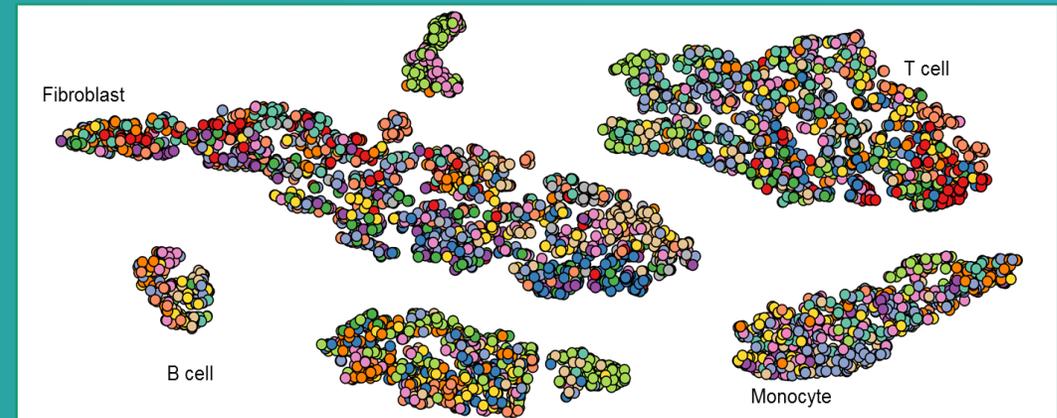


Accelerating Medicines Partnership Autoimmune and Immune-Mediated Diseases (AIM)



AMP AIM Program Goals



The cornerstone of **AMP AIM** will be the concept of *disease deconstruction/reconstruction*:

- Building on the success of AMP RA/SLE, extend *disease deconstruction* to indexing and mapping of cells and pathways in:
 - ❖ Rheumatoid Arthritis
 - ❖ Lupus
 - ❖ Psoriasis
 - ❖ Psoriatic Arthritis
 - ❖ Sjogren's Syndrome

- Discover how these pathways and cells interact through new analytics:
 - ❖ Discover how innate and adaptive cells of the immune system and tissue resident cells interact to cause inflammation and clinical disease (*disease reconstruction*);
 - ❖ Accelerate the discovery of new mechanisms of disease and new targets for intervention in therapeutic development.

Concept approved by AMP EC (Jul 2020)

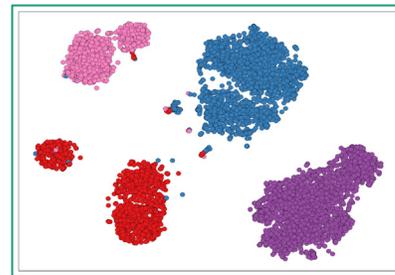
Concept clearance by NIAMS Council (Sep 2020)

AMP AIM Builds on Key Outcomes of AMP RA/SLE

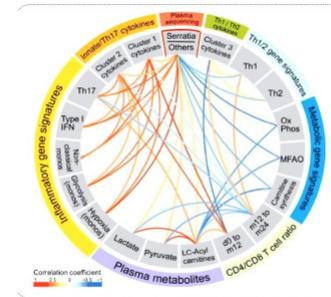


Identify the pieces of the puzzle

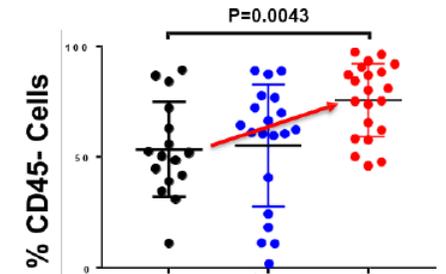
AMP RA/SLE
Disease 'Deconstruction'



CITE-Seq, ATAC-Seq & CyTOF
Identify cell types and states in disease tissue

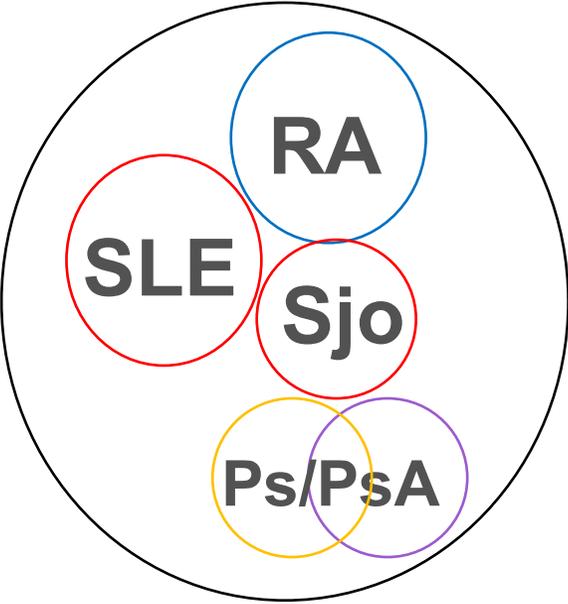
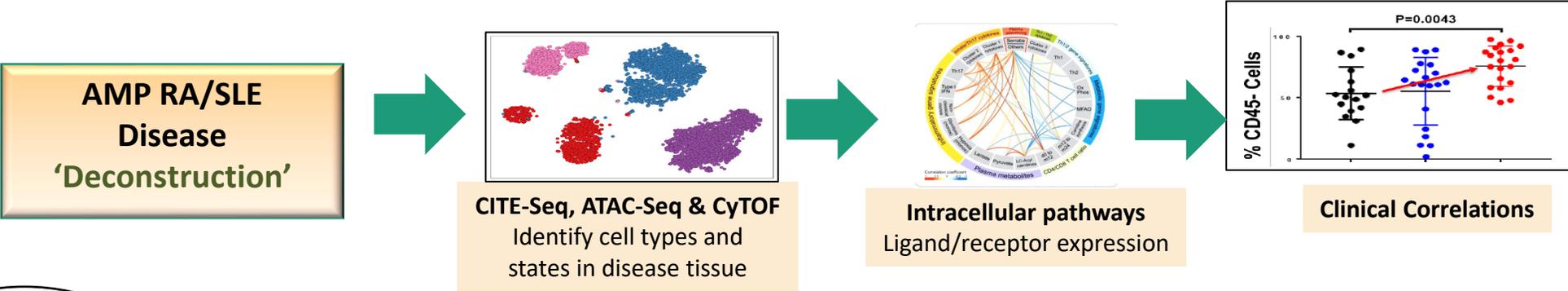


Intracellular pathways
Ligand/receptor expression



Clinical Correlations

AMP AIM Builds on Key Outcomes of AMP RA/SLE



Diseases

Disease phenotype, stage, treatment and response

Skin, Synovium, Kidney, Salivary Gland & Blood

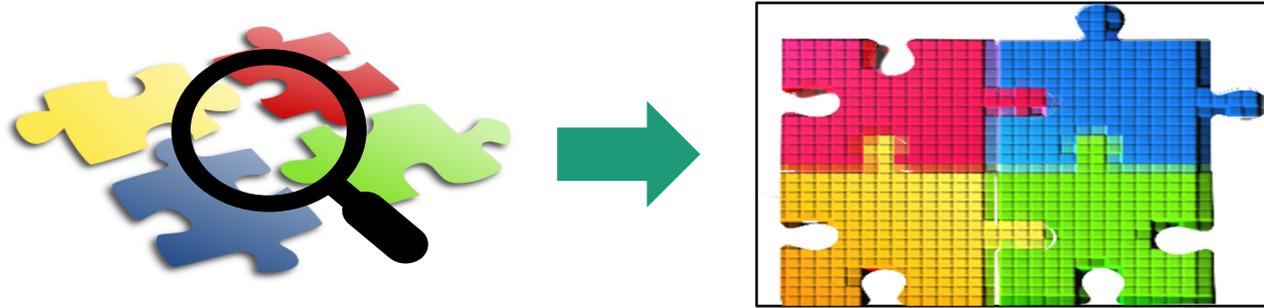
Compare Analytics across Diseases

Clinical correlation and validation

Tissues

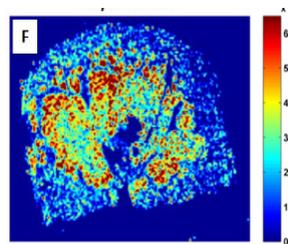
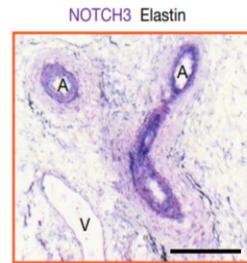
Pathways and targets

AMP AIM Expands to Mechanisms



Put the pieces back together

AMP AIM Disease 'Reconstruction'



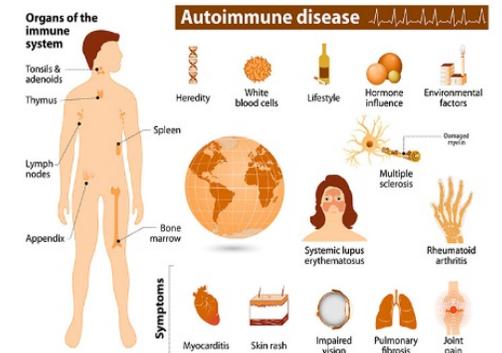
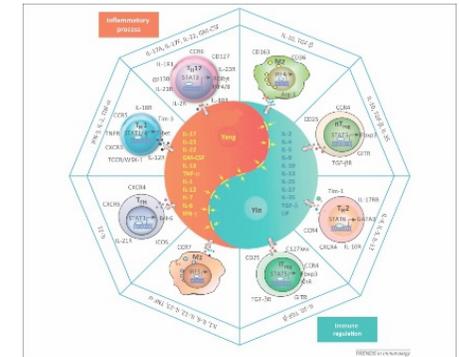
Map interactions between tissue-resident and infiltrating cells in situ

In situ analysis of mediators of crosstalk between cells that drive inflammation and damage

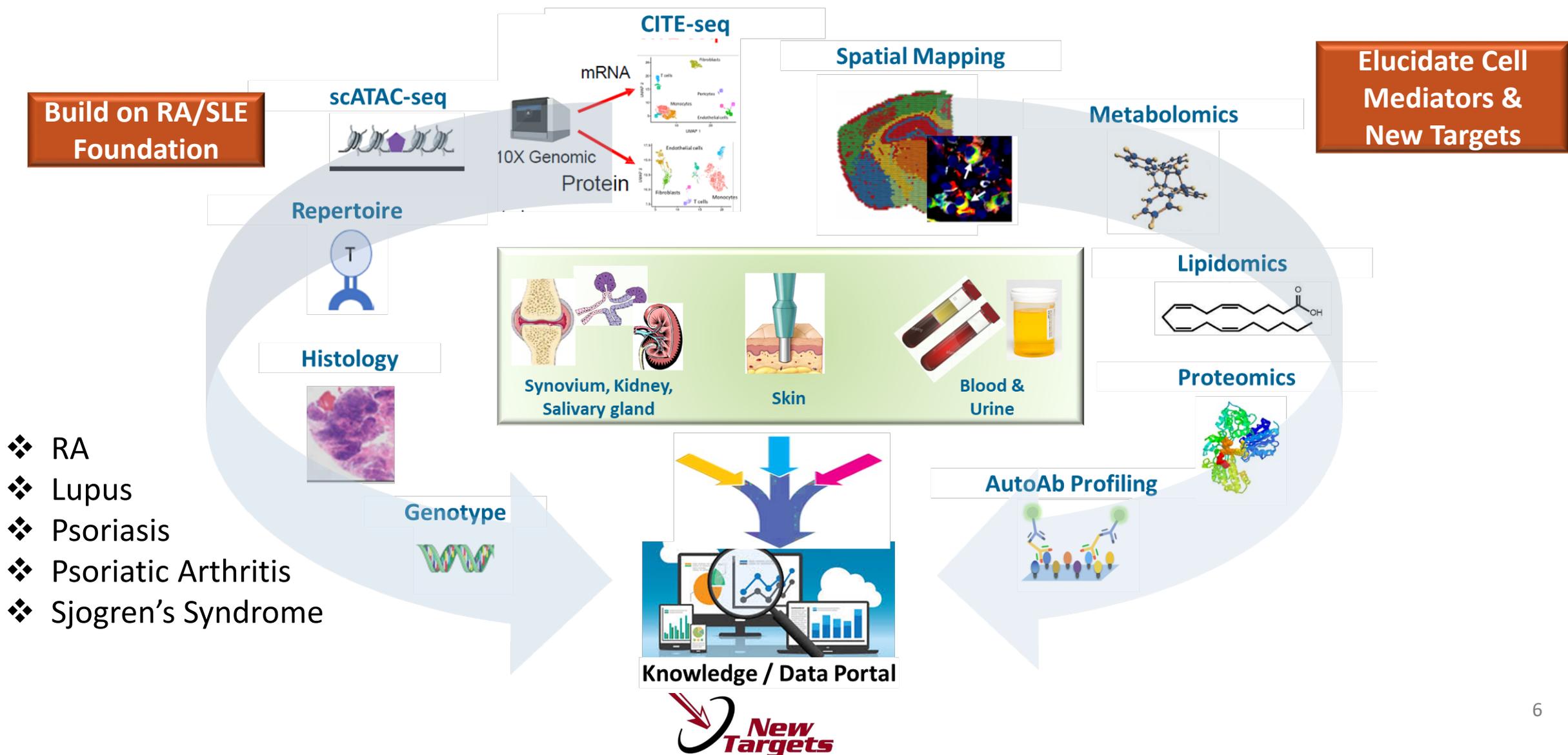
Contrast tissues in different diseases to identify specific pathways



WHAT ARE THE IMMUNE MEDIATORS BETWEEN CELLS?



AMP AIM Will Enable Unprecedented Multi-Modality Data Integration



- ❖ RA
- ❖ Lupus
- ❖ Psoriasis
- ❖ Psoriatic Arthritis
- ❖ Sjogren's Syndrome

Key Project Deliverables



- **A robust clinical dataset** that can support rigorous interrogation of clinical correlates of molecular data
- **A highly curated data set that can be used to identify potential new targets.** This will potentially include high dimensional data for tissue resident and infiltrating cells at the single cell level in blood and tissues, gene expression, spatial mapping of cell types and states and mediators
- **Advance effectiveness of therapeutic targeting strategies.** Modelling of pathways active in target tissues, skin and blood, in RA, PSD, lupus and Sjogren's syndrome, including identification of pathways involved in early and pre-clinical disease in treatment response
- **Potential disease biomarkers.** Identify changes in peripheral blood (and urine) that reflects activation of specific pathways in the tissues
- **A suite of proven tools, technologies and SOPs,** to investigate tissues at the single cell level that can be applied to other autoimmune and inflammatory diseases
- **A queryable knowledge portal for facile public data interactions.** New computational tools to analyze and integrate high dimensional, multi-modal data sets into disease pathways including clinical features. A roadmap for how to apply contemporary molecular technology to similarly assess therapeutic strategies in additional inflammatory diseases of interest

AMP AIM Structure

