Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with highly heterogeneous clinical presentation characterized by disease unpredictable features and multi-system involvement. This clinical heterogeneity calls for designing a molecular stratification to improve clinical trial design and formulate personalized treatment therapies.

Disclosure of Interests: Alan Zabotti Speakers bureau: UCB, Novartis, Janssen, Paid instructor for: Amgen, Consultant of: Janssen, Ivan Giovannini: None declared, Alen Zabotti Speakers bureau: UCB, Novartis, Janssen, Paid instructor for: Amgen, Consultant of: Janssen, Enrico Pagano Consultant of: GSK, Roche, Grant/research support from: not relevant for this study, Chiara Zuiani Consultant of: not relevant for this study, Massimo Robiony Consultant of: not relevant for this study, Michele Lorenzon Consultant of: not relevant for this study, Sara Zandonella Callegher: None declared, Valeria Manfrè: None declared, Disclosure of Interests: None declared.

Disclosure of Interests: This research was conducted to develop a reliable method to stratify SLE patients combined gene expression information and disease status. Methods: The mRNA expression profile of GSE138458 (contained 307 patients and 23 controls) and GSE49454 (contained 111 patients and 16 controls) were downloaded from the publicly GEO databases. After background adjustment, batch correction, and other pre-processing, obtaining a big gene matrix to identify the differentially expressed genes (DEGs) in SLE compared with healthy controls, which were screened by P value < 0.01. SLE subtypes were identified by non-negative matrix factorization (NMF) based on DEGs. Acquired signature genes in different SLE subtypes were conducted to process pathway enrichment analysis in Metascape. SLEDAI score and immune cell infiltration was also performed between subtypes by software package R (version 4.0.3).

Results: Total 1202 DEGs were imputed to NMF unsupervised machine learning method. Patients with SLE were stratified into two subsets based on 184 signature genes derived from obtained DEGs.(Fig.1A, 1B). GO and KEGG enrichment analysis showed that signature genes were mainly involved in negative regulation of innate immune response, toll-like receptor signaling pathway, regulation of immune effector process and so on.(Fig.1C). Patients in Sub1 group had severe disease activity measures compared with those in Sub2(Fig.1D). SLEDAI scores from GSE49454 dataset were also higher in Sub1 compared with Sub2((Fig.1E). Further, immune cell infiltration results revealed an insufficient of regulatory T cell, CD8 T cells and naive CD4 T cells in Sub1 and neutrophils cells in Sub2(P<0.05.(Fig.1F).

Conclusion: Our findings indicate that patients with SLE could be stratified into 2 subtypes which had different lymphocyte status and closely related to disease activity. This phenotyping may help us understand the etiology of the disease, inform patient in the design of clinical trials and guide treatment decision.

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