damage response, senescence, and self-destruction. Those cellular events might in turn trigger overproduction of antinuclear antibodies.

Lay Summary To gain insight into mechanisms of autoimmunity, we simultaneously investigated the presence of classical SLE autoantibodies (ANA, dsDNA, Sm/RNP, Ro, La) and gene expression in a cohort of 80 SLE patients followed longitudinally. We observed a significant association between antiantibodies titers and genes involved in cell division The aberrant expression of cell-cycle related genes might cause cell cycle arrest, DNA destruction, and enhanced antinuclear antibodies production in SLE.

Transcriptomics

2105 UCSF AUTOIMMUNOPROFILER – UNDERSTANDING THE IMMUNOMES OF AUTOIMMUNE DISEASES

[1]Consortium of UCSF, [2]Eli Lilly, [1]led by UCSF leadership team of David Erle, [1]Vincent Chan, [1]Jimmie Ye, [1]Andy Gross, [1]Max Krummel, [1]Jeroen Roose*. [1]*University of California, San Francisco (UCSF), CA, USA*; [2]*Eli Lilly, San Diego, CA, USA*

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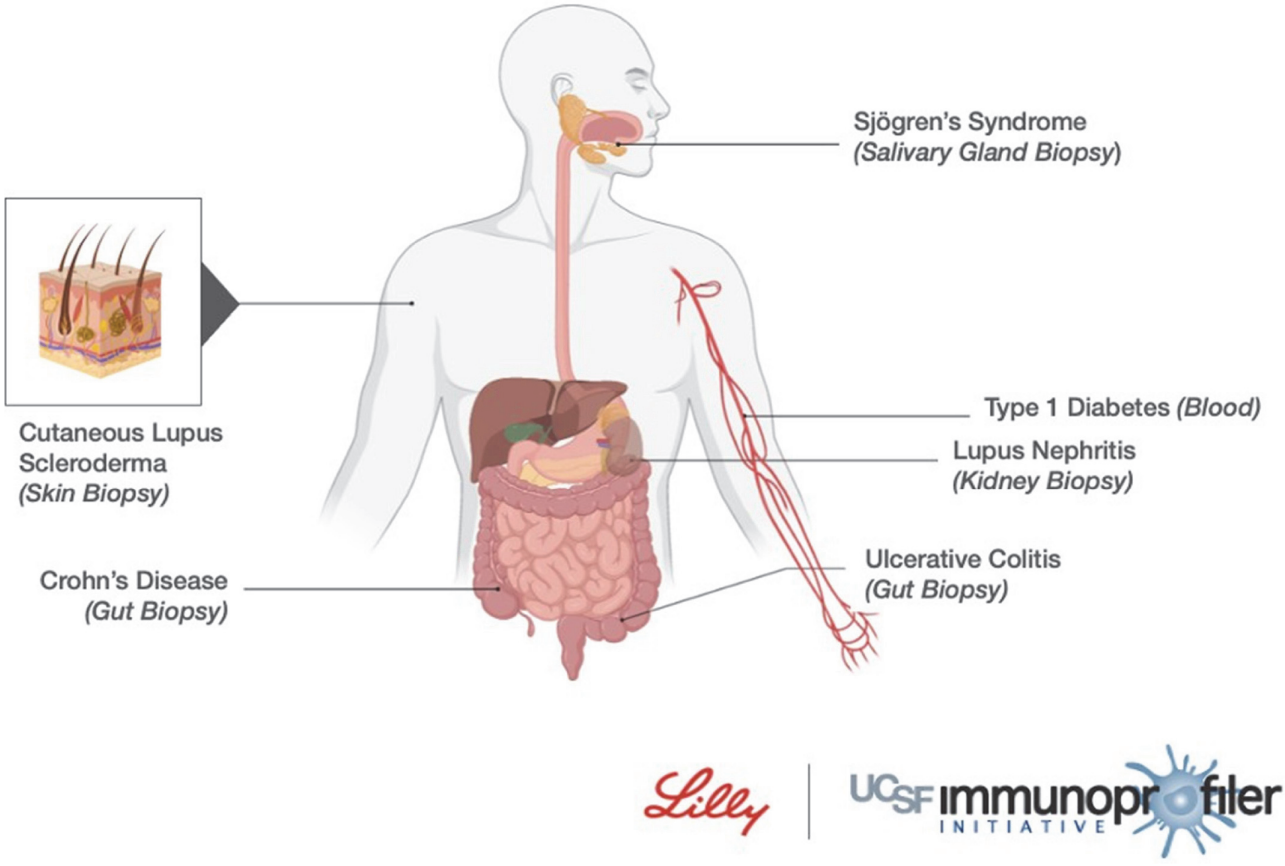
Background In autoimmune diseases, like Lupus, immune cells are entangled in stimulatory loops and attack otherwise healthy tissues. In AutoImmunoProfiler we strive to map the different configurations of immune cell interactions in tissues of patients with autoimmune diseases. Overall goals include better understanding of underlying mechanisms of autoimmune diseases, identification of the relationship between tissue and peripheral compartment, and the identification of novel pathways and targets for future drug discovery and development.

Methods In AutoImmunoProfiler, the UCSF team will initially prospectively collect tissue and blood samples from patients with the following autoimmune diseases: Systemic Lupus Erythematosus (SLE), Scleroderma (SSc), primary Sjögren's Syndrome (pSS), Ulcerative Colitis (UC), Crohn's Disease (CD), and Type 1 Diabetes (T1D), and will be complemented by samples from matched healthy controls (HC). Samples are processed and analyzed with the expertise of the UCSF CoLabs, performing: scRNAseq, CITEseq, scATACseq, bulk epigenomic assays (EPIC chip), Bulk RNAseq, Image analysis of tissue biopsies, and Organoid assays (only for IBD).

Results Autoimmunoprofiler is envisioned to be a consortium effort. Eli Lilly and UCSF are the founding partners, with the expectation to engage additional partners in the future. Since our kick-off in 2021, we have begun to profile the range of autoimmune diseases using a combination of proteomic, transcriptomic, epigenomic, and structural analyses. Emphasis will be on freshly collected tissue samples with matched peripheral blood samples from clinically well-annotated patients with autoimmune diseases.

Conclusions We have started to map the different configurations of immune cell interactions in tissues of patients with autoimmune diseases. An example of high-resolution data that is being generated in AutoImmunoProfiler is the recent publication in Science "Single-cell RNA-seq reveals cell type-specific



Abstract 2105 Figure 1

molecular and genetic associations to lupus" (PMCID: PMC9297655) from AutoImmunoProfiler leads Maria Dall'Era and Jimmie Ye. In this study, they profiled peripheral blood mononuclear cells for 162 SLE cases and 99 healthy controls with multiplexed single-cell RNA sequencing (mux-seq). We anticipate that will generate a comprehensive overview of "immune states and immune cell networks" at single cell resolution, by comparing tissue biopsies from SLE to those form other autoimmune diseases and to peripheral blood samples.

Trial Registration N/A

Lay summary We have started a new initiative called AutoImmunoProfiler at UCSF that aims to profile tissue and blood samples from patients with autoimmune diseases at single cell resolution. Autoimmunoprofiler is envisioned to be a consortium effort with up to five industry partners and Eli Lilly and UCSF are the founding partners. By capitalizing on the consortium structure of collaboration, we believe we can reveal underlying mechanisms of autoimmune diseases and particularly the relationship between tissue and the immune system. We anticipate that results from AutoImmunoProfiler will eventually lead to the identification of novel pathways and targets for future drug discovery and development.