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Title: Stratification of Systemic Lupus Erythematosus Patients Using Gene Expression Data Reveals Expression of Distinct Immune Pathways

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Abstract:
Systemic lupus erythematosus (SLE), an autoimmune disease that destroys healthy organs and tissue, is the tenth leading cause of death in females 15-24 years old in the US. SLE is one of many autoimmune diseases, which are diseases in which a patient's immune system mistakes parts of their own body as foreign, attacking their body instead of protecting it. The diversity of symptoms in SLE patients (ranging from rashes to fatigue to joint pain to destruction of the kidneys, heart, or even brain) and the diversity in the immune pathways expressed in these patients causes difficulties in treating SLE as well as in new clinical trials, and prior research has shown that the immune pathways expressed in patients can influence their responses to various current treatments.

This study used a type of machine learning called unsupervised learning to separate adult SLE patients into clusters based on their gene expression data and identify relevant immune pathways in said clusters. Because data for each patient included information on the expression of 47,323 genes, the dimensionality, or amount, of the gene expression data was reduced by three separate methods (PCA, UMAP, and a simple linear autoencoder) and the results from each of these methods were used to separate patients into six clusters with k-means clustering. The expression of genes in the SLE clusters was compared to the expression of the same genes in control patients with t-tests, indicating whether each gene was upregulated, downregulated, or neither in all of the clusters.

This analysis of the clusters revealed three separate immune pathways, each found in several clusters, which caused SLE. These pathways were: (1) high interferon levels, (2) high autoantibody levels, and (3) dysregulation of the mitochondrial apoptosis pathway. High interferon levels and high autoantibody levels are known to be associated with SLE, but mitochondrial apoptosis has not been investigated before to our knowledge as a standalone cause of SLE, independent of autoantibody production, so mitochondrial proteins could be investigated as a therapeutic target for SLE in the future.