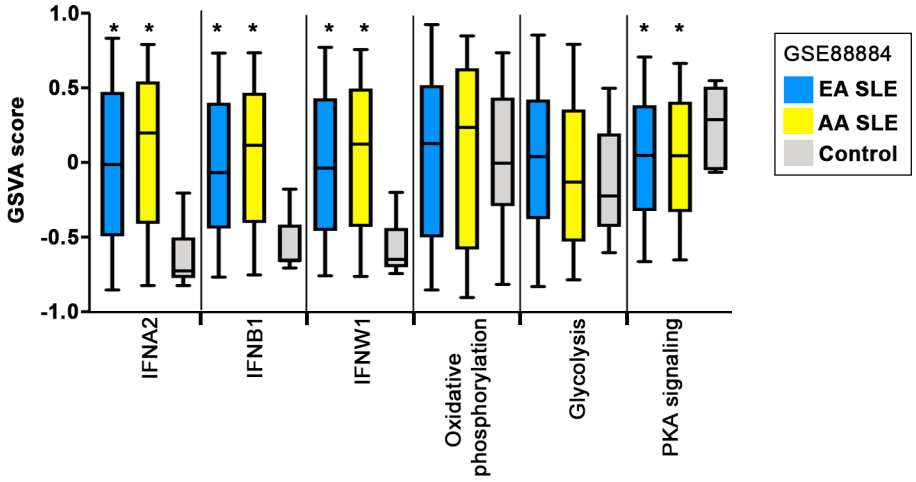

Figure S6. GSVA enrichment scores for interferon and metabolic pathways. GSVA signature scores distinguishing SLE patients from healthy controls using gene modules defining IFNA2, IFNB1, IFNW1, oxidative phosphorylation, glycolysis and PKA signaling. Asterisks (*) indicate a p-value <0.05 using Welch's t-test comparing SLE to control.