031 INTEGRATIVE ANALYSIS REVEALS A MOLECULAR STRATIFICATION OF SYSTEMIC AUTOIMMUNE DISEASES

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Background Clinical heterogeneity, a hallmark of systemic autoimmune diseases (SADs) impedes early diagnosis and effective treatment, issues that may be addressed if patients could be grouped into a molecular defined stratification.

Methods With the aim of reclassifying SADs independently of the clinical diagnoses, unsupervised clustering of integrated whole blood transcriptome and methylome cross-sectional data of 918 patients with 7 SADs and 263 healthy controls was undertaken. An inception cohort prospectively followed for 6 and 14 months was studied to validate the results in early cases and analyze if cluster assignment was modified with time.

Results

Four clusters were identified Three aberrant clusters were 'acute phase inflammatory', 'T cell immunity', and 'interferon', each including all diagnoses, were defined by genetic, clinical, serological and cellular features. A fourth cluster showed no specific molecular pattern, to which 74% of healthy controls clustered with patients. The inception cohort showed that most patients were either assigned always to the same cluster or moved from the healthy-like cluster to a single aberrant cluster resembling the relapsing-remitting dynamic of these diseases, showing that single aberrant molecular signatures characterize each individual patient.

Conclusions Patients with SADs share molecular signatures and can be therefore stratified into three disease clusters differentiating each patient into a specific molecular disease pathway. Such assignment is stable with time. These results have important implications for understanding disease progression and therapy design marking a paradigm shift in our view of SADs.

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032 SKIN PROTEOME INVESTIGATION IN CUTANEOUS LUPUS ERYTHEMATOSUS (CLE) REVEALS NOVEL UNIQUE DISEASE PATHWAYS

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Background Cutaneous Lupus Erythematosus (CLE) is an autoimmune disease. It can be limited to the skin or be one of