Background Systemic lupus erythematosus (SLE) is a complex autoimmune disease stemming from a poorly understood preclinical stage of autoantibody and symptom accrual. Antinuclear autoantibodies (ANAs) accumulate during this preclinical period. As many healthy individuals are also ANA-positive, this study aimed to identify further immune dysregulation that may contribute to disease pathogenesis.

Materials and methods SLE-associated autoantibodies, serum IFN-alpha activity and soluble mediators from multiple immune pathways were measured in serial serum samples from the Department of Defense Serum Repository by bead-based assays and cell-based reporter assays. Eighty-four patients with samples available pre- and post-SLE classification (average time span = 5.98 years) were compared to 86 matched healthy controls. Temporal and predictive connexions between autoantibodies, soluble mediators, and SLE classification were determined by mixed linear regression, growth curve modelling, path analysis, analysis of covariation and random forest analyses.

Results In cases, but not matched controls, autoantibody specificities and IFN-associated mediators accumulated over a period of years, plateauing near the time of disease classification (p < 0.001). Nine soluble mediators, including IL-5 (q = 4.33 x 10^-4) and IL-6 (q = 8.26 x 10^-5), were significantly elevated in cases vs. controls >3.5 years pre-classification. Th1-type, Th17-type, and TNF superfamily soluble mediators increased longitudinally in cases approaching SLE classification, but not in controls. Autocoid B cells from BXD2 mice exhibit autocrine stimulation by intracellular IFNb. IFNb, compared to IFNa, exhibited a signal to enhance type I IFN expression in BXD2 B cells. IFNb, compared to IFNa, exhibited a signal to enhance type I IFN expression in BXD2 B cells.

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