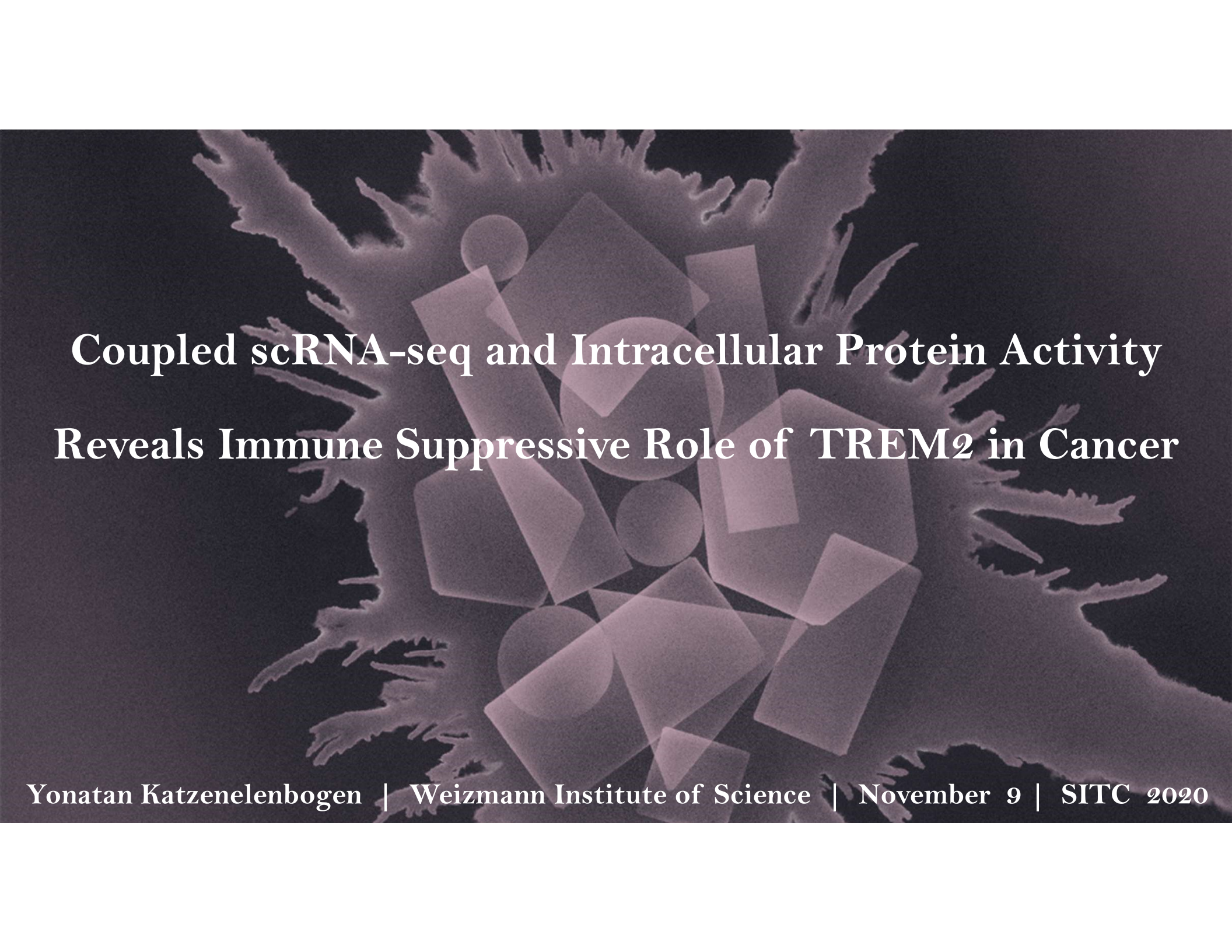
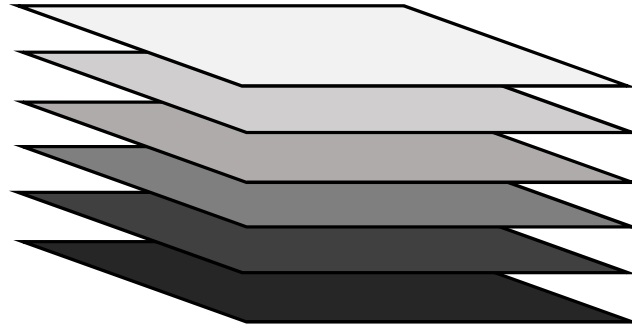
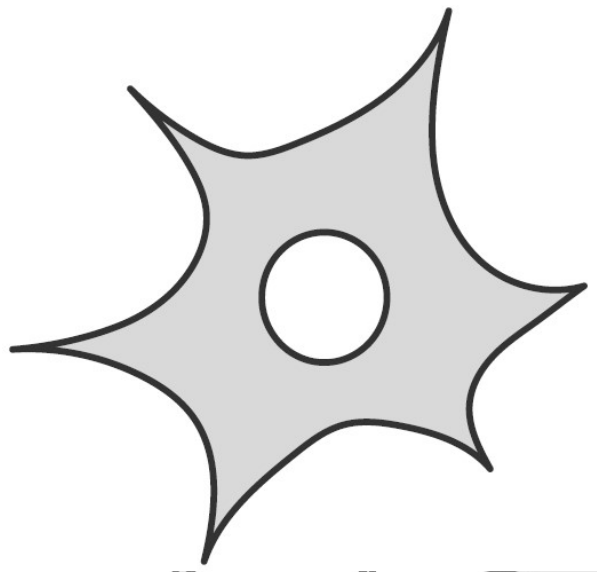




Coupled scRNA-seq and Intracellular Protein Activity Reveals Immune Suppressive Role of TREM2 in Cancer

Yonatan Katzenelenbogen | Weizmann Institute of Science | November 9 | SITC 2020

Defining cell identity



Transcriptome

Proteome

Lineage

Morphology

Location

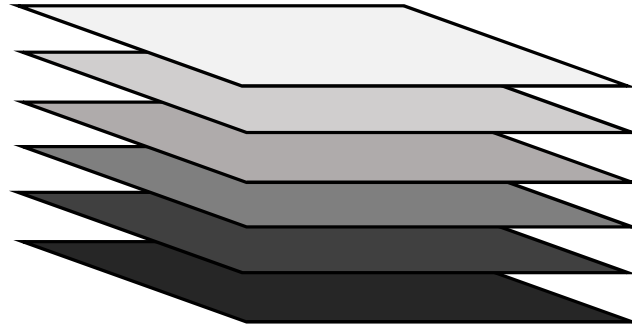
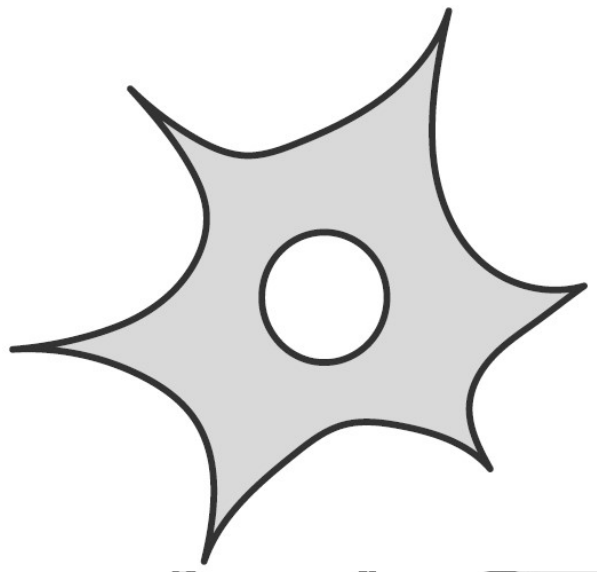
Neighbors

Function

Genome

Epigenetics

Defining cell identity



Transcriptome

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Location

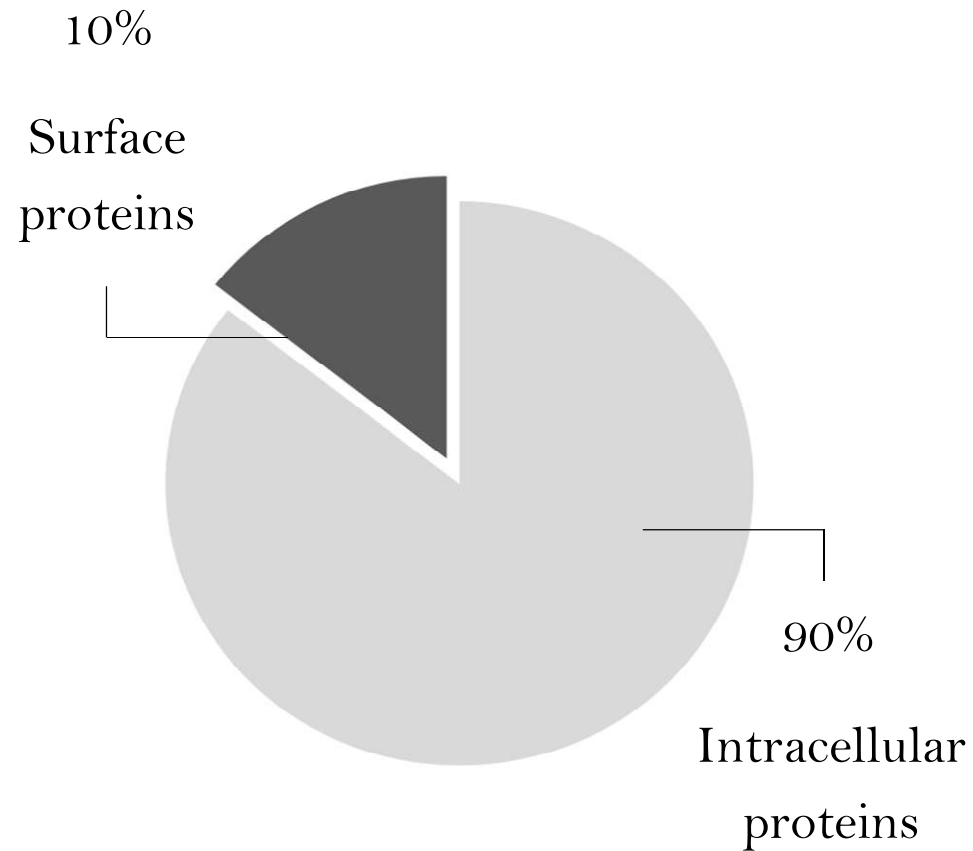
Neighbors

Function

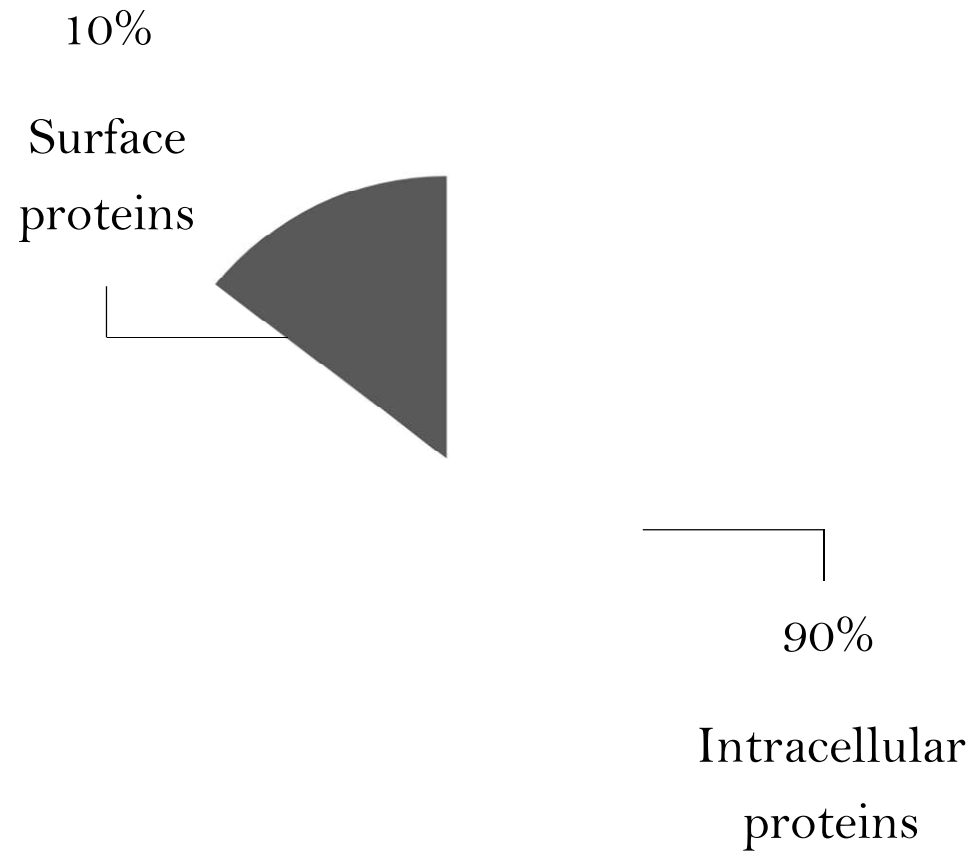
Genome

Epigenetics

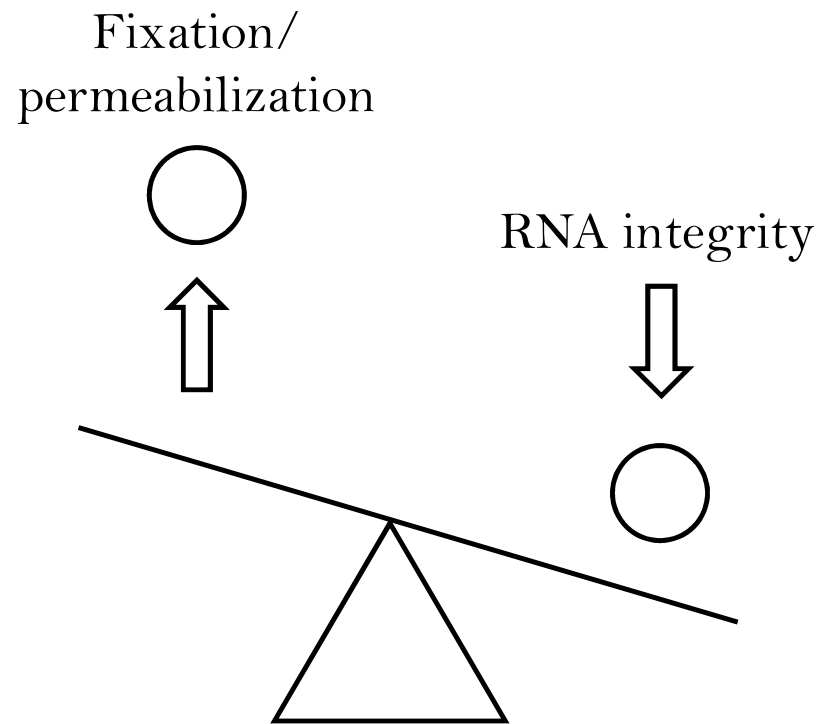
Single cell RNA-seq + protein measurement



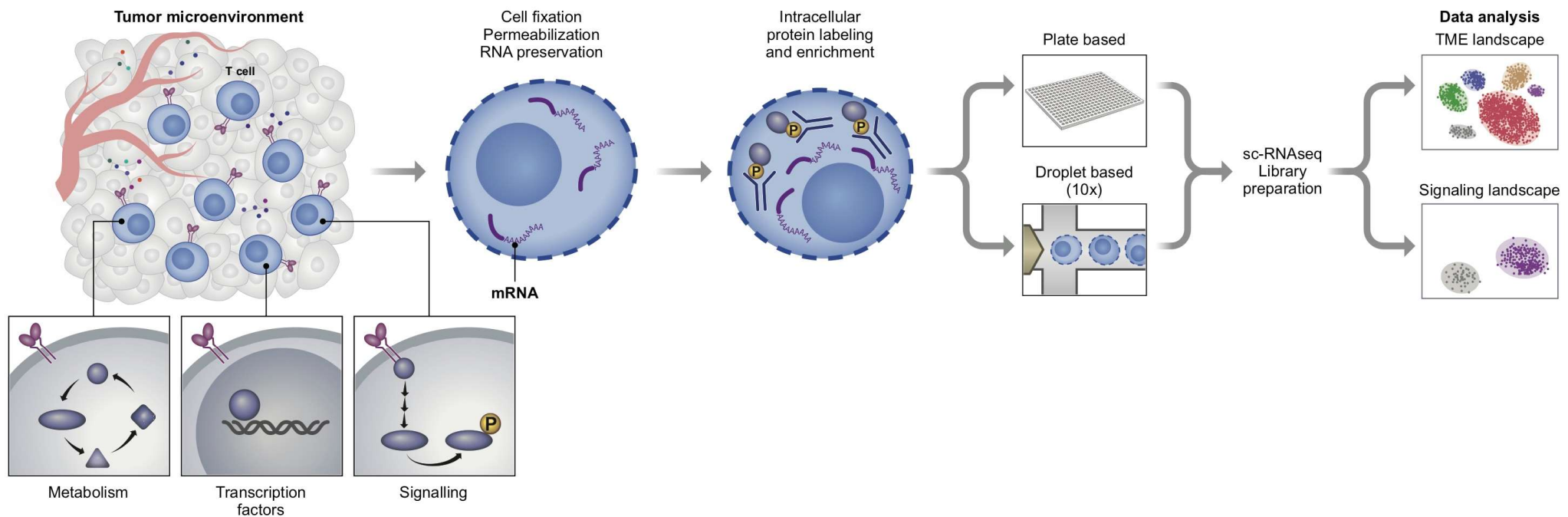
Single cell RNA-seq + protein measurement



Challenge

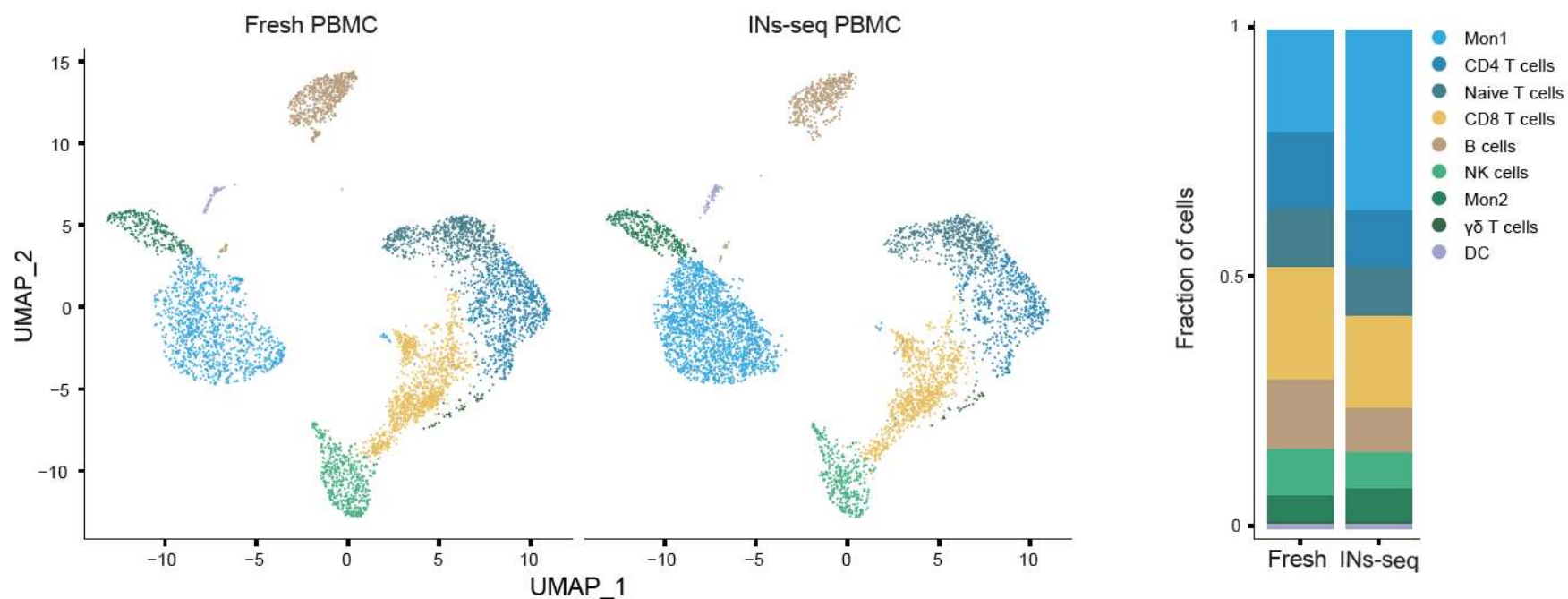


INs-seq: cell fixation technology enabling simultaneous intracellular protein recording and scRNA-seq



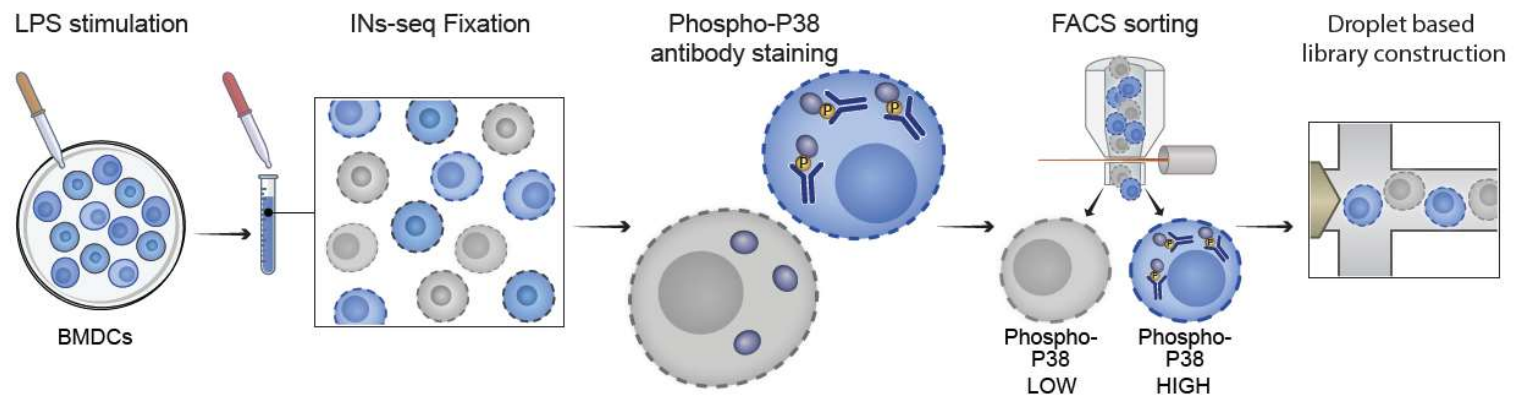
Katzanellenbogen et al. Cell, 2020

Comparison between fresh and INs-seq human PBMC

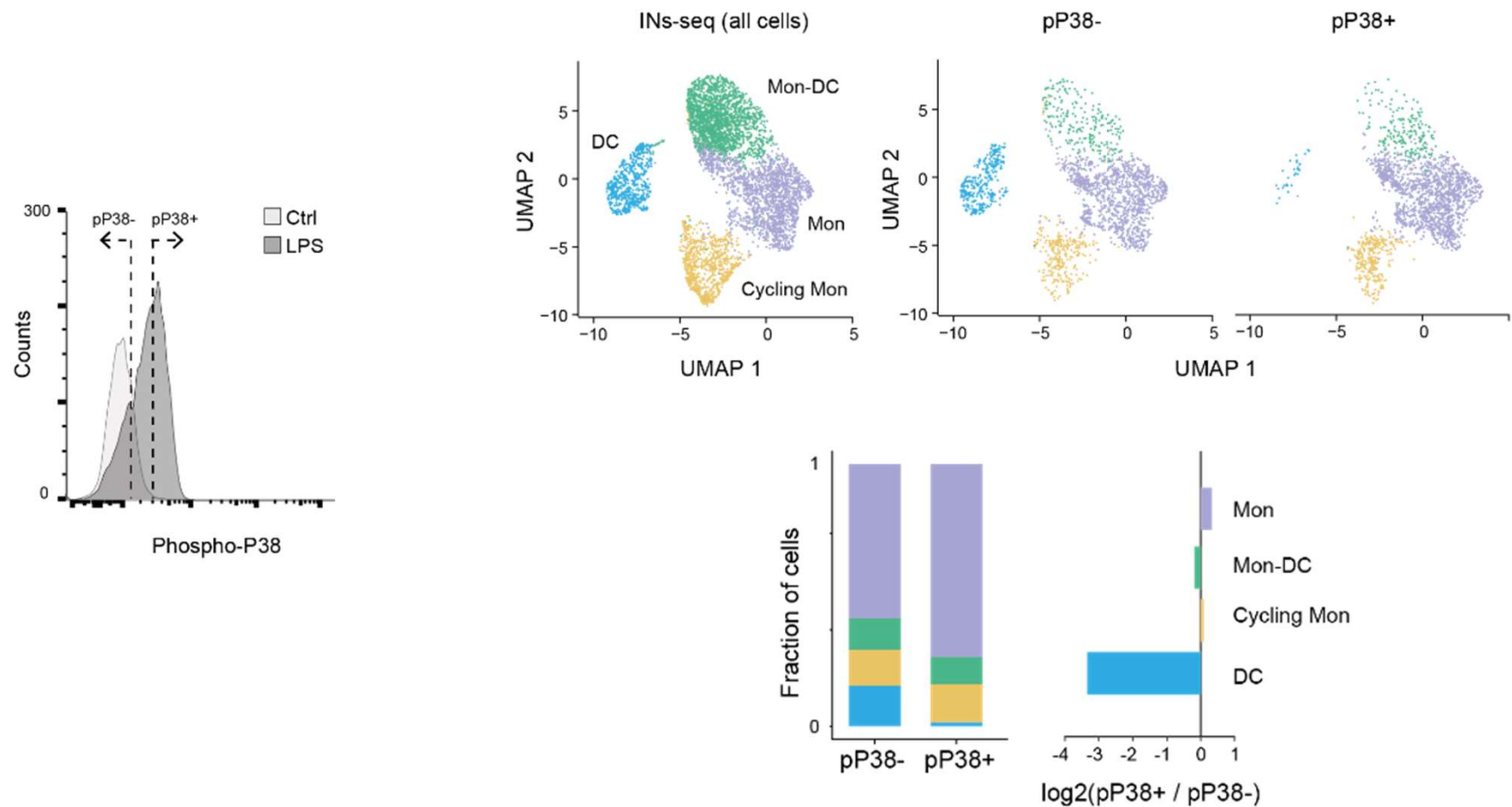


Using Seurat v3.1.0 data integration
Tim Stuart, Andrew Butler, ... , Rahul Satija. *Cell* 2019

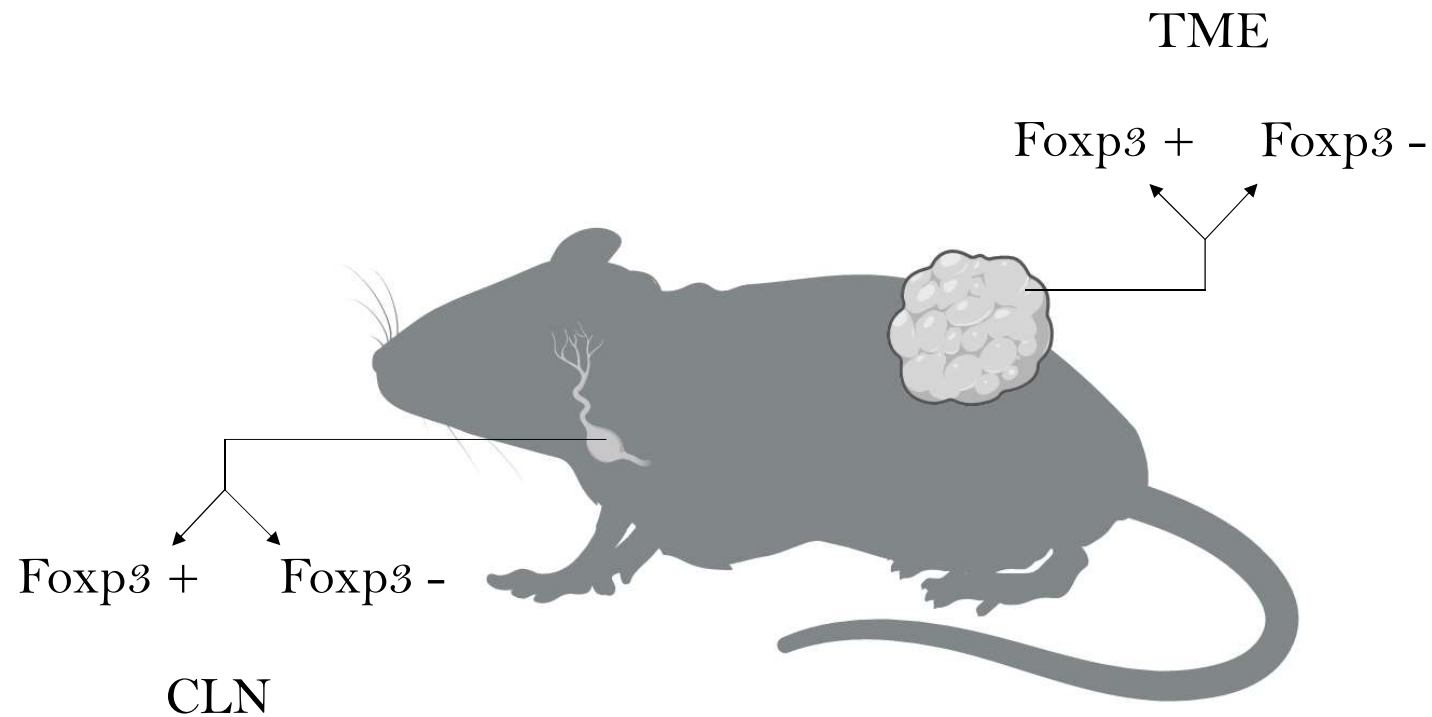
INs-seq analysis of MAPK signaling pathway



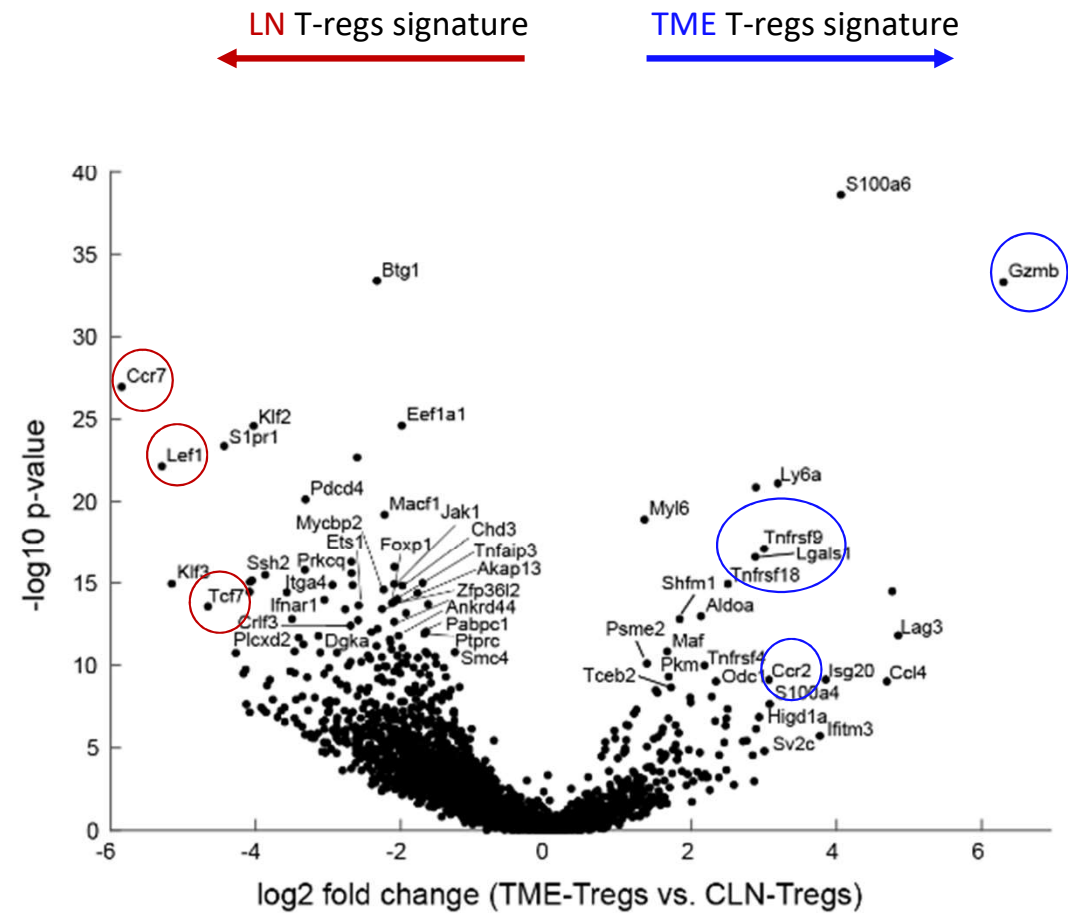
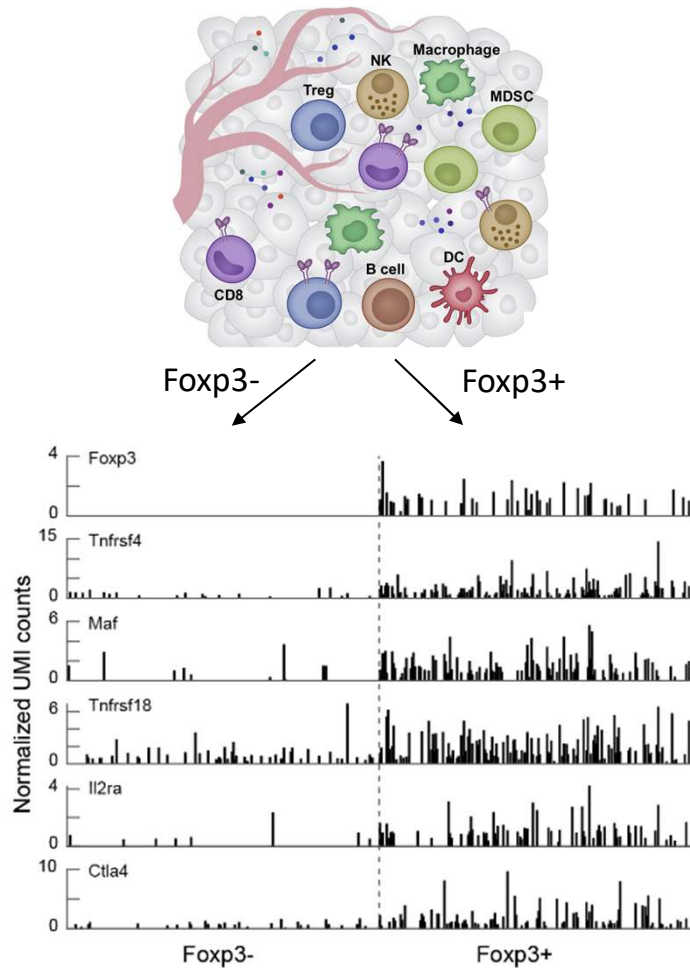
INs-seq separate responders and non-responders



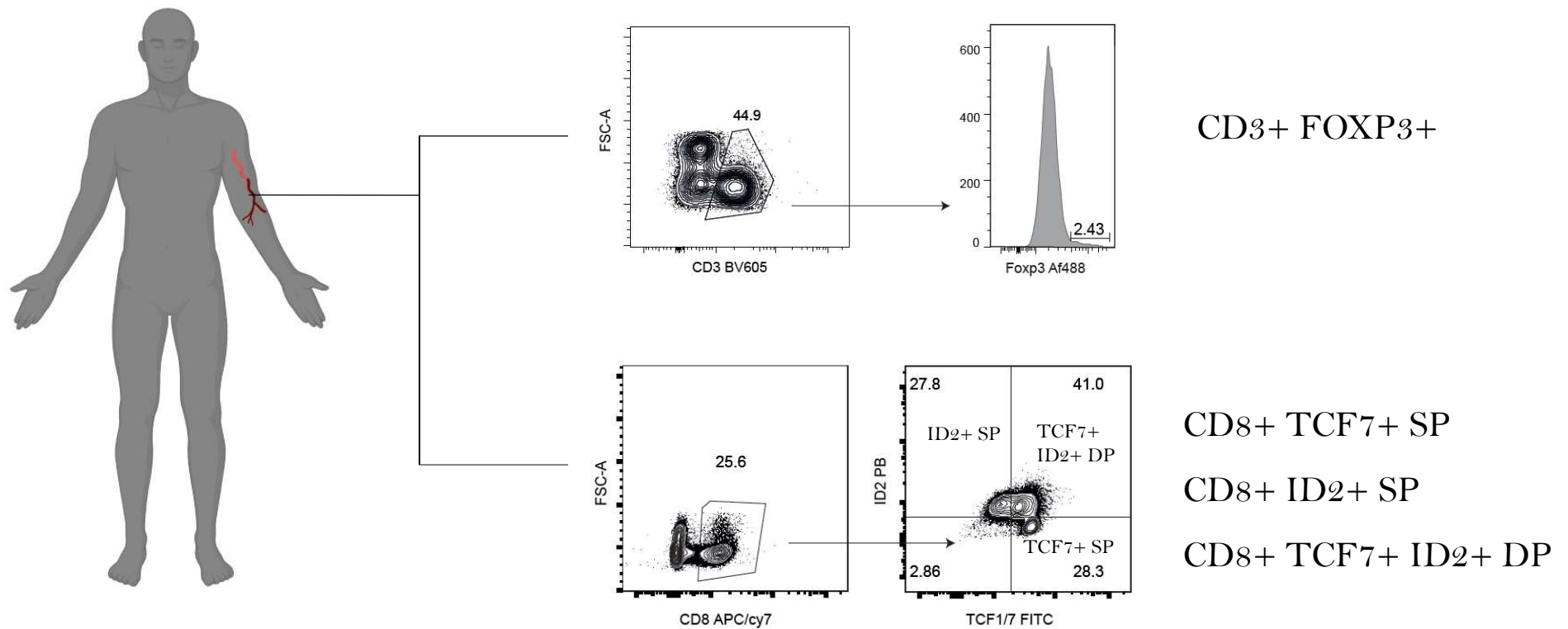
in-vivo T-reg profiling using INs-seq



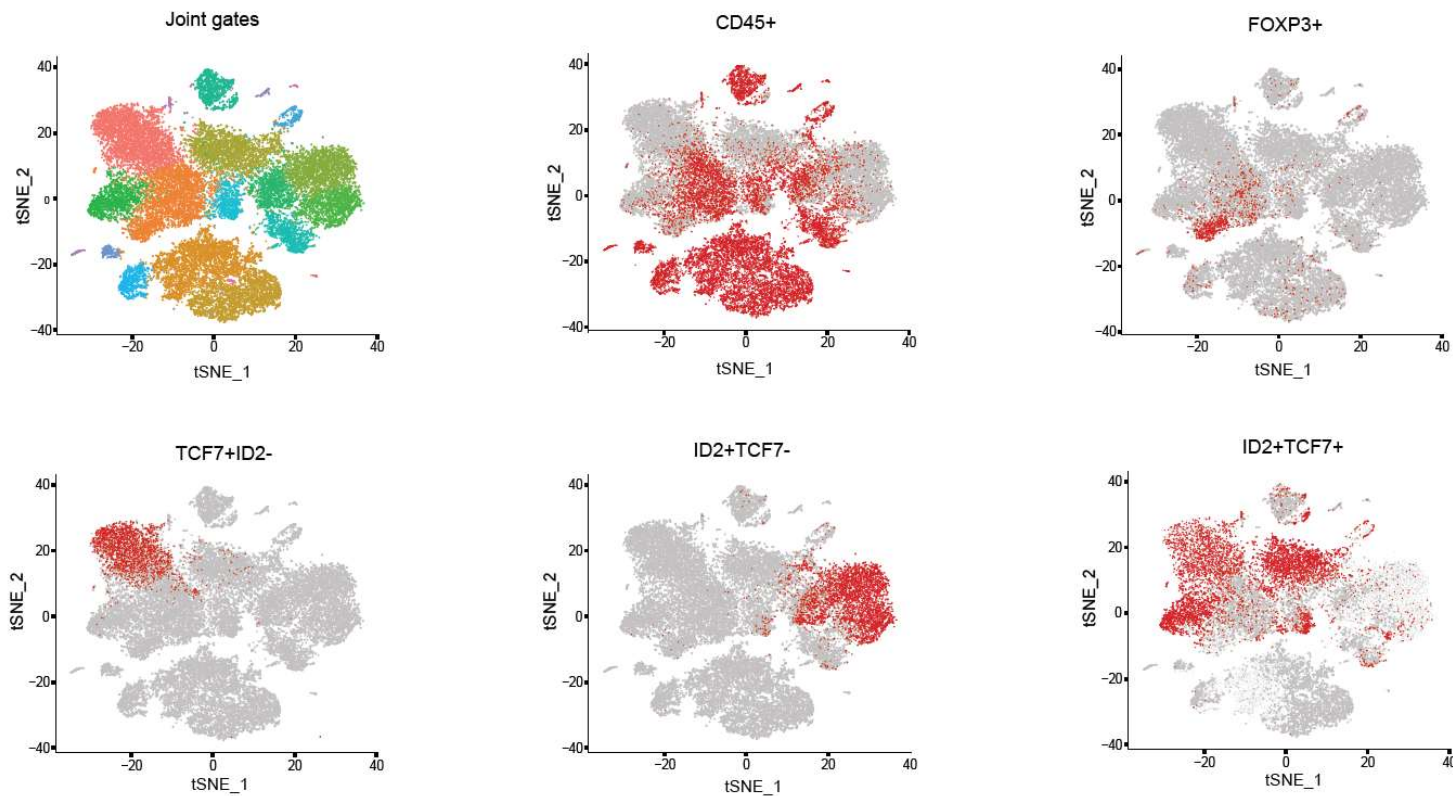
in-vivo T-reg profiling using INs-seq.



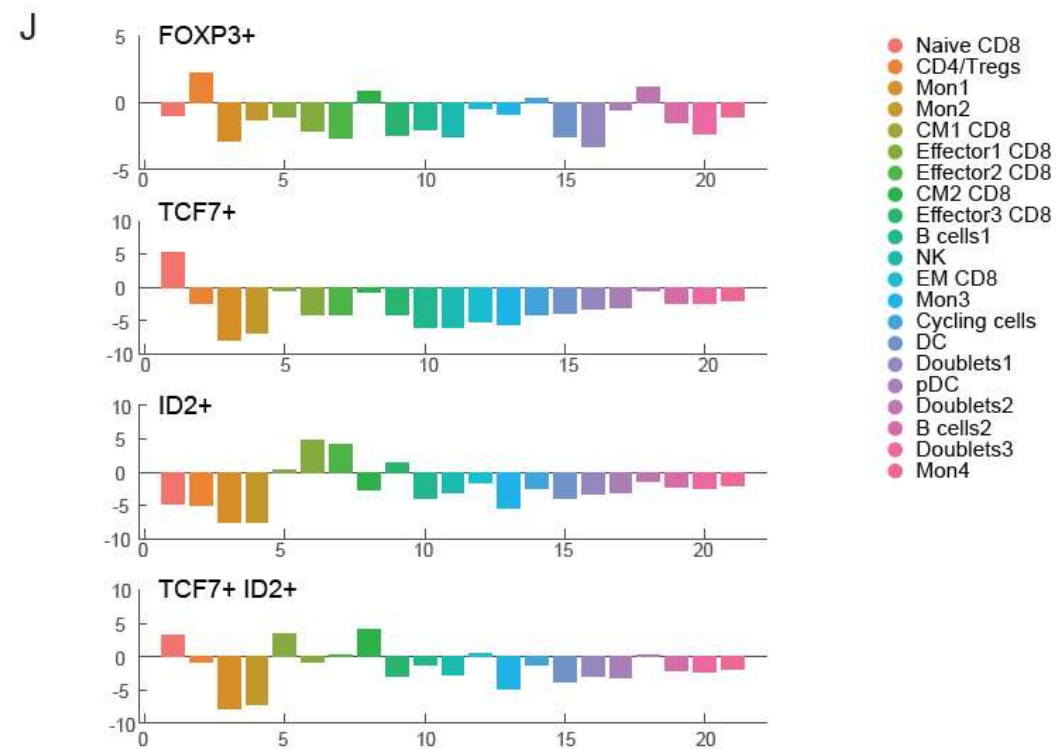
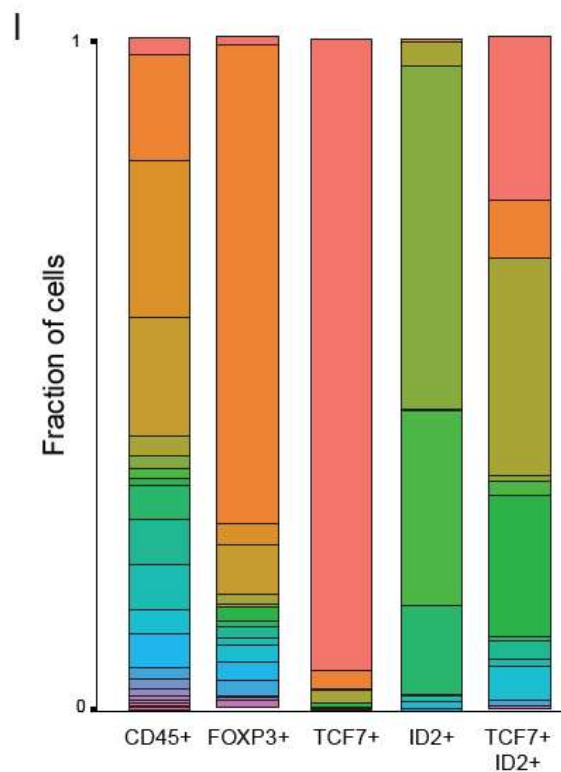
in-vivo characterization of human T cell subtypes by INs-seq transcription factors map



in-vivo characterization of human T cell subtypes by INs-seq transcription factors map



in-vivo characterization of human T cell subtypes by INs-seq transcription factors map



Myeloid derived suppressor cells: “lineage vague” tumor related immune regulatory cells

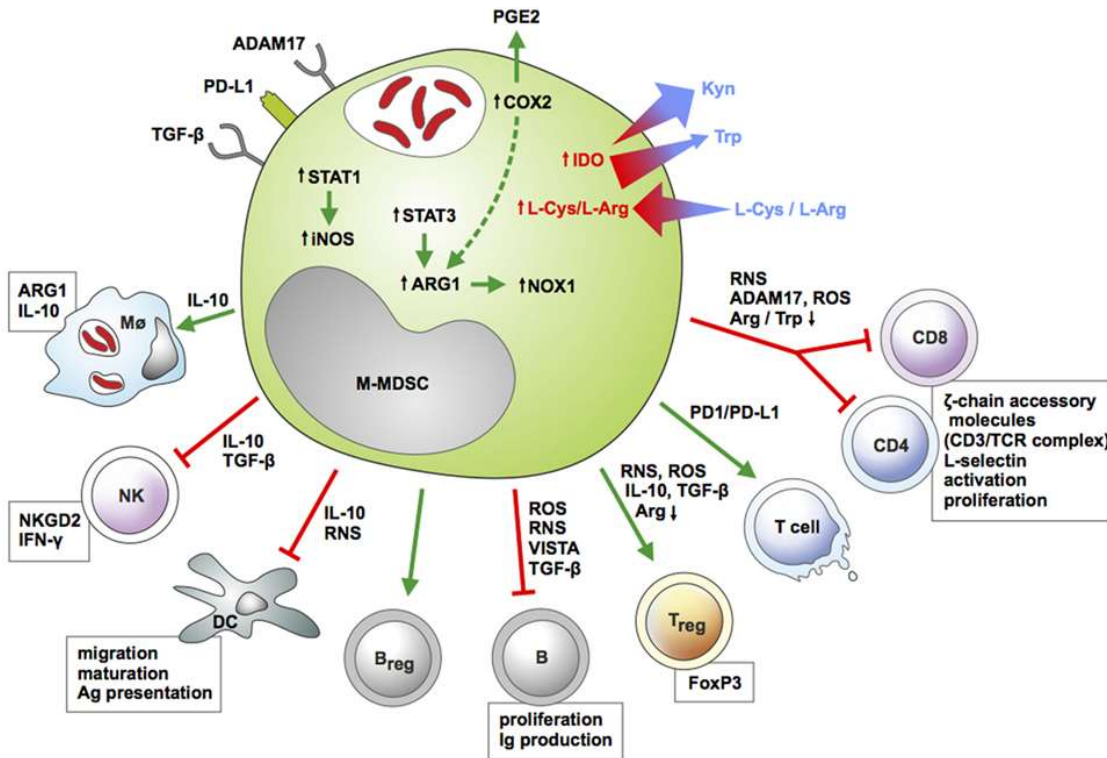
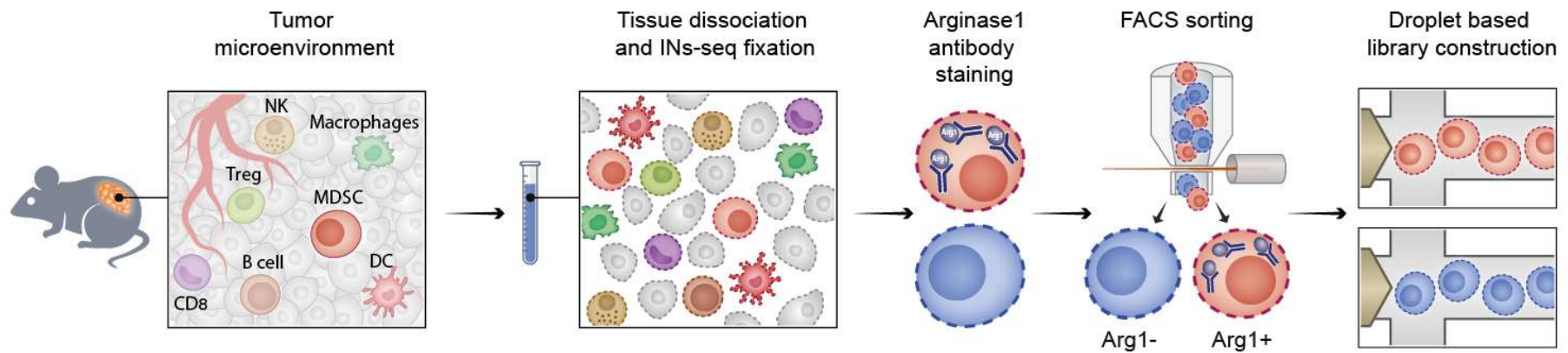


Table 1 | Phenotypical, molecular and functional properties of neutrophils, monocytes and MDSCs

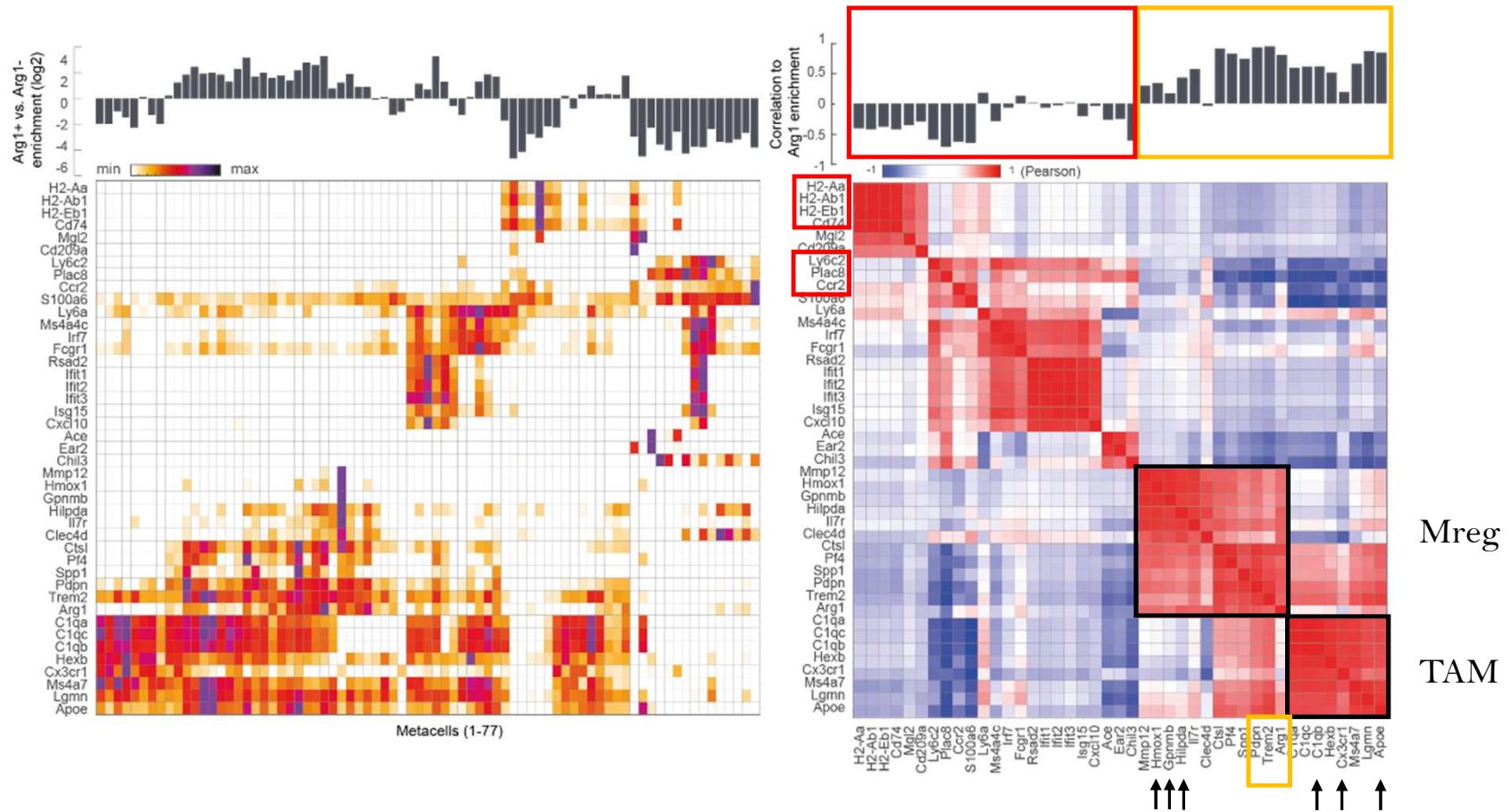
Human	Neutrophils	PMN-MDSCs	Monocytes	M-MDSCs	e-MDSCs	TAMs
Surface phenotype	CD11b ⁺ CD14 ⁺ CD15 ⁺ CD66b ⁺ LOX-1 ⁺	CD11b ⁺ CD14 ⁺ CD15 ⁺ CD66b ⁺ LOX-1 ⁺	CD14 ⁺ CD15 ⁺ HLA-DR ⁺	CD14 ⁺ CD15 ⁺ HLA-DR ^{low}	CD3 ⁺ CD14 ⁺ CD15 ⁺ CD19 ⁺ CD56 ⁺ HLA-DR ⁺ CD33 ⁺	CD206 ⁺ CD163 ⁺ C D204 ⁺ CD45 ⁺
Density	High	Low	Low	Low	Low	Not applicable
Immune suppression	-	+	-	++	++	+++
ROS	+	+++	-/+	-/+	++	++
NO	-	+	+	+++	++	+++
ARG1	+	++	-	-	-/?	-
PGE2	-	++	-	+	N/A	-
S100A8/A9	+	++	-/+	+	N/A	-
ER stress	-/+	++	-/+	++	N/A	N/A
STAT3	-/+	++	-/+	++	N/A	N/A
Mouse						
	Neutrophils	PMN-MDSCs	Monocytes	M-MDSCs	TAMs	
Minimal surface phenotype	CD11b ⁺ Ly6G ⁺ Ly6C ⁺		CD11b ⁺ Ly6G ⁺ Ly6C ⁺		CD11b ⁺ F4/80 ⁺ Ly6C ⁺ Ly6G ⁺ CD115 ⁺	
Immune suppression	-	+	-	++	+++	
ROS	-/+	++	-/+	-/+	++	
NO	-	+	+	++	++	
ARG1	-	++	+	++	++	
PGE2	-	++	-	+	N/A	
S100A8/A9	+	++	-/+	+	-	
ER stress	-/+	++	-/+	++	N/A	
STAT3	-/+	++	-/+	++	-/+	
IRF8	+	-/+	+	N/A	++	
C/EBP-β	-/+	++	-/+	+	N/A	
RB1	+	-/+	+	-/+	N/A	

Comparisons between cells are shown separately for each factor. Therefore, different factors should not be compared with each other. e-MDSCs, early-stage MDSCs; N/A, not available.

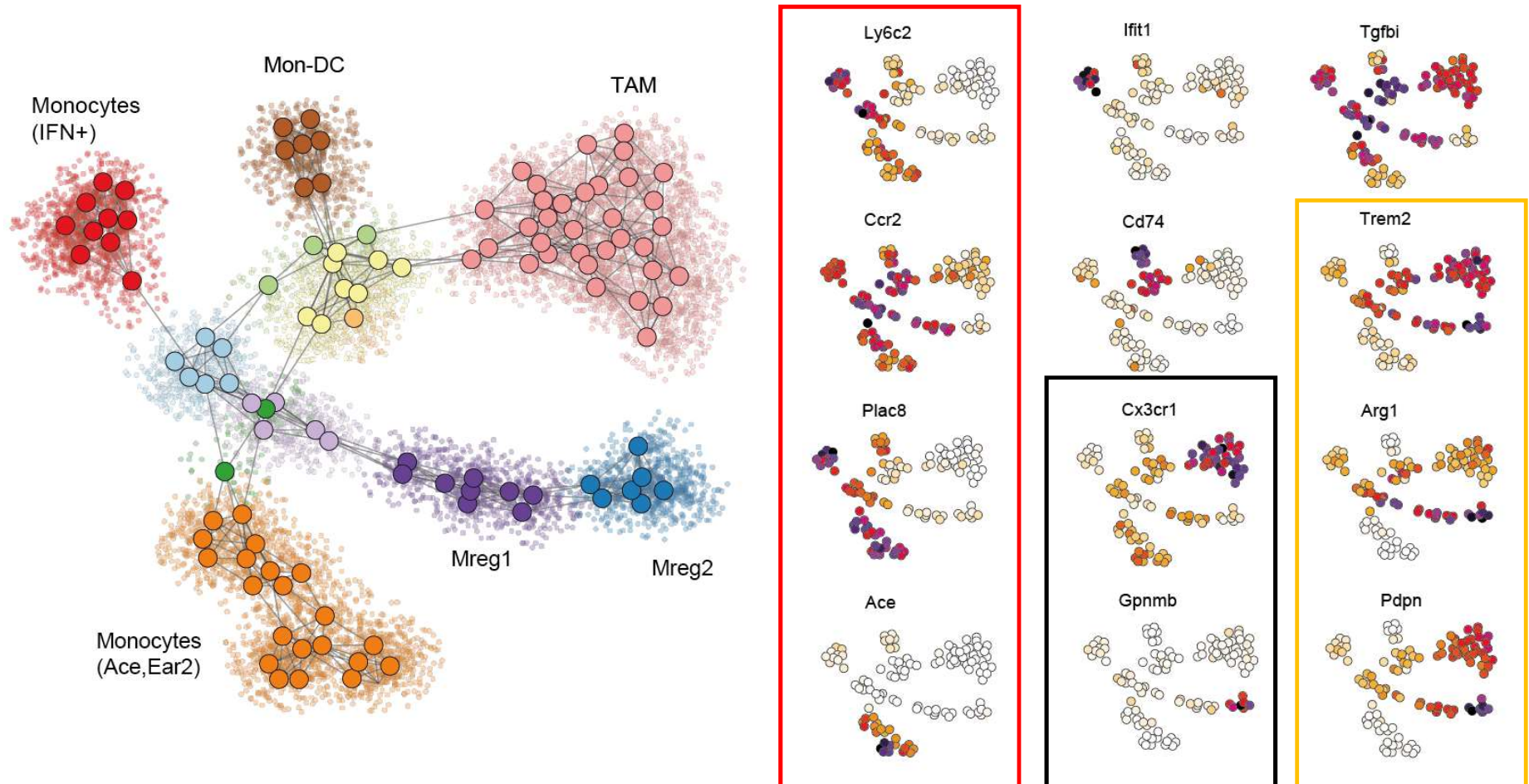
in-vivo TME myeloid suppressor cells profiling using INs-seq



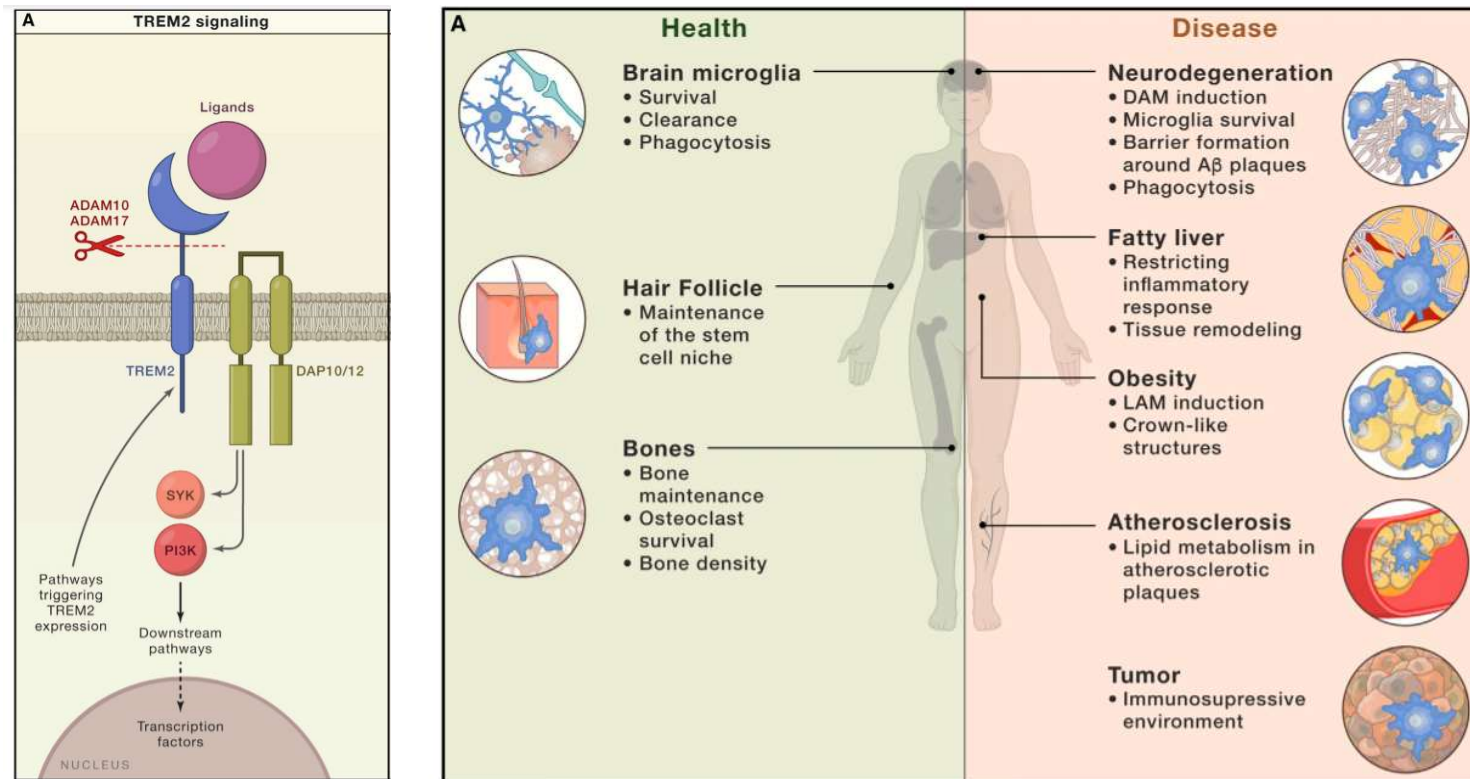
Arg1⁺ Arg1⁻ sub-populations



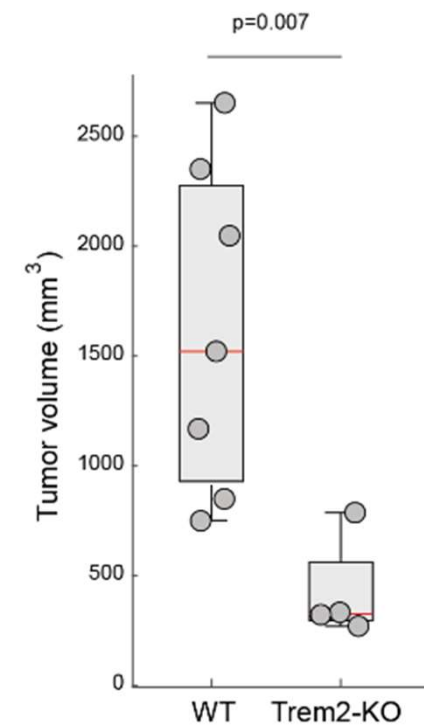
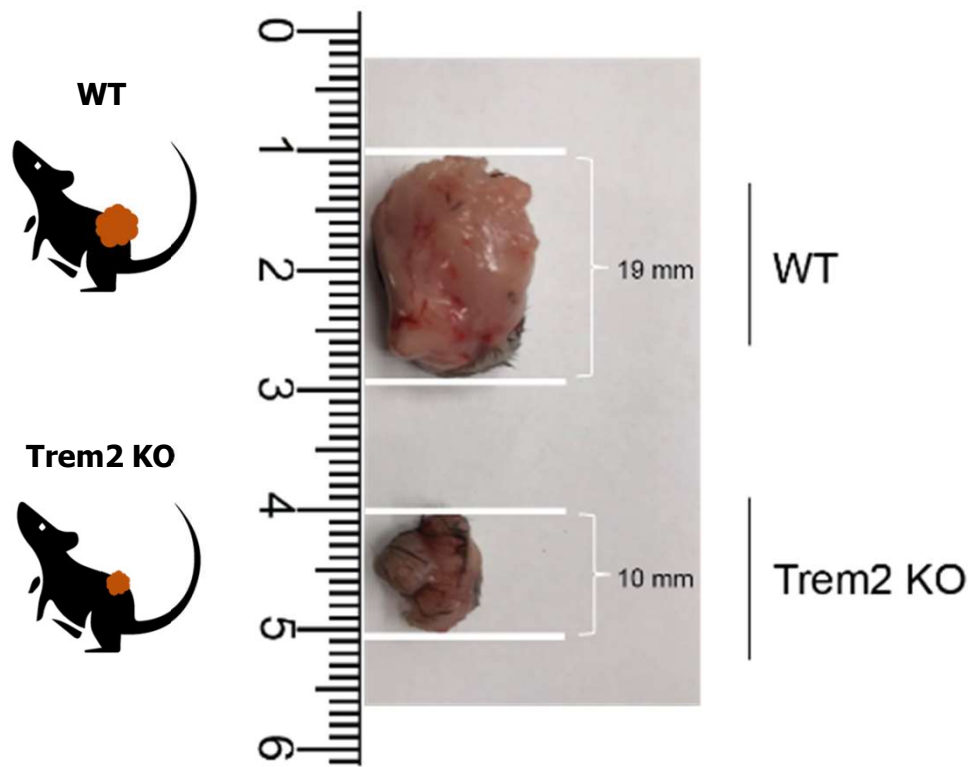
Single-cell analysis of the CD45⁺ TME myeloid compartment



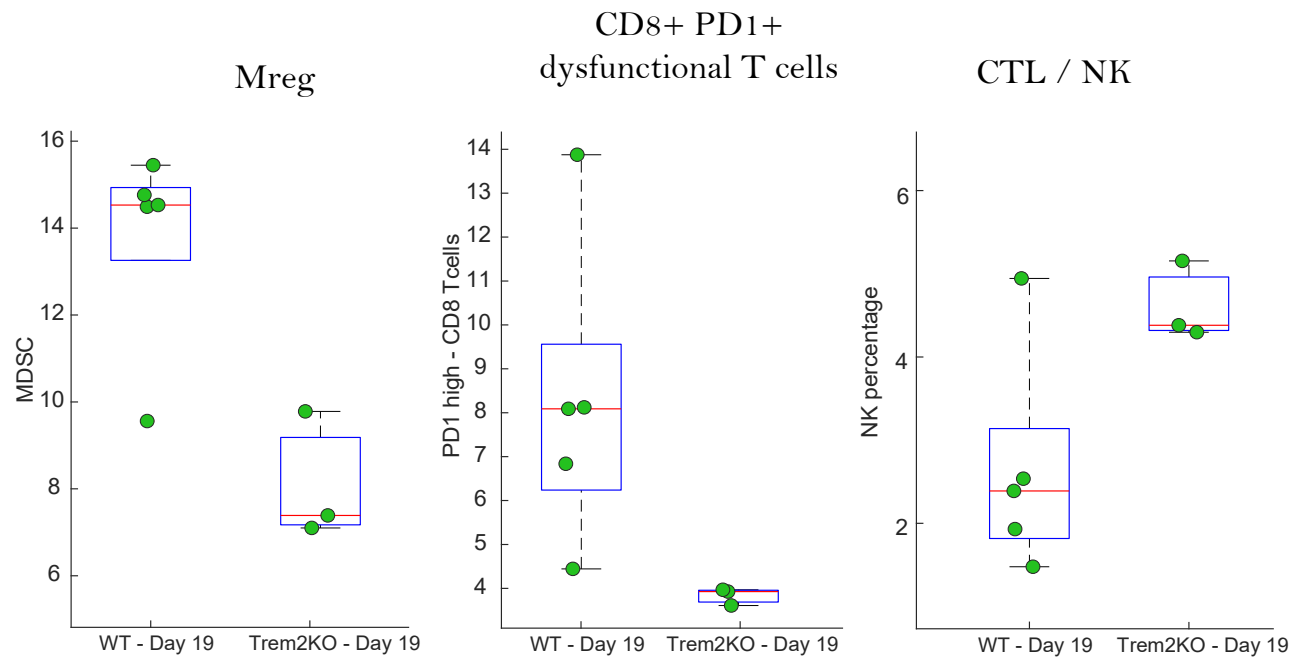
Trem2: a major pathology-induced immune signaling hub



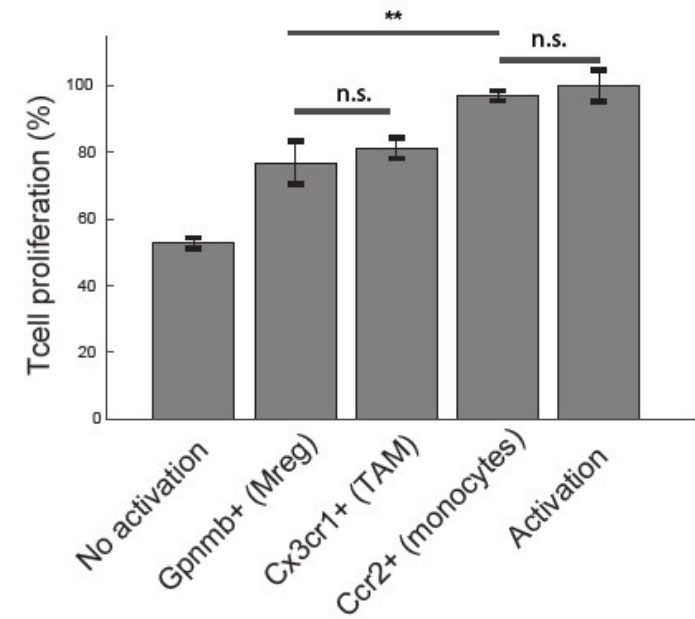
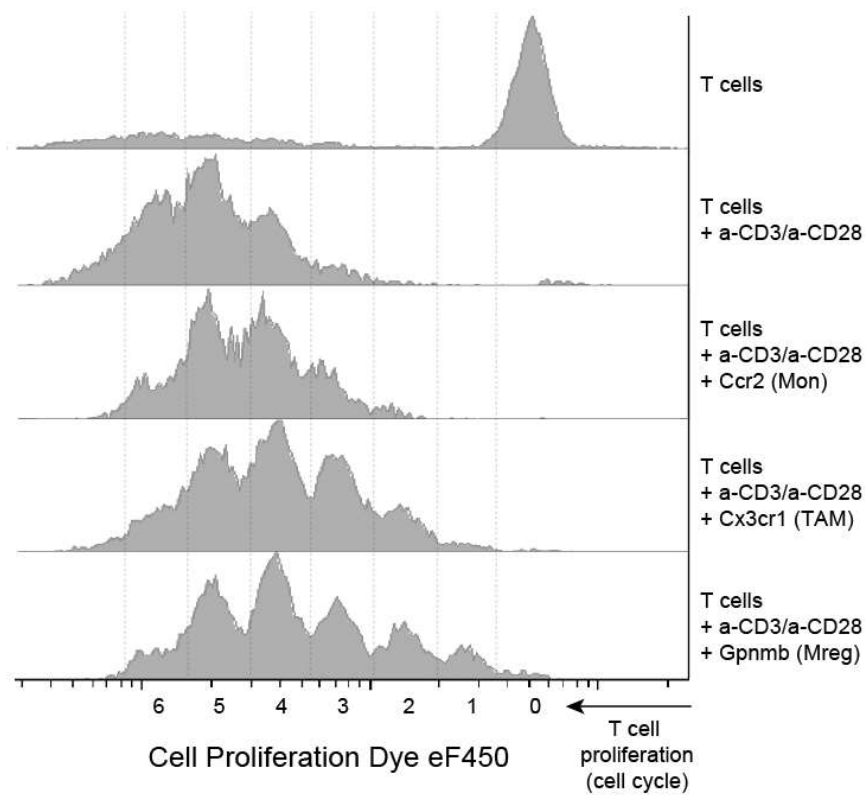
Trem2 KO mice show significant reduction in tumor size



Trem2 KO mice show ablation of Mreg and reduction of PD1+ CD8 dysfunctional



Mreg suppress T cell proliferation



Fadi Sheban



Adam Yalin



Assaf Weiner



Ido Amit



Thank you.

