

# Epigenetic Regulation of Rapid Recall Response of Memory CD4+ T-cells

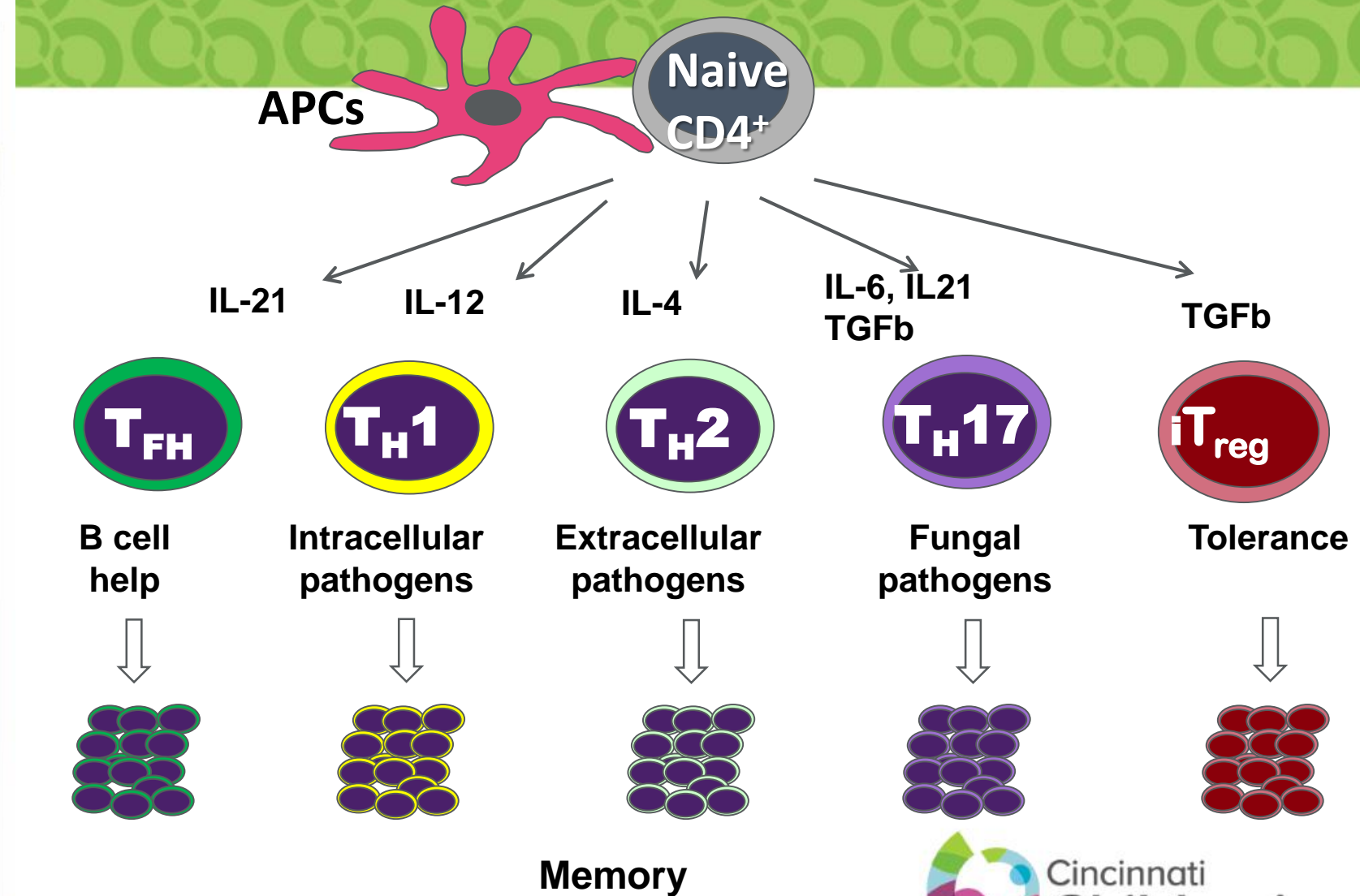
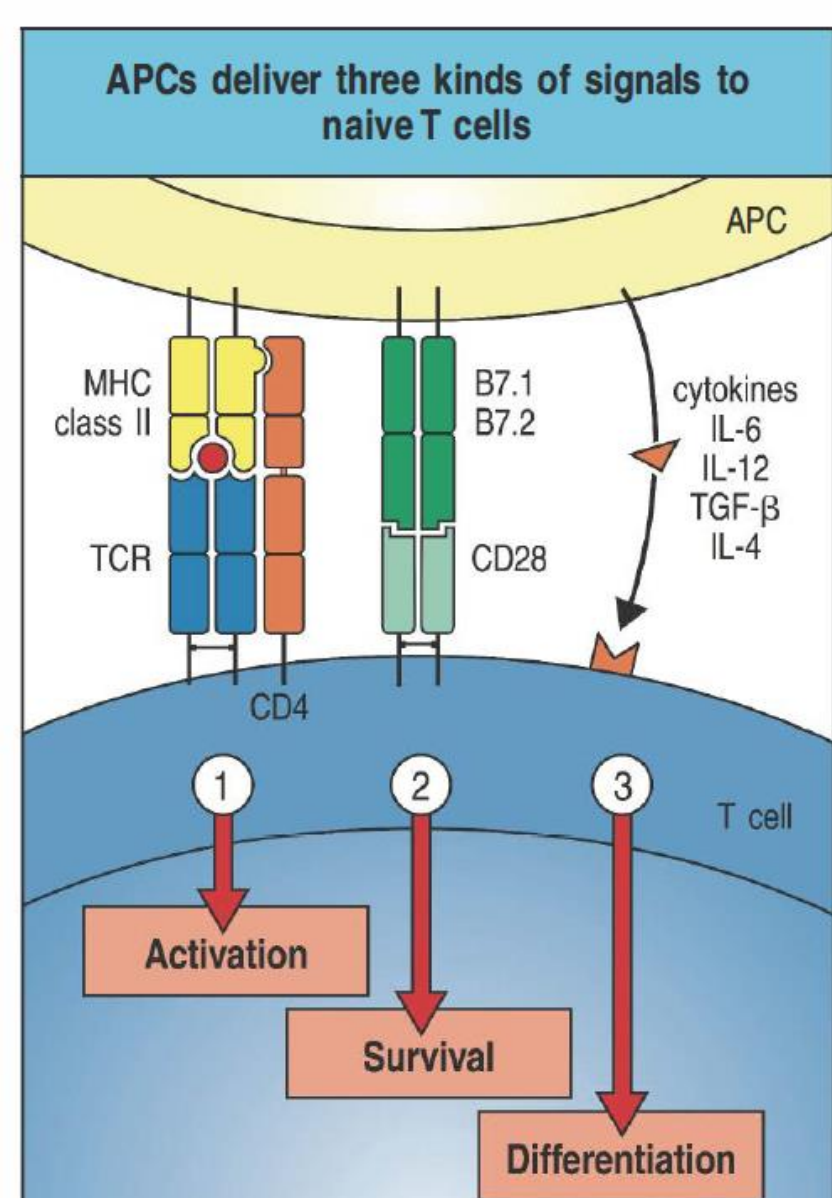
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August 16<sup>th</sup>, 2019

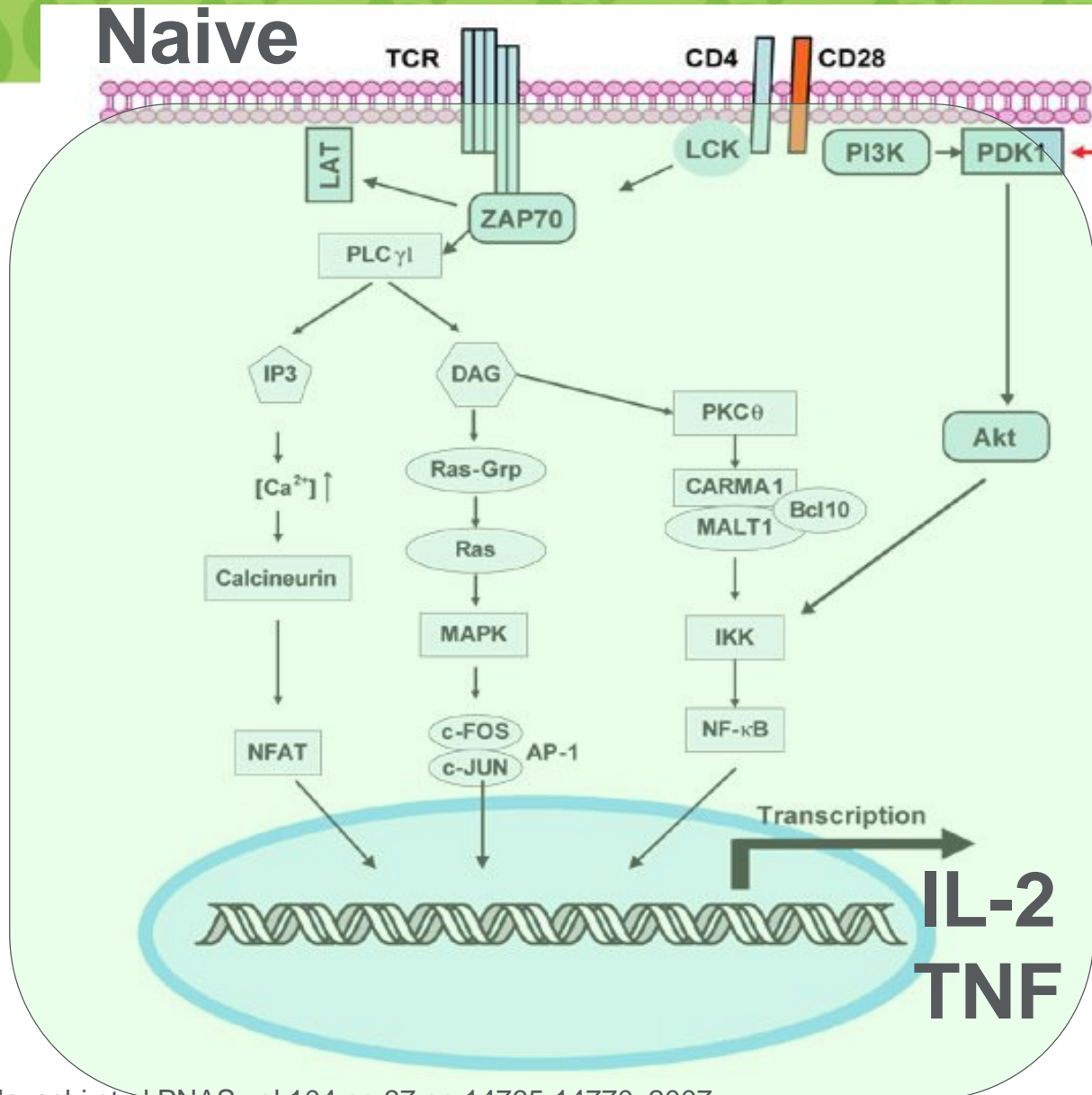


# T-cell Response and CD4+ T-cell Differentiation

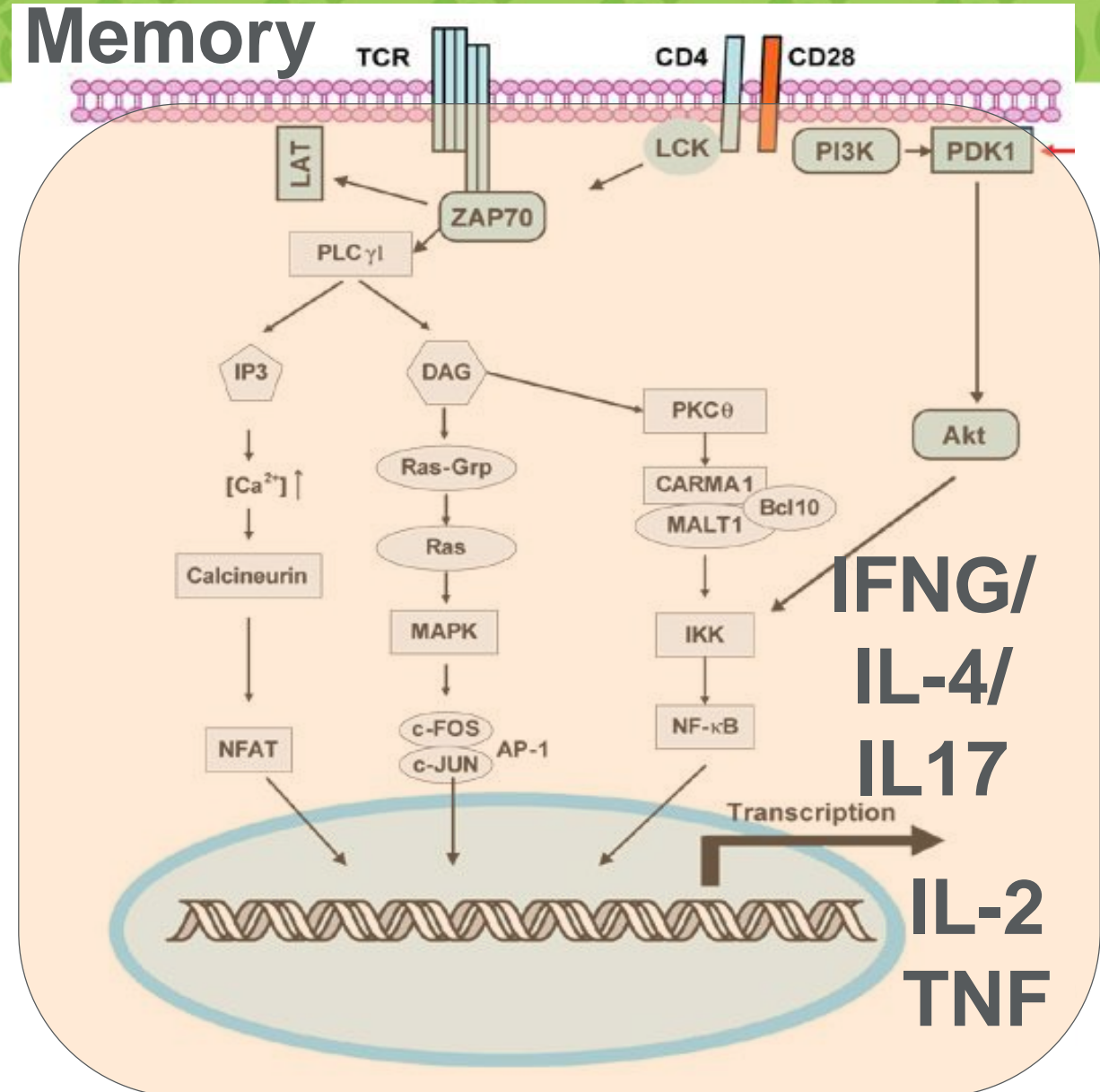


# Memory cells respond differently to TCR/CD28 signal

## Naive

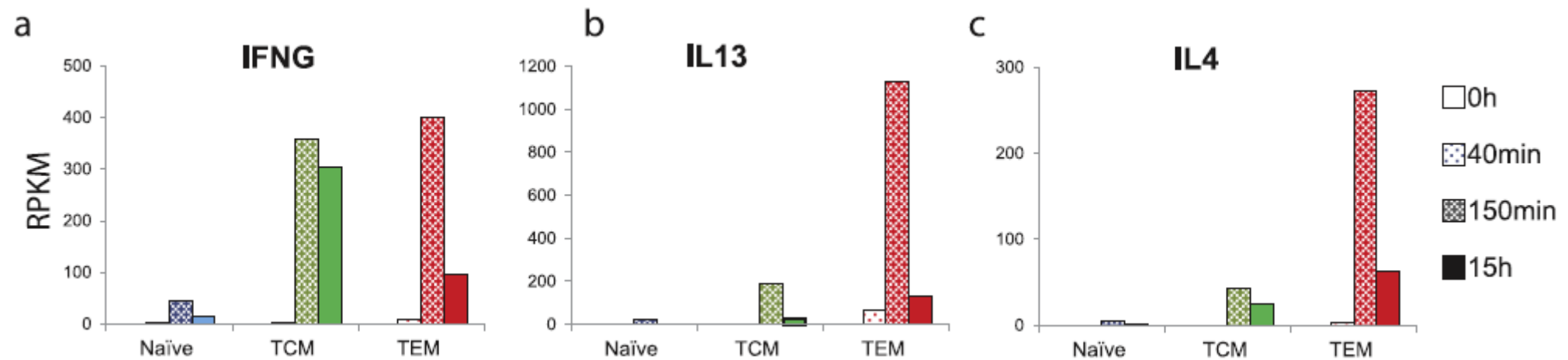


## Memory

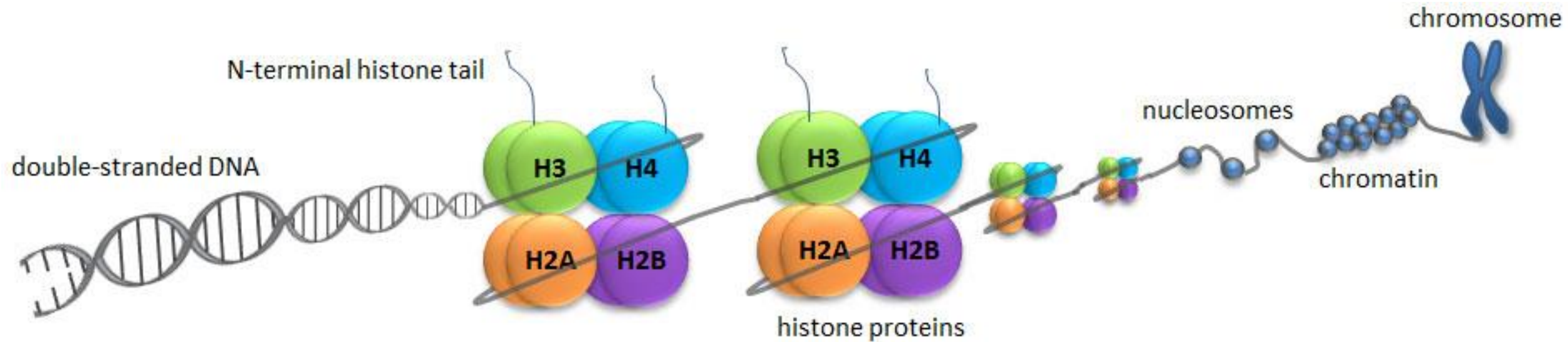




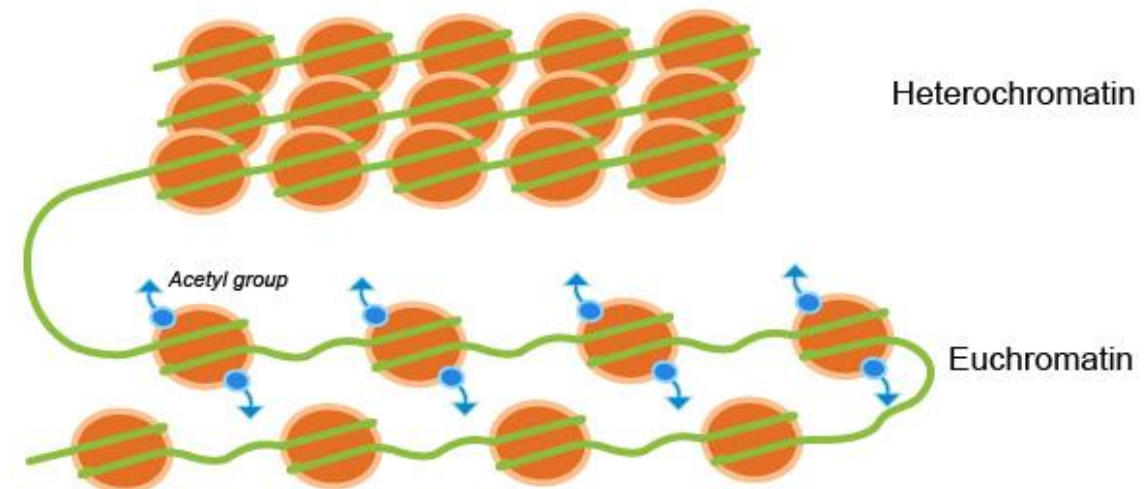
# Cytokine gene mRNA transcript expression during T helper-cell activation



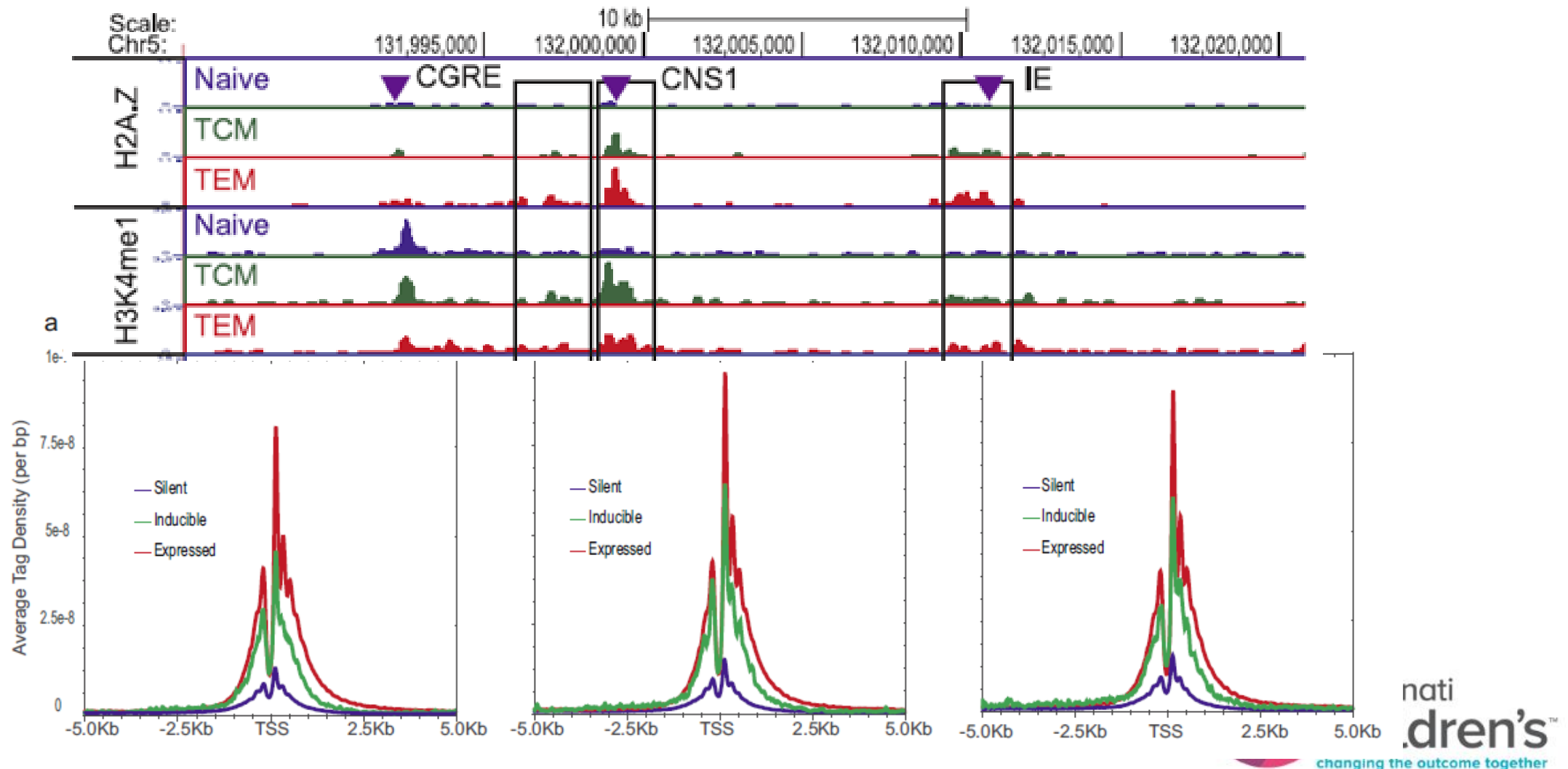
# Intracellular DNA organization: histones and chromatin



**Epigenetics:** heritable changes in phenotype or gene expression caused by mechanisms other than changes in underlying DNA sequence

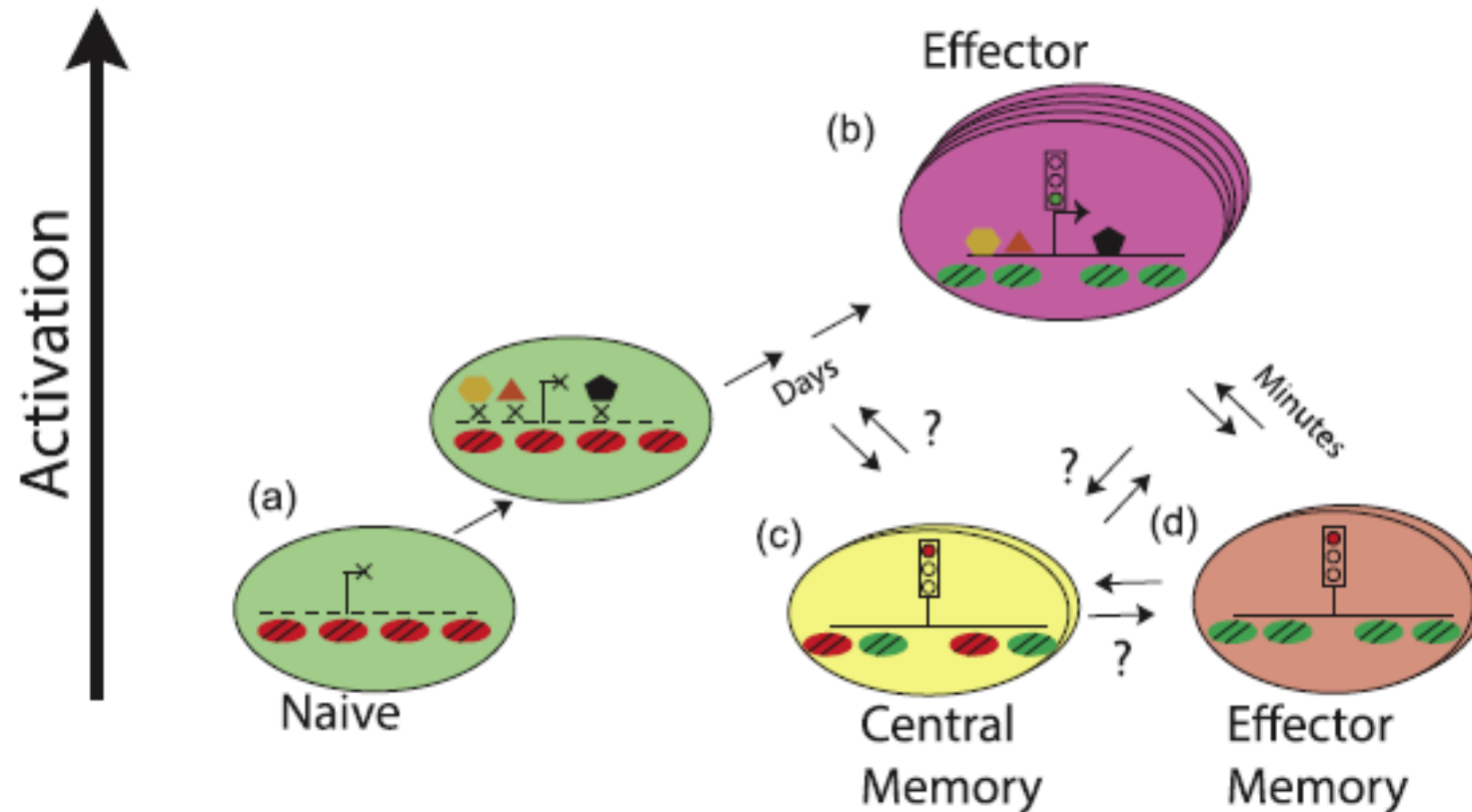


# Inducible genes are modified prior to induction: “poised”

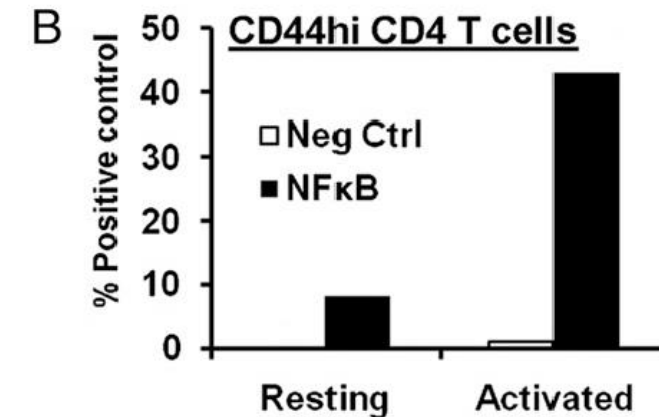
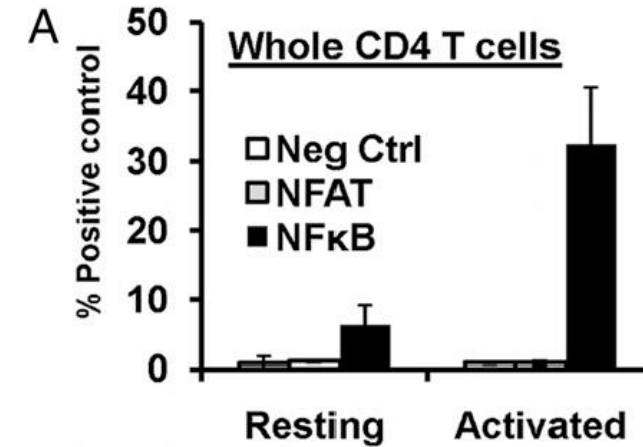
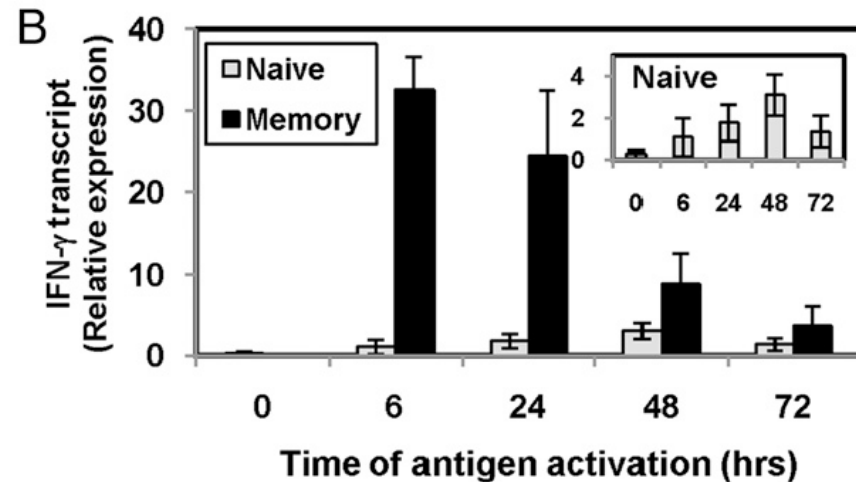
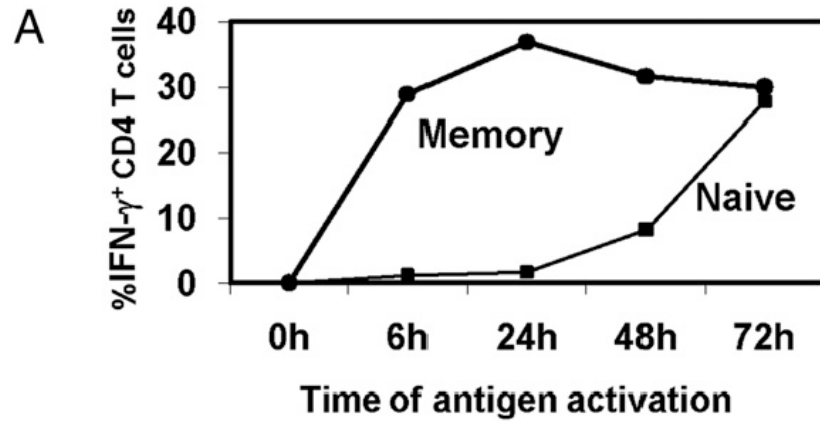




# Model for rapid recall of T-cell activation



# IFN $\gamma$ and NF $\kappa$ B in Murine Memory Cells

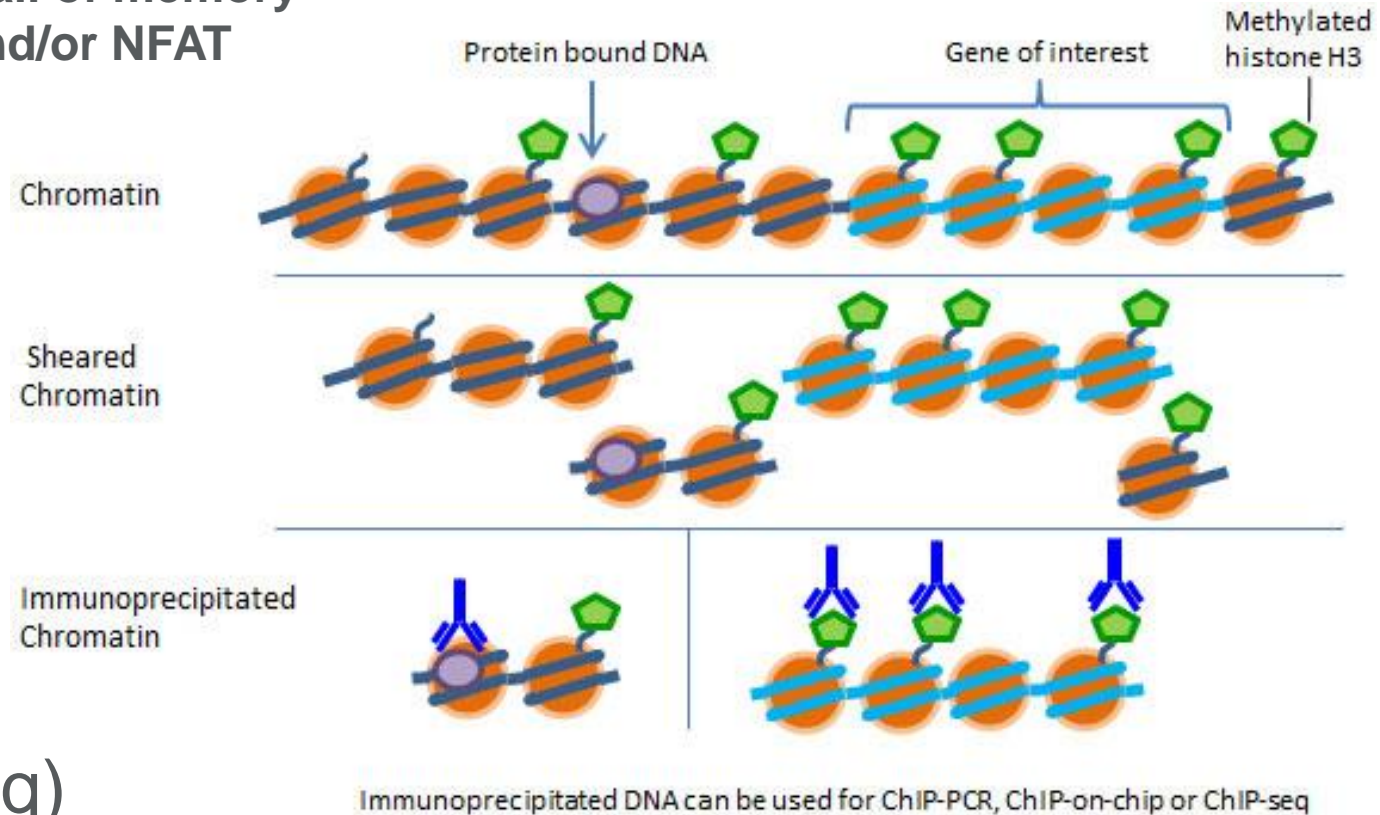




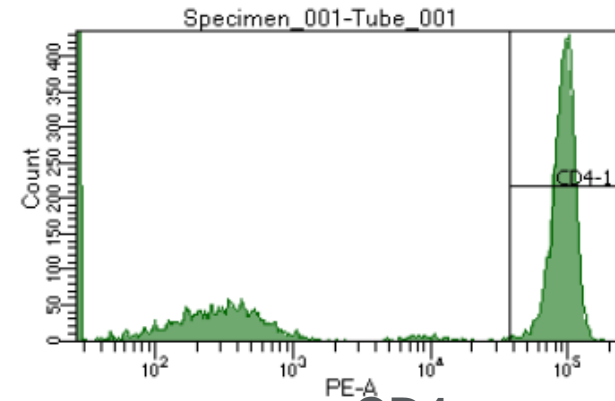
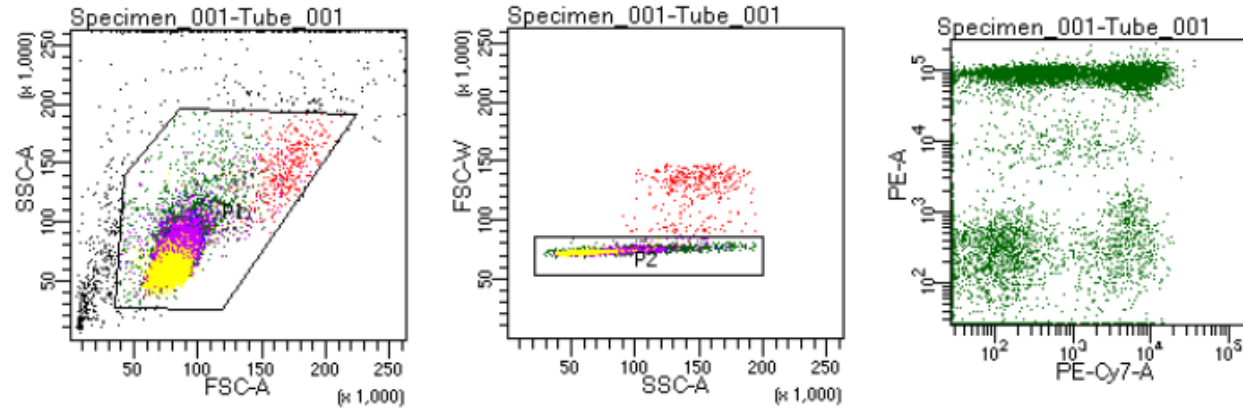
# Hypothesis and Experimental approach

**Hypothesis:** the epigenetically encoded rapid recall of memory CD4<sup>+</sup> T-cells is mediated by activation of NF $\kappa$ B and/or NFAT

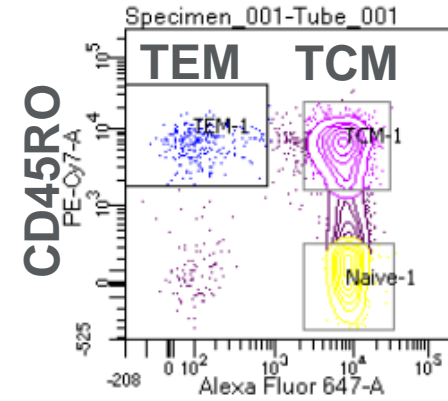
- Isolate blood from human donor
- Isolate PBMCs
- Negative selection for CD4<sup>+</sup> T-cells
- Cell sorting
- Activation
- Chip-seq for NF $\kappa$ B and NFAT
- (data already collected: ATAC Seq)
- Data analysis



# BD FACSDiva 8.0.1

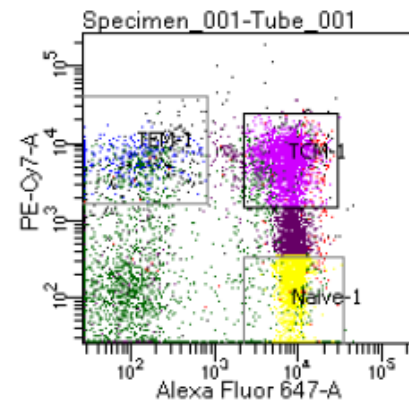


CD4



CD27

Naive



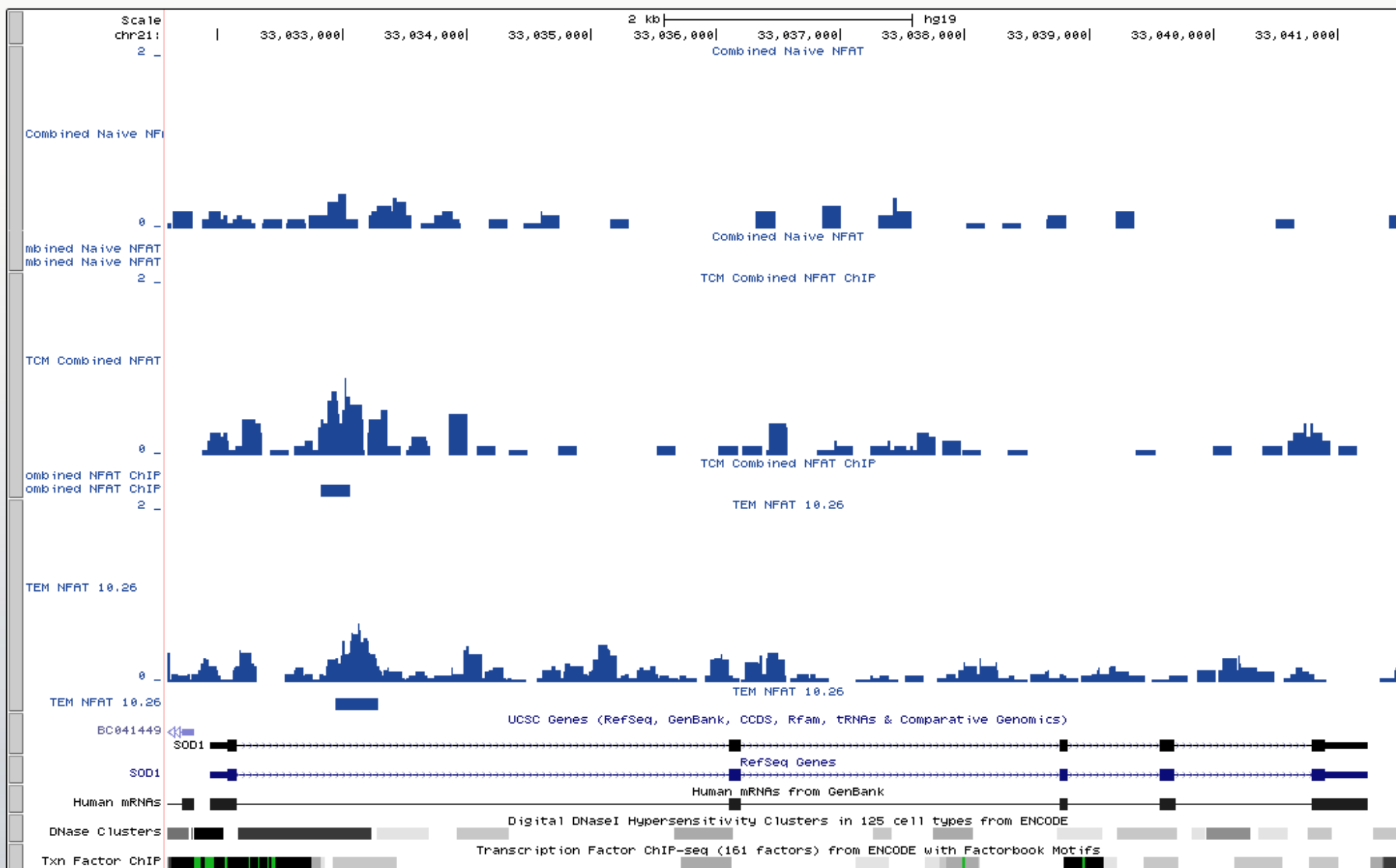
Tube: Tube_001			
Population	#Events	%Parent	%Total
All Events	10,000	####	100.0
P1	9,286	92.9	92.9
P2	8,943	96.3	89.4
CD4-1	5,218	58.3	52.2
TEM-1	259	5.0	2.6
TCM-1	2,048	39.2	20.5
Naive-1	1,732	33.2	17.3

chr19:50390639-50400147 9,509 bp.

piens interleukin 4 induced 1 (IL4I1), transcript variant 1, mRNA.)

go

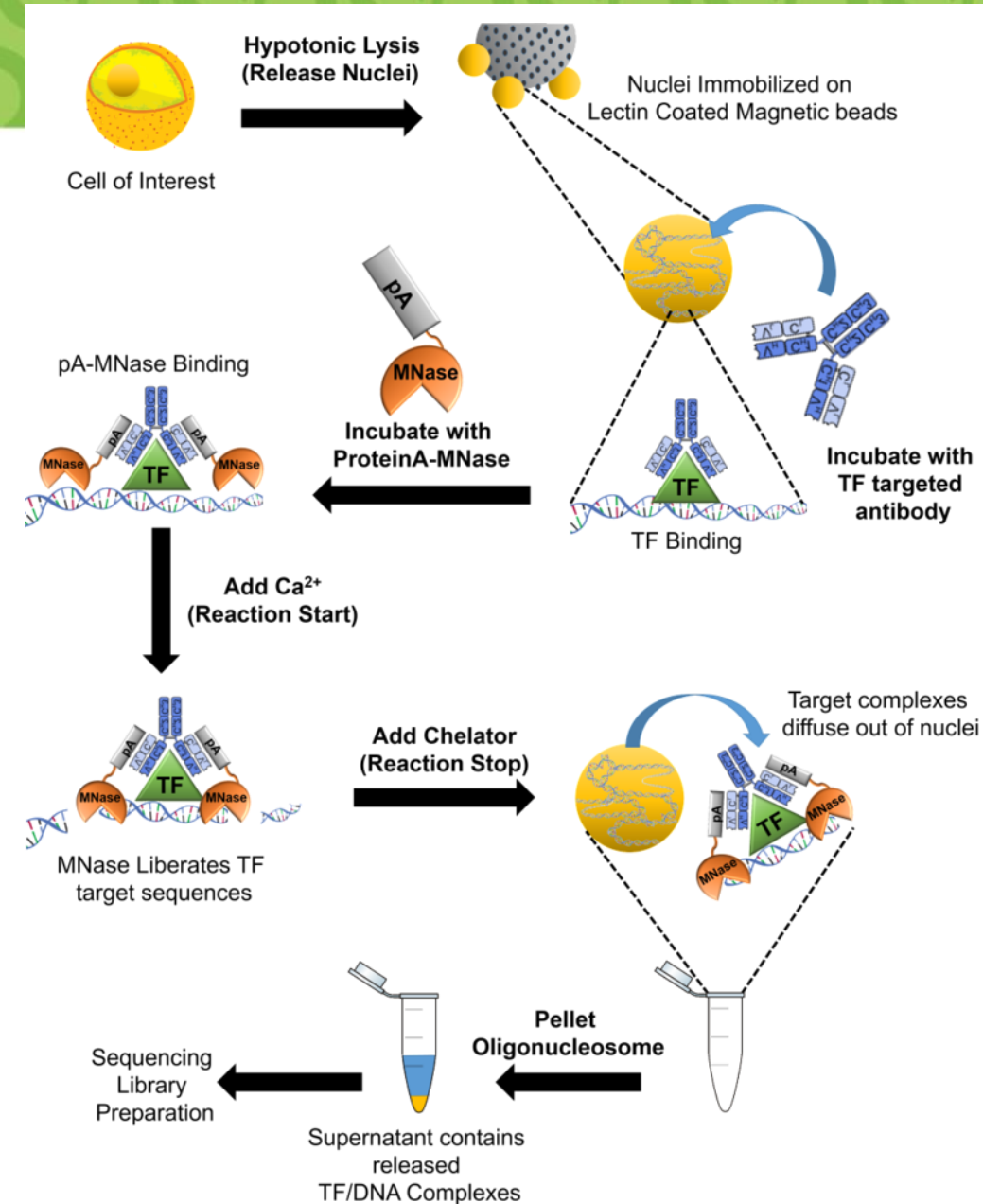
chr21 (q22.11) 21p13 21p12 21p11.2 q11.2 21q21.1 21q21.2 21q21.3 21q22.11 22.12 22.13 21q22.2 21q22.3





# Future directions

- Further analysis of NF $\kappa$ B and NFAT ChIPs
- ChIPs of multiple NFAT and NF $\kappa$ B antibodies sent for sequencing
- Sample size issue, particularly for TEM cells – attempting to optimize Cut and Run



# Acknowledgements

- Artem Barski, PhD
- Andrew Lindsley, MD, PhD
- Masashi Yukawa, PhD
- Kurtis Stefan
- Sushmitha Vallabh
- Ben Wronowski
- Andrey Kartashov
- Michael Kotliar
- Lakshmi RaoVenkata
- Eric Eymard

