

27.06.2026

2^{ΟΣ} ΕΚΠΑΙΔΕΥΤΙΚΟΣ ΚΥΚΛΟΣ

ΜΥΟΣΚΕΛΕΤΙΚΟ ΣΥΣΤΗΜΑ

ΒΑΣΙΚΕΣ ΑΡΧΕΣ ΑΝΟΣΟΛΟΓΙΑΣ
ΚΑΙ ΜΗΧΑΝΙΣΜΟΙ ΙΣΤΙΚΗΣ ΒΛΑΒΗΣ
ΣΤΑ ΡΕΥΜΑΤΙΚΑ ΝΟΣΗΜΑΤΑ

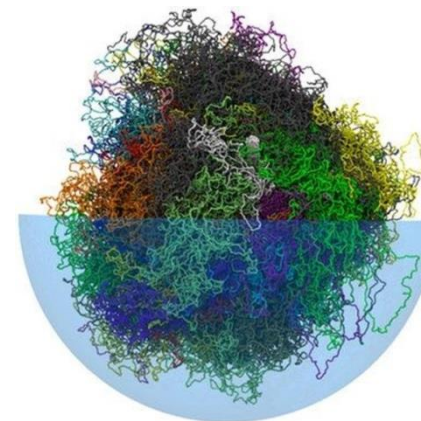
Webinars

ΕΛΛΗΝΙΚΗΣ ΡΕΥΜΑΤΟΛΟΓΙΚΗΣ
ΕΤΑΙΡΕΙΑΣ



ΕΛΛΗΝΙΚΗ ΡΕΥΜΑΤΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ
& ΕΠΑΓΓΕΛΜΑΤΙΚΗ ΕΝΩΣΗ
ΡΕΥΜΑΤΟΛΟΓΩΝ ΕΛΛΑΔΟΣ

Βιολογία συστημάτων (Systems Biology) στα ρευματικά νοσήματα



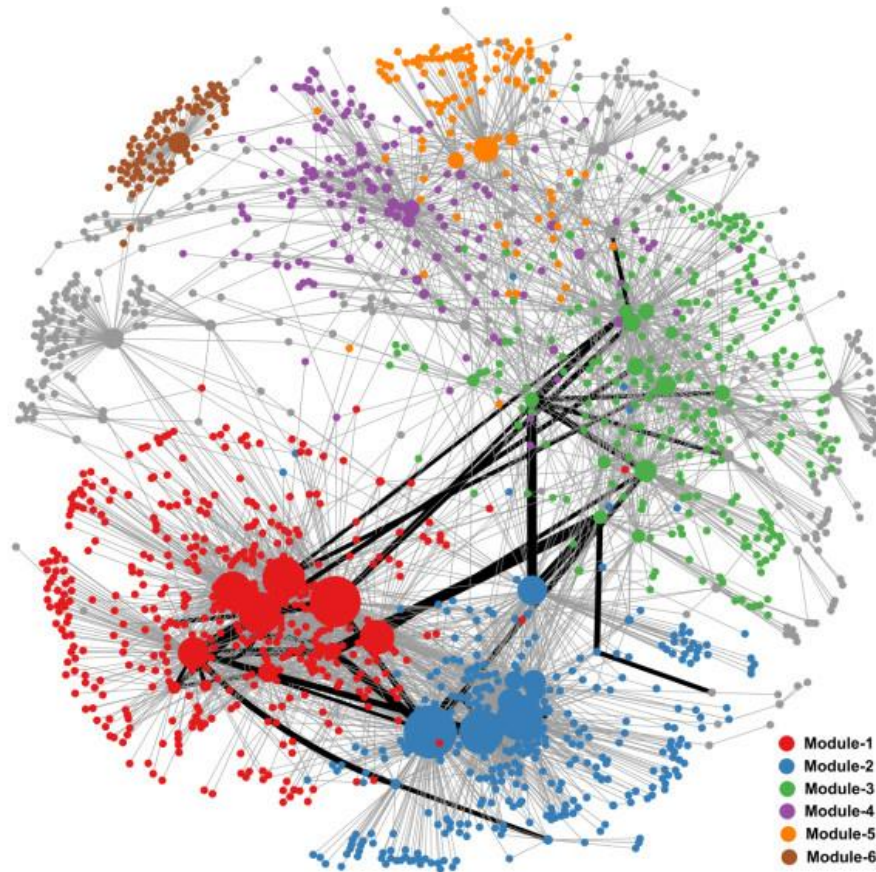
27.06.2026

Aggelos Banos, MD PhD

Assistant Professor of Internal Medicine/Rheumatology,
D PPK, Attiko Hospital
Affiliated Researcher - Laboratory of Inflammation and
Autoimmunity - BRFAA

Omics

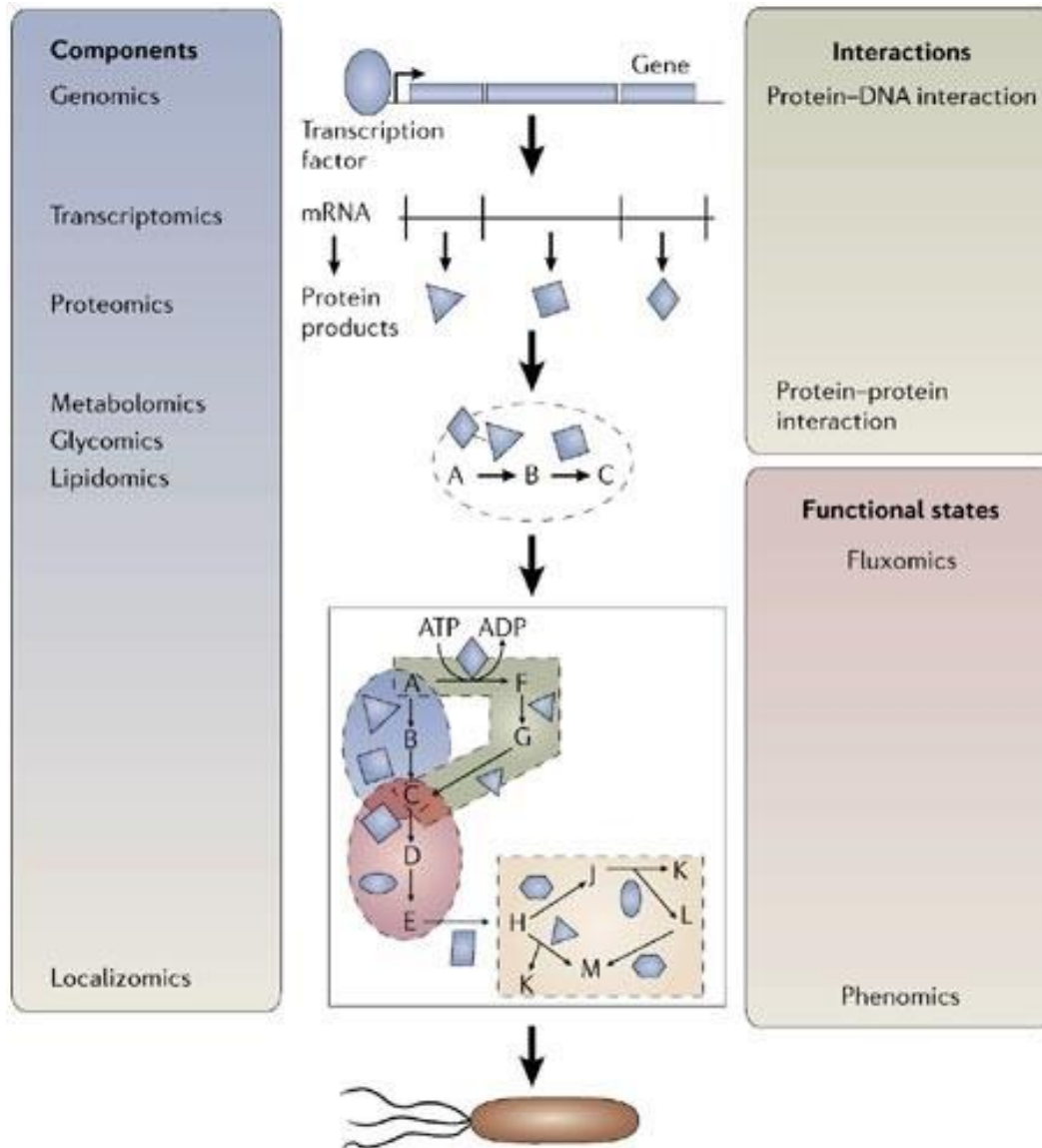
Big data/Next Generation Techniques



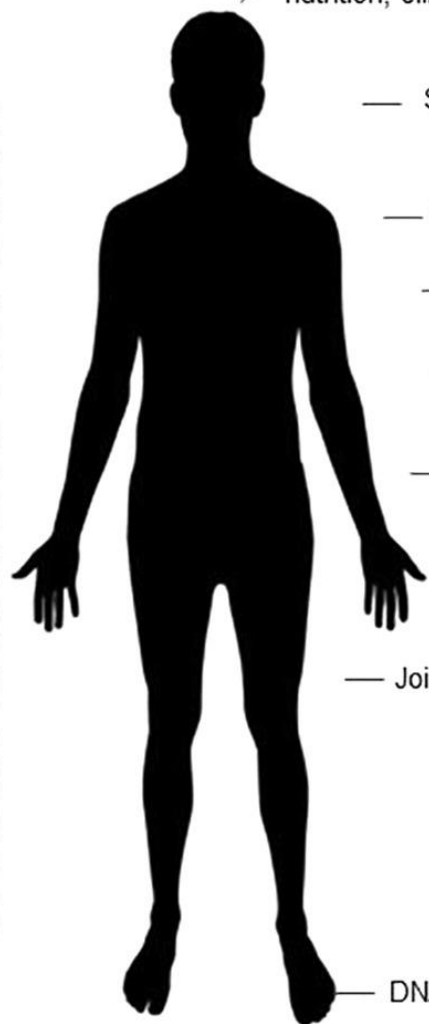
Gene regulatory networks in
Hepatocellular Carcinoma

-Omics: Large scale dataset in specific species of biomolecules or biological entities (holistic approach)

Communication of biological entities – Pathophysiology in detail



- Serial layers of –omics
- Elucidation of mechanisms
- Pathophysiological maps
- Casuality
- Therapeutical targets
- Personalized medicine



ENVIRONMENT

Behaviour, socioeconomic factors,
nutrition, clinical data, life history

— Saliva, oral mucosa —

— CSF —

— Skin (swabs, biopsies) —

— Sputum, BAL —

— Blood, Serum —

— Stool, Gut biopsies —

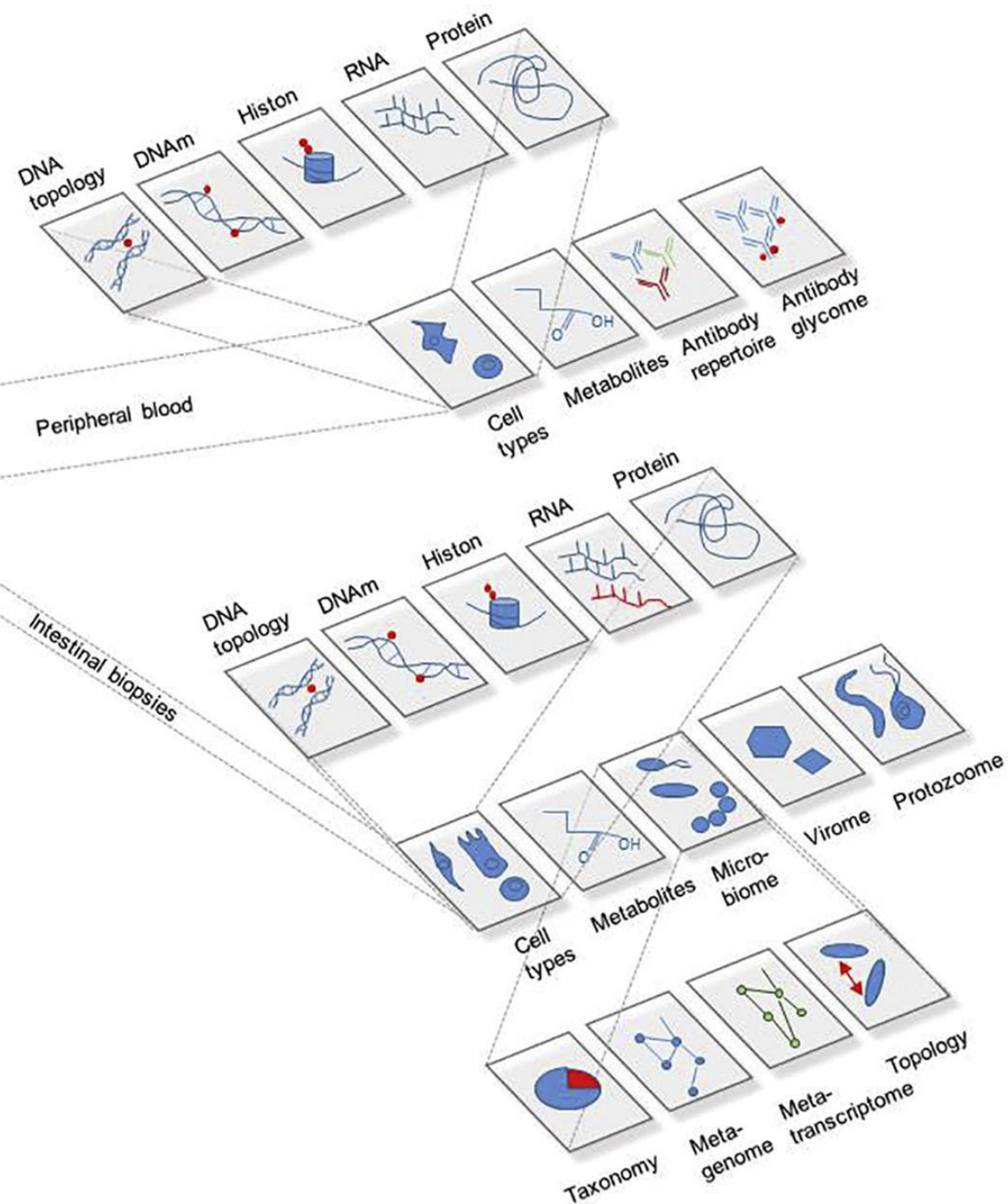
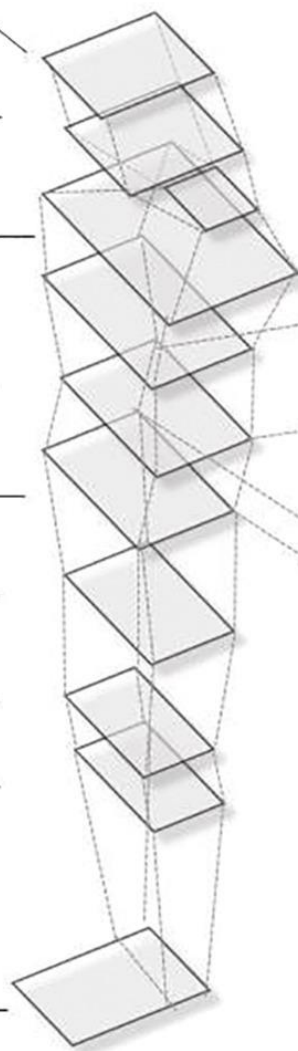
— UGT (Urine) —

— Joint (biopsy, aspirate) —

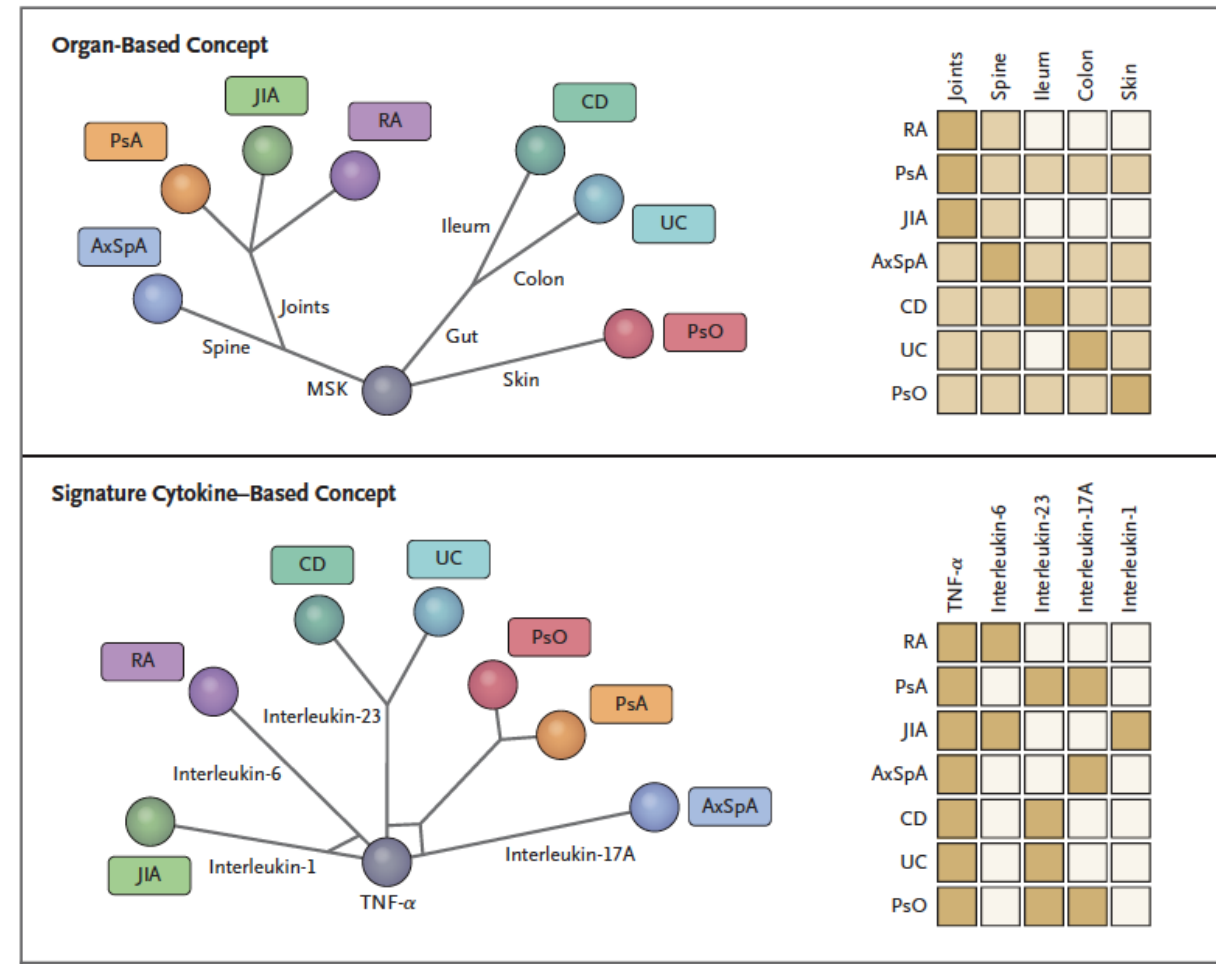
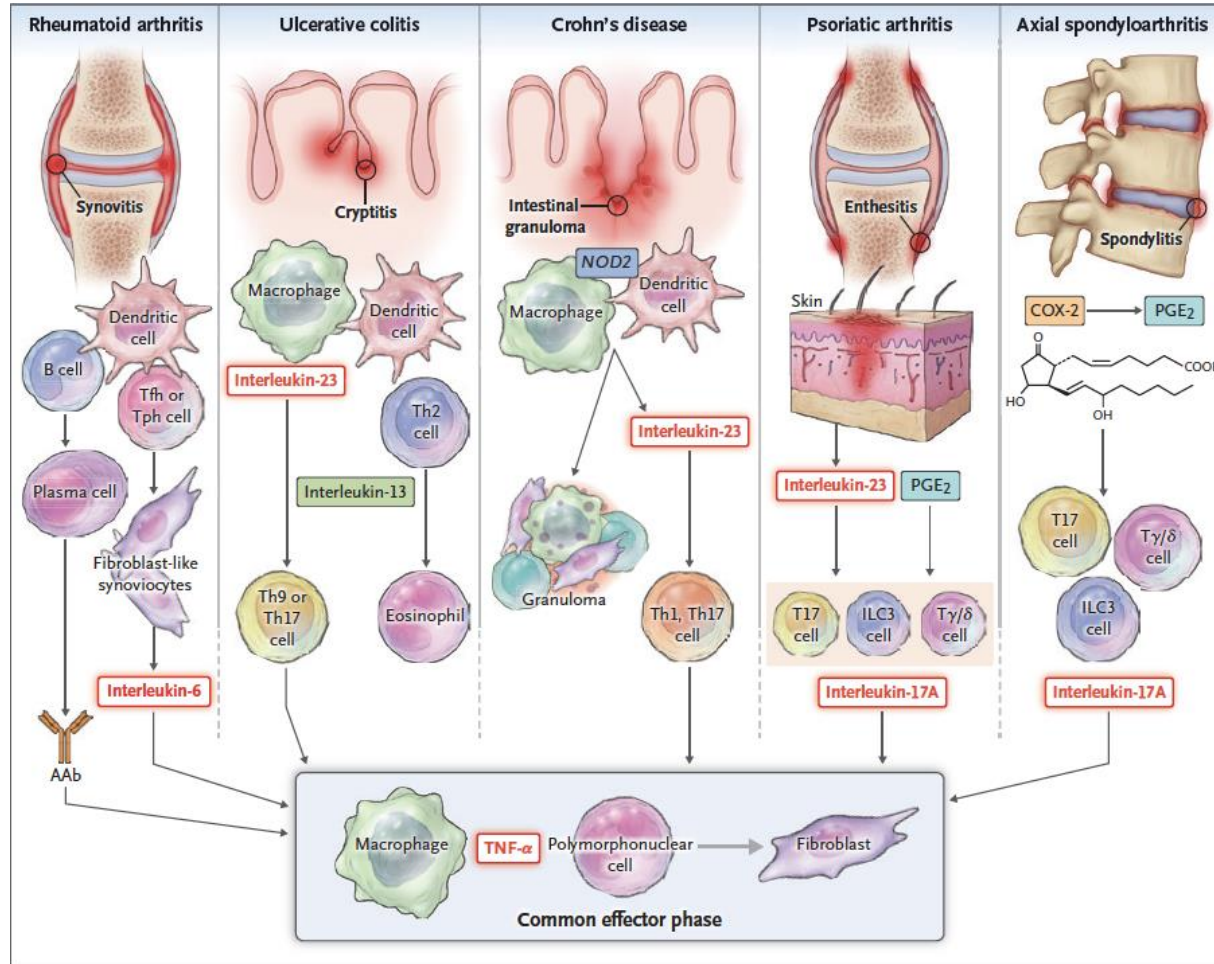
— Bone marrow —

— DNA Individual Genome —

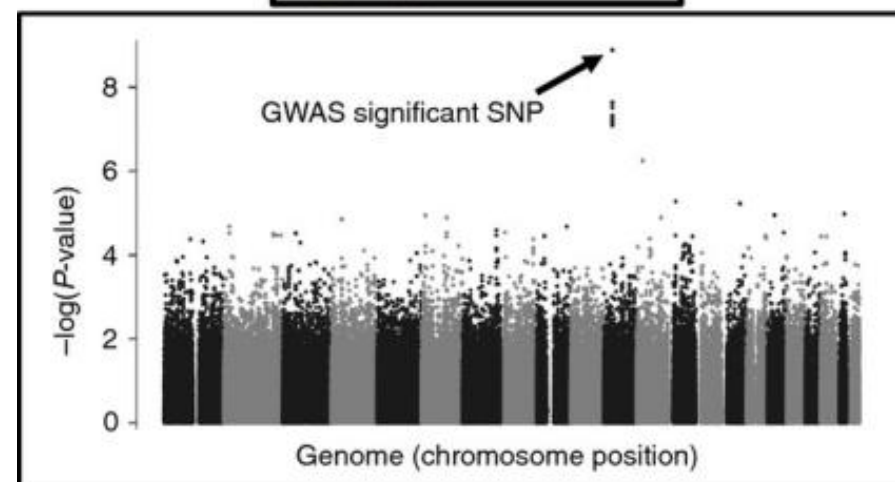
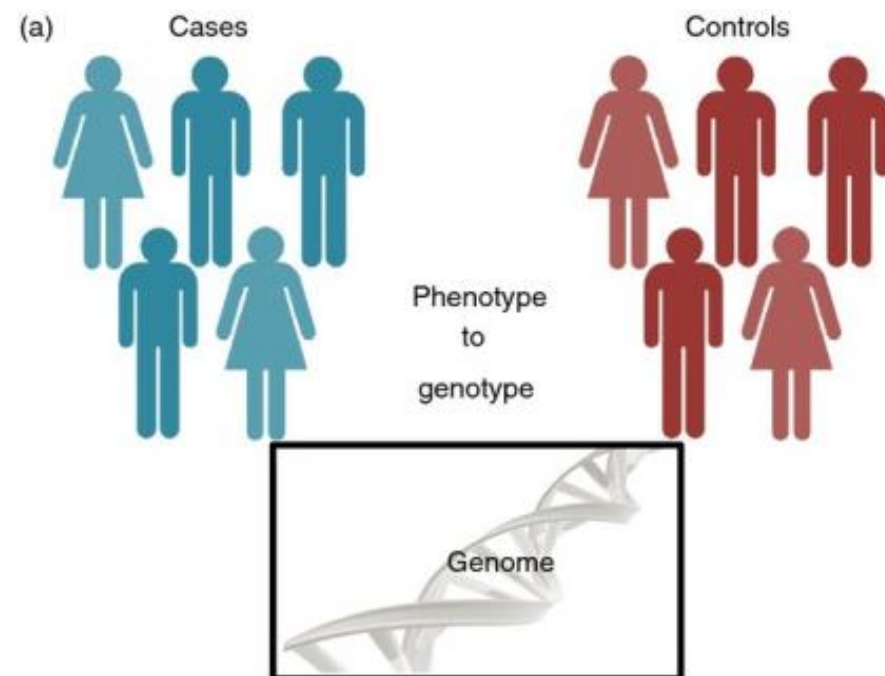
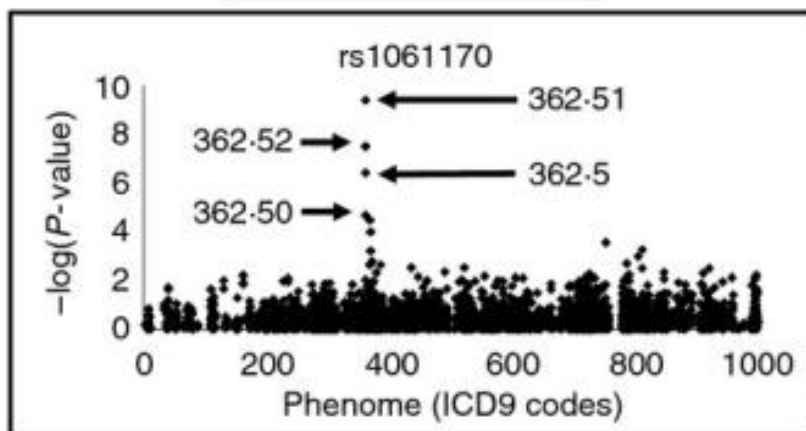
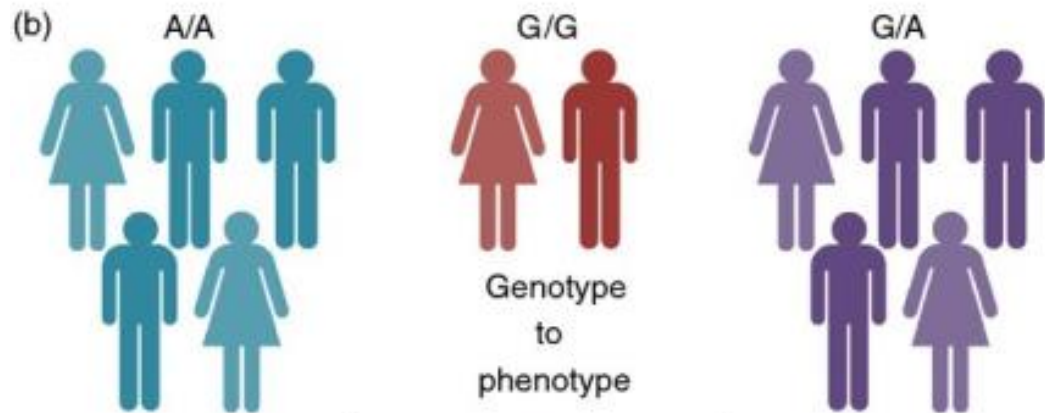
GENETICS



Reframing Immune-Mediated Inflammatory Diseases through Signature Cytokine Hubs



GWAS data



Generations of Sequencing Technologies

1st Generation



Sanger Sequencing

- Infer nt identity with dNTPs and visualize with capillary electrophoresis
- 500-1000 bp fragments
- Expensive, laborious, time consuming

Next Generation (2nd Generation)



Massive Parallel Sequencing

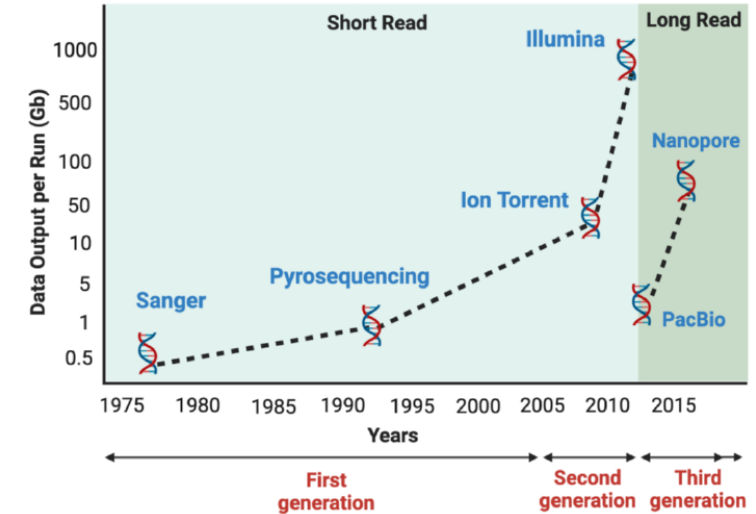
- High throughput from the parallelization of millions of sequencing reactions
- ~50-500 bp fragments

3rd Generation



Single Molecule Real Time
Long Reads Sequencing

- Sequence native DNA and/or RNA in real time with single-molecule resolution
- Tens of kb fragments



The Human Genome Project

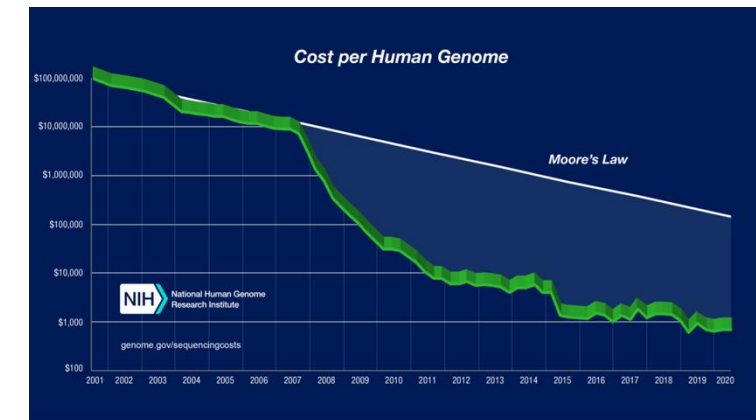


World's largest collaborative biological project

- Duration: 13 years (1990-2003)
- Cost: 3 Billion \$

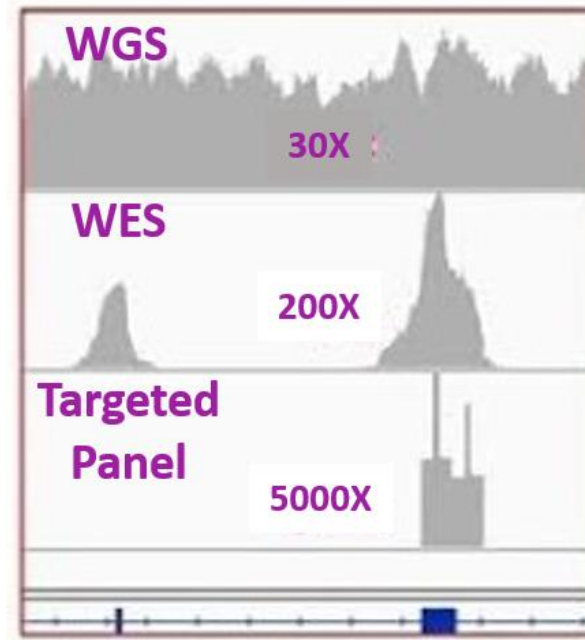
1 human Whole Genome:

- Duration: 48 hrs
- Cost: < 1000 \$



Flavors of genome sequencing

- **Whole Genome Sequencing:** every single bit, depending on depth, de novo assembly
- **Whole Exome Sequencing:** focus on protein-important events, cheaper, weak at regulatory events
- **Targeted Sequencing:** Evolution towards translational research, sequencing for less curious people



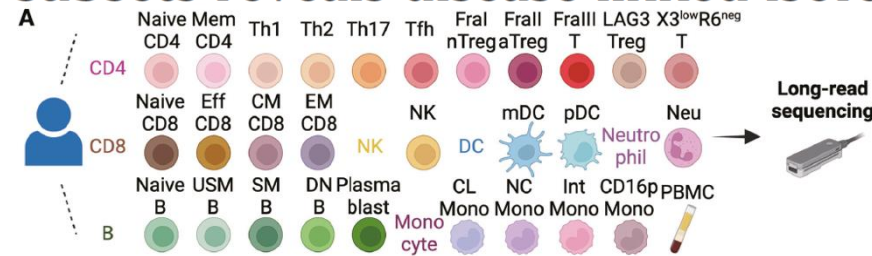
- 2% of genome
- 85% of disease causing variants
- Only targets of interest
- Seek specific disease causing variants

Long-read sequencing in diverse transcriptome usage in autoimmunity

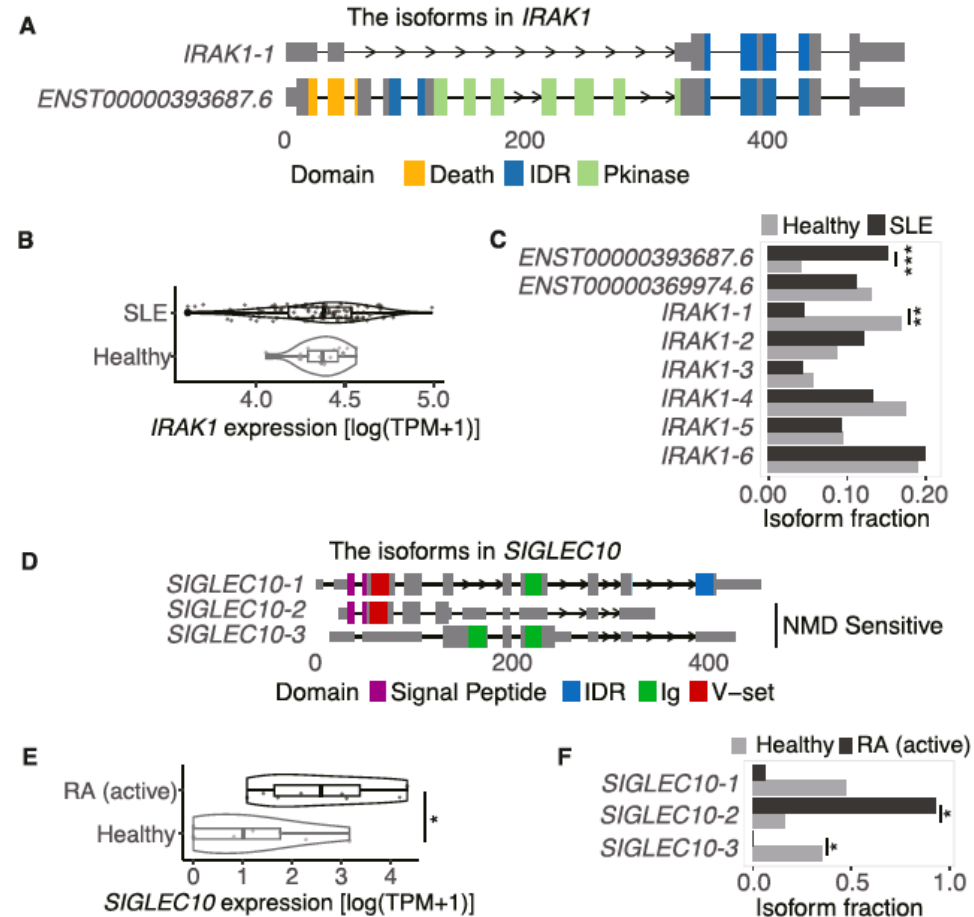
Article

<https://doi.org/10.1038/s41467-024-48615-4>

Long-read sequencing for 29 immune cell subsets reveals disease-linked isoforms



- Alternative splicing events → complex traits
- Full-length isoform annotation of 29 human immune cells (long-read sequencing)
- Characteristic isoforms and repetitive element → diversity
- Alternative 3' -UTR usage
- Disease-associated isoforms by isoform switch analysis



Genetic predisposition in EGPA

ARTICLE

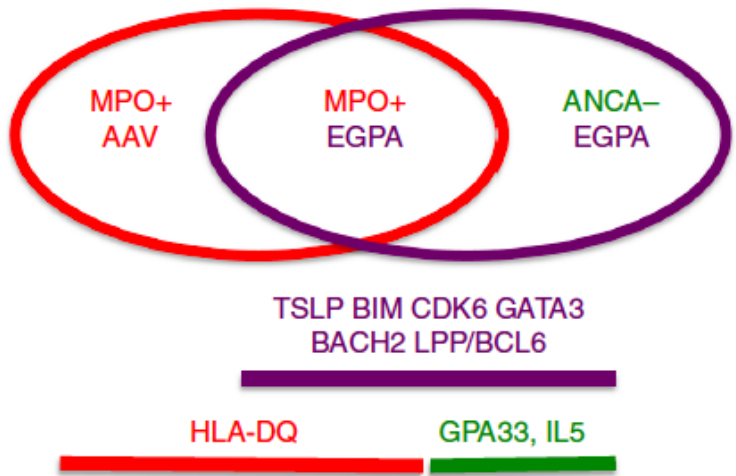
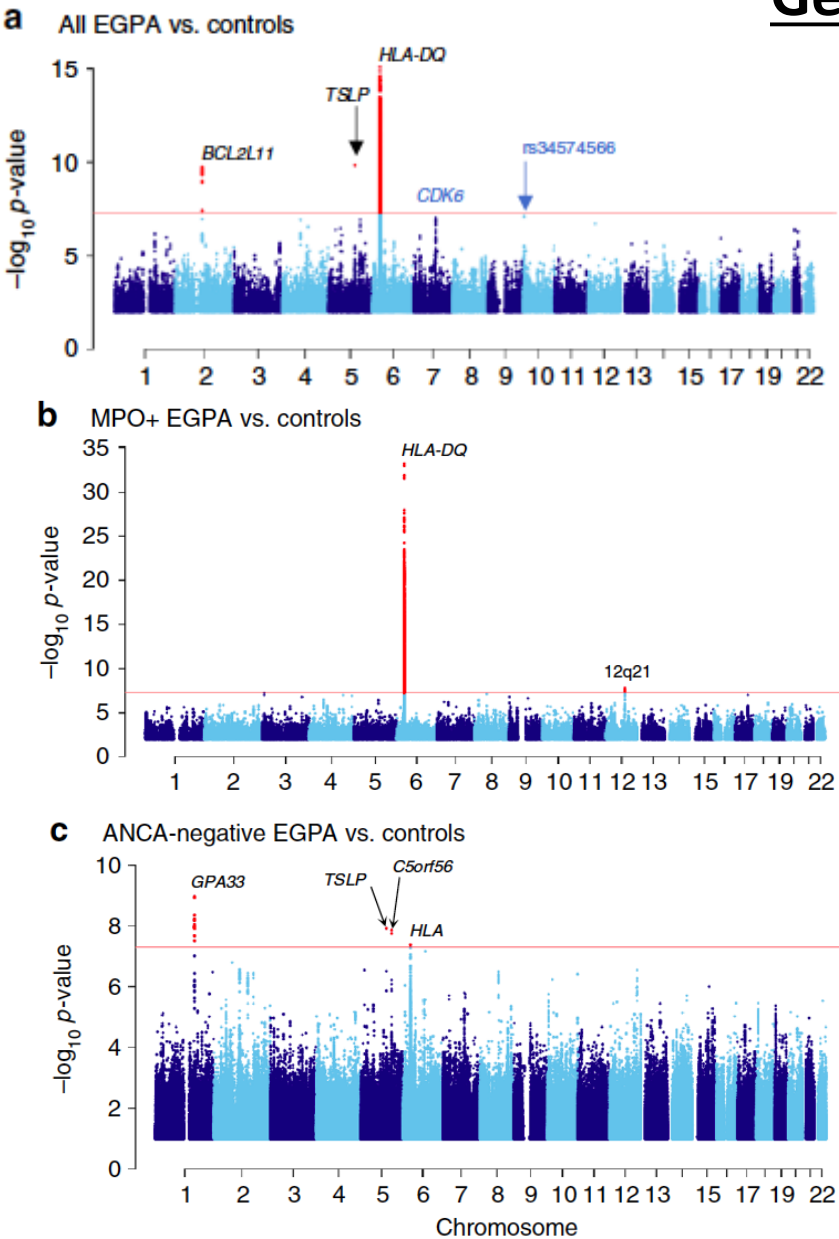
<https://doi.org/10.1038/s41467-019-12515-9> OPEN

Genome-wide association study of eosinophilic granulomatosis with polyangiitis reveals genomic loci stratified by ANCA status

Paul A Lyons et al.[#]

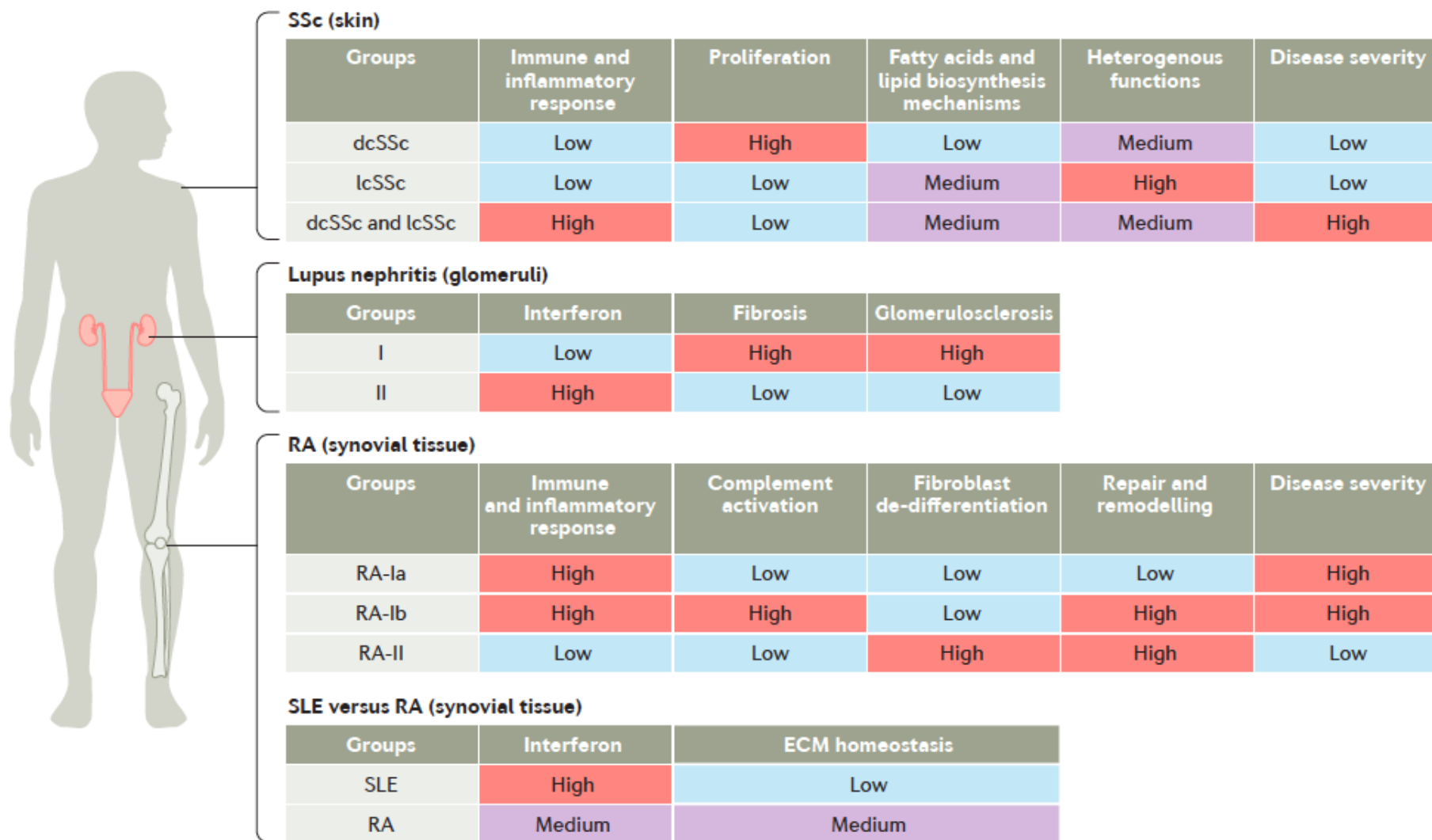
Table 2 Genetic associations with EGPA												
Chr	Variant rsid	Gene/ Region	Cont maf	Case maf	OR	Total EGPA N = 534			MPO+ EGPA N = 159		ANCA –ve EGPA N = 352	
						LMM P	Meta OR	Meta P	MPO OR	MPO P	OR	P
2	rs72946301	BCL2L11	0.1	0.17	1.66	1.9 × 10^{−10}	1.81	9.0 × 10^{−11}	1.89	7.7 × 10 ^{−5}	1.76	3.6 × 10 ^{−7}
5	rs1837253	TSLP	0.26	0.17	1.42	1.5 × 10^{−10}	1.52	5.2 × 10^{−11}	1.46	0.0008	1.53	1.2 × 10^{−8}
6	rs9274704	HLA-DQ	0.17	0.27	1.98	8.2 × 10^{−16}	2.01	1.2 × 10^{−20}	5.68	1.1 × 10^{−28}	1.32	0.004
10	rs34574566	10p14	0.31	0.24	0.73	8.0 × 10 ^{−8}	0.7	2.9 × 10^{−8}	0.66	0.0004	0.7	9.9 × 10 ^{−6}
7	rs42041	CDK6	0.24	0.31	1.32	1.9 × 10 ^{−6}			1.34	0.014	1.36	9.7 × 10 ^{−5}
5	rs11745587†	IRF1/IL5	0.35	0.4	1.31	2.1 × 10 ^{−7}			1.16	0.17	1.47	1.8 × 10^{−8}
6	rs6454802	BACH2	0.4	0.31	0.8	2.2 × 10 ^{−6}			0.81	0.024	0.74	3.8 × 10 ^{−6}
3	rs9290877	LPP	0.3	0.38	1.27	4.7 × 10 ^{−6}			1.48	0.0007	1.24	0.0006
1	rs72689399	GPA33	0.01	0.03	2.7	6.7 × 10 ^{−7}			0.89	0.96	5.34	1.1 × 10^{−9}
6	rs6931740	HLA	0.39	0.25	0.62	1.7 × 10^{−10}			0.55	1.6 × 10 ^{−5}	0.61	4.2 × 10^{−8}
12	rs78478398	12q21	0.03	0.05	0.59	0.0017			0.17	1.7 × 10^{−8}	0.81	0.37

Genetic predisposition in EGPA



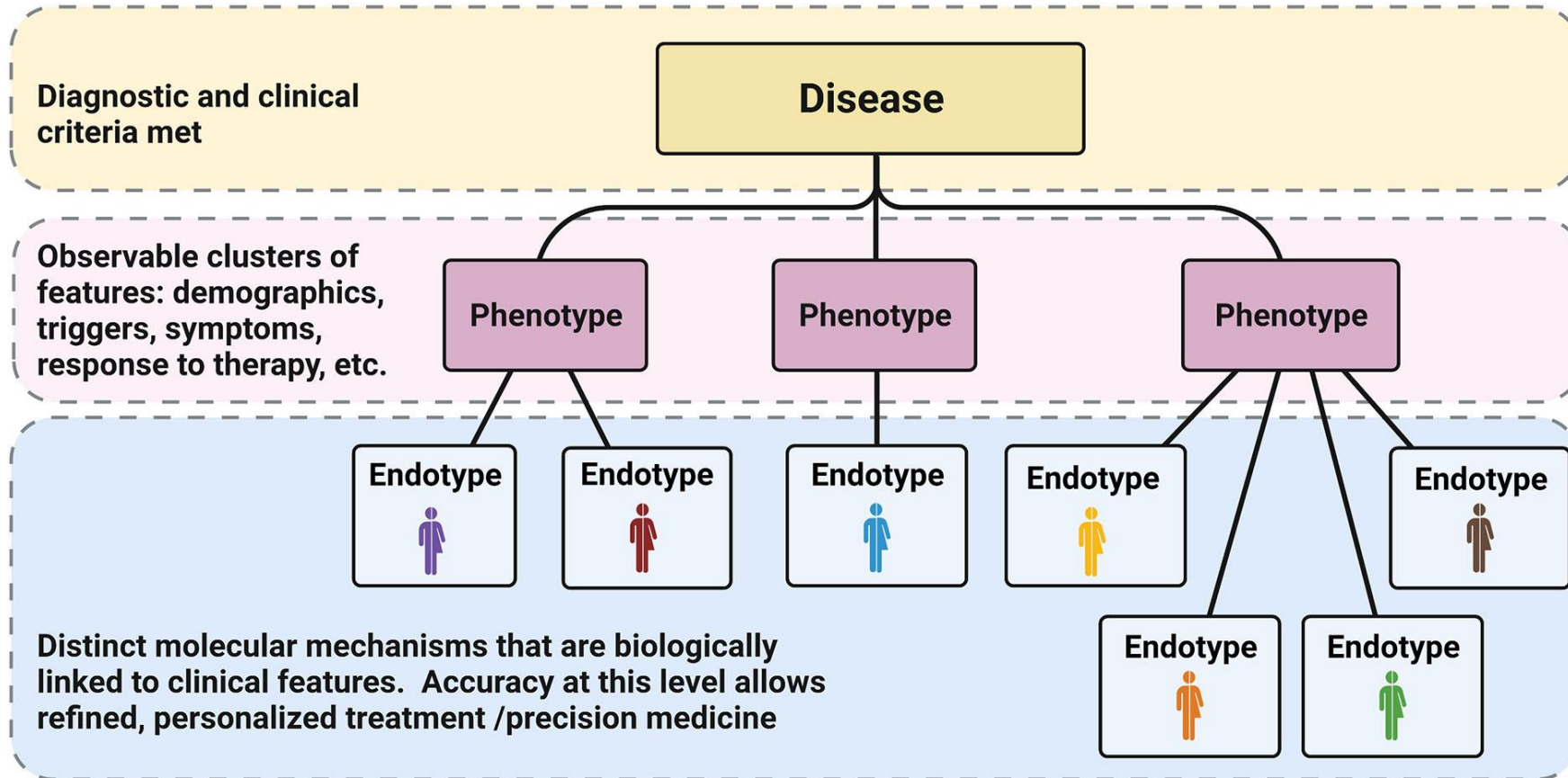
Clinical feature	% of patients with feature		
	MPO+ AAV (non EGPA)	MPO+ EGPA	ANCA- EGPA
Glomerulonephritis	85	29*	9
Neuropathy	20	79*	57
Asthma	n.d.	100	100
Eosinophilia	4.5	100	100
Pulmonary hemorrhage	17	4	4
Ear nose or throat	32	81	88
Pulmonary infiltrates	20	45	61*
Cardiac involvement	3	15	30*
Rituximab response	98	80	38

Molecular Taxonomy in Rheumatic Diseases



Molecular taxonomy based on transcriptome analysis

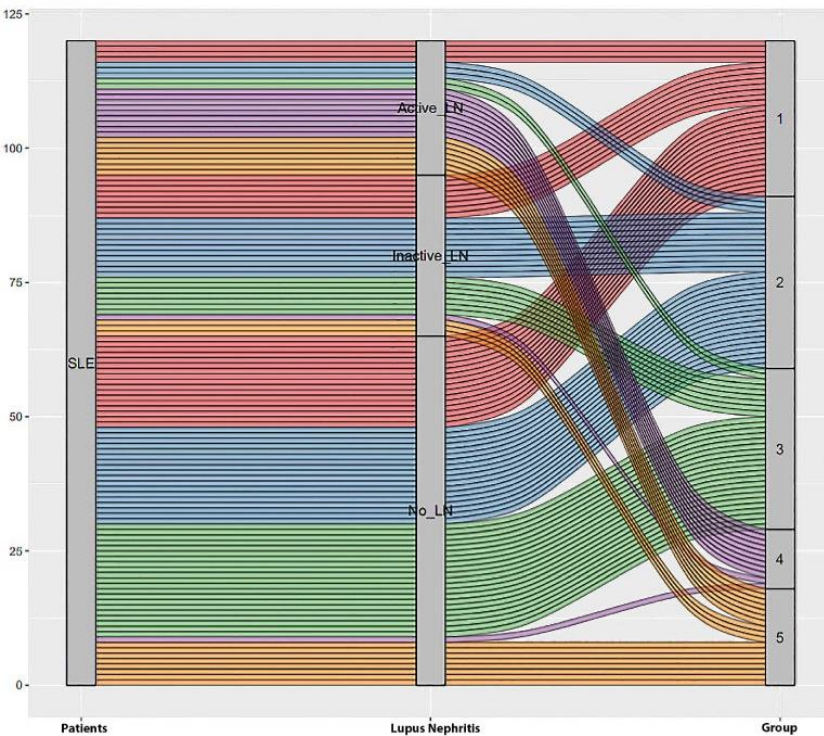
Molecular Disease Endotypes



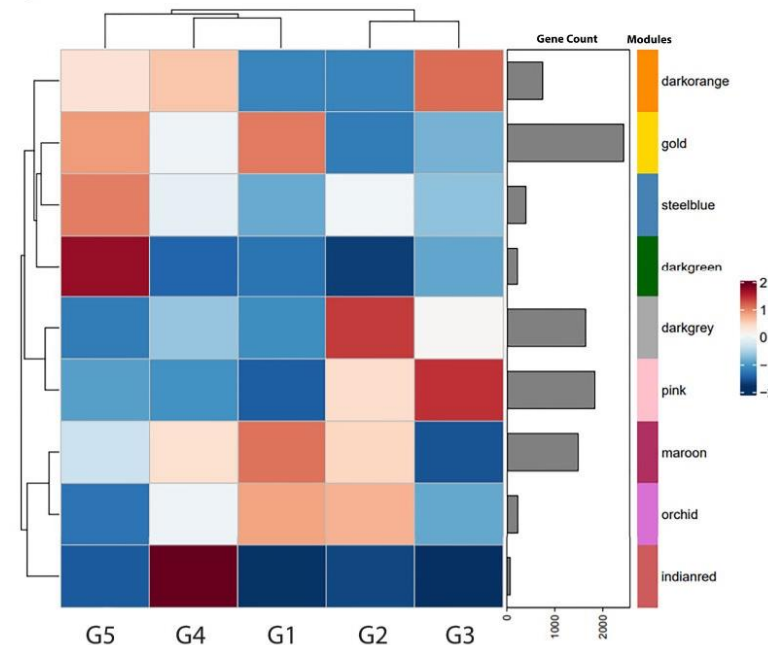
Molecular Taxonomy of Systemic Lupus Erythematosus Through Data-Driven Patient Stratification: Molecular Endotypes and Cluster-Tailored Drugs

frontiers | Frontiers in Immunology

B



C

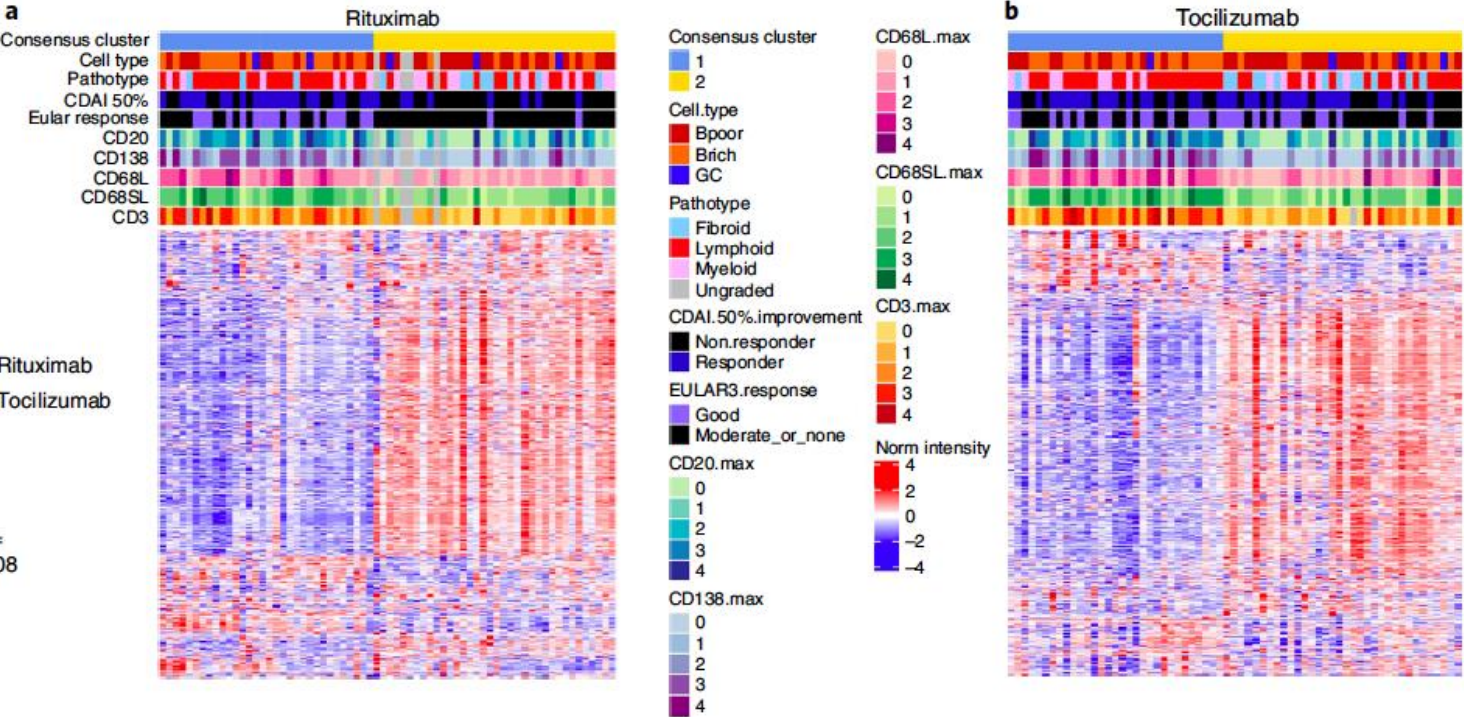
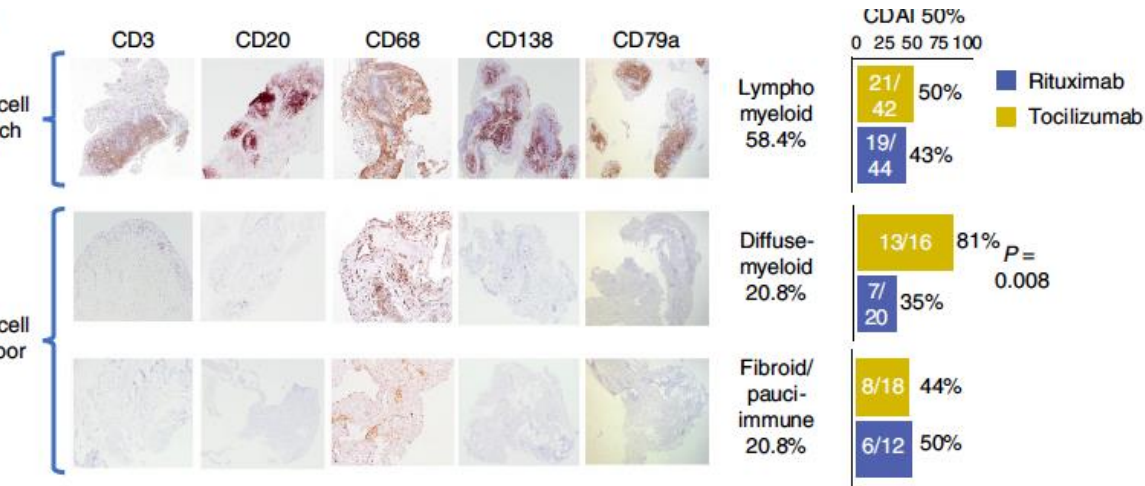


- 5 SLE endotypes characterized by a unique gene module.
- Neutrophilic signature consisted primarily of patients with active LN
- B-cell group included patients with constitutional features.
- Patients with moderate severity and serologic activity exhibited a signature enriched for metabolic processes.
- Mild disease was distributed in 2 groups, exhibiting enhanced basic cellular functions, myelopoiesis, and autophagy

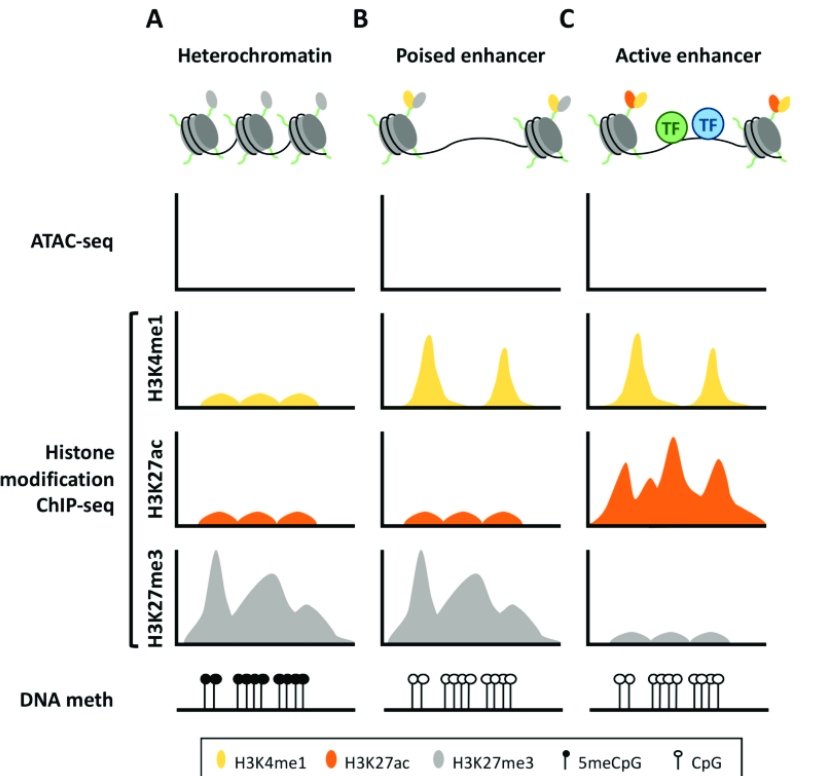
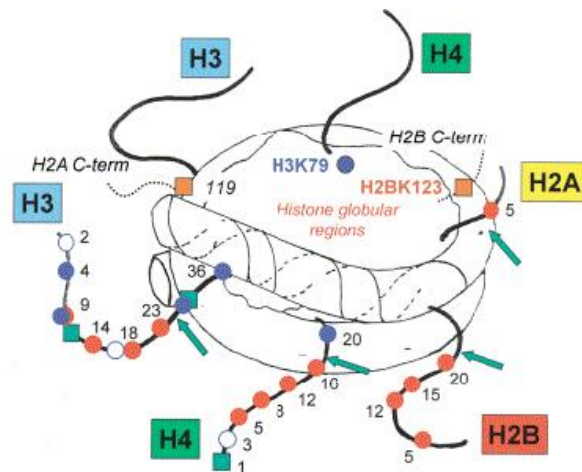
Biopsy-based disease endotyping before and after therapy in RA reveals diverse clinical and treatment–response phenotypes

ARTICLES
<https://doi.org/10.1038/s41591-022-01789-0>
 nature
 medicine

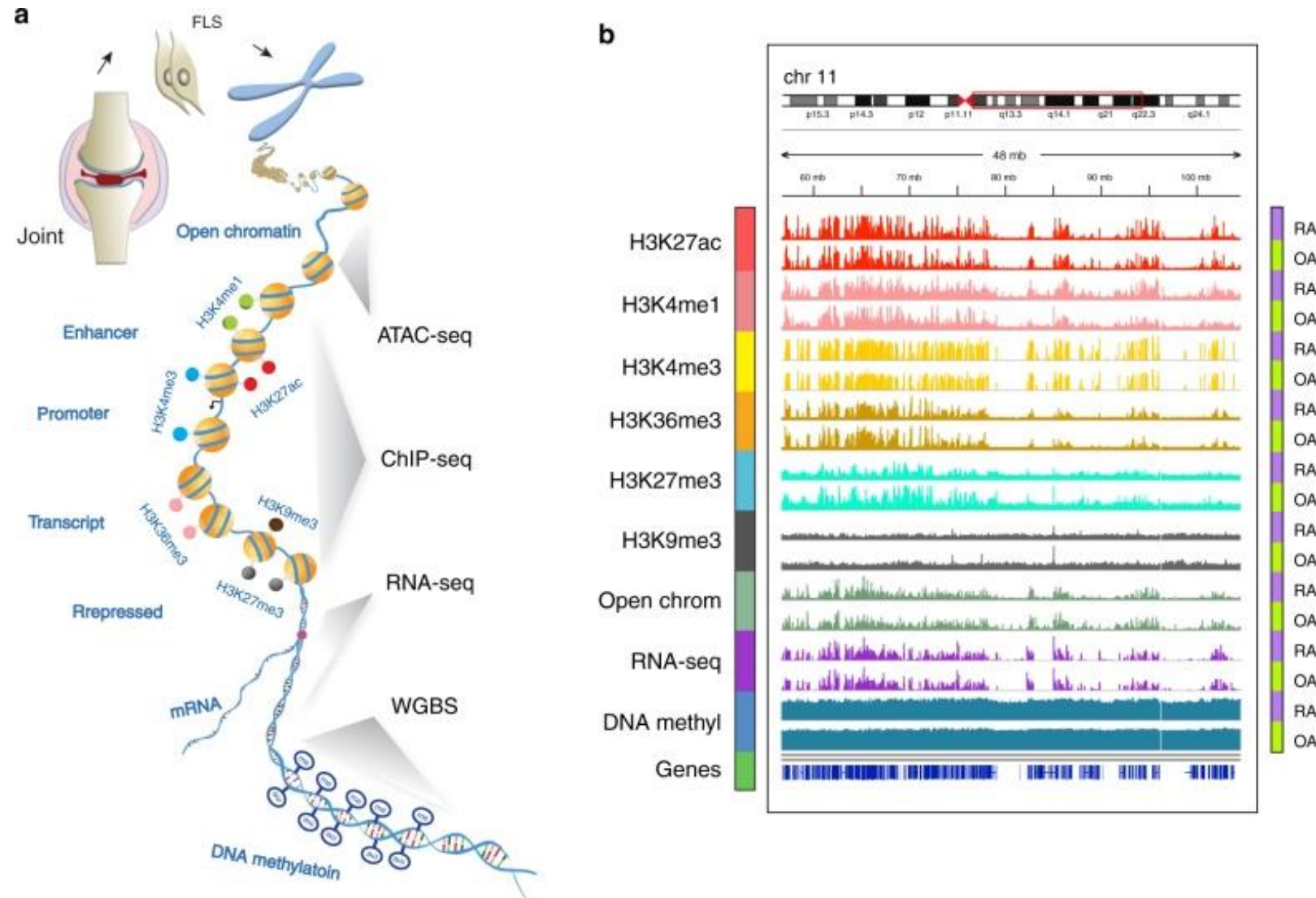
OPEN
 Rituximab versus tocilizumab in rheumatoid arthritis: synovial biopsy-based biomarker analysis of the phase 4 R4RA randomized trial



The diagram illustrates the hierarchical organization of DNA in a cell. It begins with a cell containing a nucleus, from which a **Chromatin Fiber** is extracted. This fiber is shown as a long, thin strand that can form loops containing **Genes**. A detailed view of the fiber shows it is composed of **Nucleosome** units, where DNA is wrapped around histone cores. **Regulatory DNA** is also indicated. The diagram further details the structure of a nucleosome, showing **DNA methylation** (green dots) and **Histone Modifications** (various colored shapes) on the histone tails. A section of the fiber is also shown with **RNA** being transcribed.



Comprehensive epigenetic landscape of rheumatoid arthritis fibroblast-like synoviocytes



- Characterization of DMERs
- Differentially modified epigenetic regions
- Integration of different omics
- Epigenetic landscape sets new light on the genetic load and its pathophysiological mechanisms

Spatial transcriptomics: Cell-specific gene expression in spatial detail



Bulk RNASeq

Assess unbiased gene expression

Can measure mean gene expression in high fidelity

Cannot delineate cell type heterogeneity based on gene expression



Single-Cell RNASeq

Characterize cellular heterogeneity

Can delineate cell type heterogeneity based on gene expression

Cannot put the cell type phenotype into the tissue context

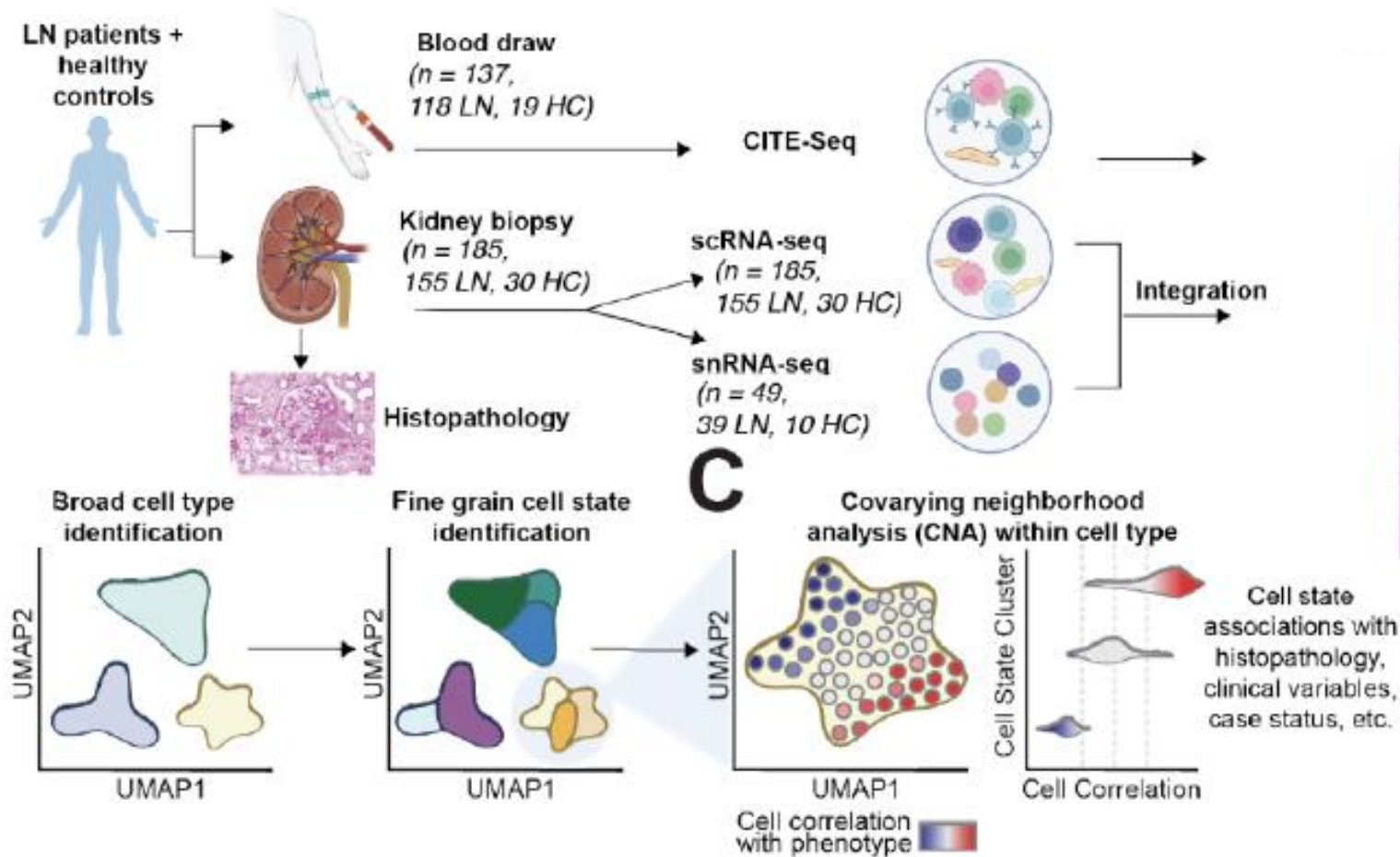


Spatial transcriptomics

Spatial context of tissue architecture

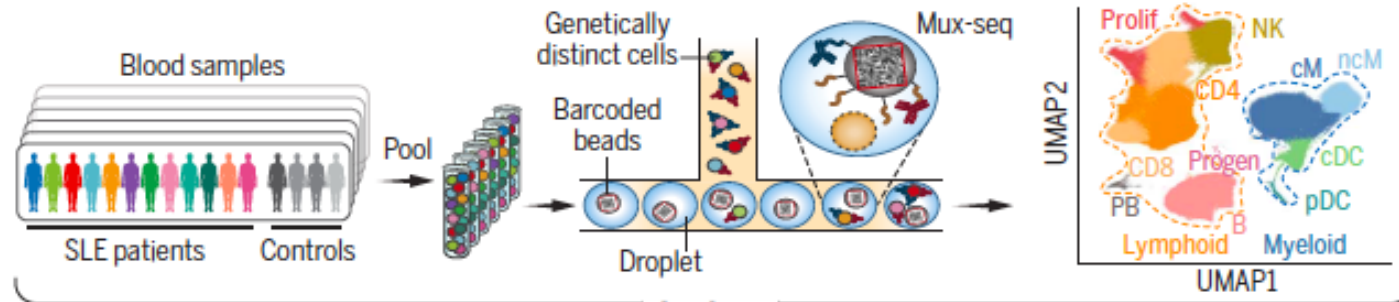
Tissue context cell type specific gene expression map

A population-scale atlas of blood and tissue in lupus nephritis



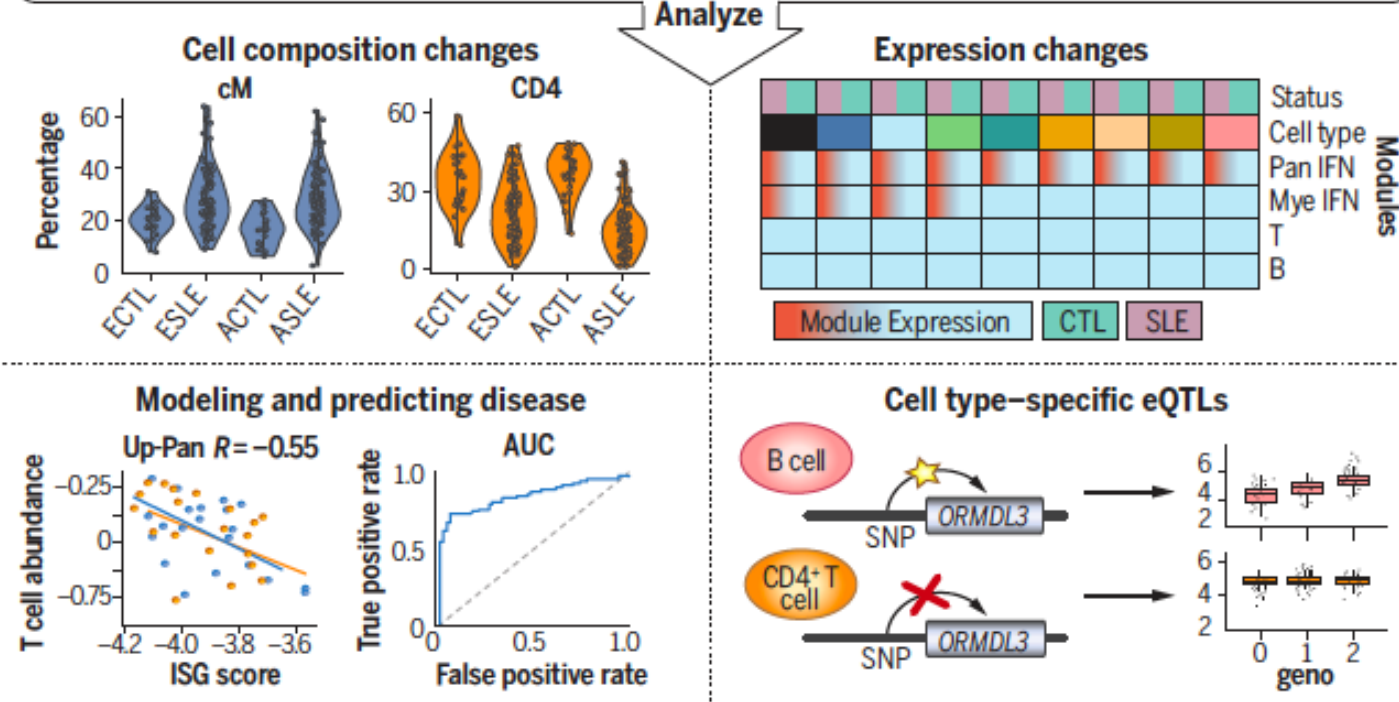
- 538k single-cell and 140k single nuclear profiles from kidney biopsies ($n=155$)
- Tissue specific cell states
- Association with irreversible chronic tissue damage
- **SAMs (Scar Associated Macrophages)** → appear with increasing inflammatory disease activity and drive LN fibrosis
- Myeloid populations as therapeutic targets in LN

Census of immune cells in systemic lupus erythematosus

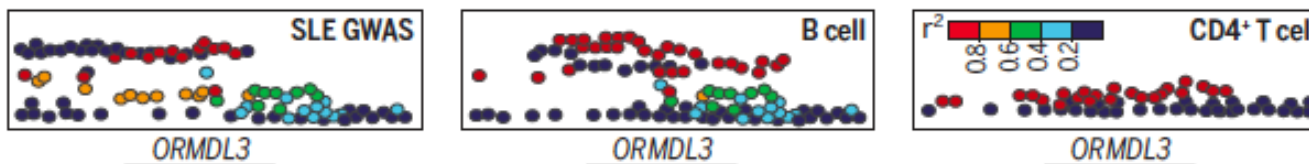


IMMUNOGENOMICS

Single-cell RNA-seq reveals cell type-specific molecular and genetic associations to lupus

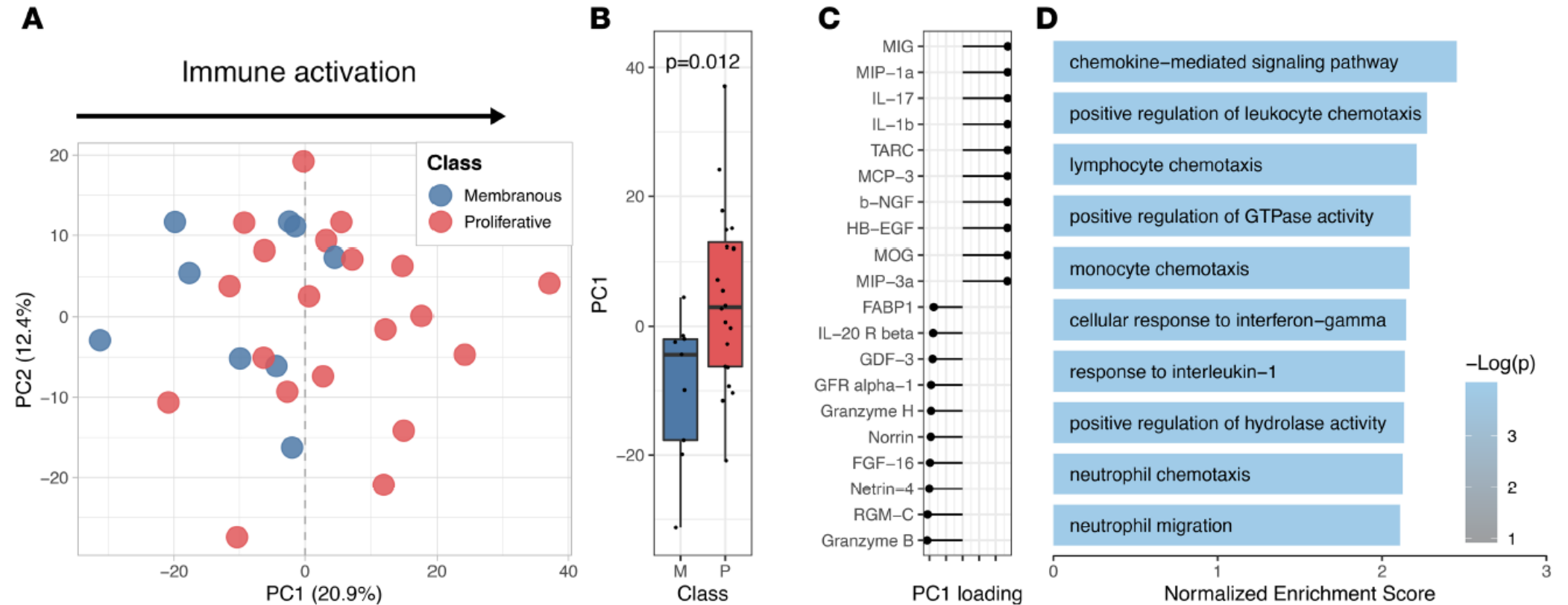


Annotation of GWAS with cell type-specific eQTLs

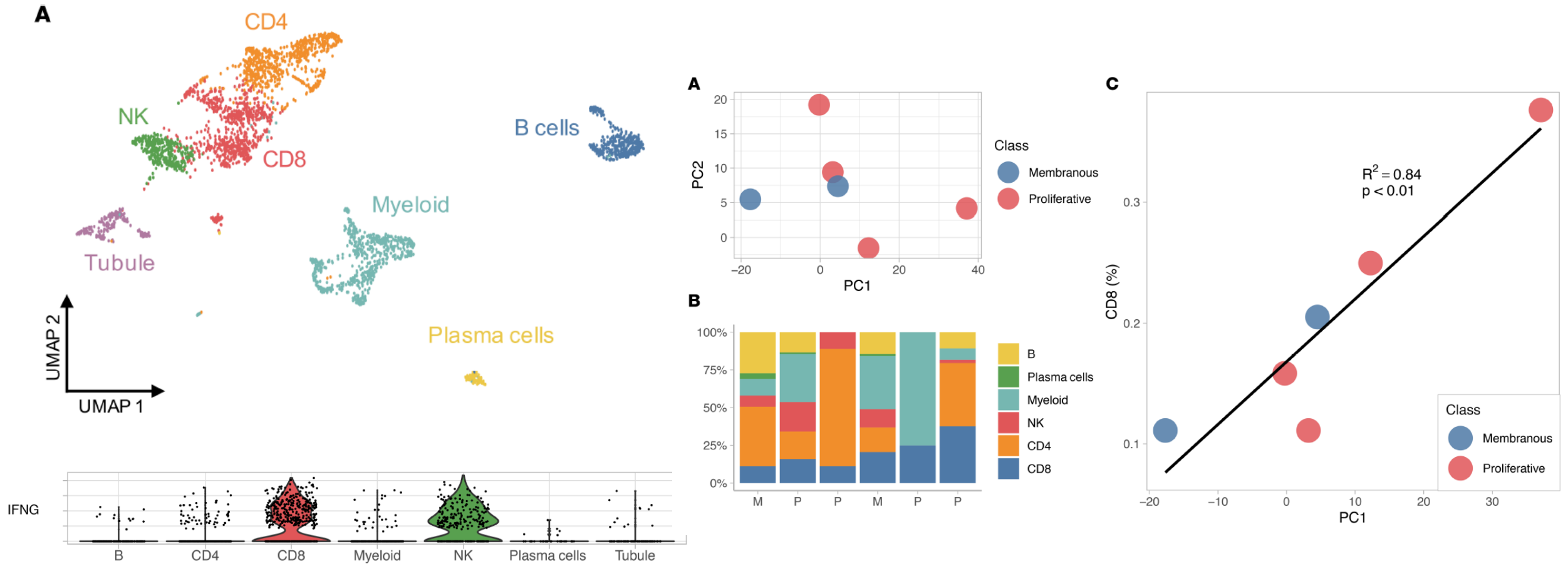


- Unique maps of cell heterogeneity within hundreds of patients
- Integration with genetic and epigenetic layer
- Cell-type specific effects
- Gene modules for disease prediction

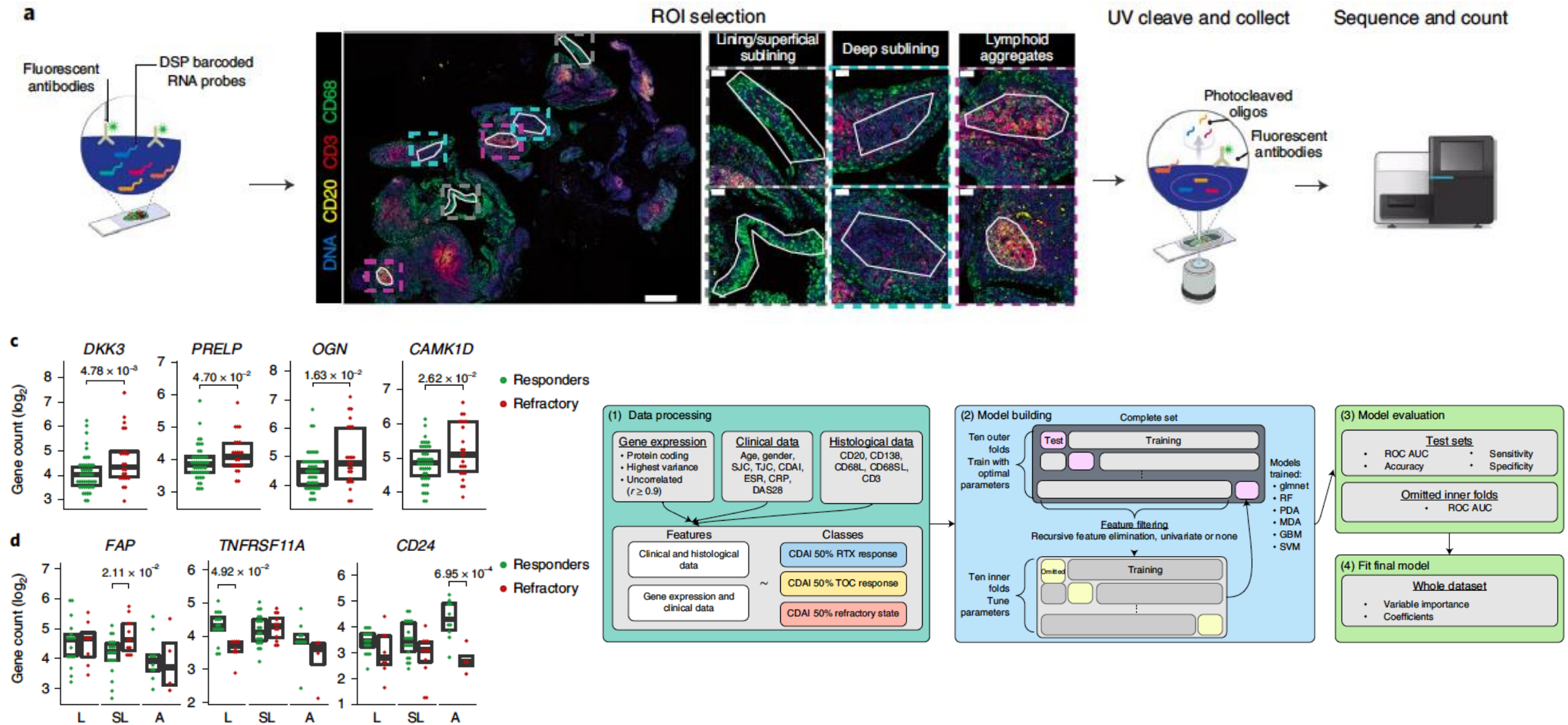
Proteomics analysis in urine leads to stratification of SLE patients according to kidney damage



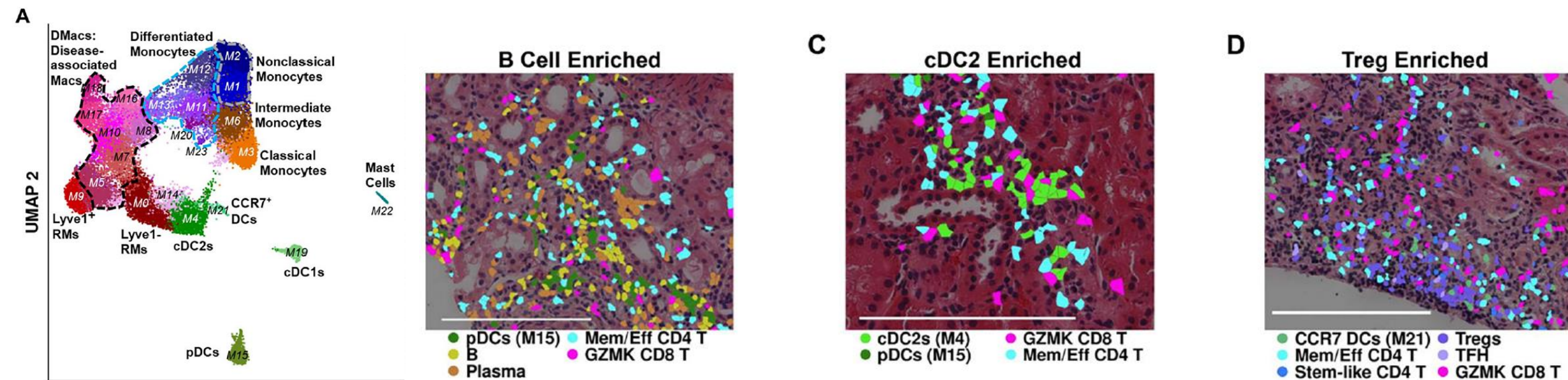
Proteomics analysis in urine leads to stratification of SLE patients according to kidney damage



The future of Transcriptomics and Personalized Medicine – Spatial Transcriptomics



Deep profiling of lupus nephritis kidneys reveals dynamic changes in myeloid cells associated with disease progression

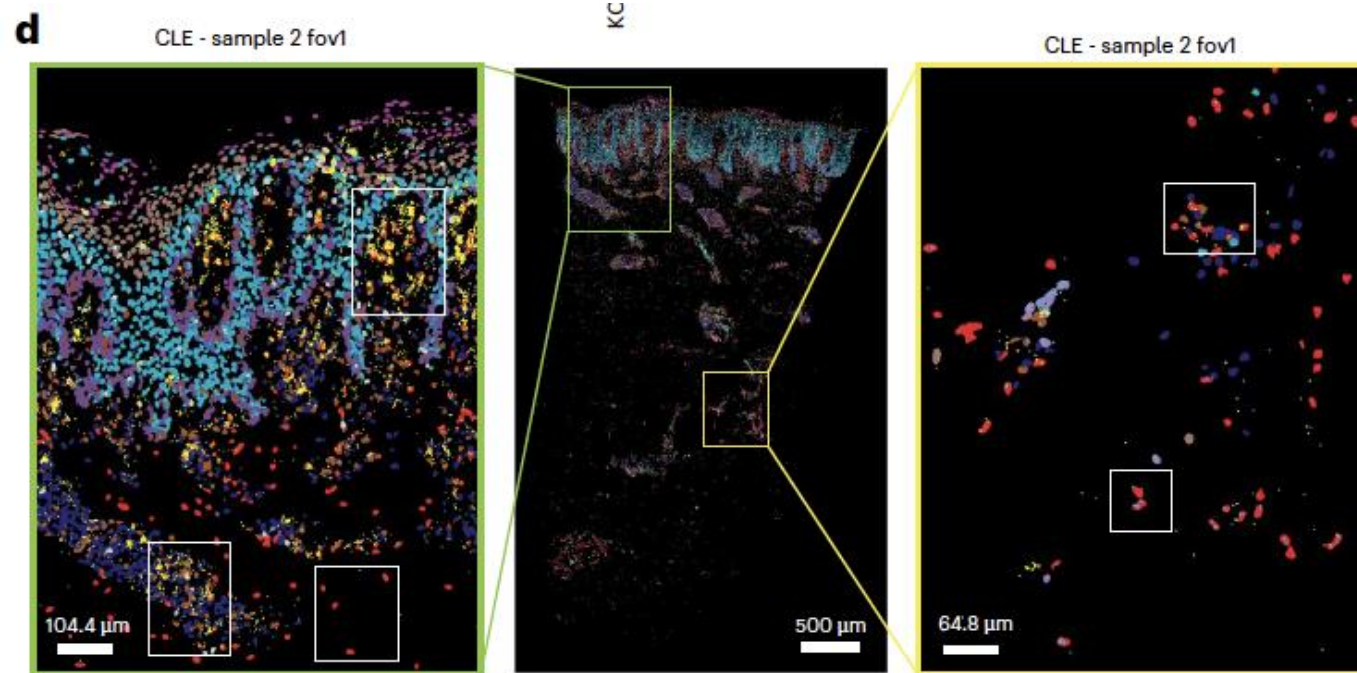


scRNA-seq of kidney samples from 156 LN patients – spatial transcriptomics(ST), myeloid –focusing

Chronicity index (CI) – association with **switch of the local immune response from Mo/Mφs to expanded CD4T, GZMK⁺ CD8 T, B and dendritic cells** – parallel decrease in IFN response

Proliferative/mixed LN → expansion of **disease-specific Mφs (DMac)**, arising from both infiltrating monocytes and tissue-resident macrophages; and interacting with parietal epithelial cells, promoting glomerulosclerosis.

A spatially coordinated keratinocyte–fibroblast circuit recruits MMP9⁺ myeloid cells to drive type I interferon-driven inflammation in photosensitive autoimmunity



Myeloid cells as critical mediators of photosensitivity in Lupus and DM

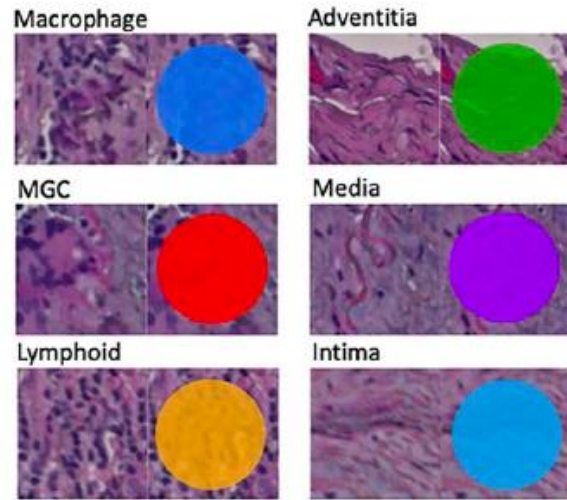
Expansion in lesional skin, **production of IFN β** and colocalization with cytotoxic CD4⁺ T cells at the dermal–epidermal junction

Keratinocytes activate fibroblasts, prompting them to release chemokines

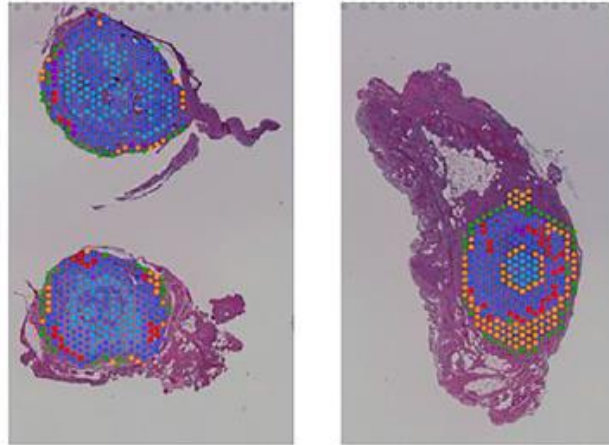
Anti-type I interferon treatment with **anifrolumab** prevented UVB-induced myeloid infiltration and reduced photosensitivity

Matrix metalloproteinase 12 (MMP12) as a novel signature molecule in systemic vasculitis

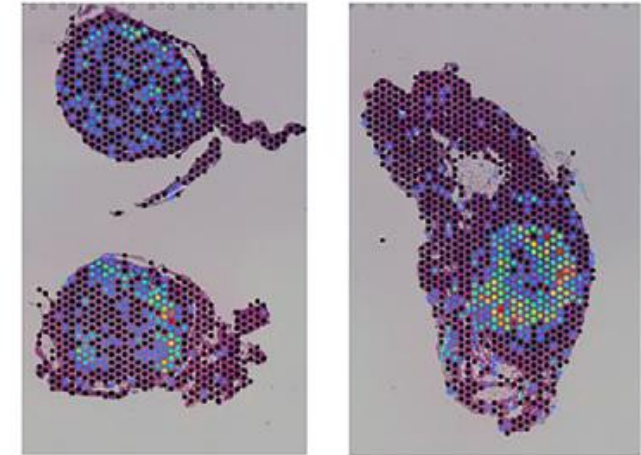
Temporal arteries in patients with giant cell arteritis



B

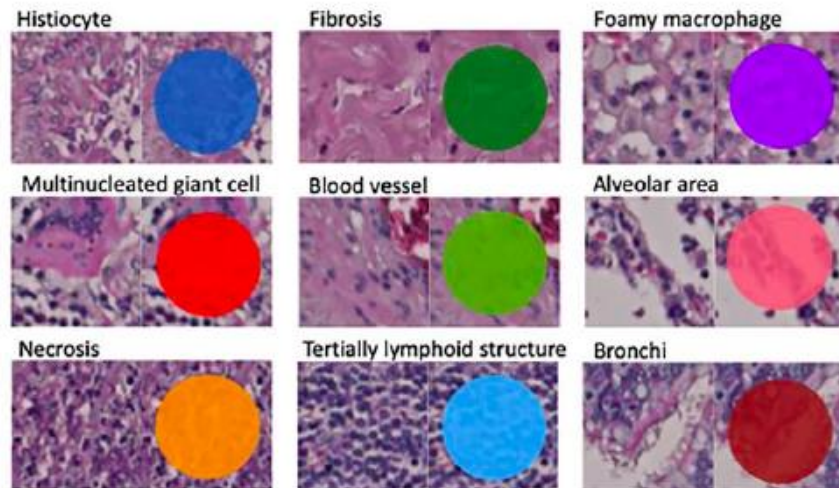


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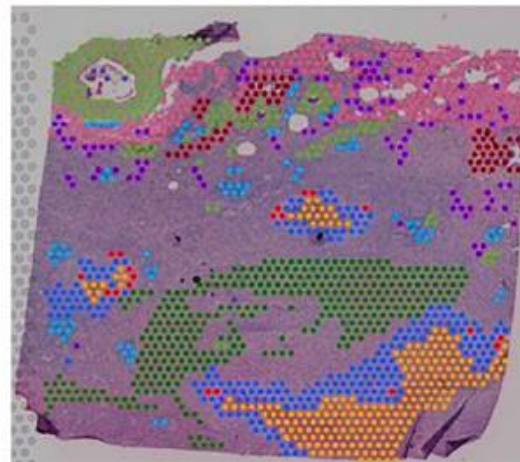


Log2 Exp - MMP12
0.0 6.0

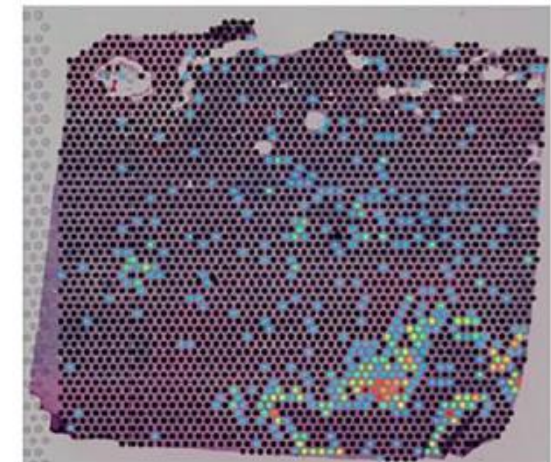
Lung of a patient with granulomatosis with polyangiitis



B



C

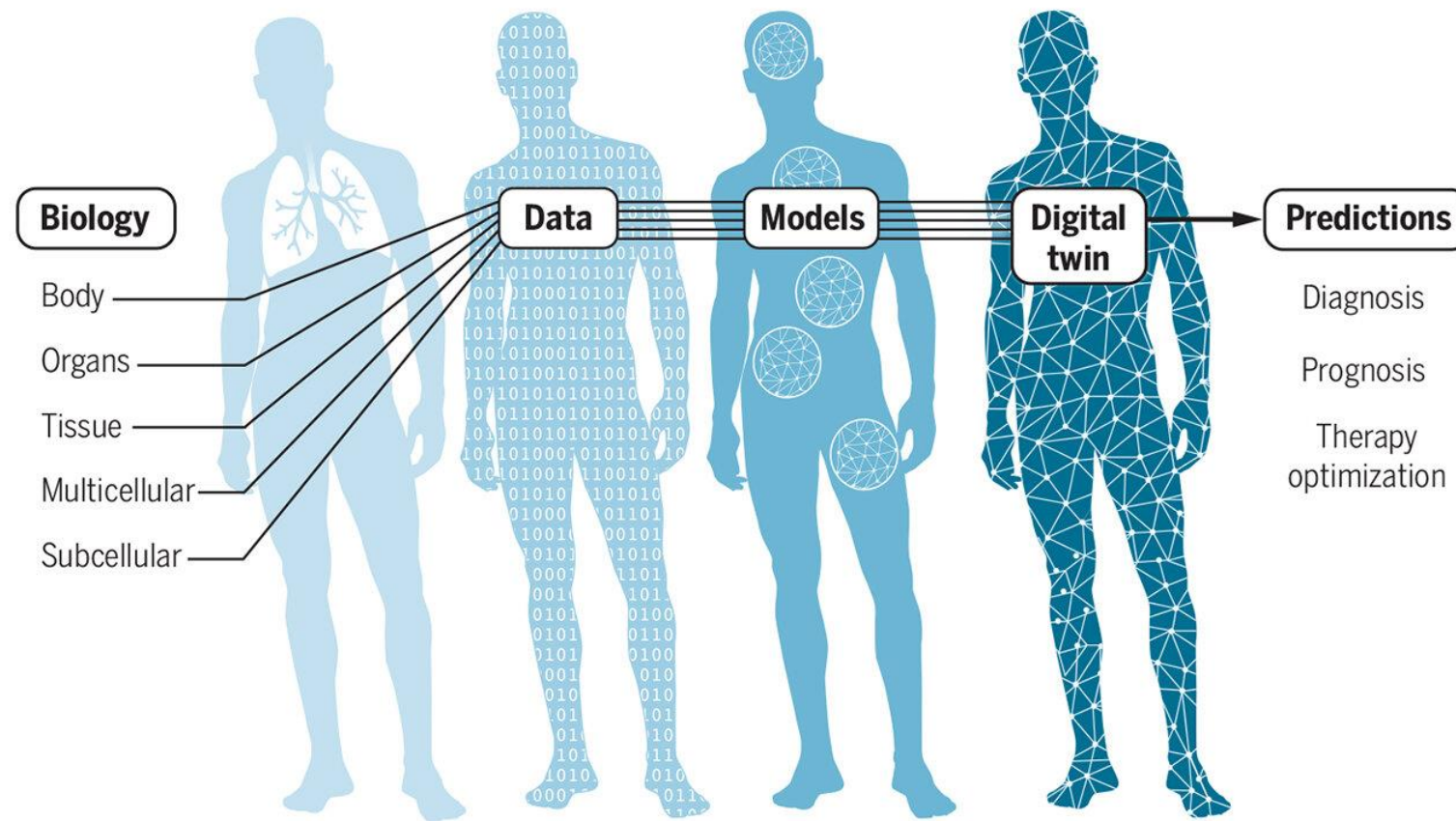


Log2 Exp - MMP12
0.0 6.0

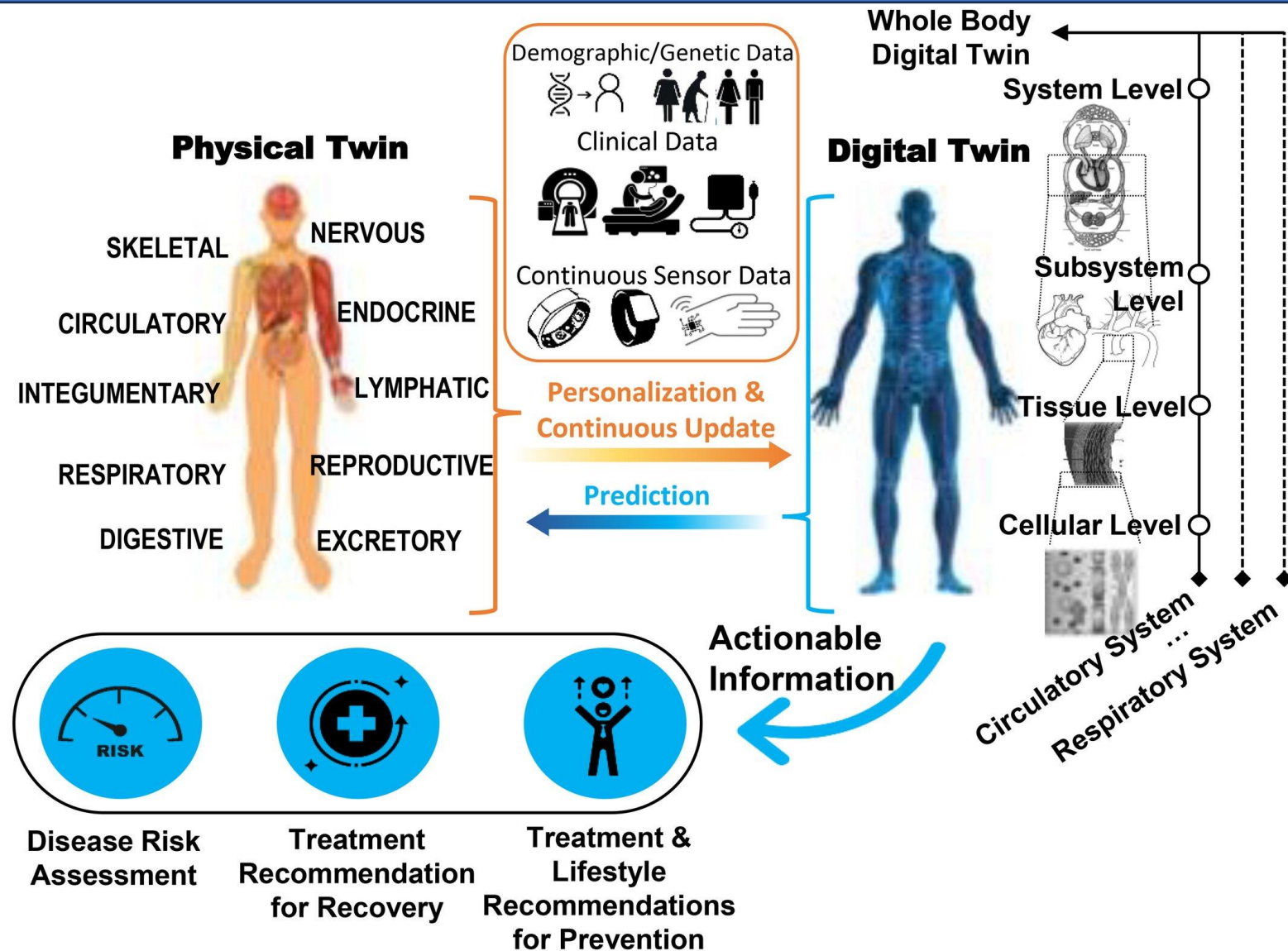
The idea of the digital twin

Building a personalized digital twin

Data from multiple scales are needed to build computational representations of biological processes and body systems that are affected by viral infection. These submodels are integrated and personalized with clinical data from individual patients. The digital twin can then be used to derive predictions about diagnosis, prognosis, and efficacy and optimization of therapeutic interventions.



The idea of the digital twin



Take-home messages

- Systems Medicine initiates a new era in Rheumatology, providing novel tools in clinical practice
- Pathophysiological mechanisms, previously unknown are elucidated through -omics
- Genetic basis of each disease is seen through a new lens
- Single cell studies are conquering almost all rheumatic diseases from various aspects
- Personalized medicine is based solely on systems approach
- Future studies will analyze spatial cell characteristics of causal and inflamed tissues



Thank you!