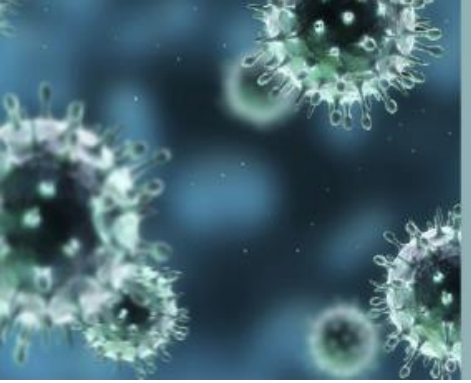

3ο ΣΧΟΛΕΙΟ ΒΑΣΙΚΗΣ ΑΝΟΣΟΛΟΓΙΑΣ ΓΙΑ ΚΛΙΝΙΚΟΥΣ

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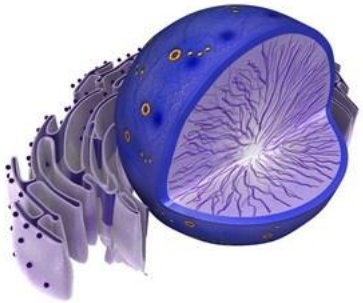
8–10 ΟΚΤΩΒΡΙΟΥ 2021 ΗΡΑΚΛΕΙΟ ΚΡΗΤΗ

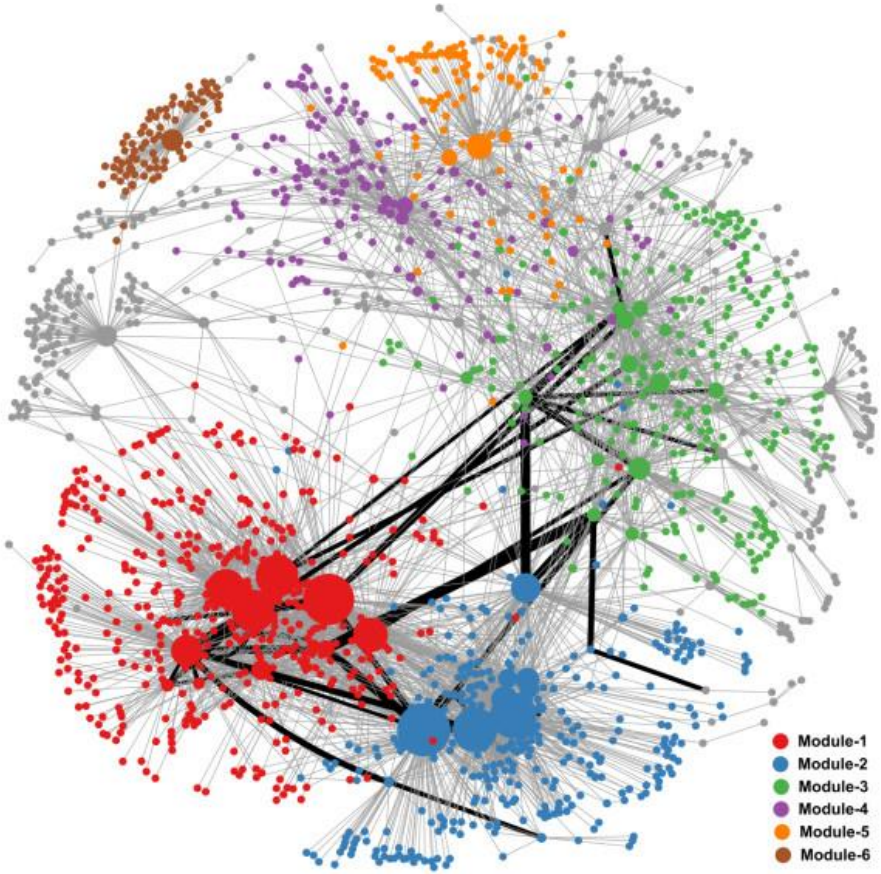
ΔΙΟΡΓΑΝΩΣΗ ΠΑΓΚΡΗΤΙΑ ΕΝΩΣΗ ΥΓΕΙΑΣ

Genetics, Epigenetics in Inflammation/Cancer Omics



Άγγελος Μπανός
Μεταδιδακτορικός Ερευνητής, ΙΙΒΕΑΑ &
Ειδικευόμενος Παθολογίας, Β' Παθολογική Κλινική,
Ιατρική Σχολή ΕΚΠΑ, ΓΝΑ «Ιπποκράτειο»

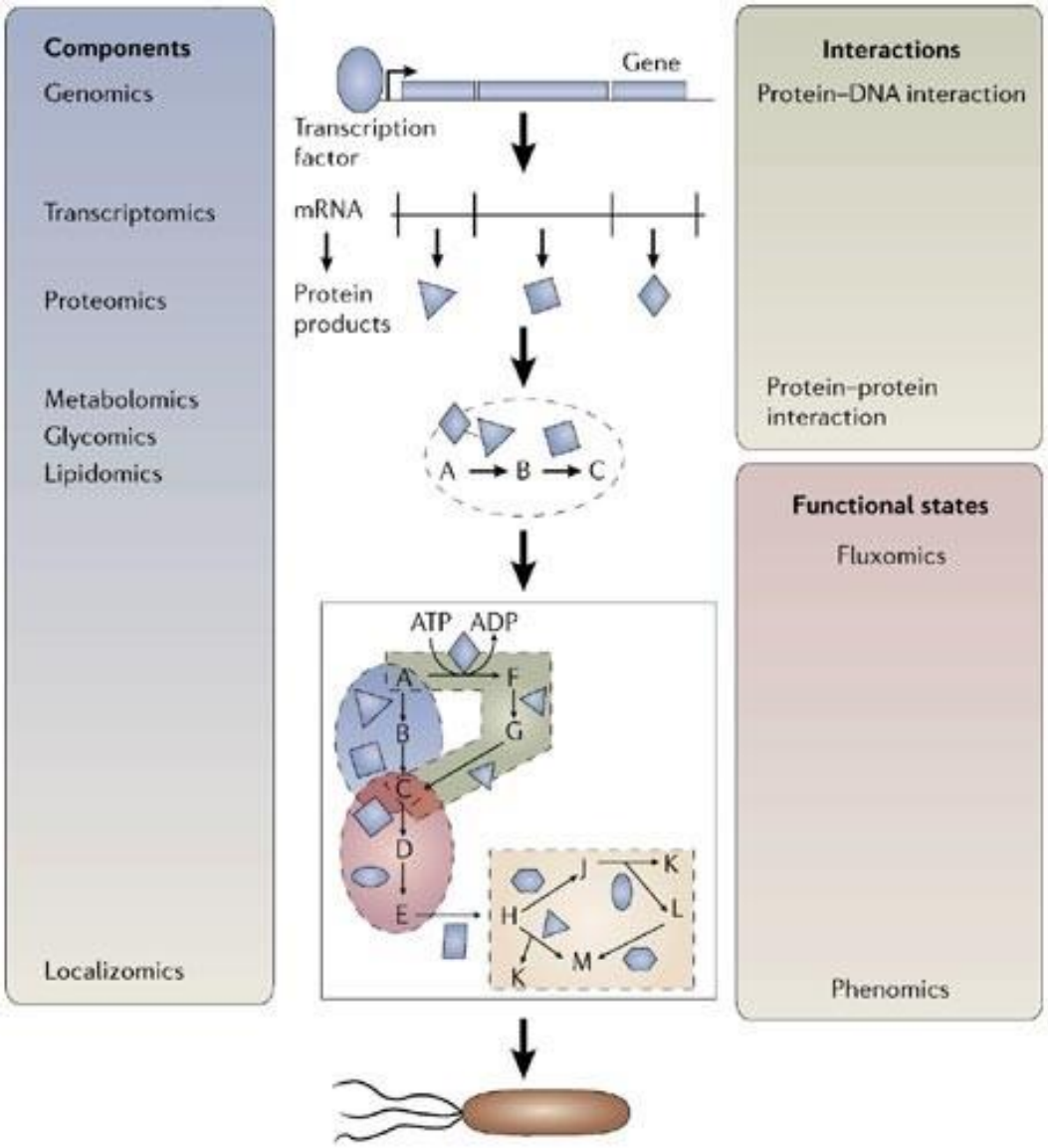
Omics – Anarchy in Biology



Gene regulatory networks in Hepatocellular Carcinoma

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

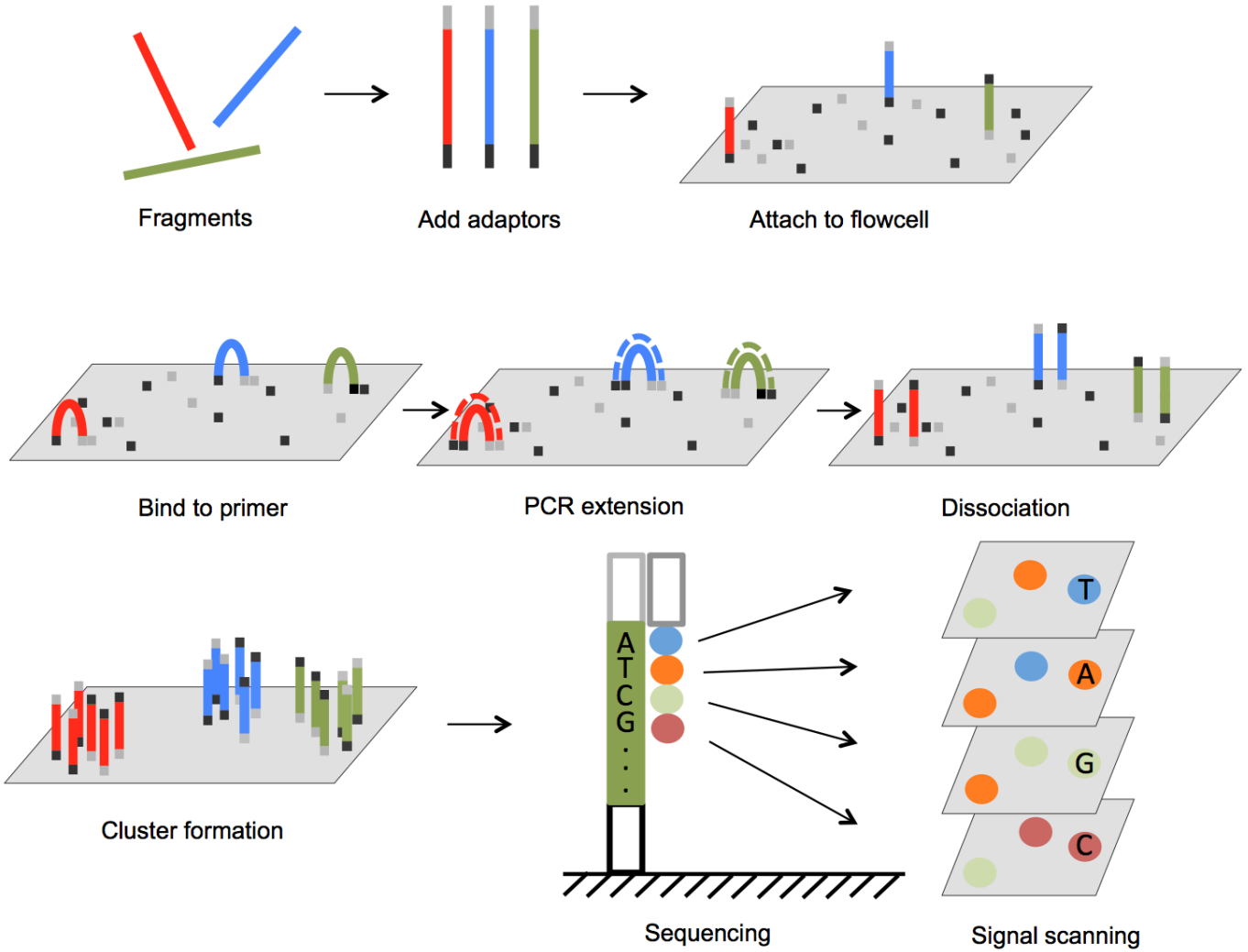
Gu et al, *BMC Syst Biol*. 2012 May 1;6:32



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

Joyce, A. *Nat Rev Mol Cell Biol* **7,** 198–210 (2006)

NGS technology



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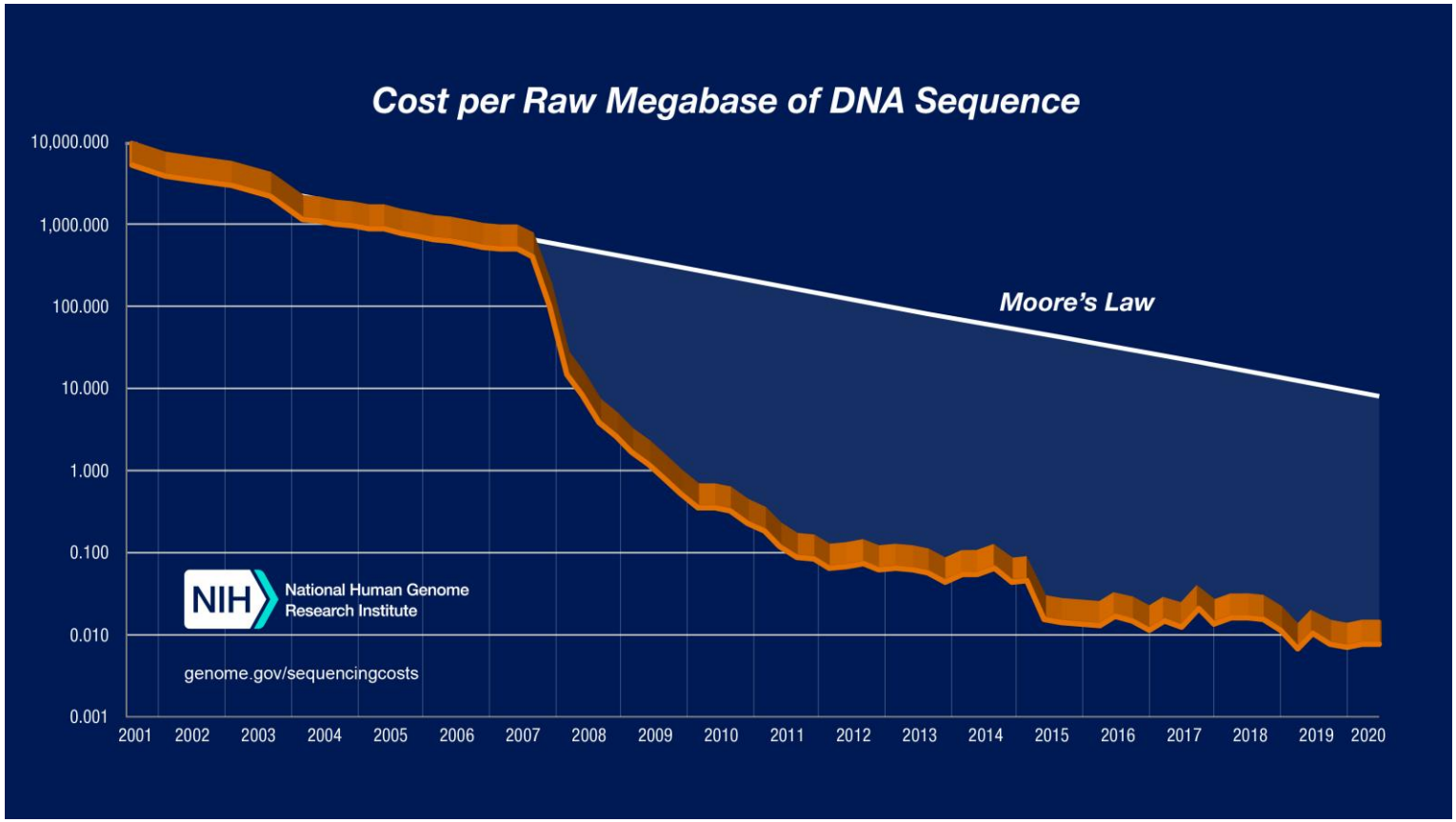
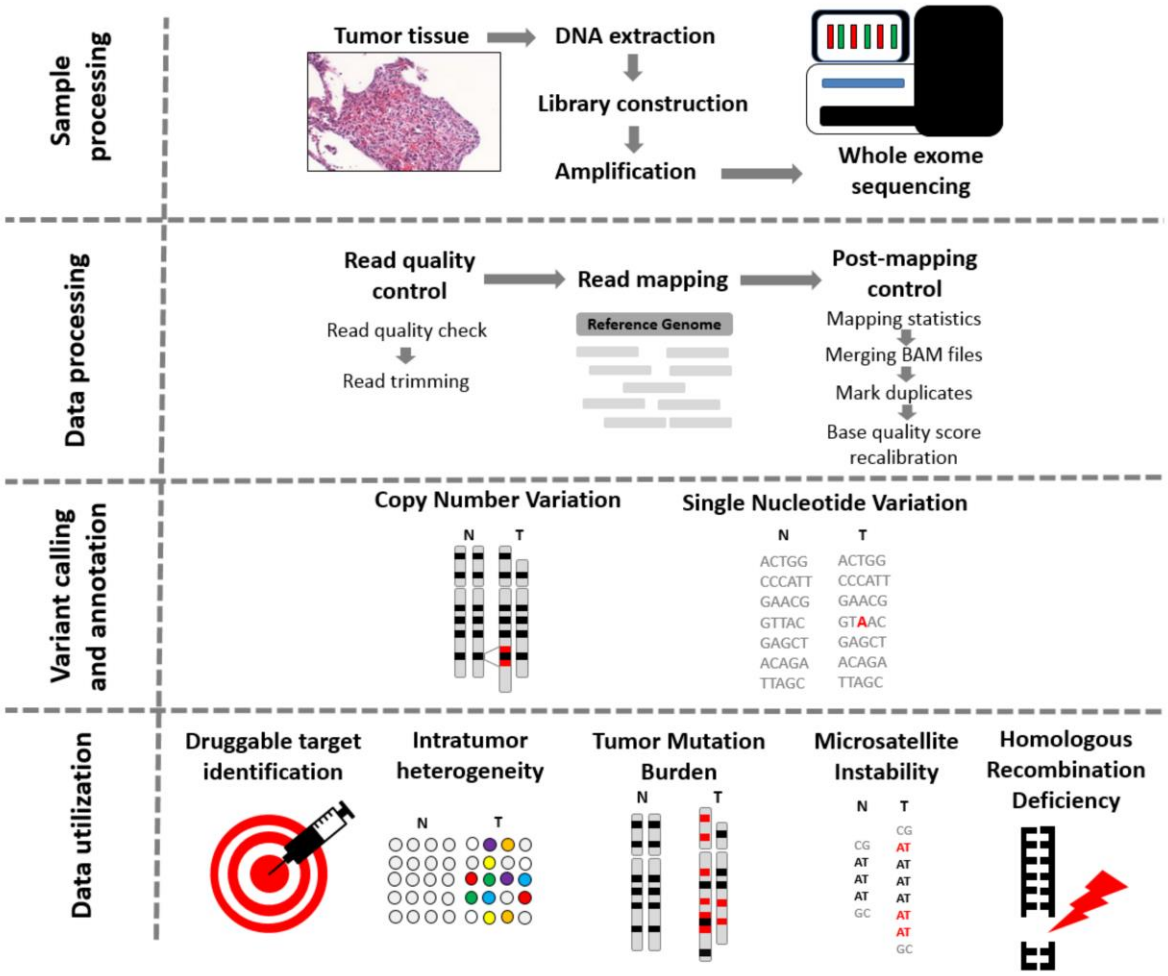


Exome sequencing



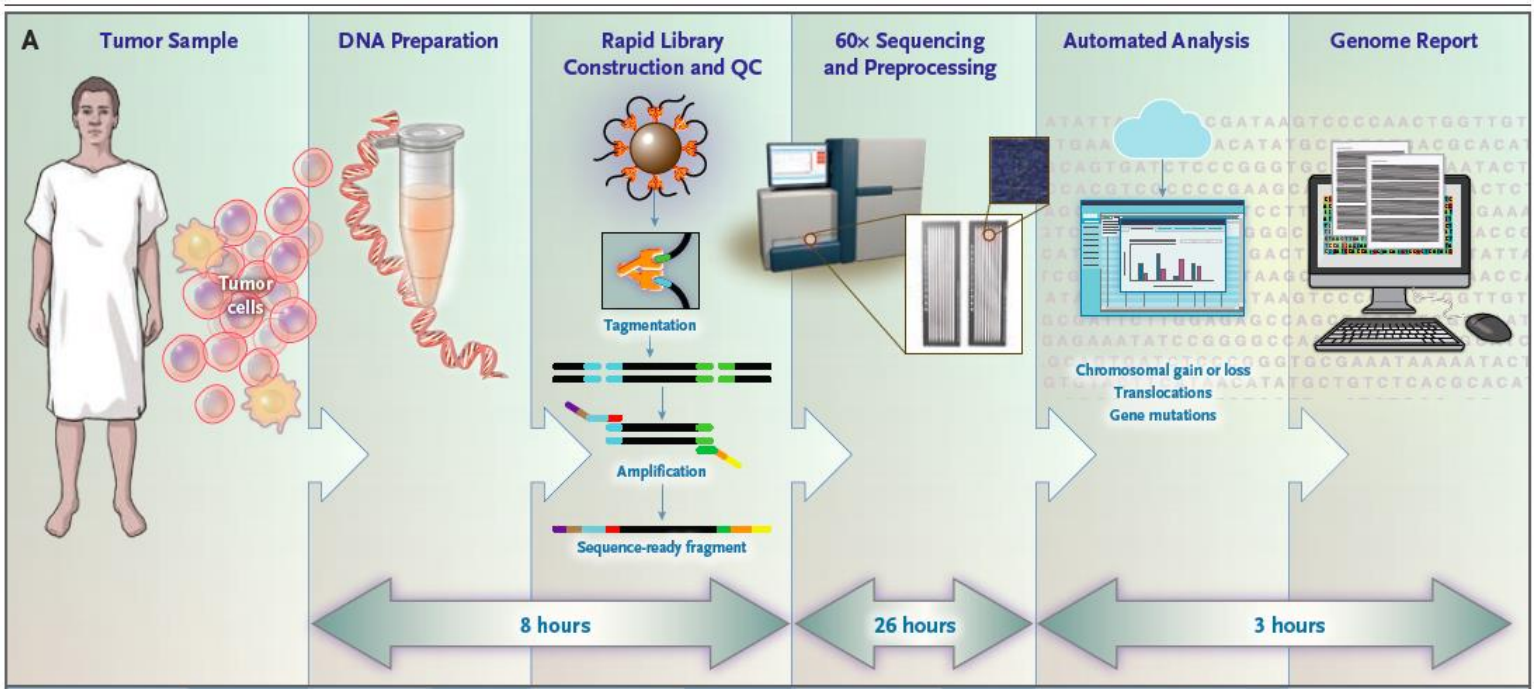
Exome sequencing in clinical practice

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

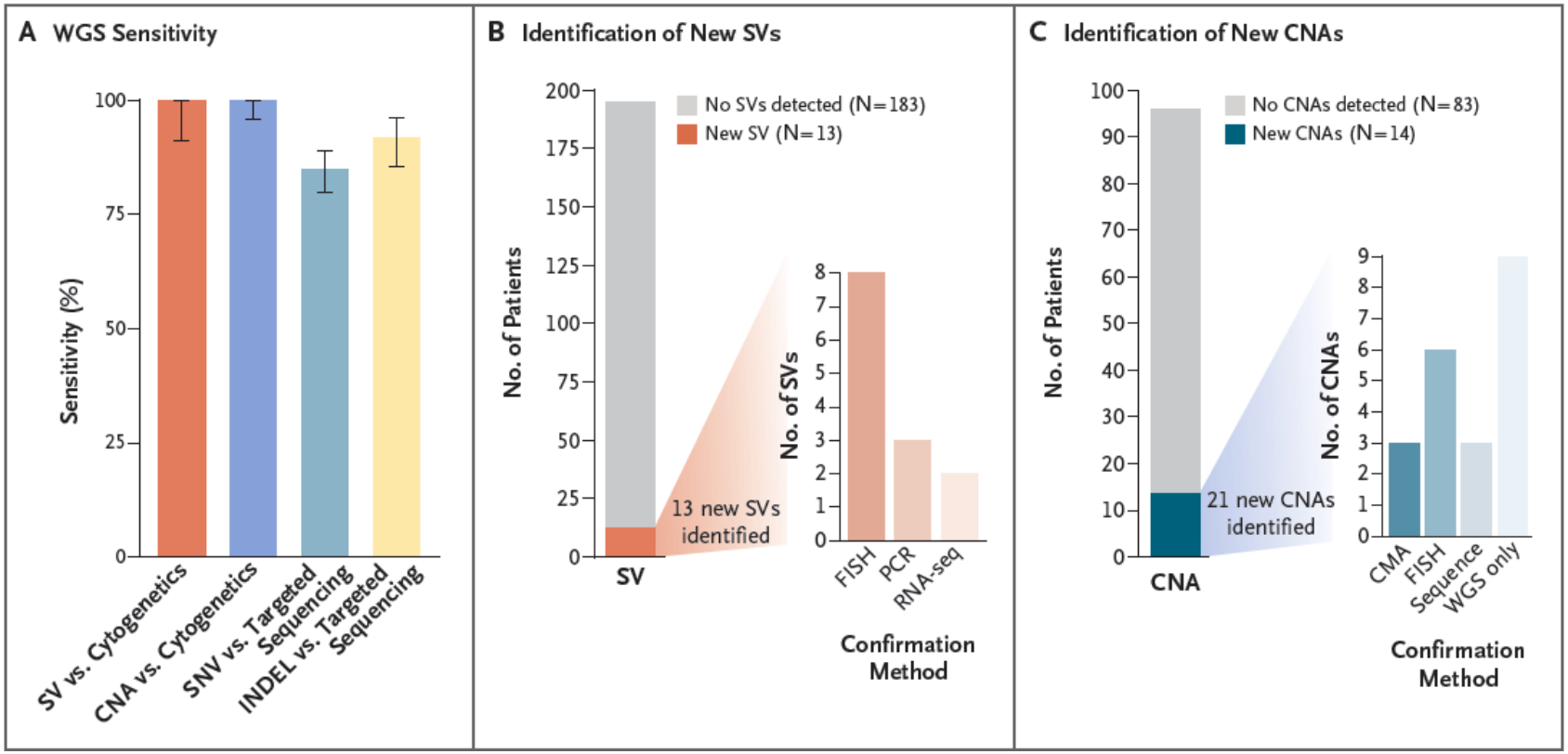
Genome Sequencing as an Alternative to Cytogenetic Analysis in Myeloid Cancers

Question: Replacement for conventional cytogenetic and sequencing approaches in the diagnosis of MDS and AML



Duncavage et al, *N Engl J Med* 2021; 384:924-935

Exome sequencing in clinical practice



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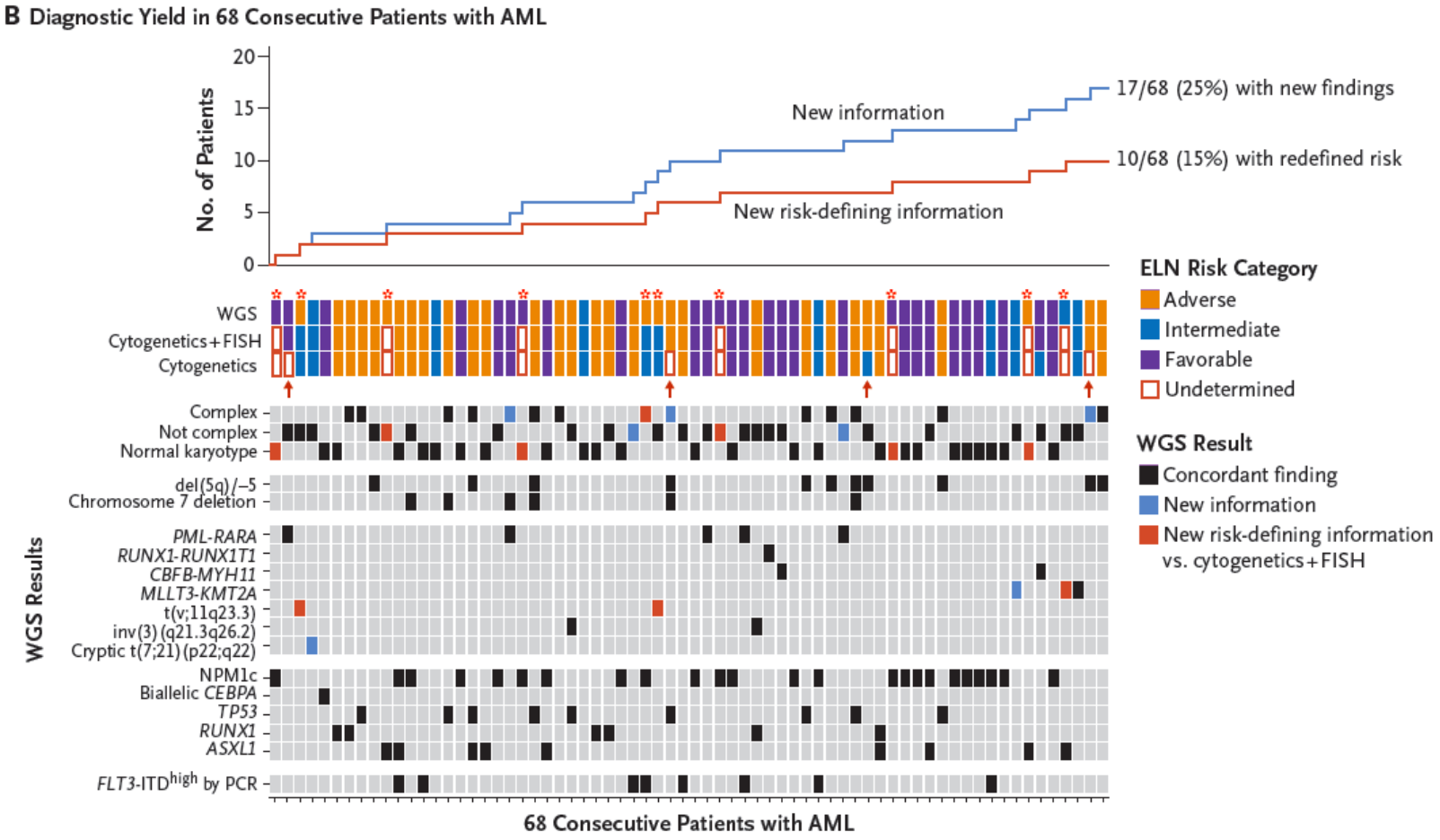
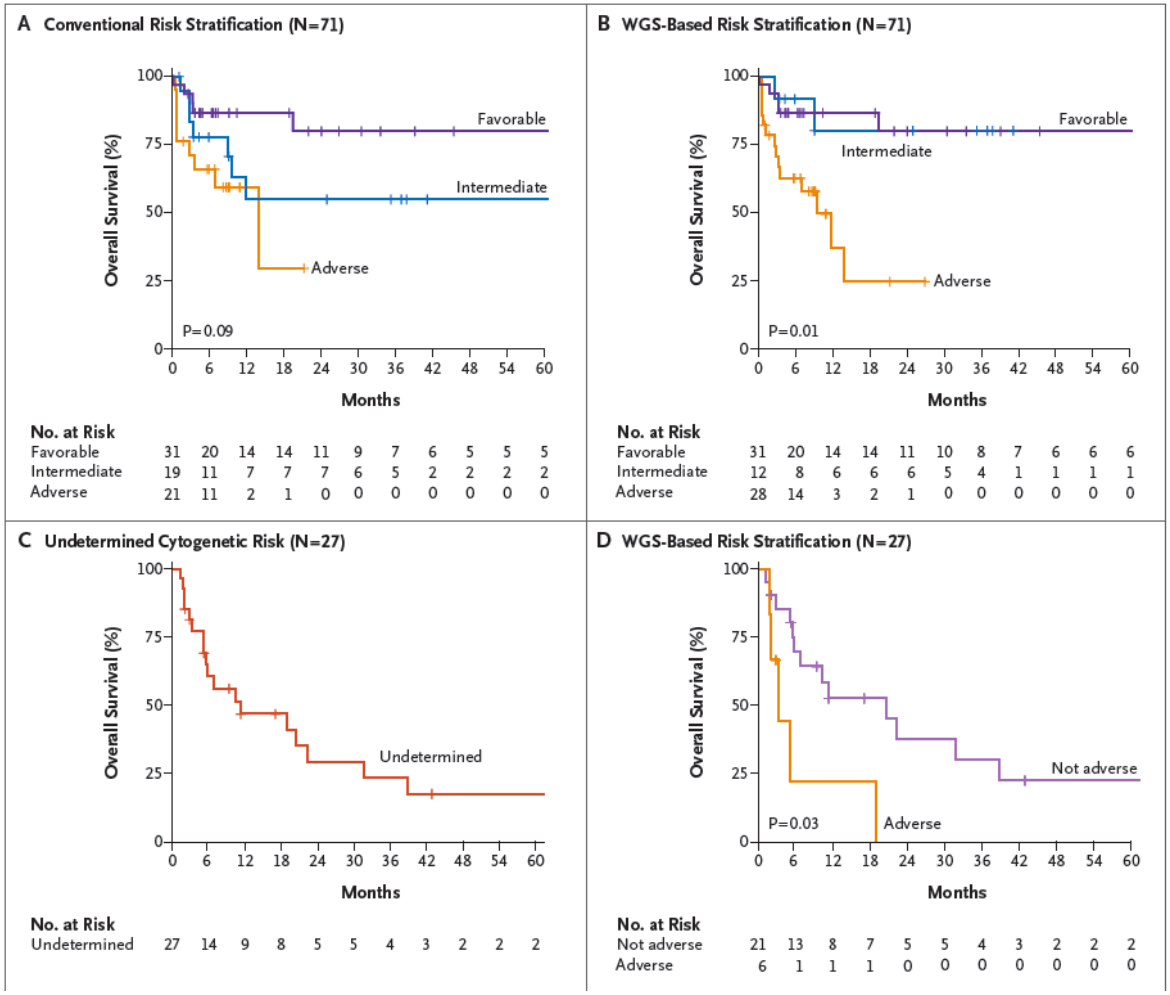
Exome sequencing in clinical practice



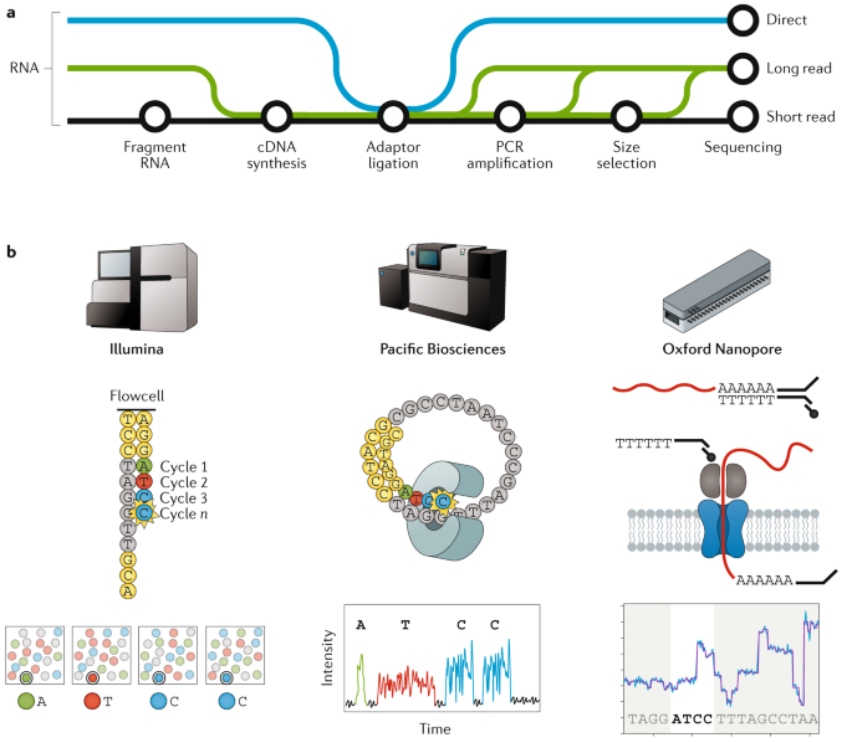
Duncavage et al, *N Engl J Med* 2021; 384:924-935

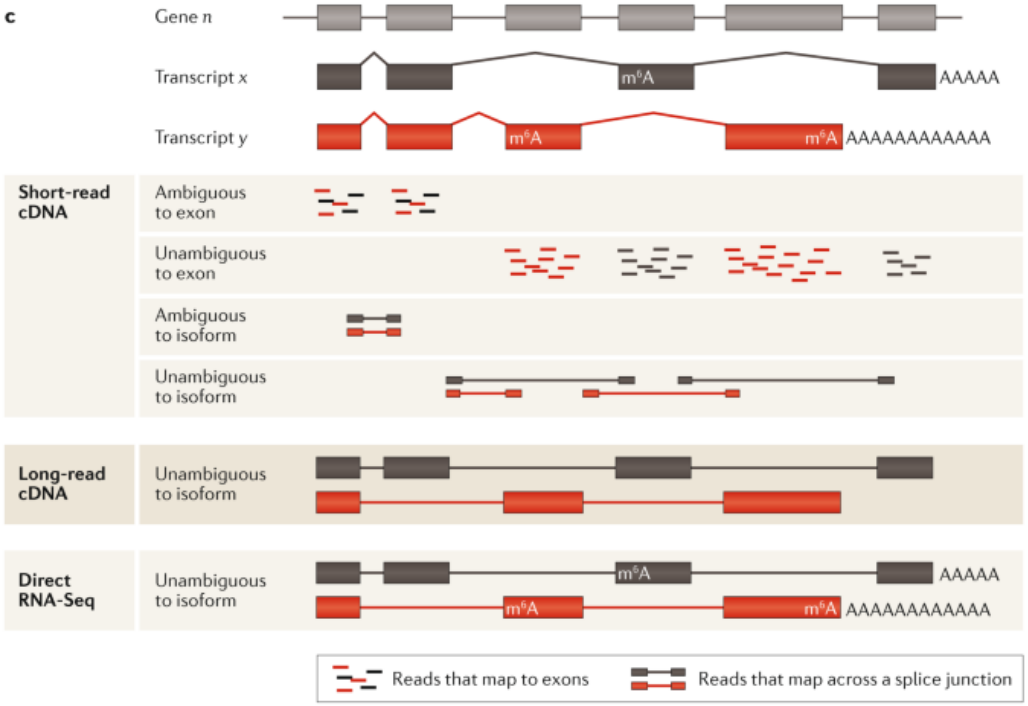
Exome sequencing in clinical practice



Duncavage et al, *N Engl J Med* 2021; 384:924-935

RNA-sequencing





Transcriptome based patient classification in SLE

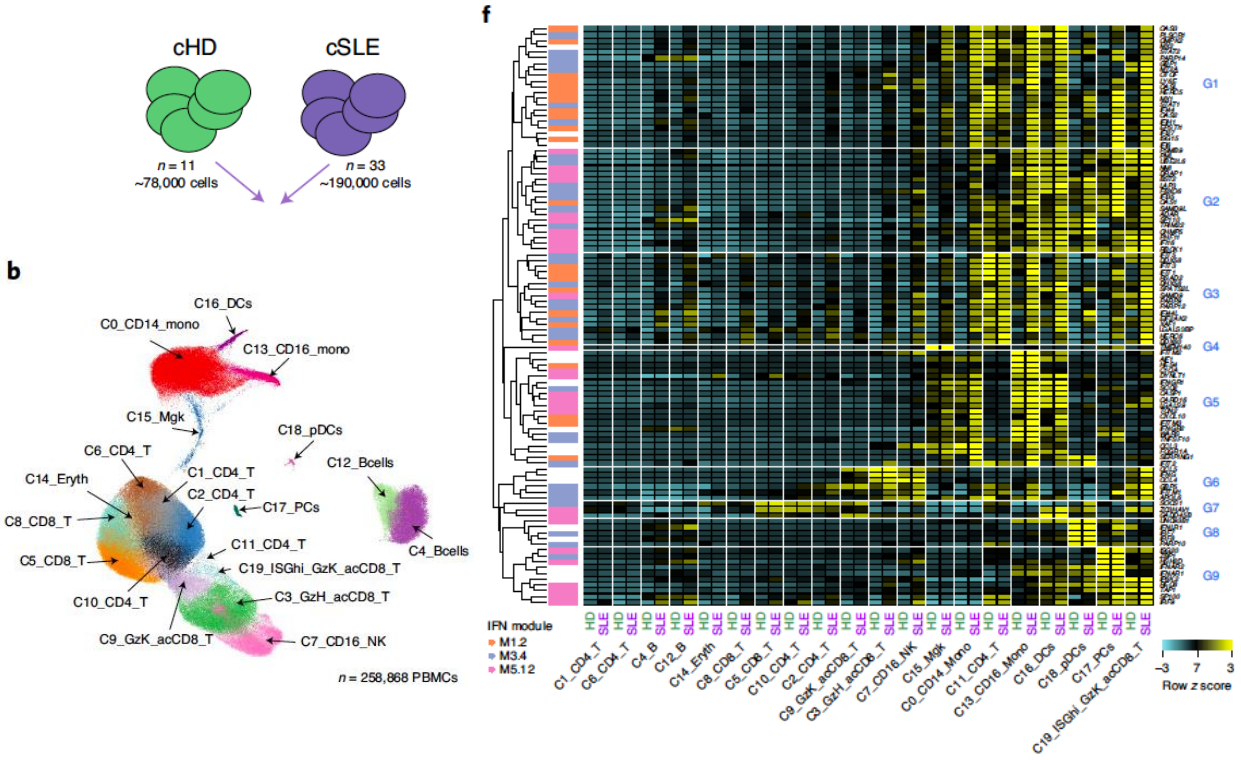
nature immunology

RESOURCE

https://doi.org/10.1038/s41590-020-0743-0

Check for updates

Mapping systemic lupus erythematosus heterogeneity at the single-cell level



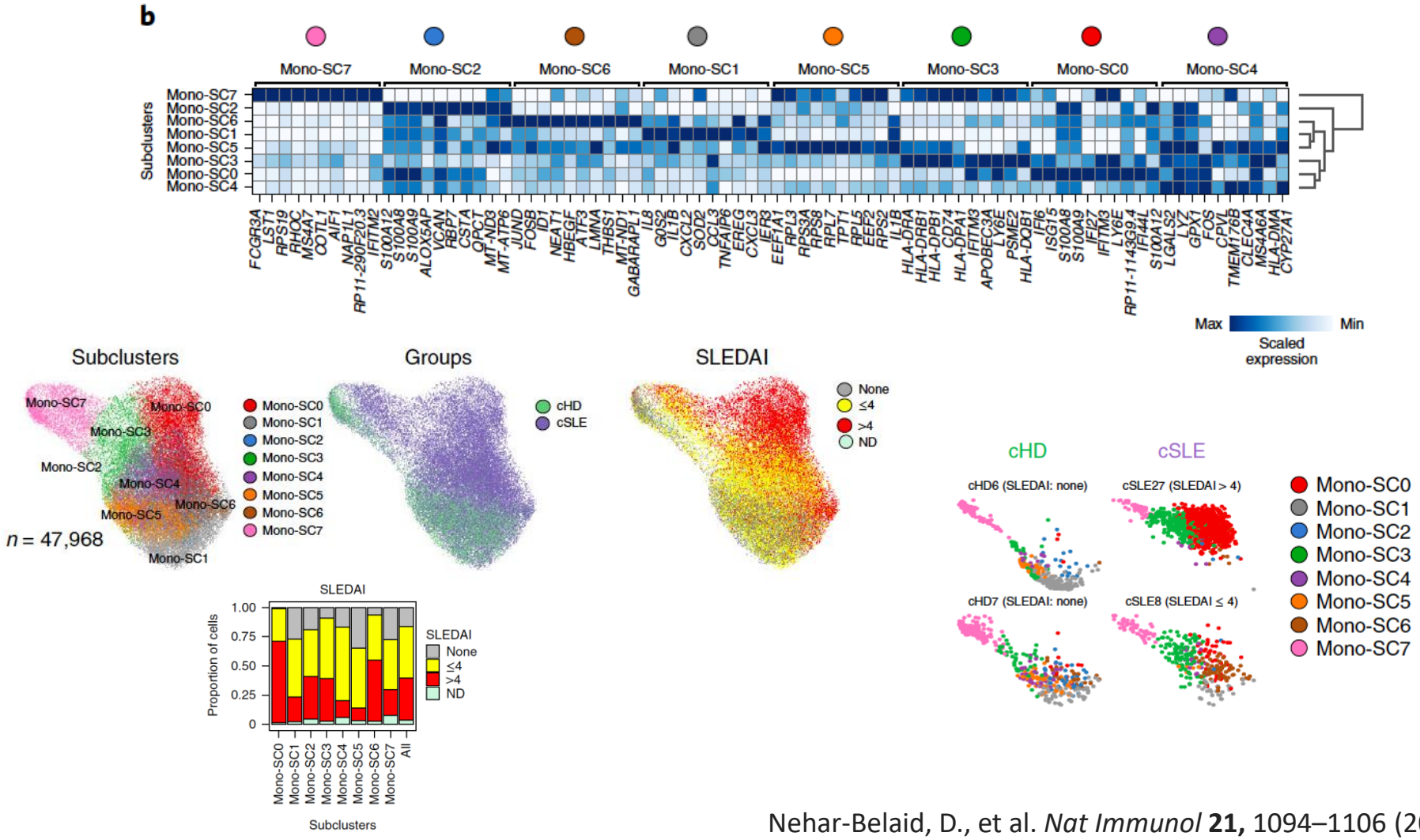
Question: Examine cellular heterogeneity and originin blood of SLE patients

Results: High ISG expression signature derived from a small number of transcriptionally defined subpopulations, including monocytes, $CD4^+$ and $CD8^+$ T cells, NKs, pDCs, B and plasma cells.

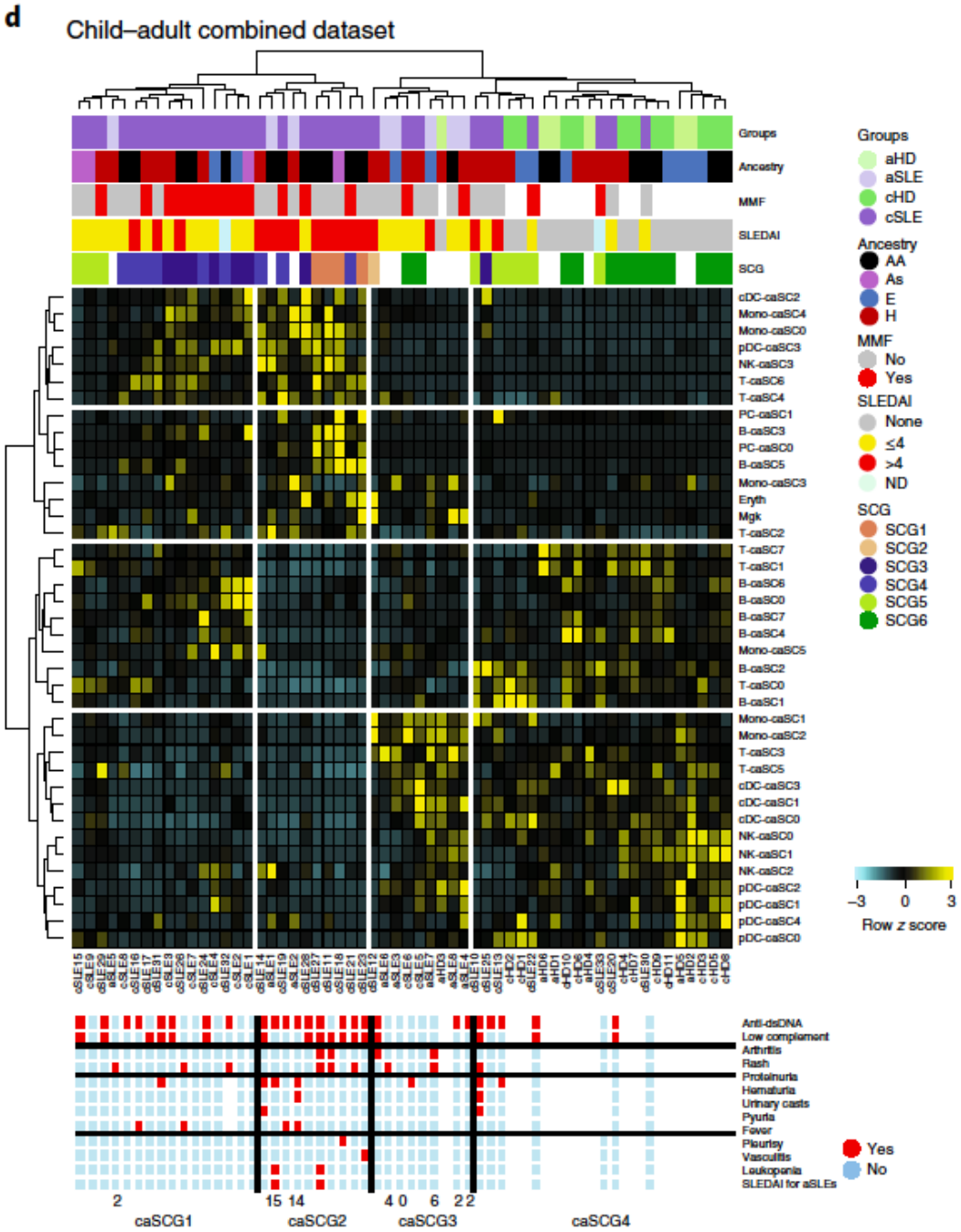
Classification and correlation with disease activity

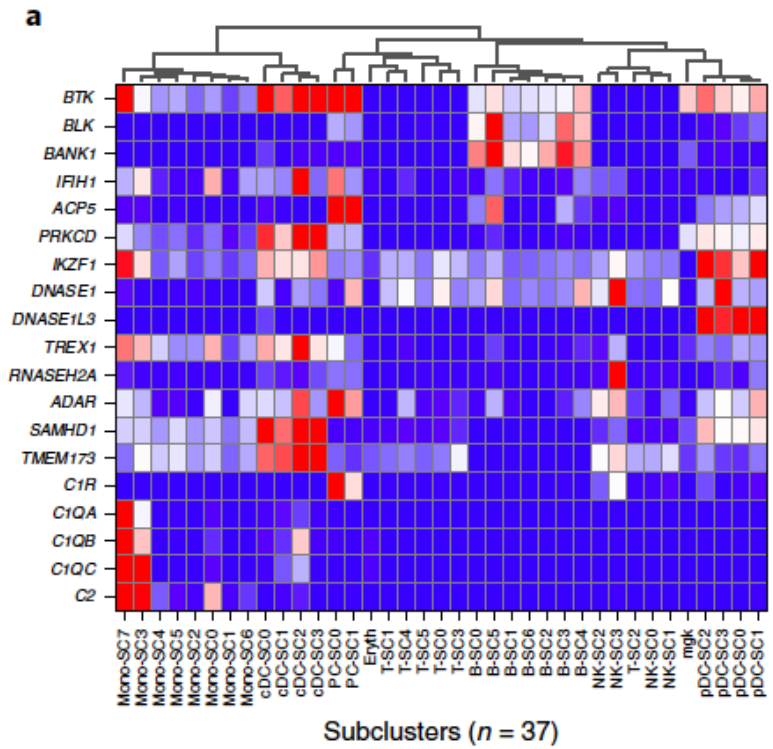
Nehar-Belaid, D., et al. *Nat Immunol* **21,** 1094–1106 (2020).

Transcriptome based patient classification in SLE



Nehar-Belaid, D., et al. *Nat Immunol* **21,** 1094–1106 (2020).

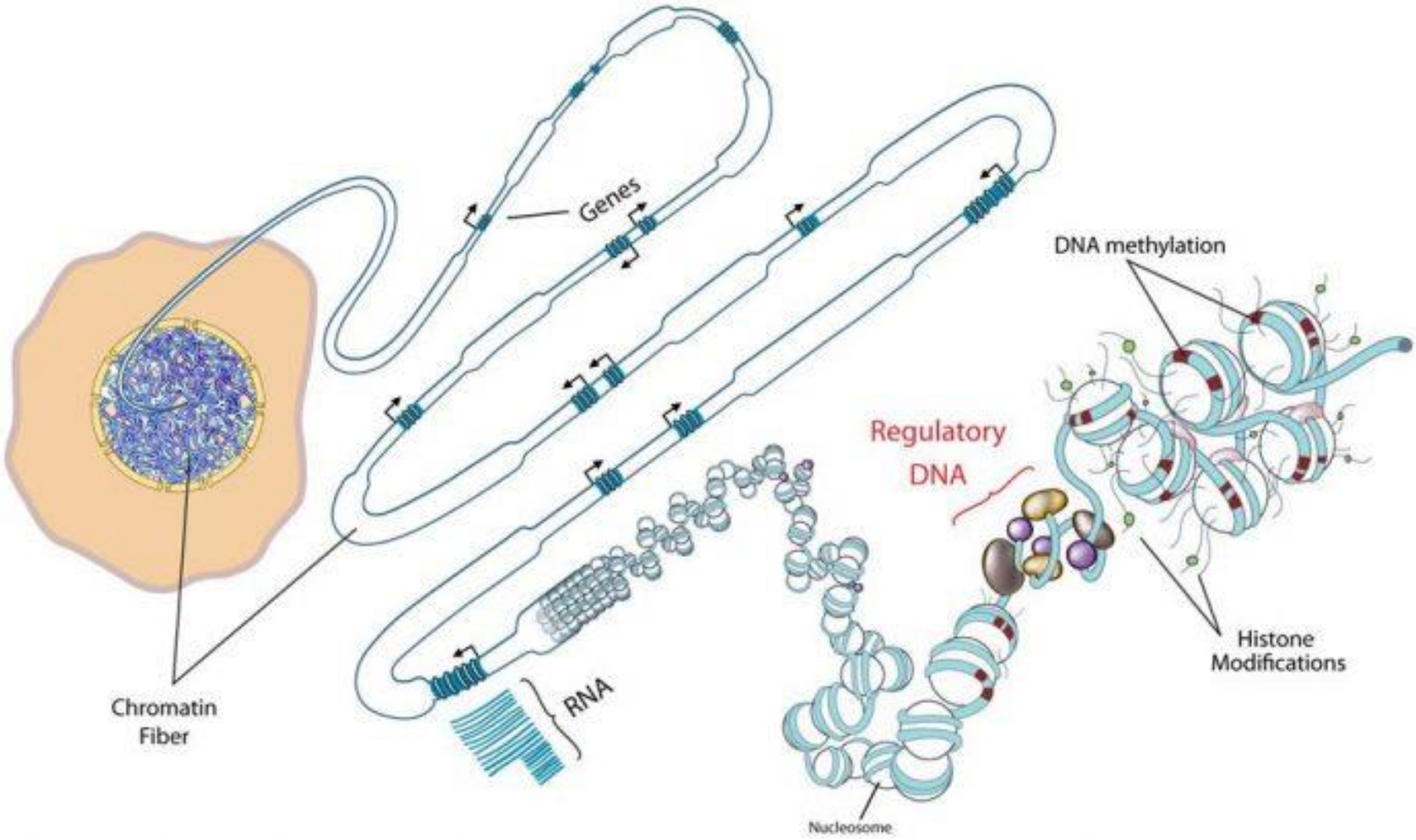




Monogenic SLE

Menar-Belaid, D., et al. *Nat Immunol* **21,** 1094–1106 (2020).

Methylome Profiling



Genome wide analysis of methylome impact on RA pathogenesis and heritability

TRANSLATIONAL SCIENCE

Genetic variants shape rheumatoid arthritis-specific transcriptomic features in CD4$^+$ T cells through differential DNA methylation, explaining a substantial proportion of heritability

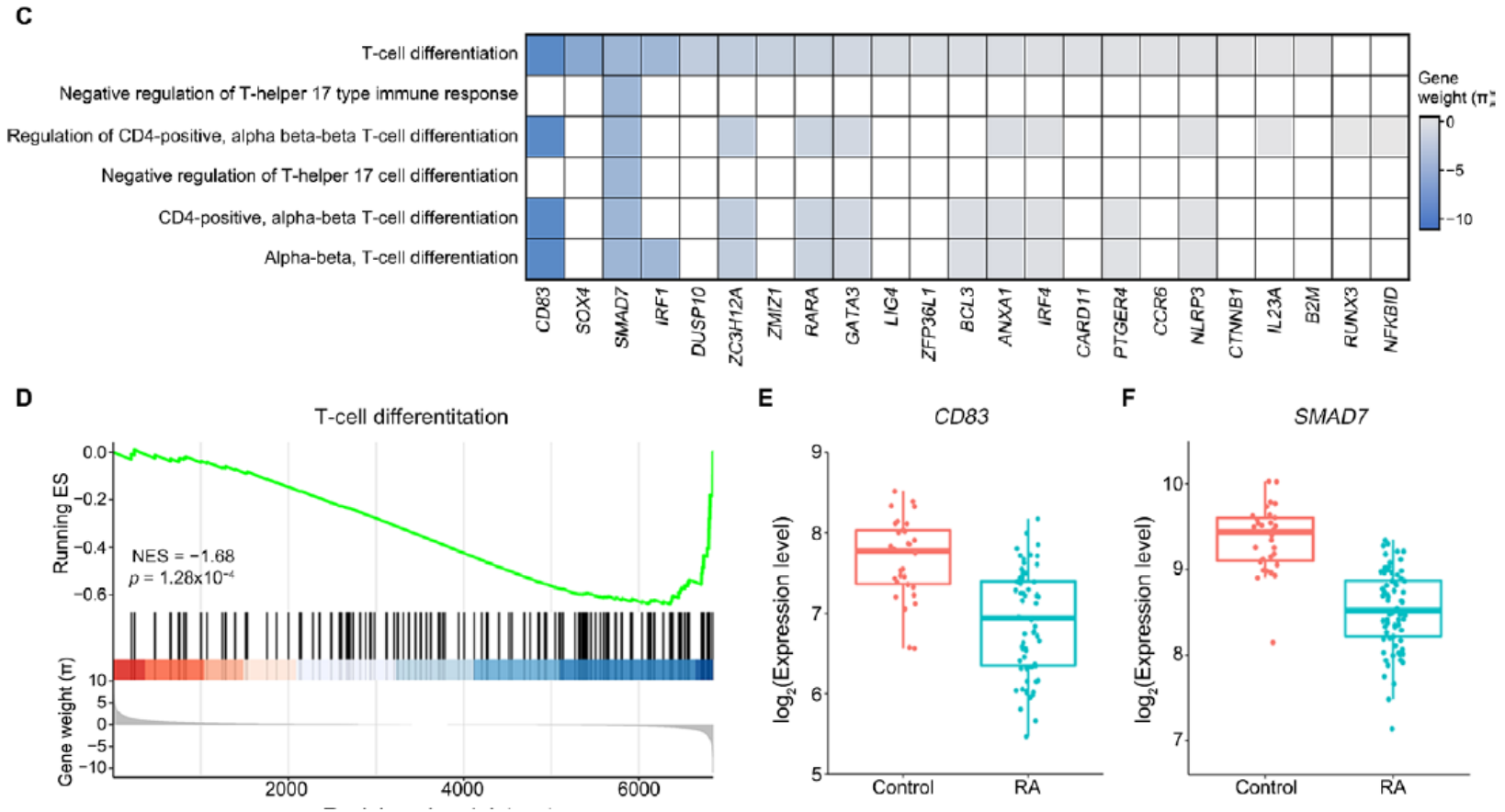
			Methylome (n=122)	Transcripotme (n=103)	Genome (n=104)
			Methylation 450K BeadChip (n=122) or MBD-Seq (n=68)	HumanHT-12 v4 BeadChip	Genome-wide SNP array (KoreanChip)
	Cases	Controls			
Sample size (n)	64	26	✓	✓	✓
	9	4	✓	✓	
	7	7	✓		✓
	2	3	✓		

Question: Map transcriptome of blood CD4$^+$ cells in RA patients, integrate genome/epigenome

Results: Differentially methylated regions coincide with RA variants explaining part of heritability

Ha E, et al. *Ann Rheum Dis* 2021;80:876–883.

Genome wide analysis of methylome impact on RA pathogenesis and heritability



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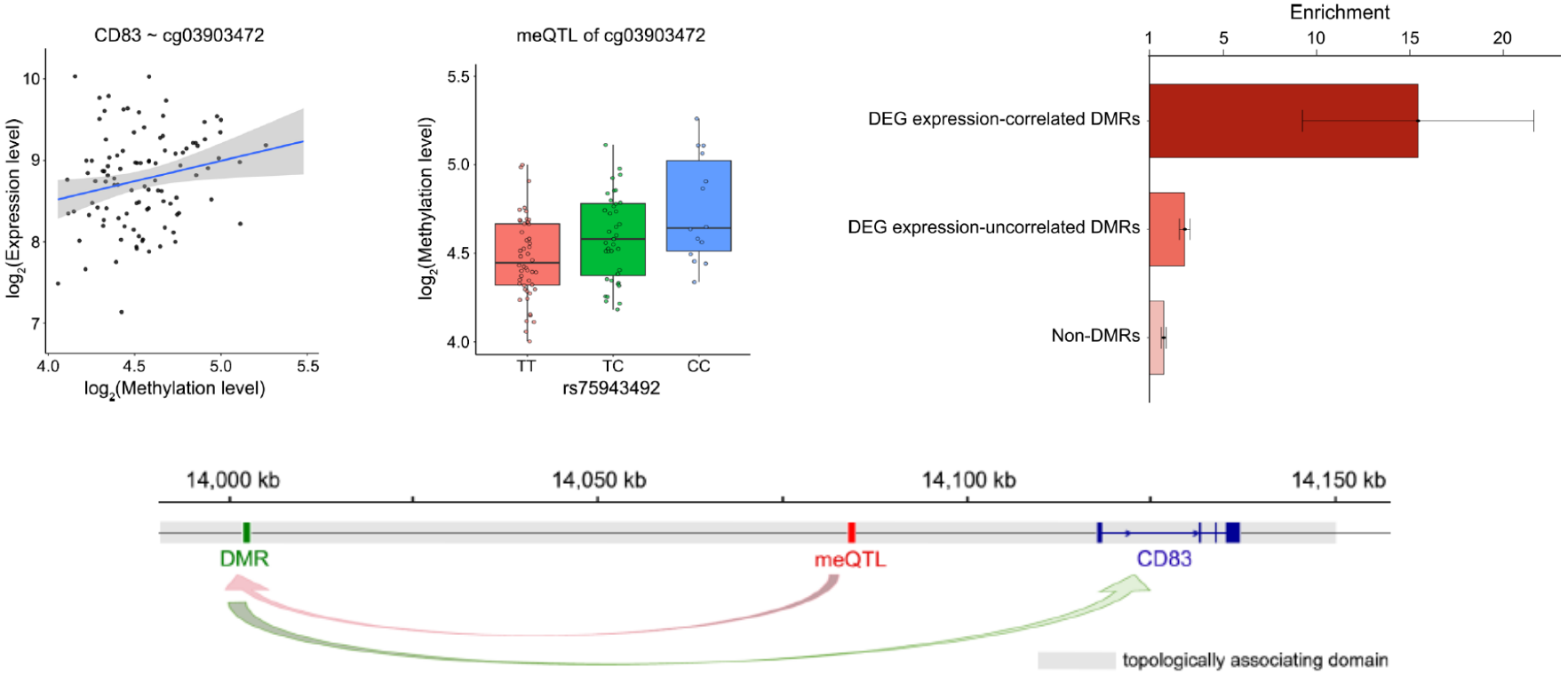
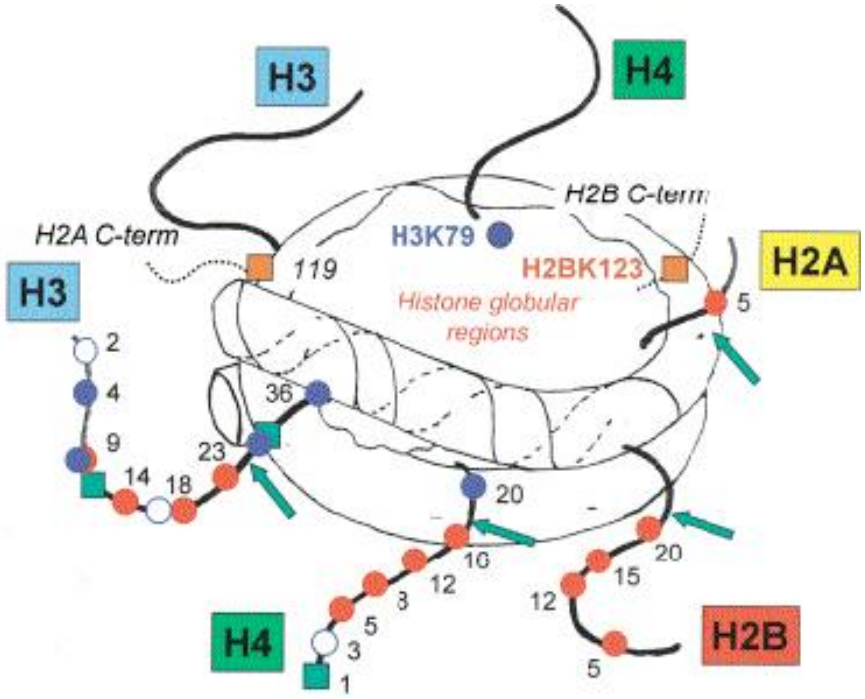
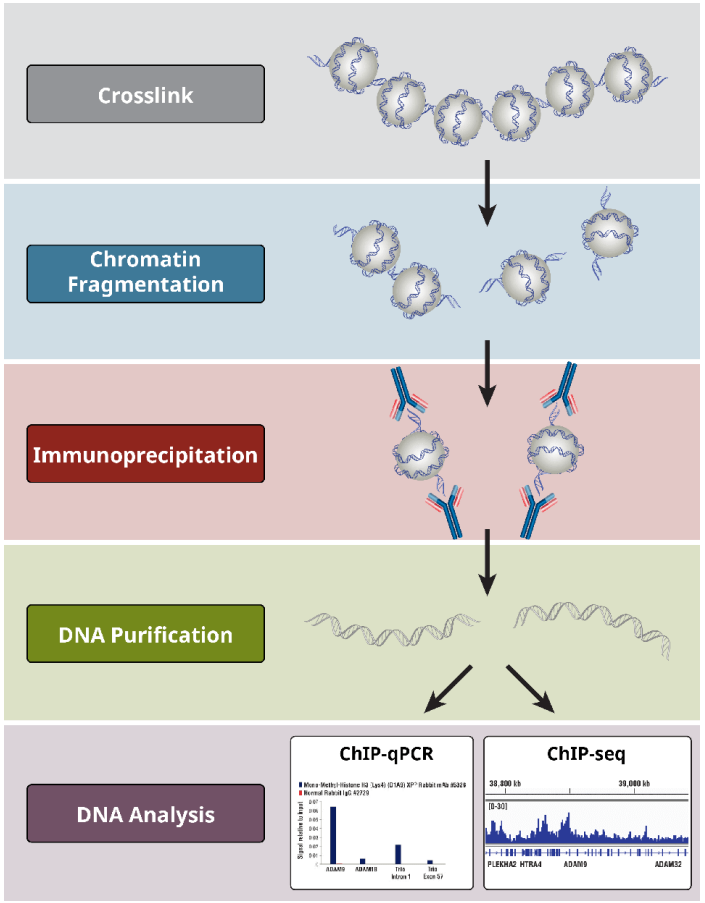
Genome wide analysis of methylome impact on RA pathogenesis and heritability



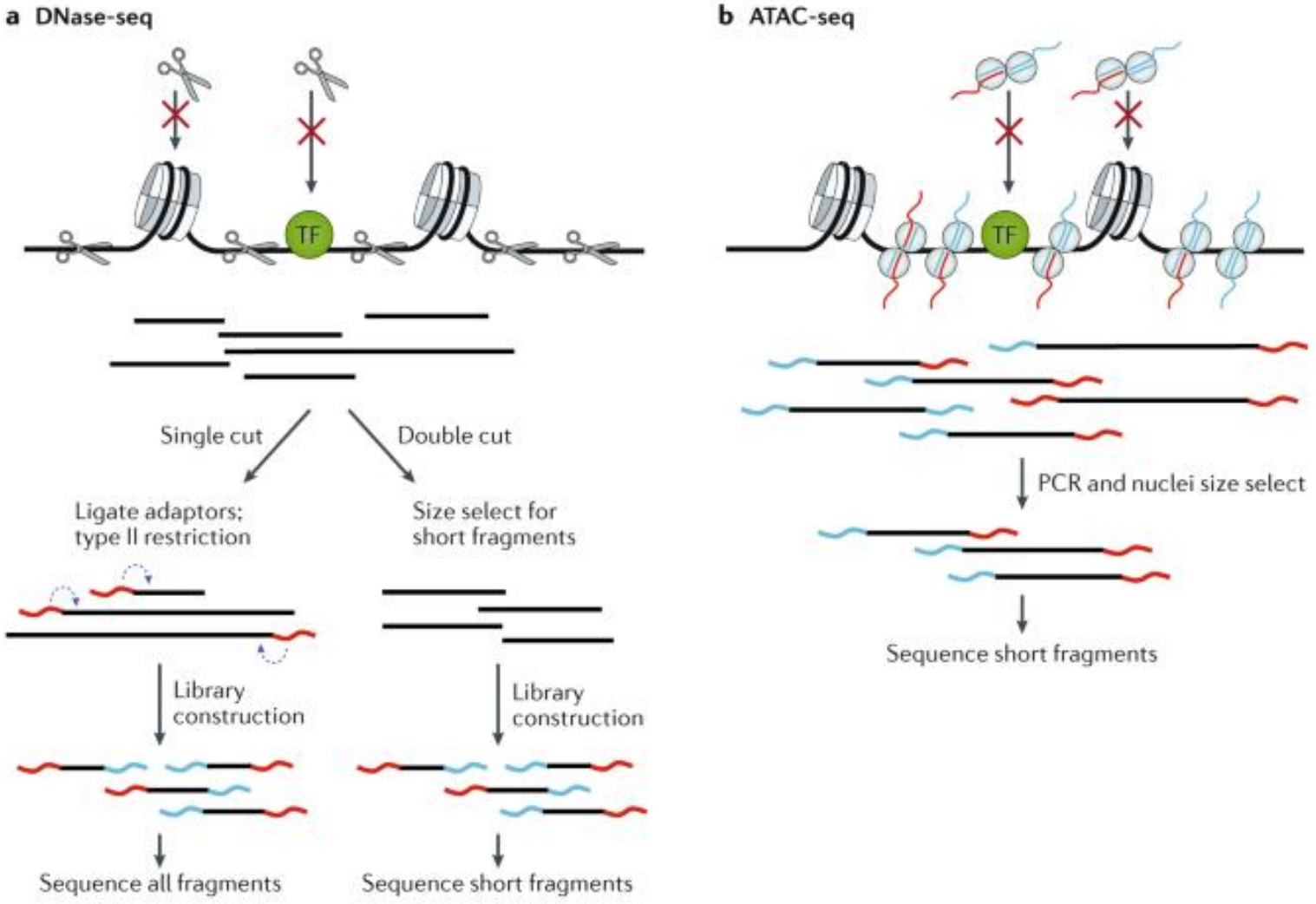
Ha E, et al. *Ann Rheum Dis* 2021;80:876–883.

Chromatin Mapping

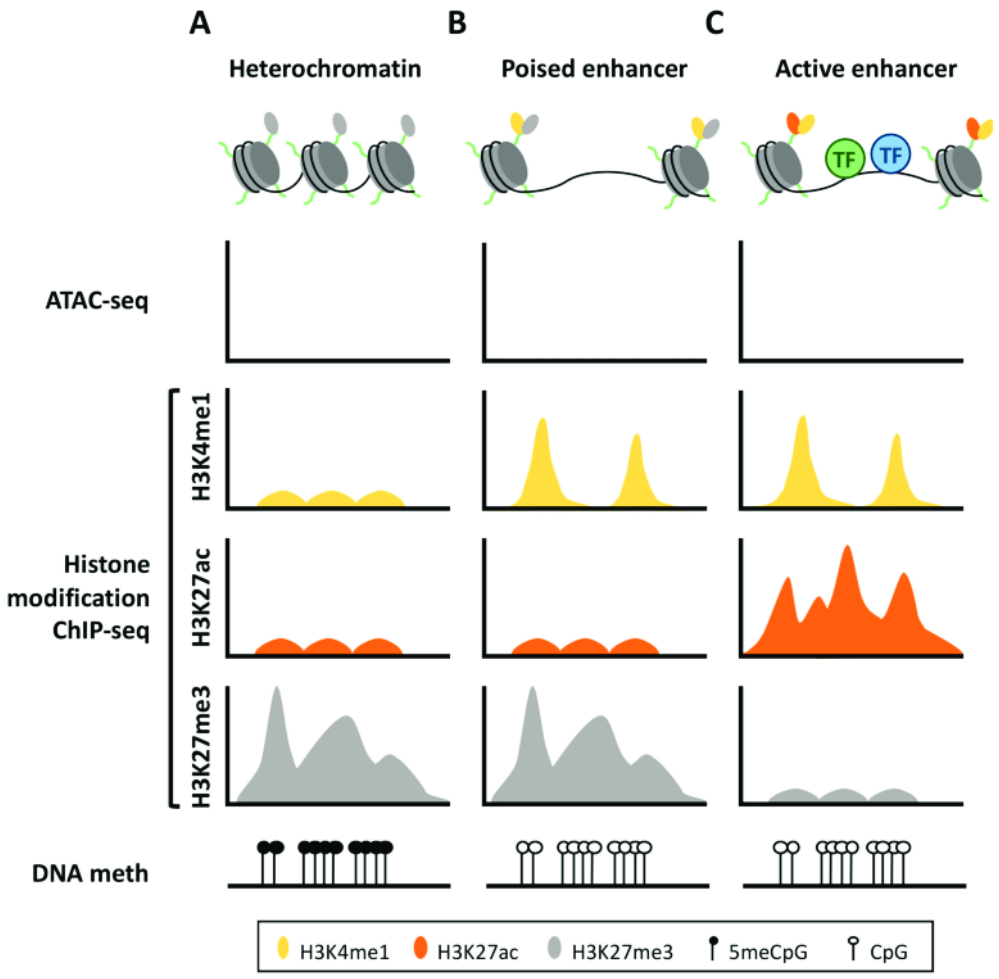




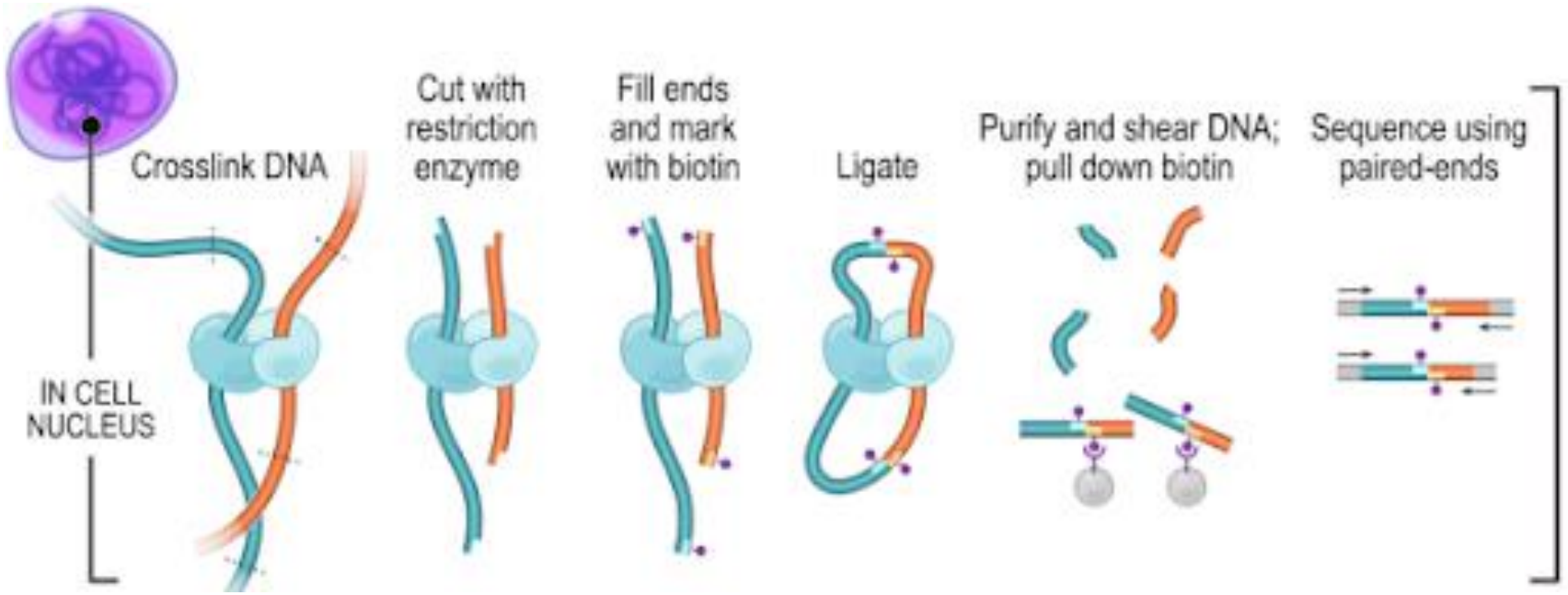
Chromatin Accesibility



Chromatin Accesibility



Nuclear Structure - HiC

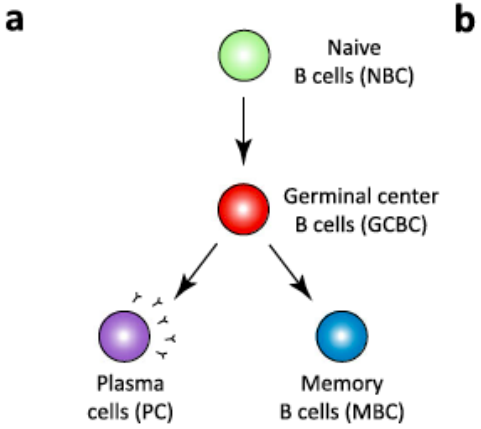


Nuclear structure and choreography during B-cell differentiation

https://doi.org/10.1038/s41467-020-20849-y OPEN

Dynamics of genome architecture and chromatin function during human B cell differentiation and neoplastic transformation

nature COMMUNICATIONS



b

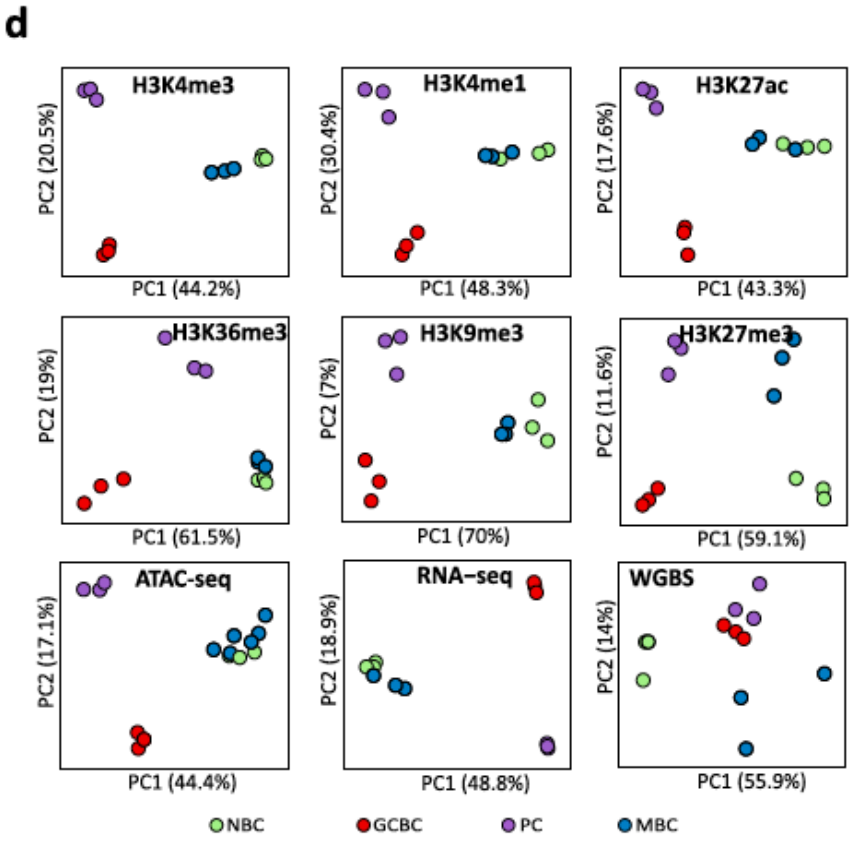
	NBC	GCBC	PC	MBC
Sorting scheme	$CD19^+$ IgD^+ $CD27^-$	$CD19^+$ $CD20^{++}$ $CD38^+$	$CD19^+$ $CD20^+$ $CD38^{++}$	$CD19^+$ $IgA^+/IgG^+/IgM^+/IgD^+$ $CD27^+$
Source	Peripheral blood	Tonsil	Tonsil	Peripheral blood
Biological replicates	3	3	3	3

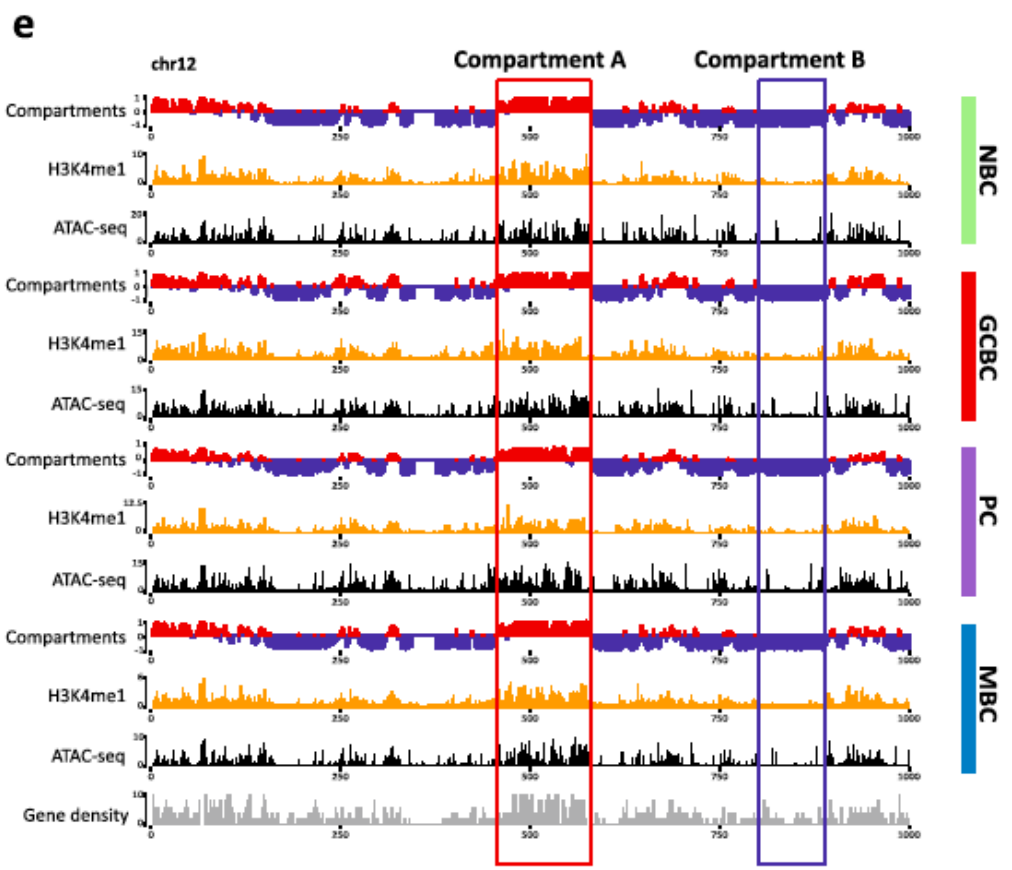
Question: Study genome rearrangements during B-cell differentiation in steady-state and disease

Results: Leukemia-derived B-cells possess a tumor like genome organization

Vilarrasa-Blasi, R., et al. *Nat Commun* 12, 651 (2021).

Nuclear structure and choreography during B-cell differentiation





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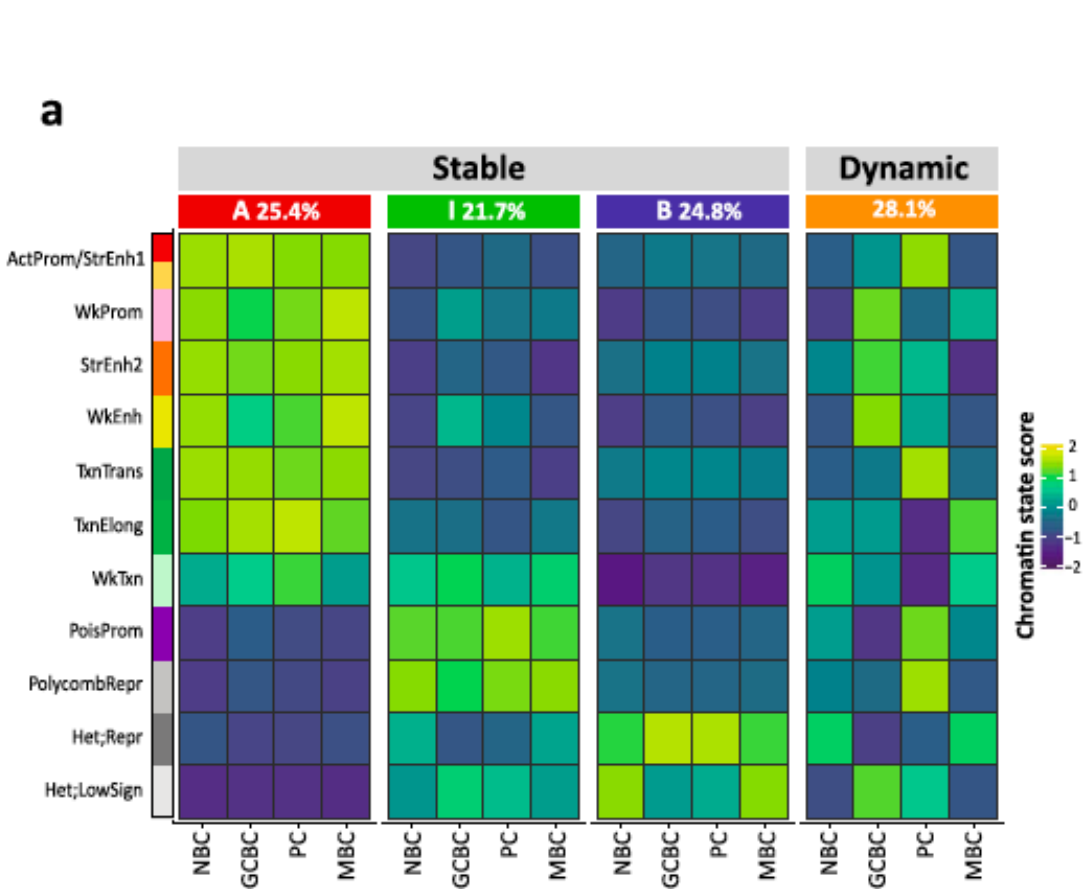
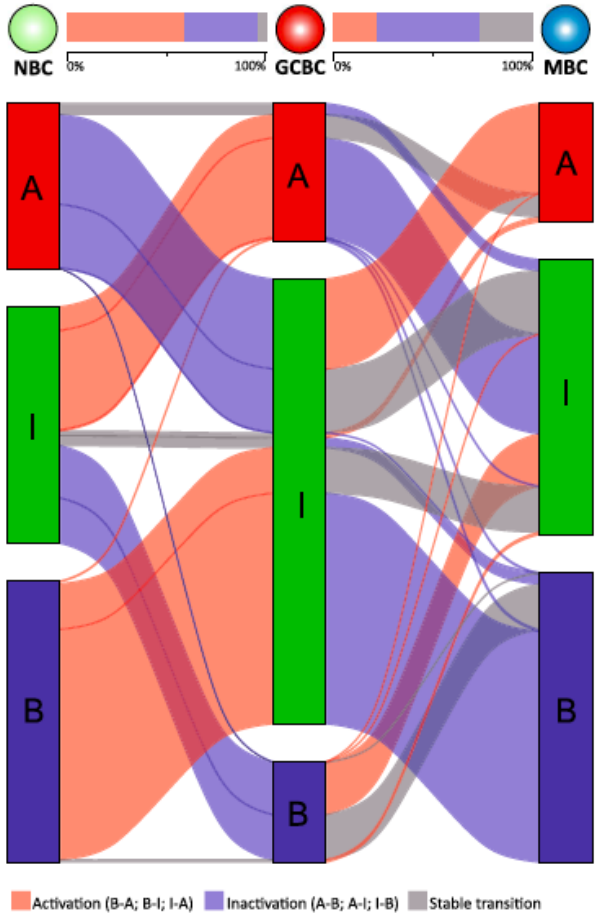
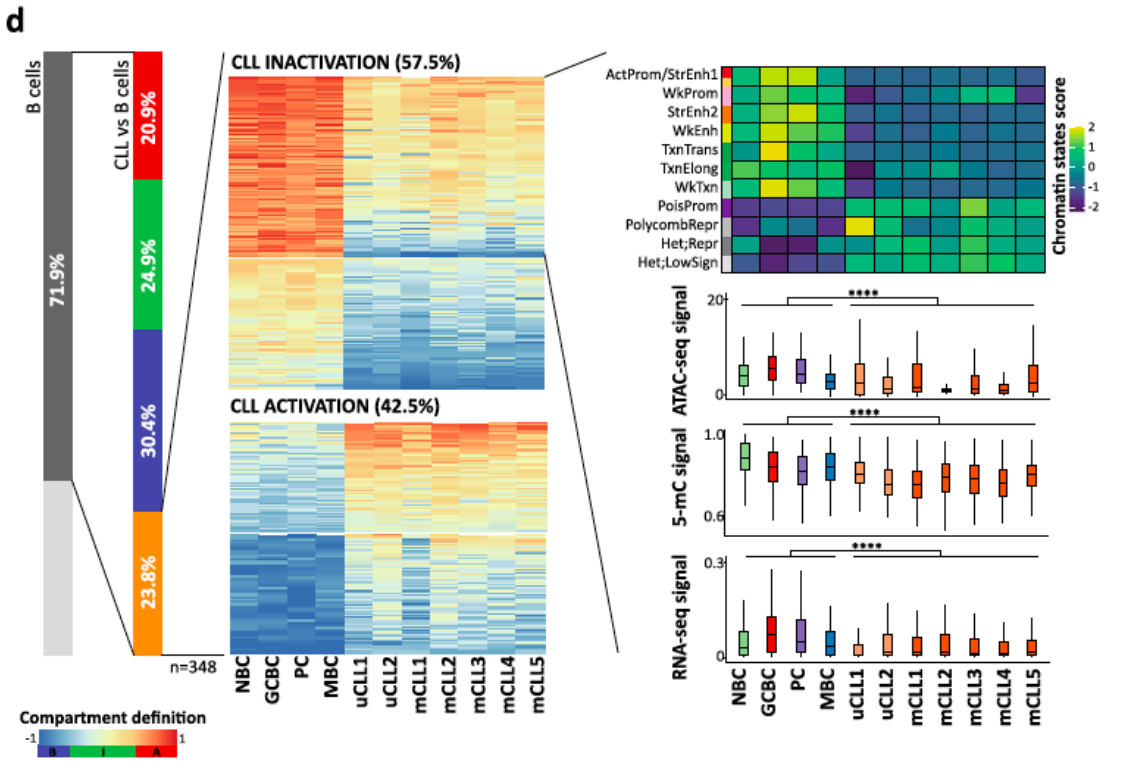




Vilarrasa-Blasi, R., et al. *Nat Commun* 12, 651 (2021).

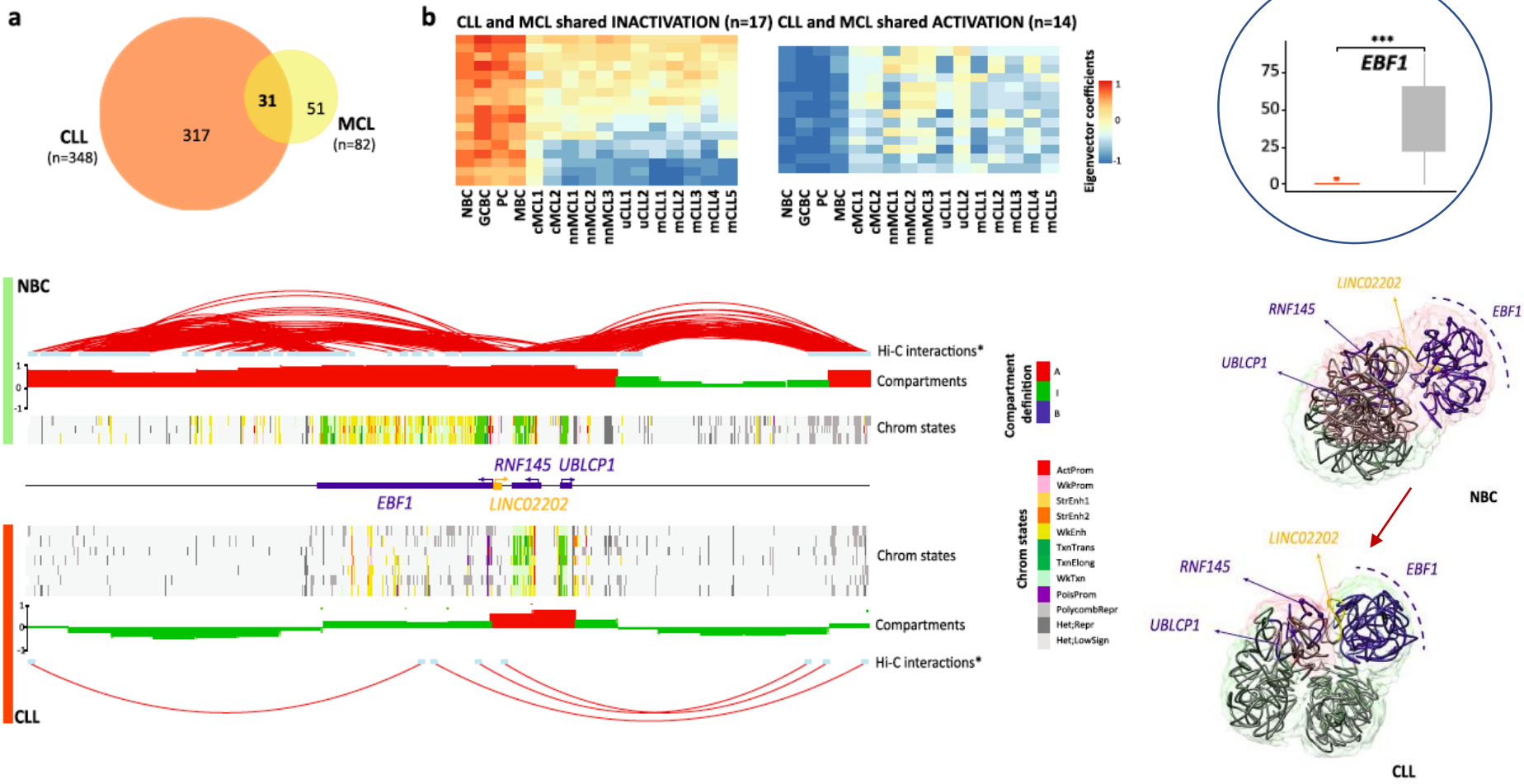
Nuclear structure and choreography during B-cell differentiation

	Chronic Lymphocytic Leukemia (CLL)		Mantle Cell Lymphoma (MCL)	
	Unmutated IGVH (uCLL)	Mutated IGVH (mCLL)	Conventional MCL (cMCL)	Non-nodal MCL (nnMCL)
Sorting scheme	$CD19^+$		$CD19^+$	
Source	Peripheral blood		Peripheral blood	
Samples	2	5	2	3



Vilarrasa-Blasi, R., et al. *Nat Commun* 12, 651 (2021).

Nuclear structure and choreography during B-cell differentiation

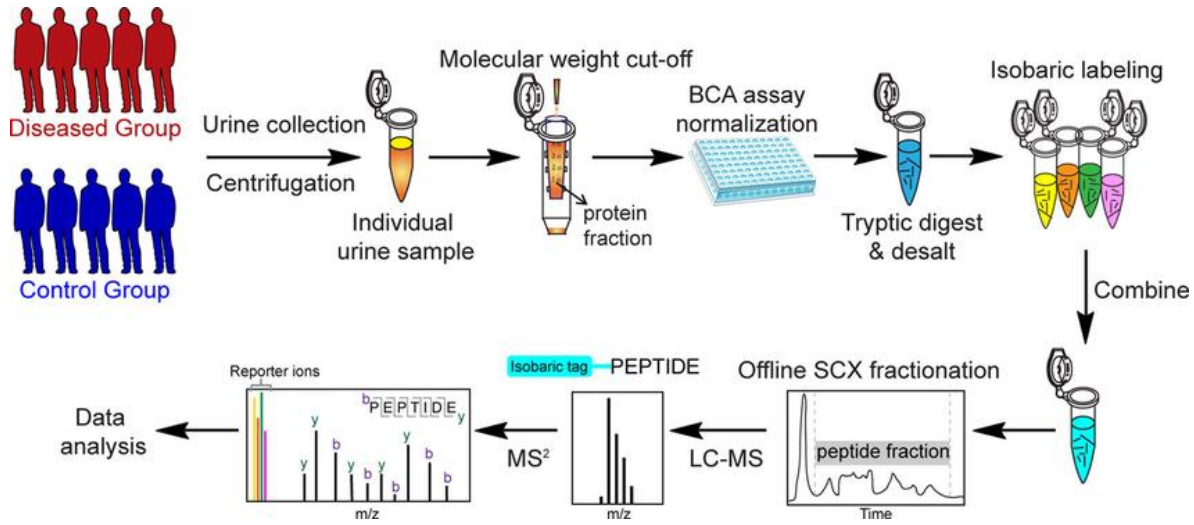


Vilarrasa-Blasi, R., et al. *Nat Commun* 12, 651 (2021).

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

JCI insight

Integrated urine proteomics and renal single-cell genomics identify an IFN-γ response gradient in lupus nephritis



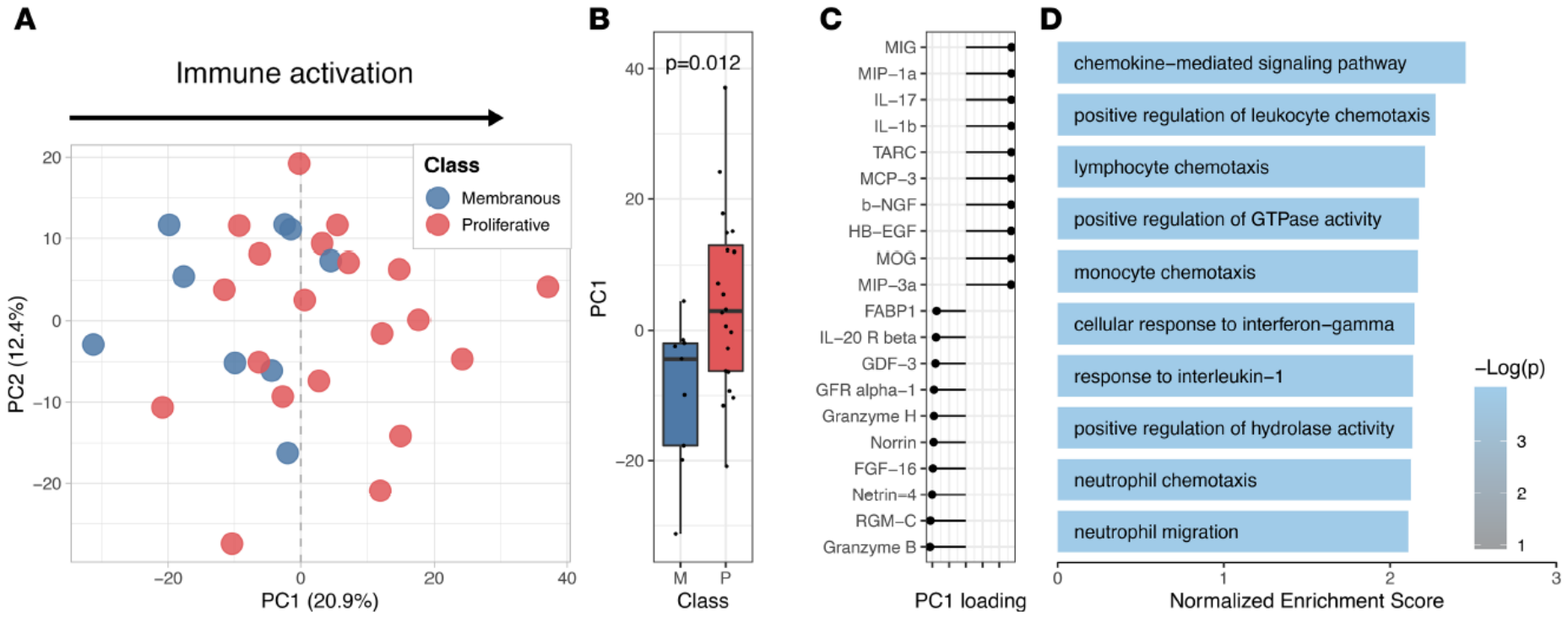
Question: Capture of inflammatory response is absent in histopathological morphology

Results: Stratification of chemokine gradient inducible of IFN-γ

Chemokines produced by kidney infiltrating $CD8^+$ cells

Fava a. et al, *JCI Insight*. 2020;5(12):e138345

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



Fava a. et al, *JCI Insight*. 2020;5(12):e138345

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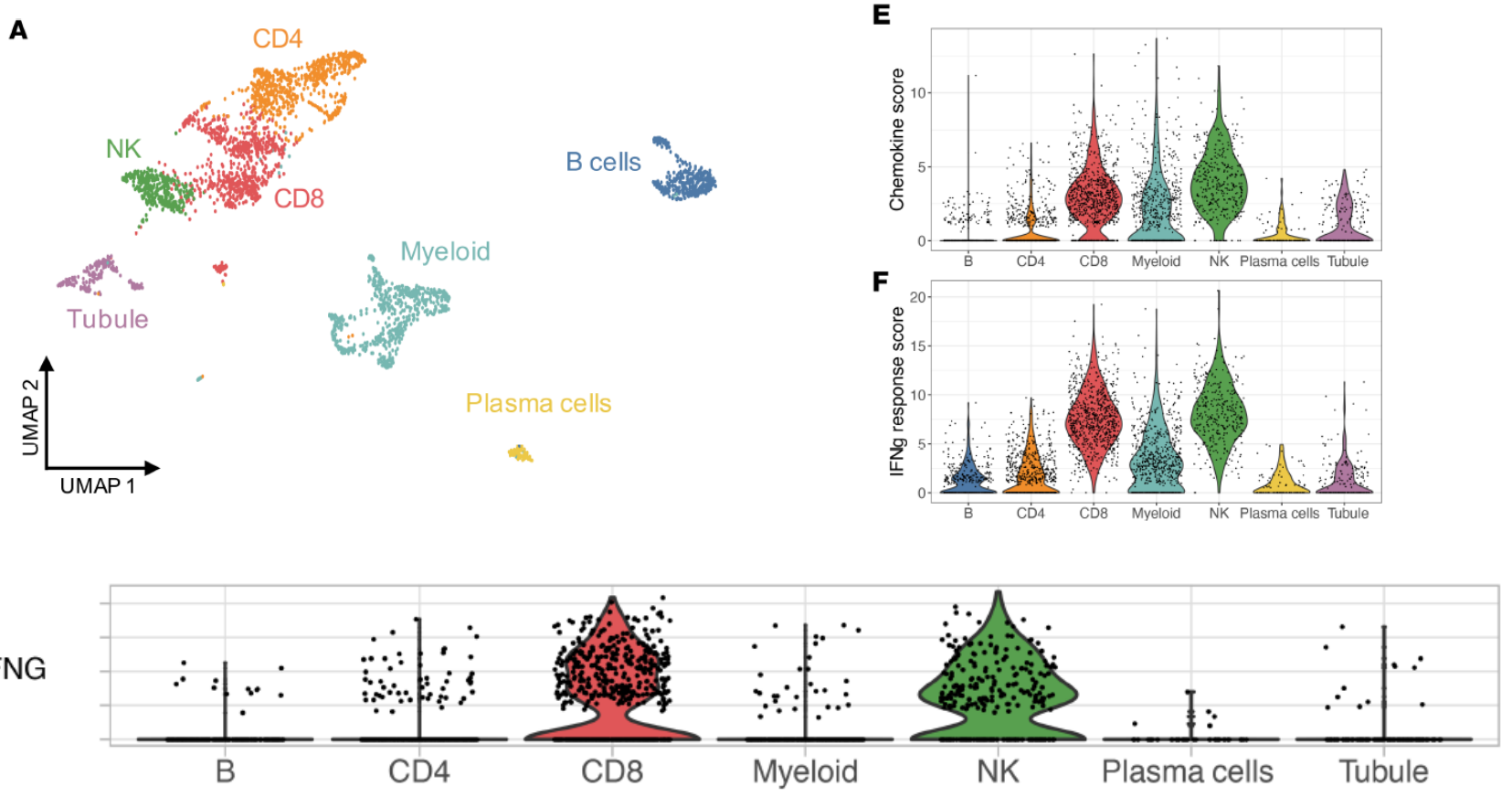
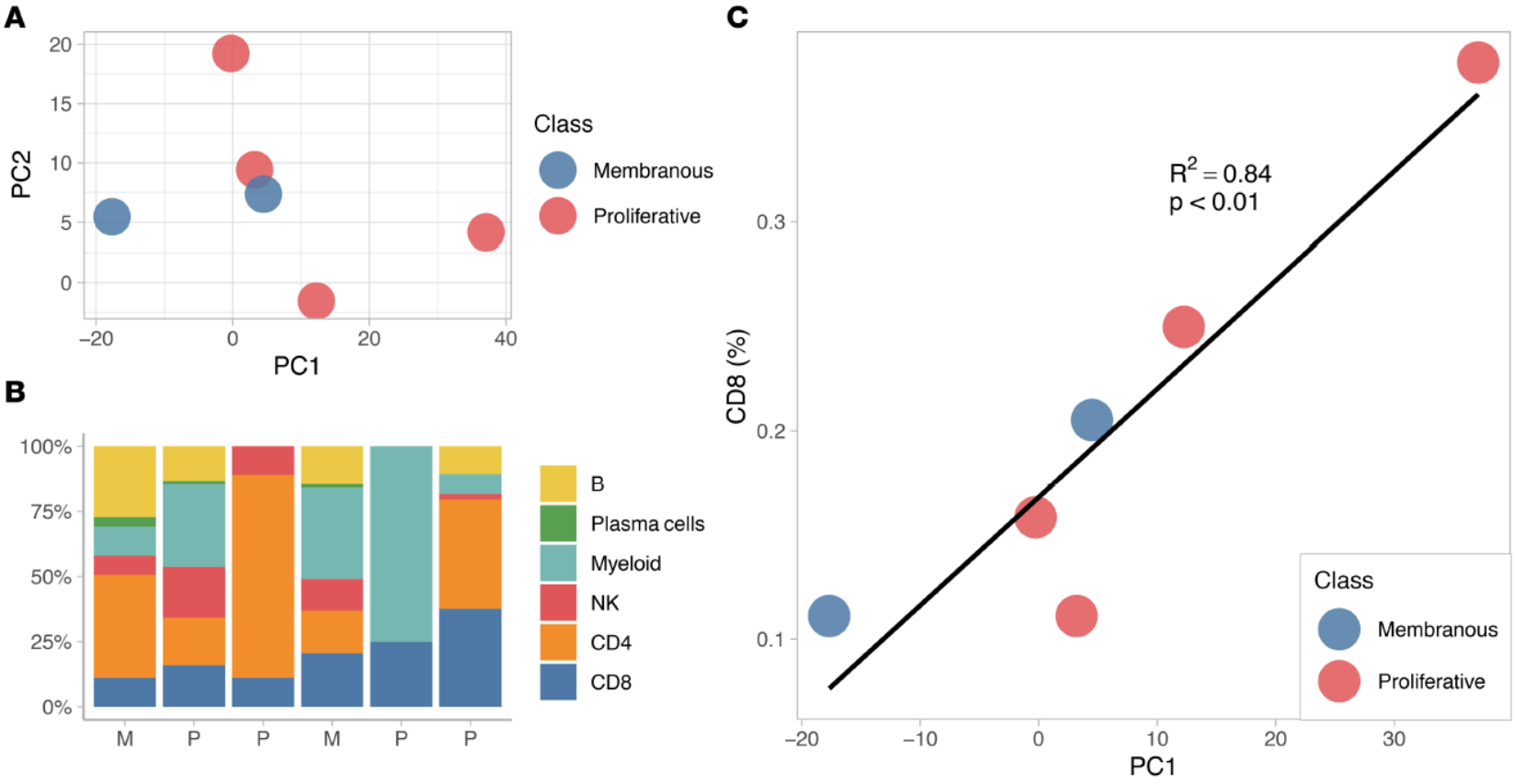


Fava a. et al, *JCI Insight*. 2020;5(12):e138345

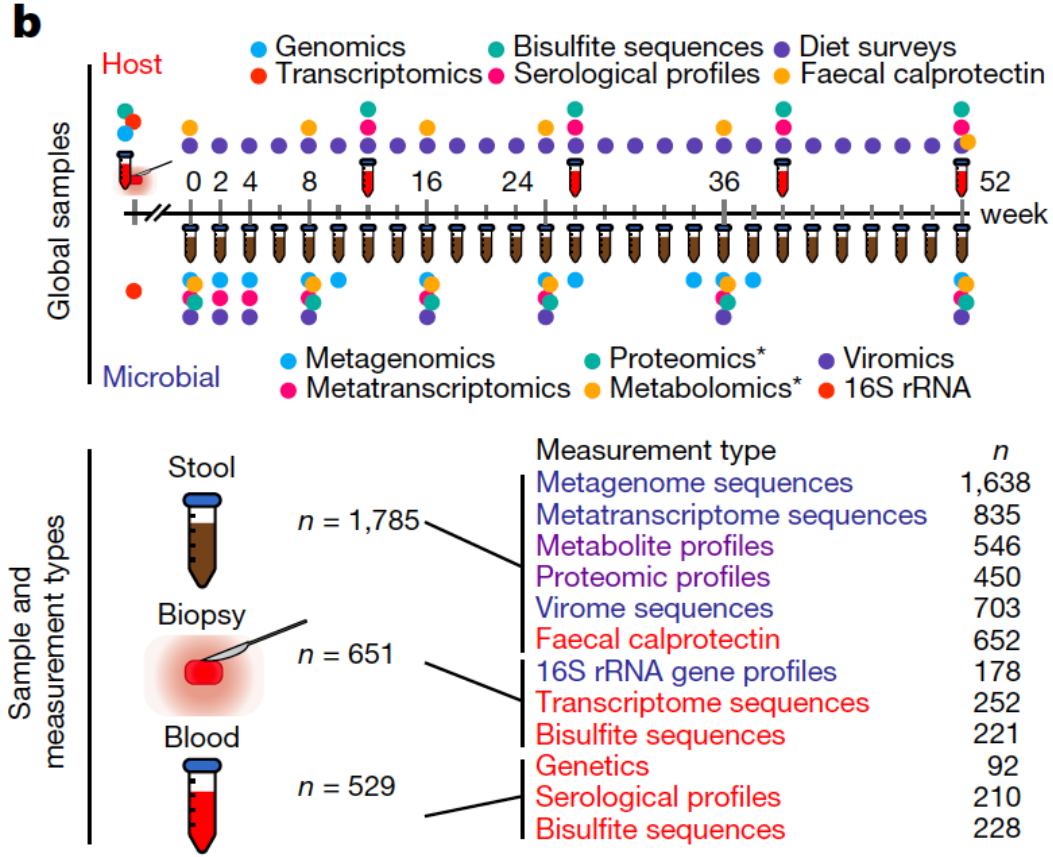
Proteomics analysis in urine leads to stratification of SLE patients according to kidney damage



Fava a. et al, *JCI Insight*. 2020;5(12):e138345

Microbiomics of IBDs
Host/Microbial interaction map

Multi-omics of the gut microbial ecosystem in inflammatory bowel diseases



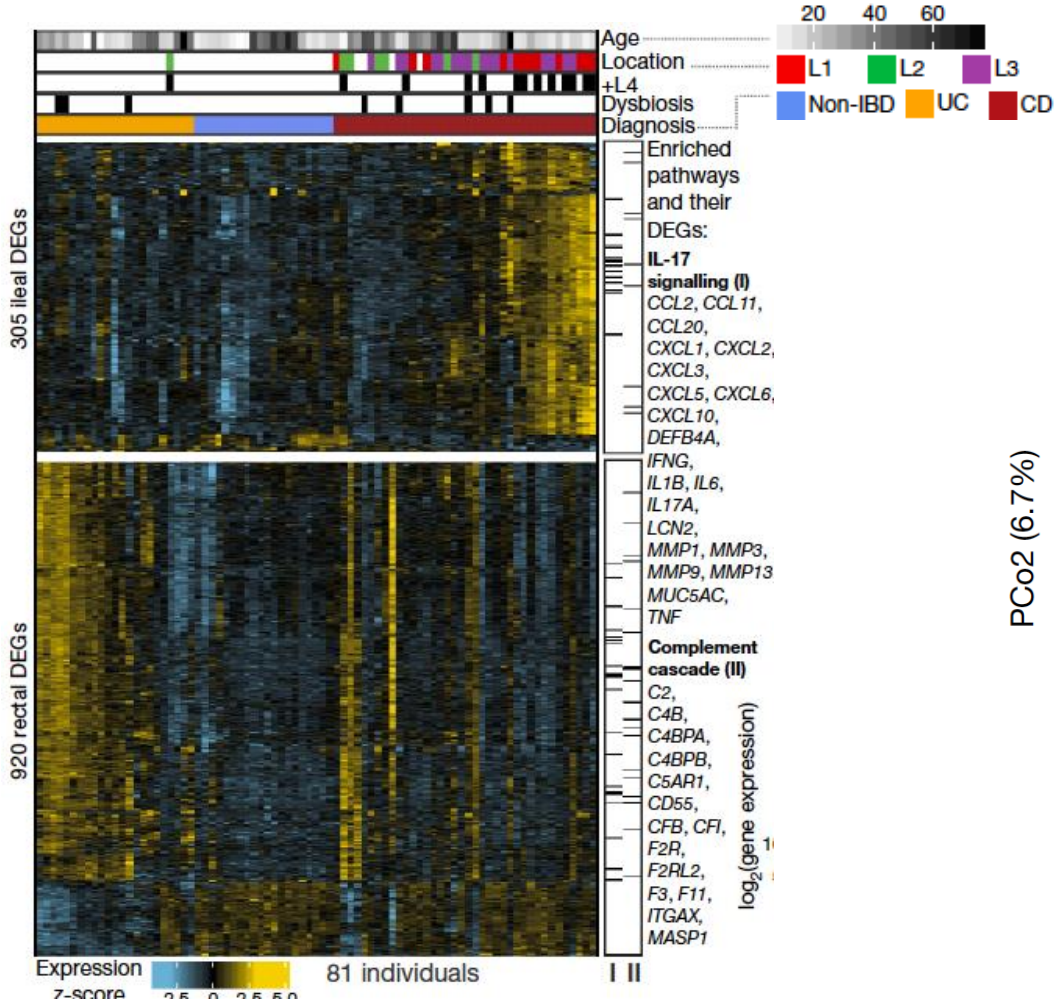
Question: Explore dysbiosis of microbiome in IBD patients

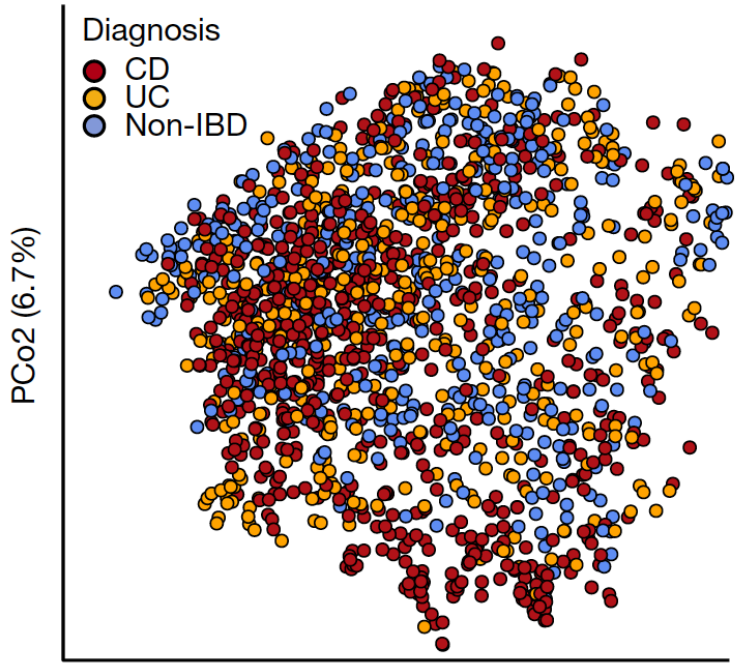
Results: Shifts in temporal variability, taxonomy, functions and biochemistry of phyla during marked disease activity

Map of the crosstalk with the host

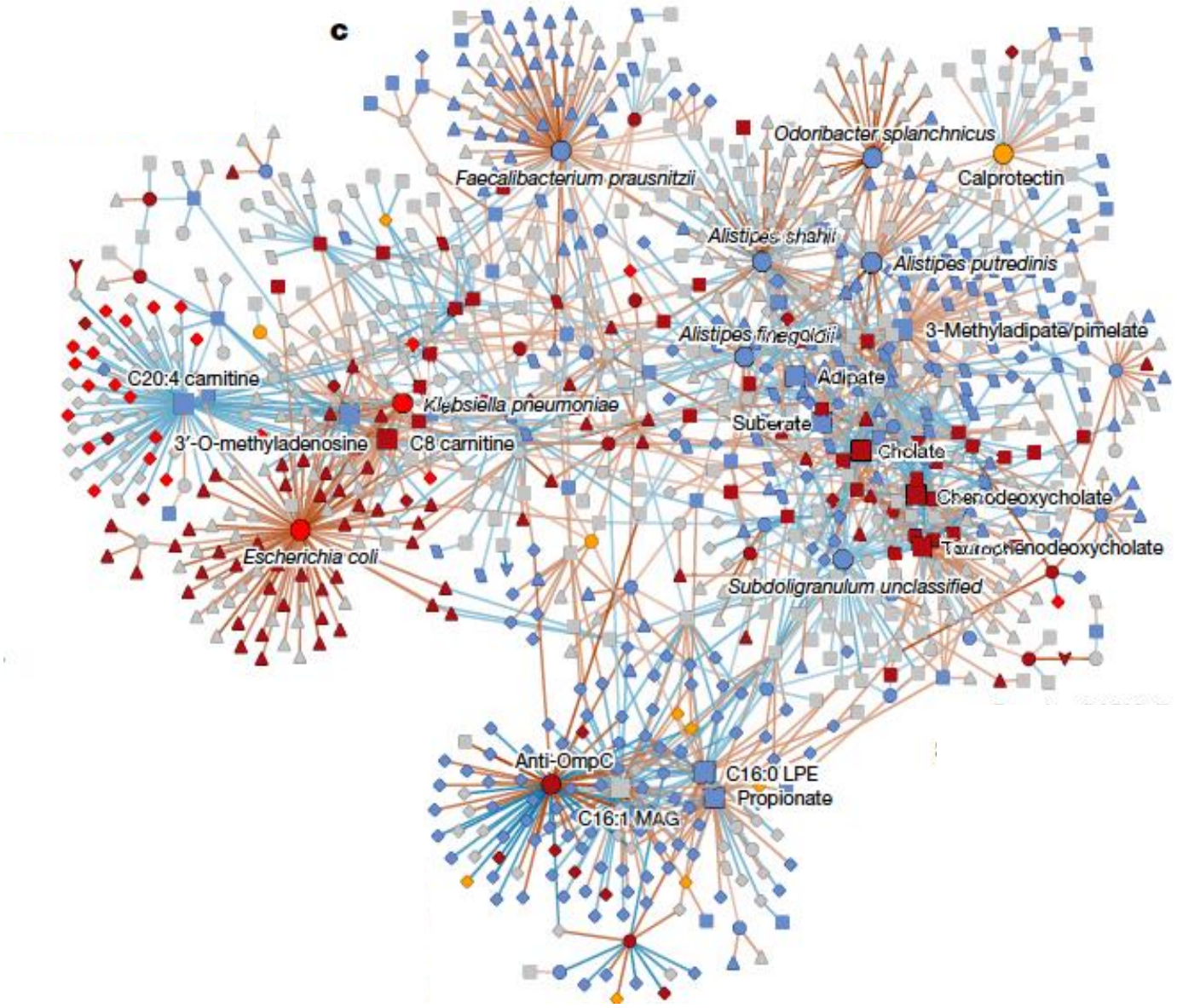
Lloyd-Price, J *et al. Nature* **569,** 655–662 (2019)

Microbiomics of IBDs
Host/Microbial interaction map





Lloyd-Price, J *et al. Nature* **569,** 655–662 (2019)



Lloyd-Price, J *et al. Nature* **569,** 655–662 (2019)

"There's your problem...
You've got an extra parenthesis in line 18."

Thank you!