
Resident CD4⁺ T cells accumulate in lymphoid organs after prolonged antigen exposure

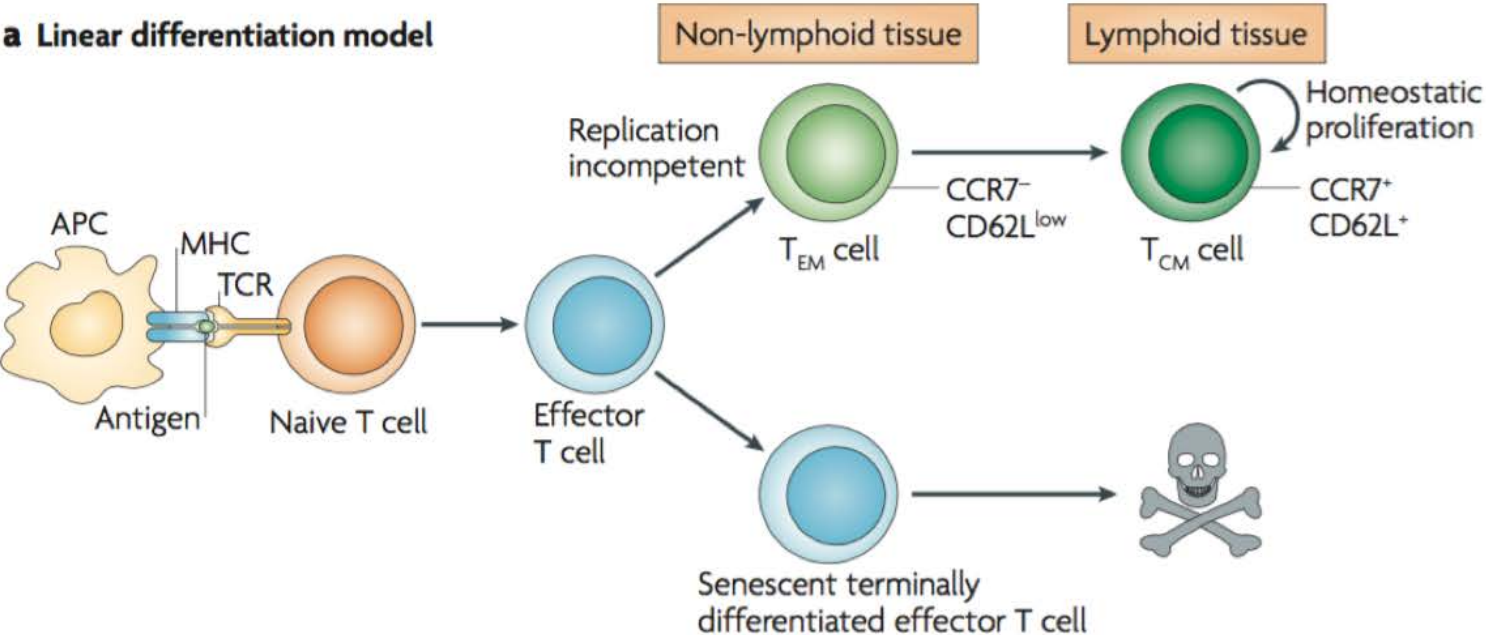
Milas Ugur¹, Olga Schulz¹, Manoj B. Menon², Andreas Krueger¹ & Oliver Pabst^{1,3}

Lukas Altenburger

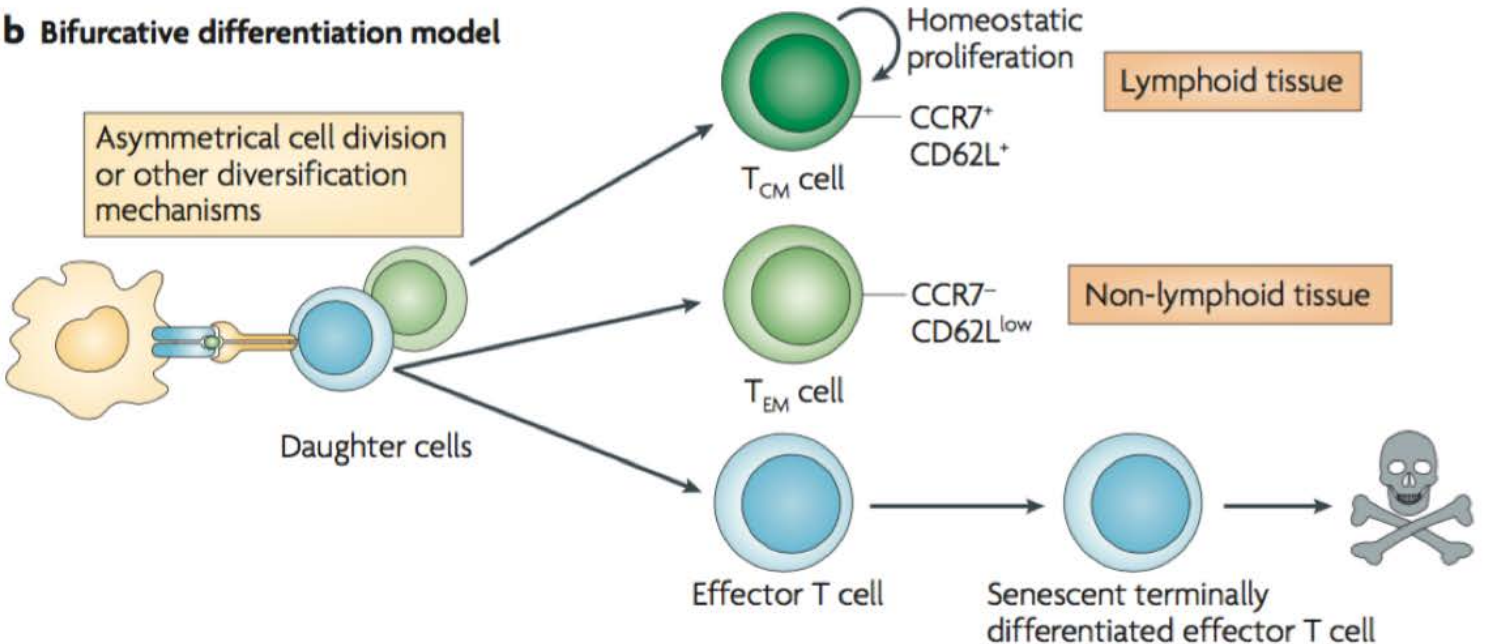


T cell activation:

a Linear differentiation model

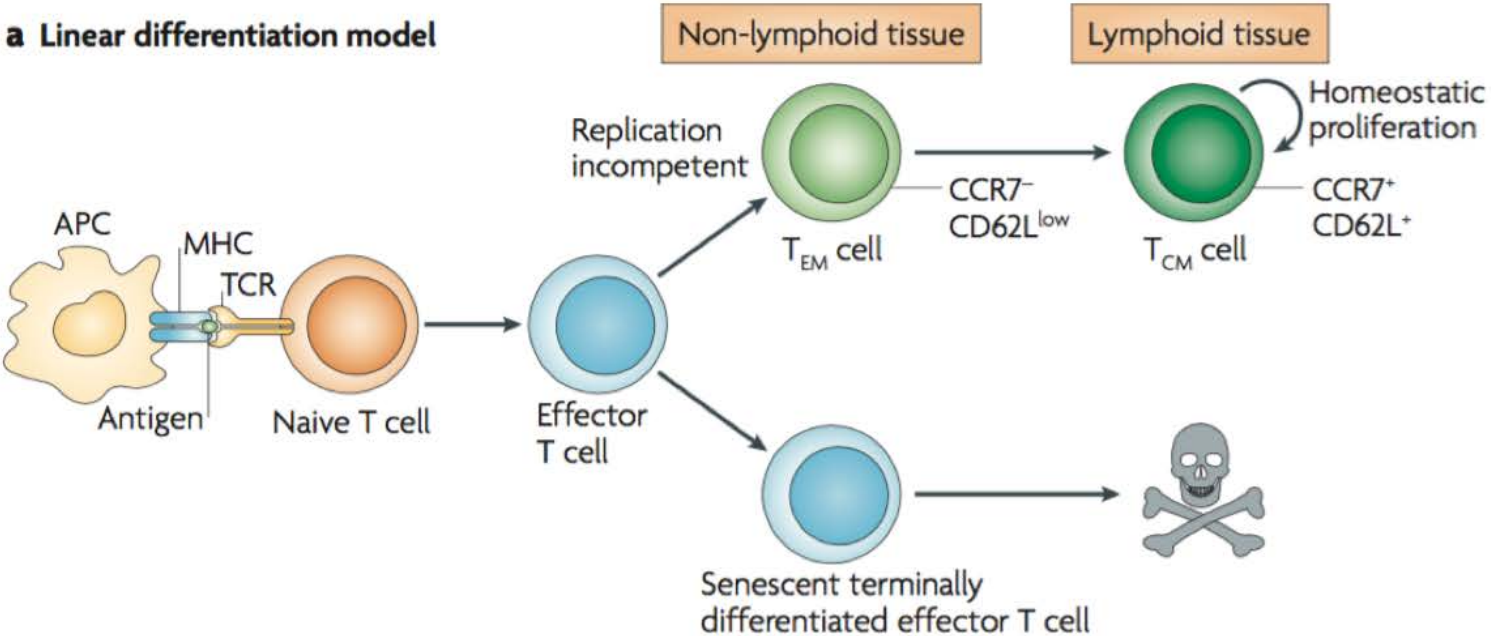


b Bifurcative differentiation model

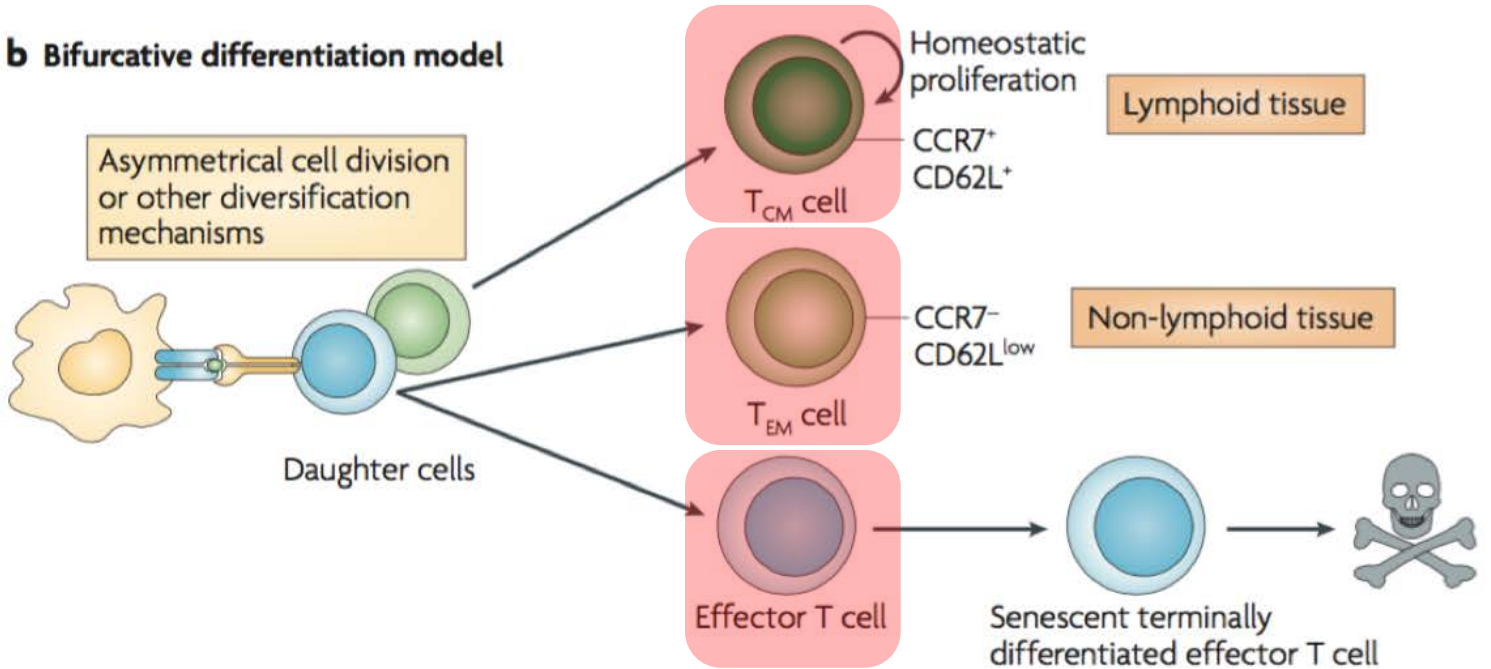


T cell activation:

a Linear differentiation model



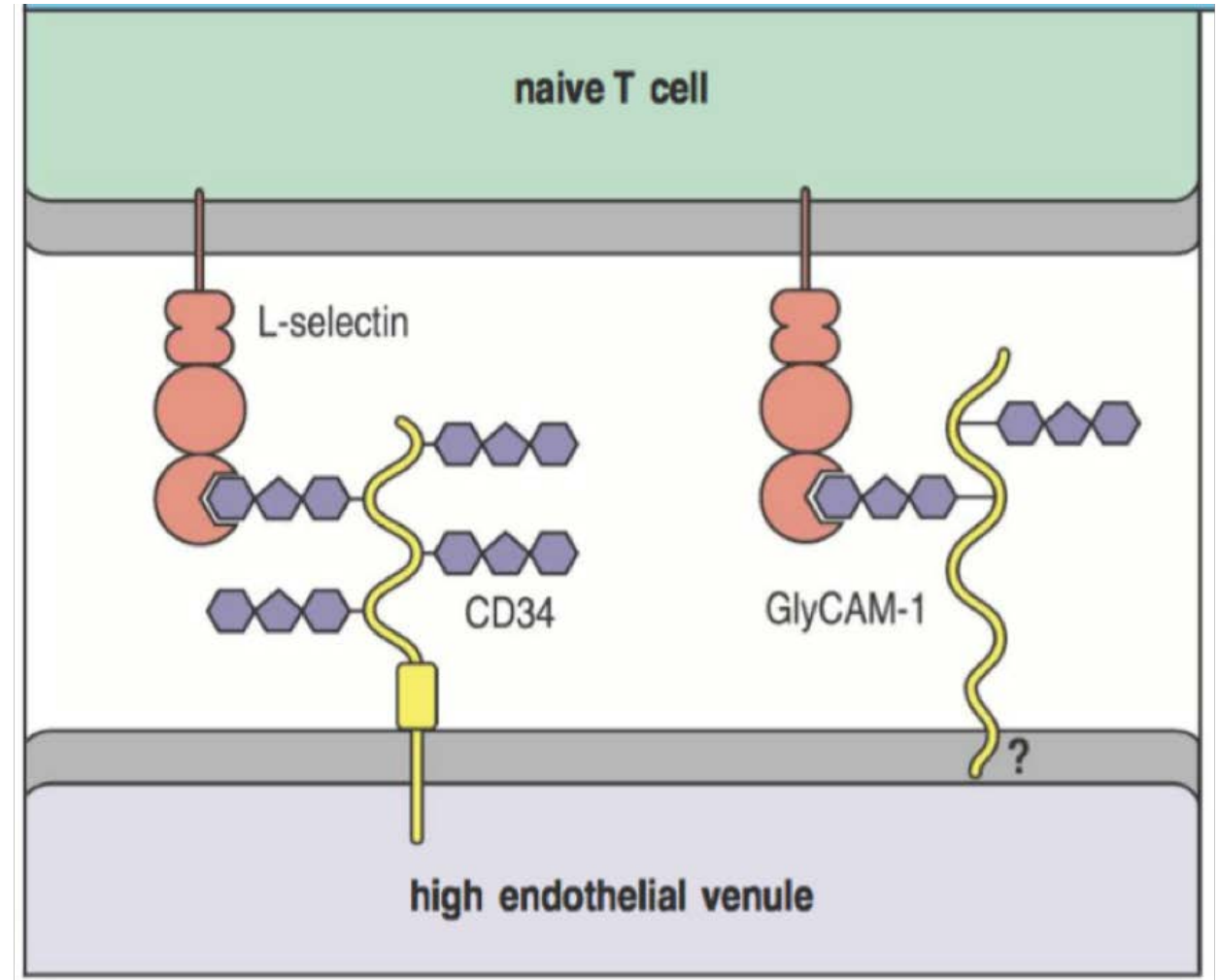
b Bifurcative differentiation model



CD62L

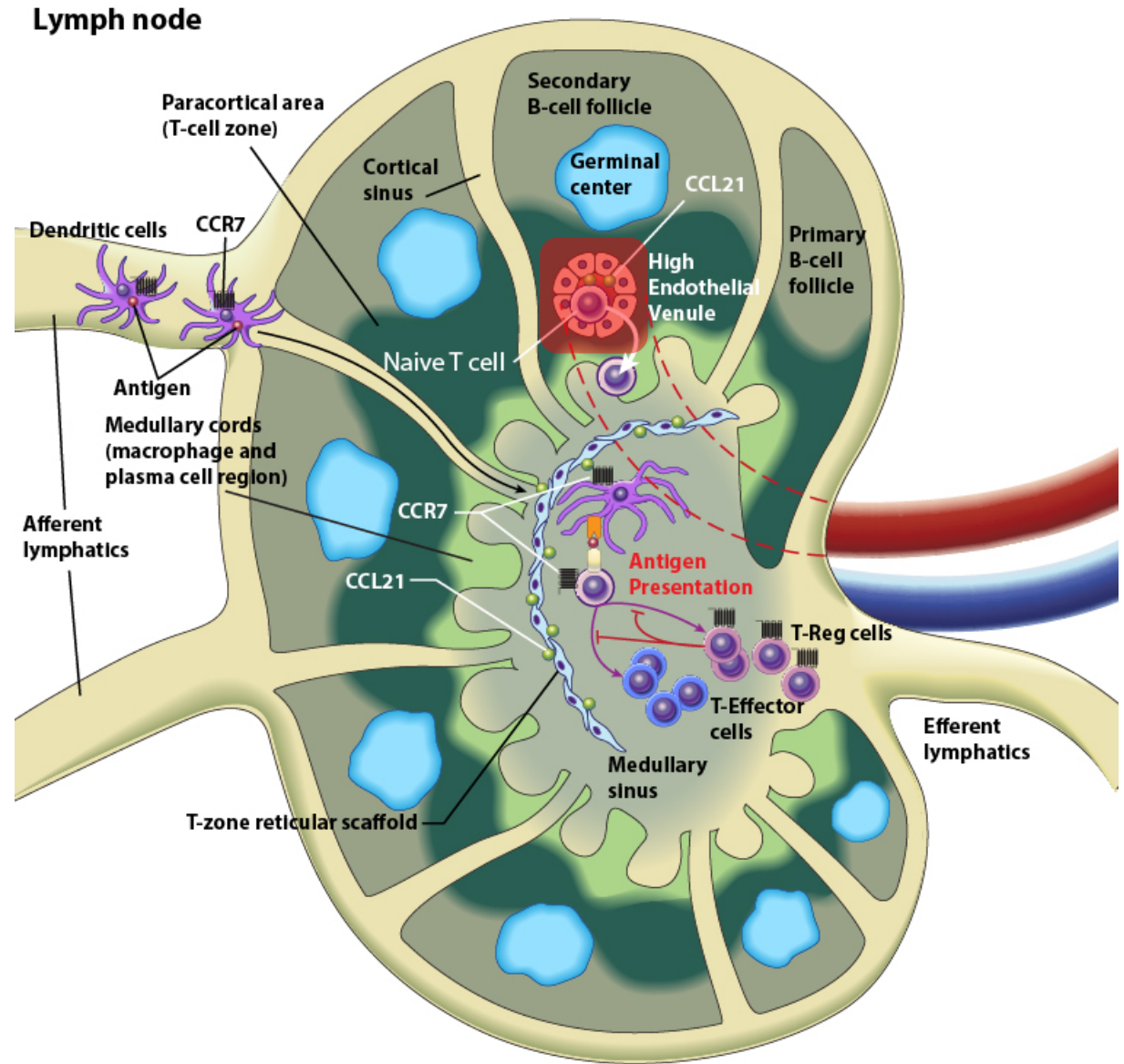
- CD62L: L selectine

- Leukocyte adhesion molecule (LAM)
- binds CD34, GlyCAM
- mediates rolling interactions with endothelium
- lymph-node homing receptor
- binds on HEV



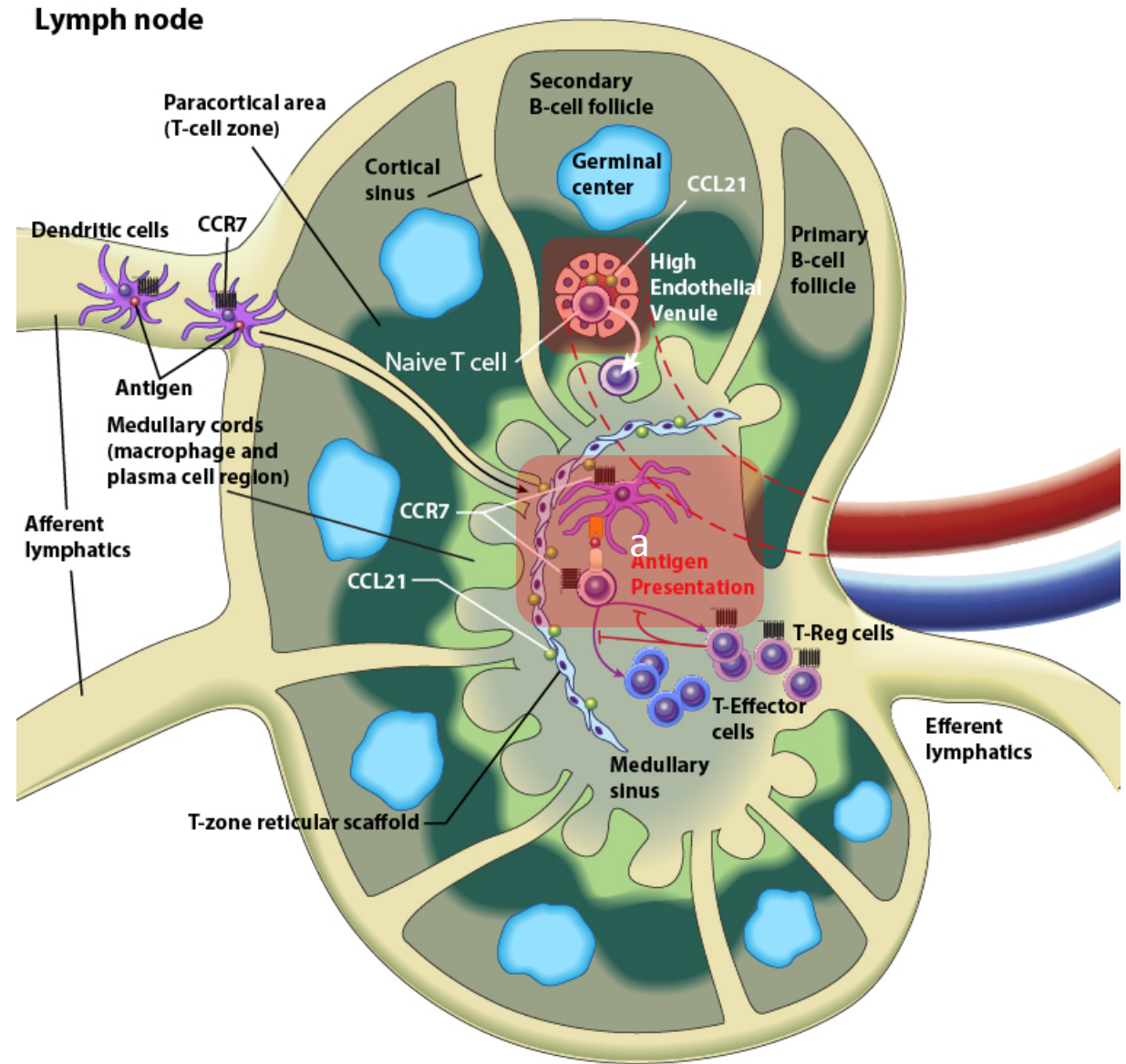
CD62L

- CD62L binds on HEV in lymph nodes
- Naïve T cells migrate to the T cell zone
- Scan for antigen presented on APC's

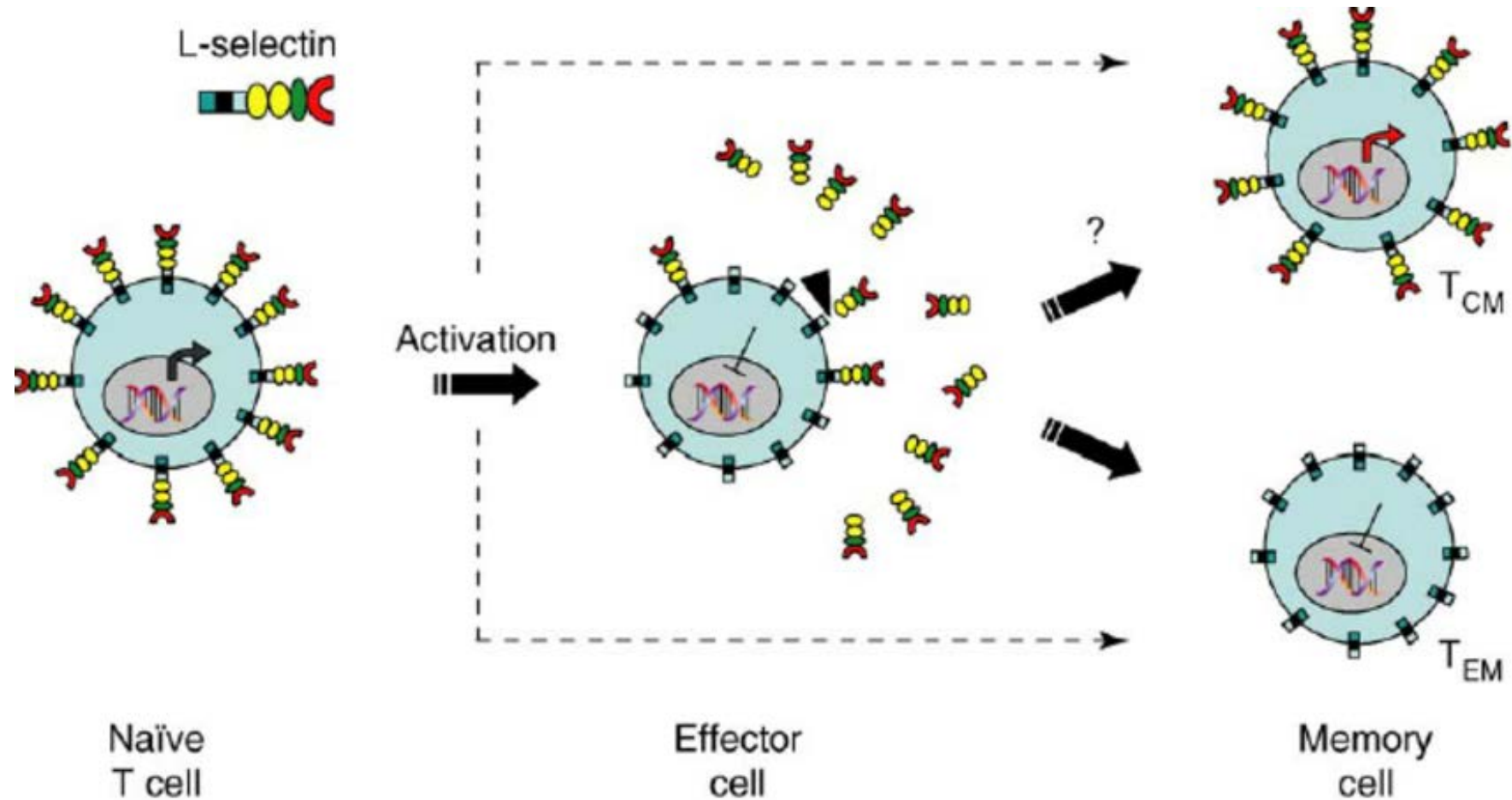


CD62L

- CD62L binds on HEV in lymph nodes
- Naïve T cells migrate to the T cell zone
- Scan for antigen presented on APC's
- Clonal expansion into:
 - Effector (CD62L^{-/lo})
 - Central memory (CD62L^{+/hi})
 - Effector memory (CD62L^{-/lo})

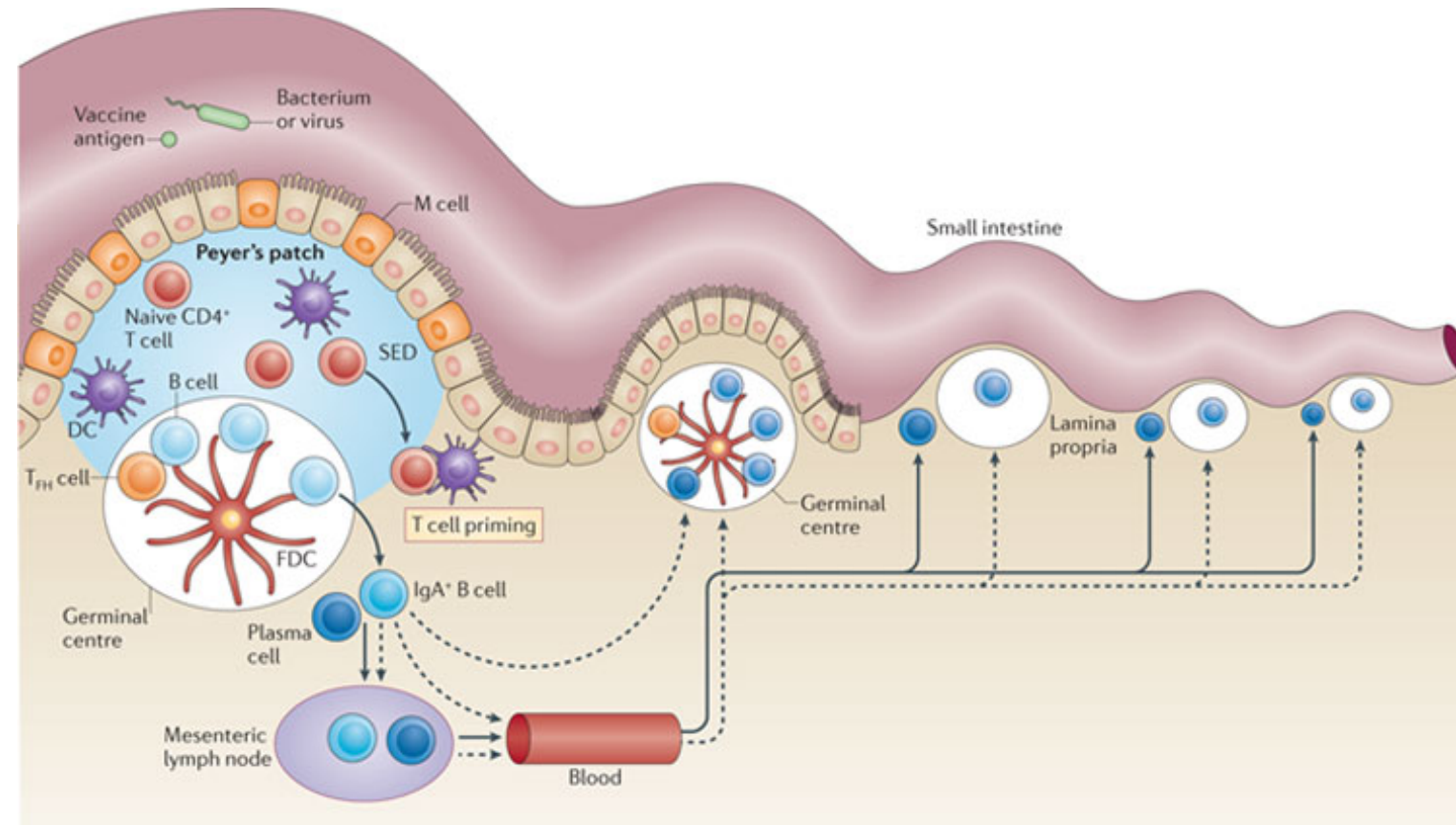


CD62L on memory T cells



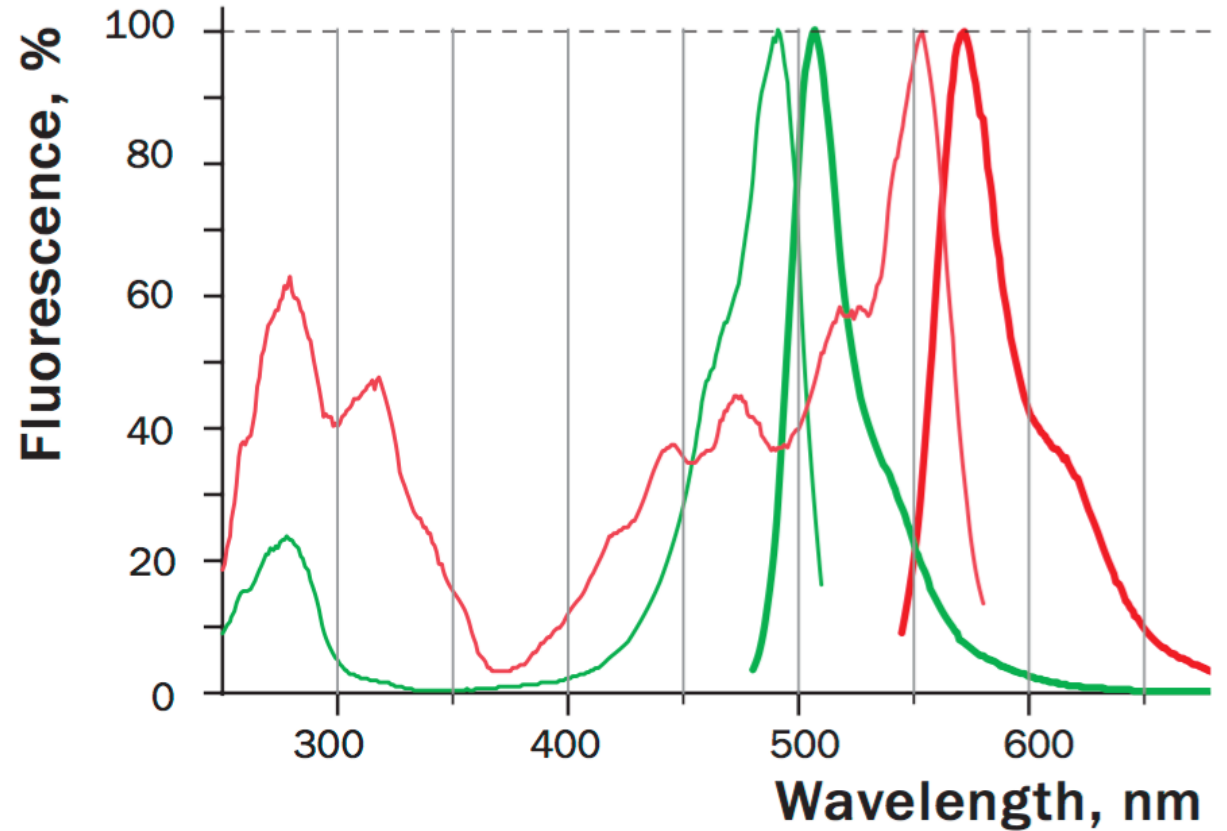
Peyer's patch

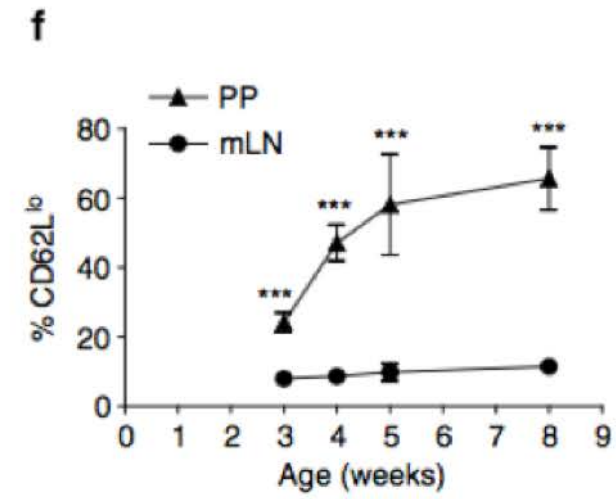
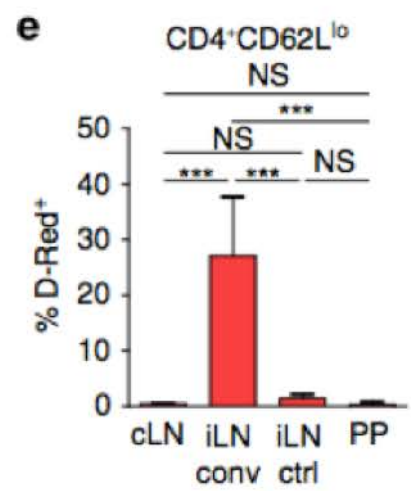
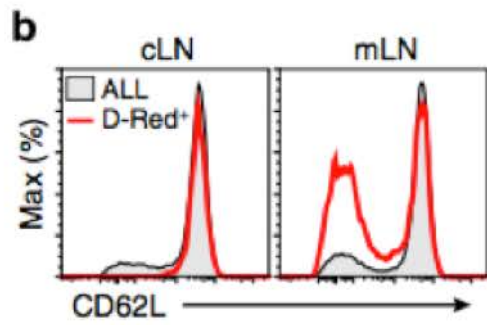
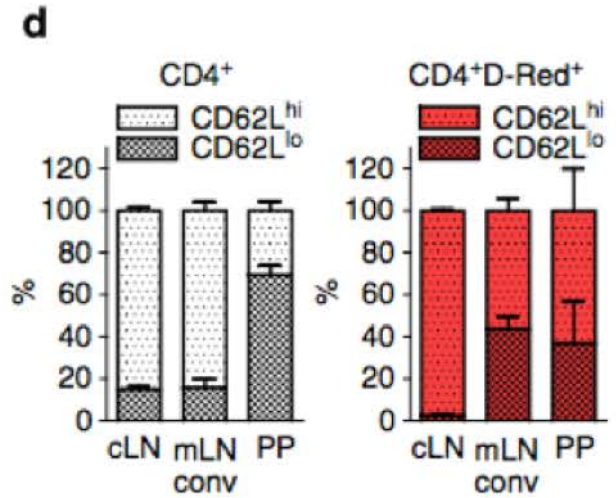
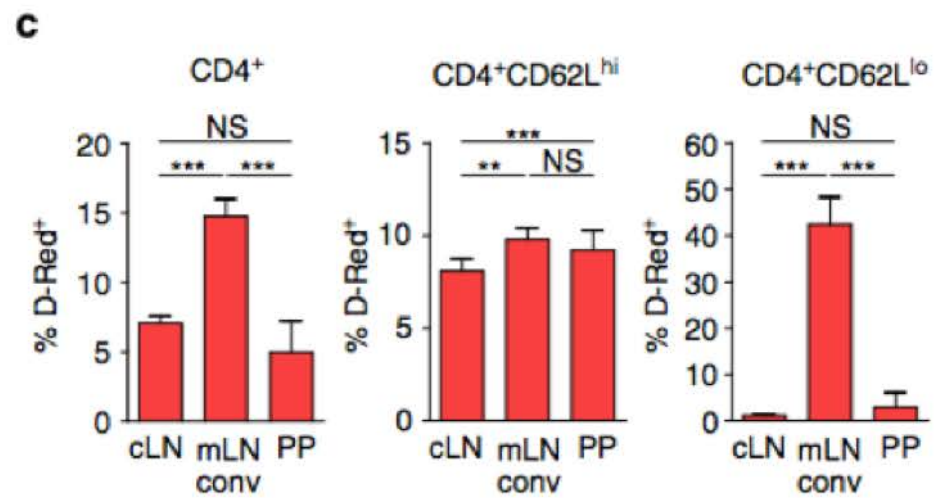
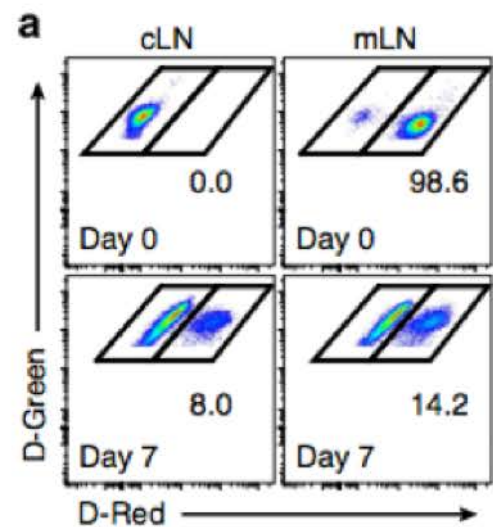
- Oval lymphoid follicles in SI.
- Mediate first mucosal immune responses.
- Comprise T cells, B cells, DC's, Macrophages .
- Activated cells pass to MLN's which amplifies responses.

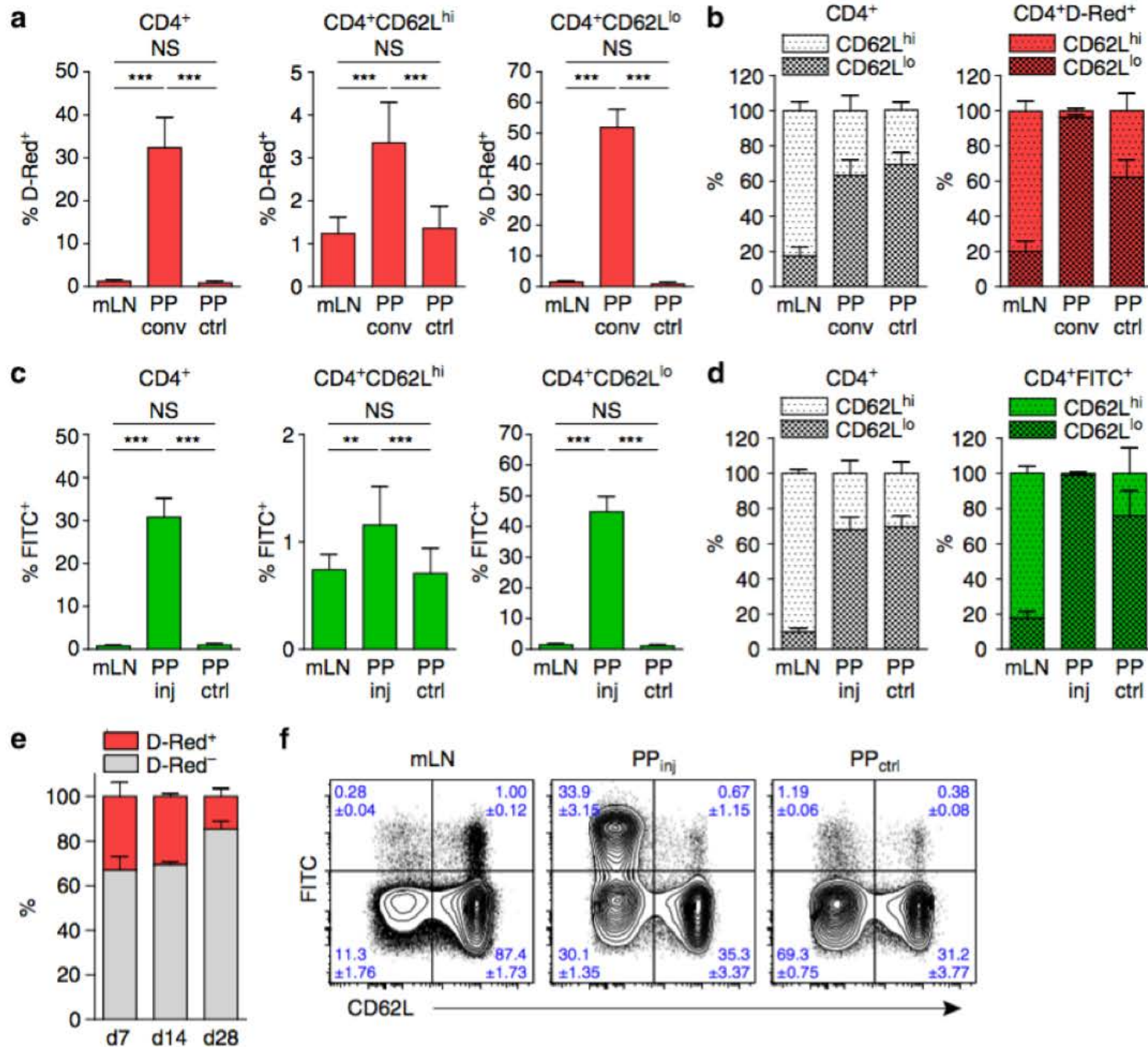


Photoswitchable fluorescent proteins

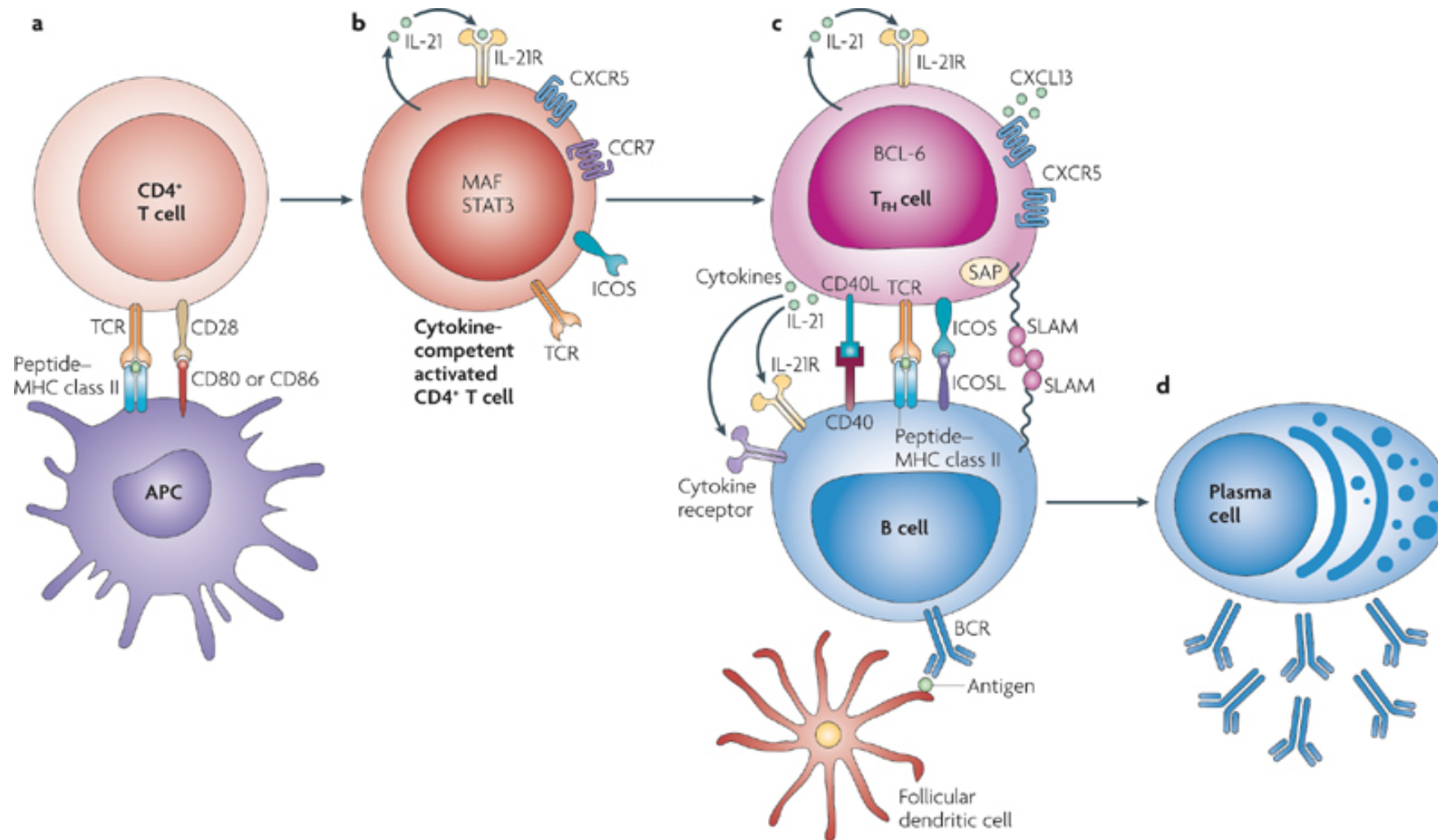
- Long-term protein tracking
- 450nm light irradiation
- Irreversible photoconversion
- Green – red fluorescence
- Histone 2B-Dendra fusion chimeras
- Long term tracking



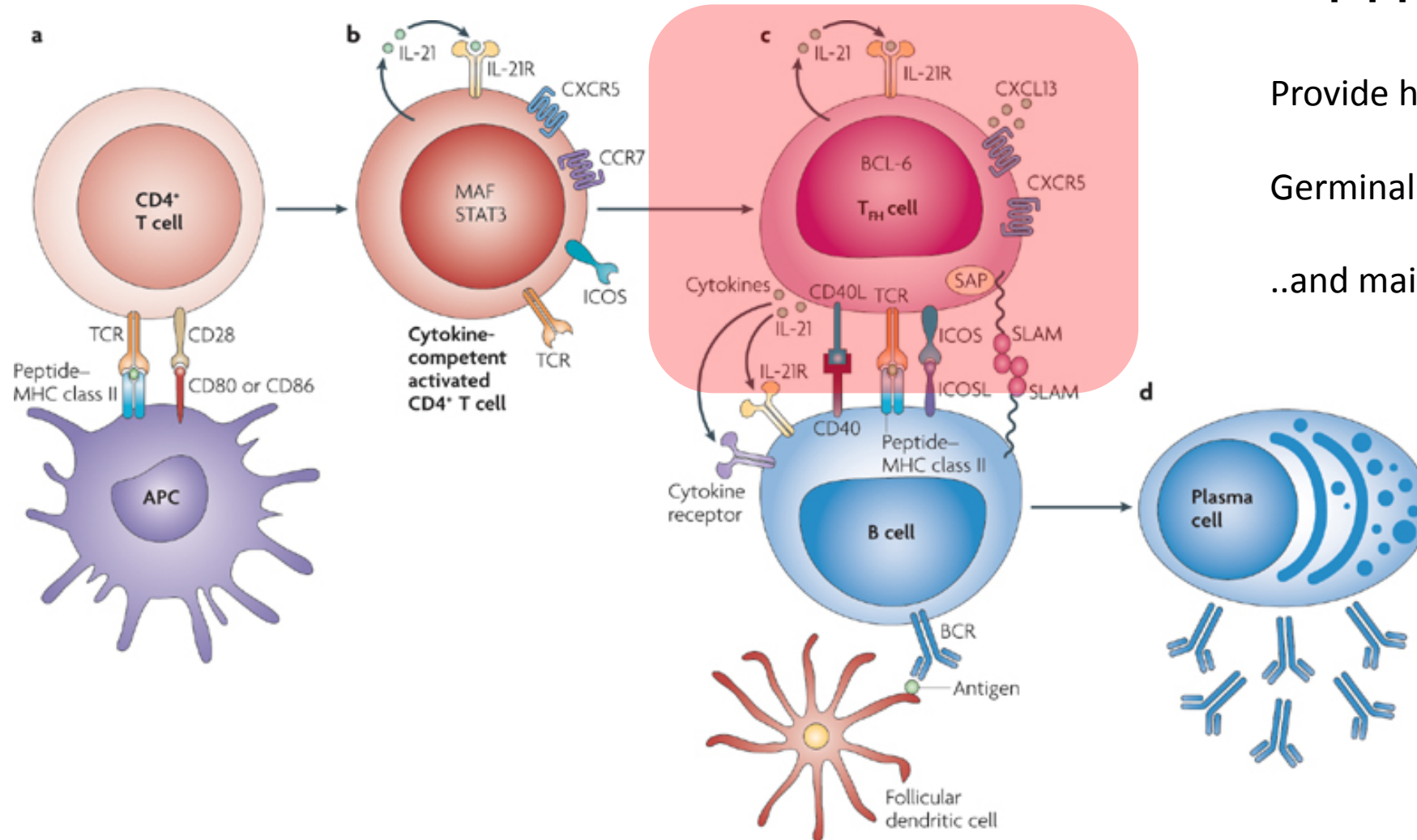




Follicular helper CD4 T cells (T_{FH})

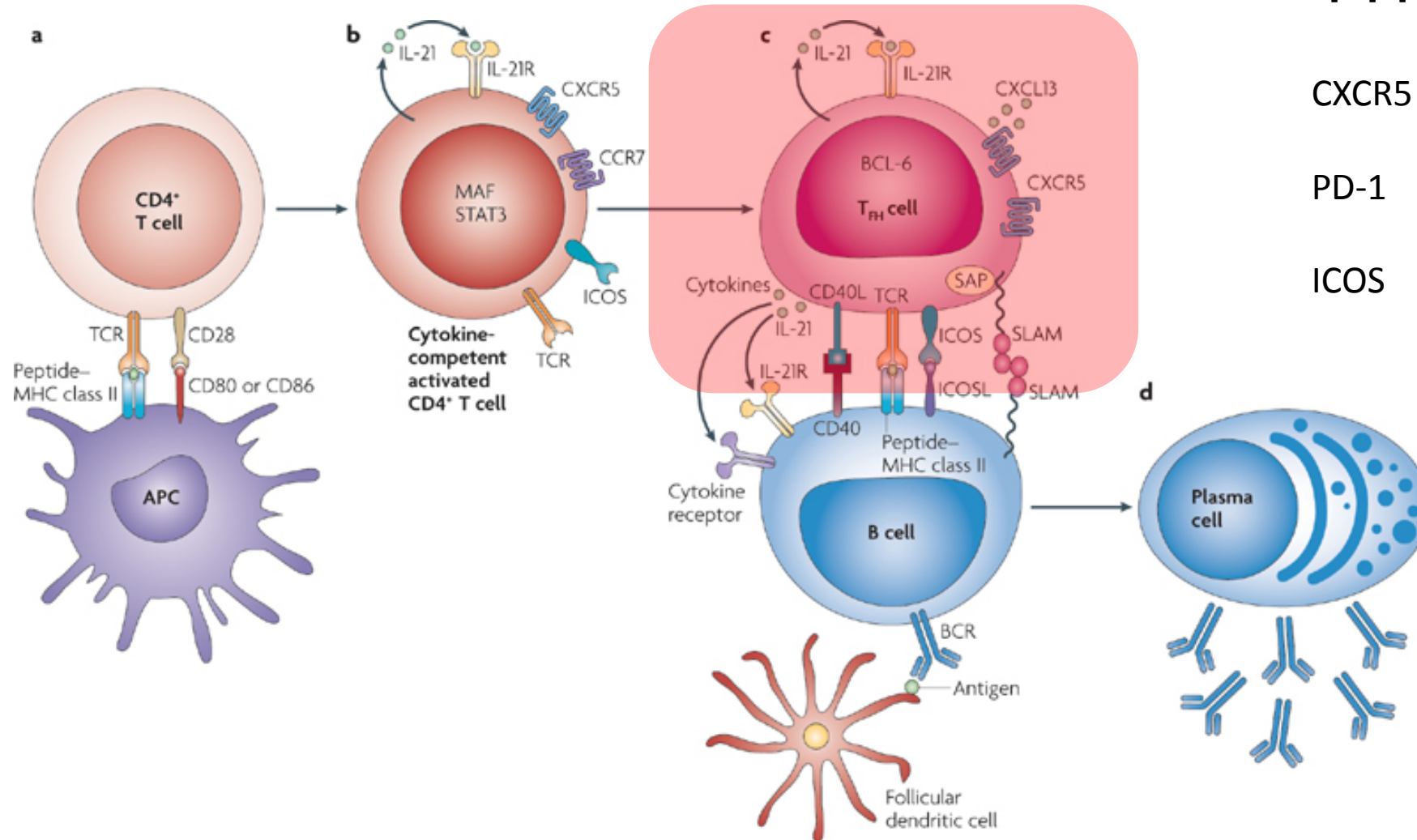


Follicular helper CD4 T cells (T_{FH})



Provide help for B cells
Germinal center formation
..and maintenance

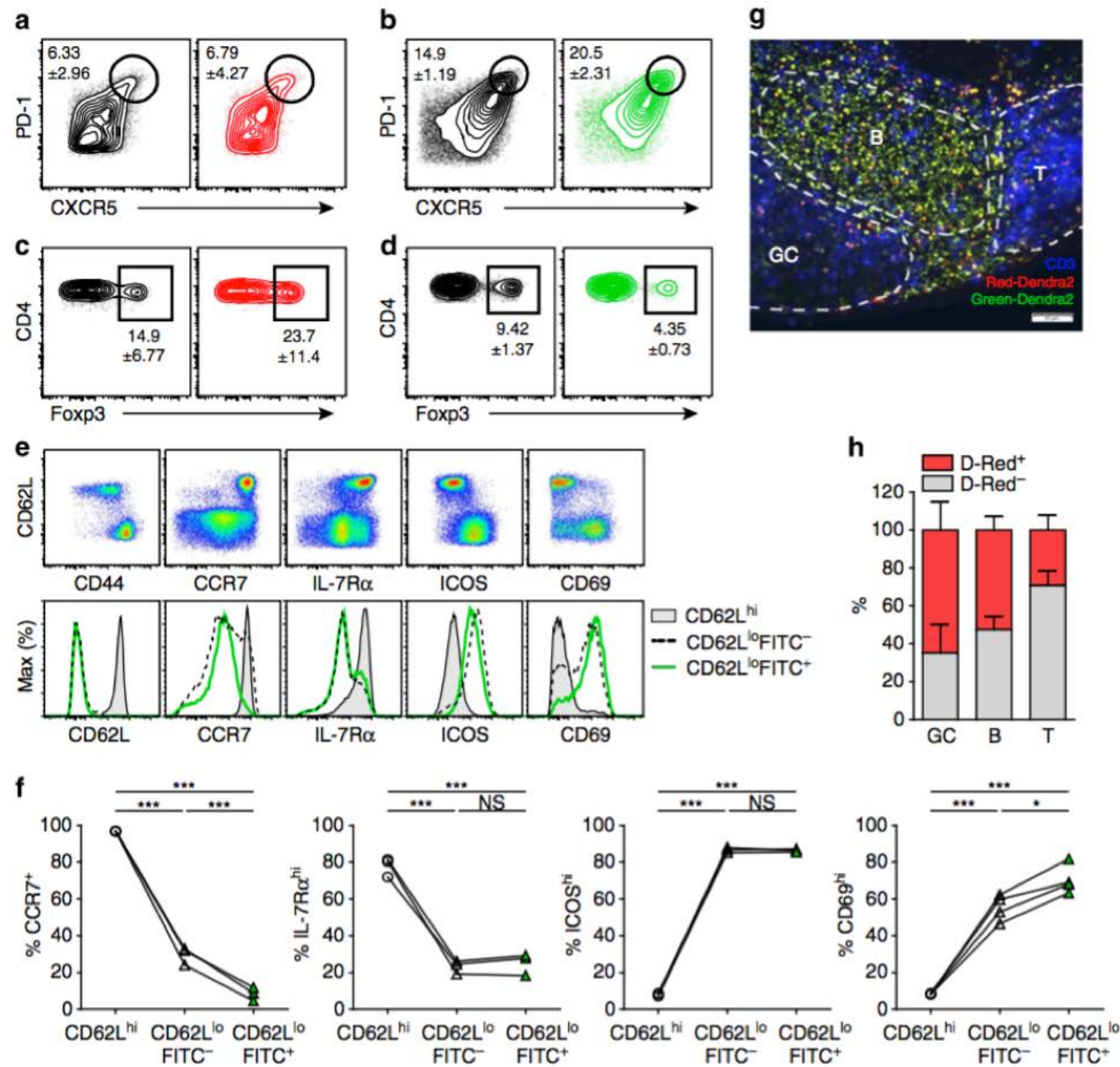
Follicular helper CD4 T cells (T_{FH})

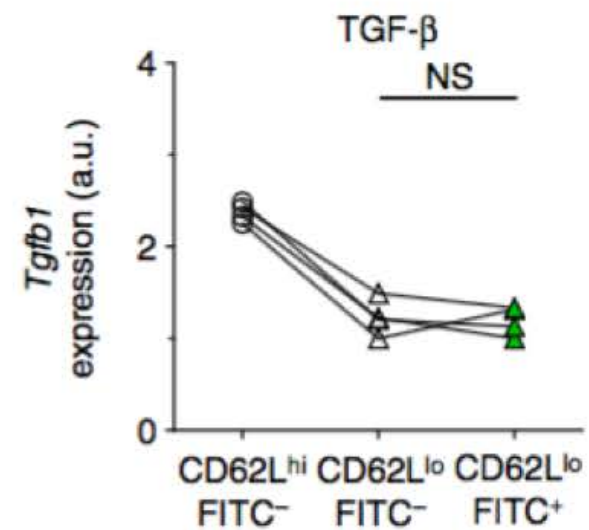
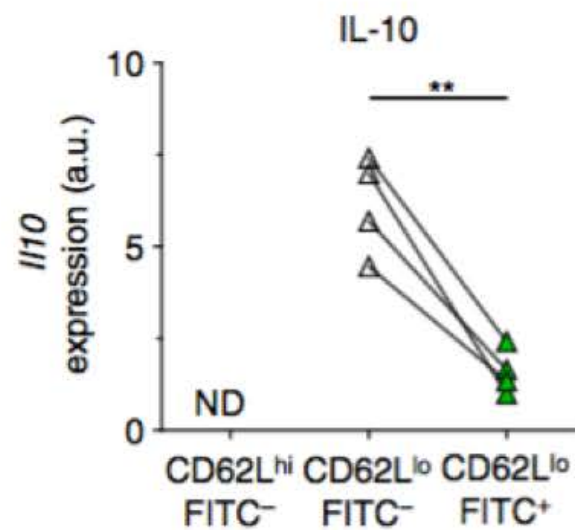
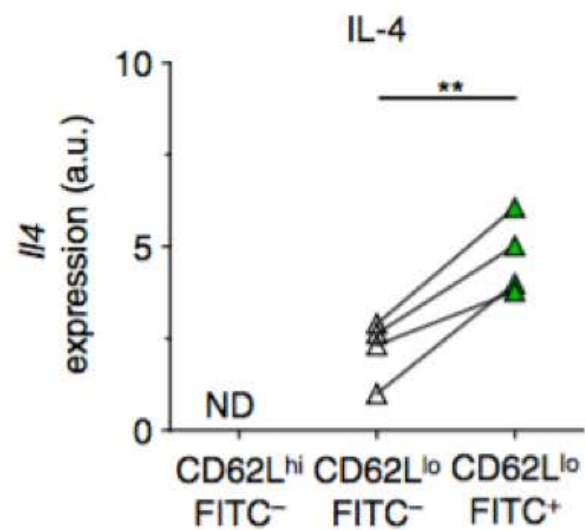
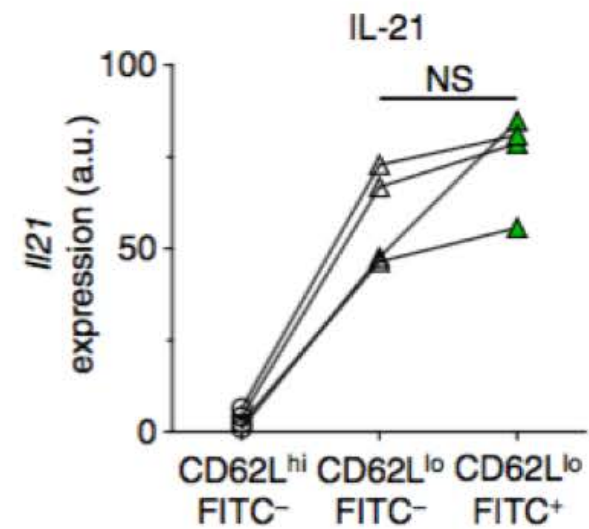
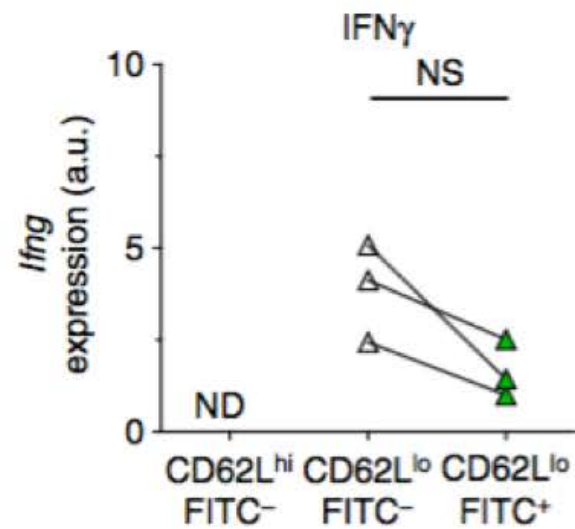
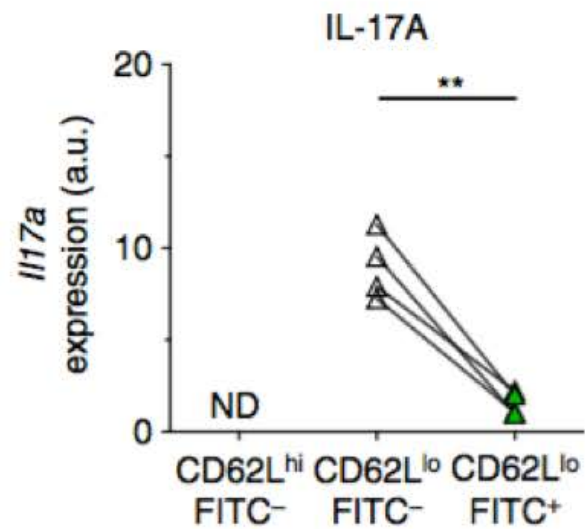


CXCR5

PD-1

ICOS





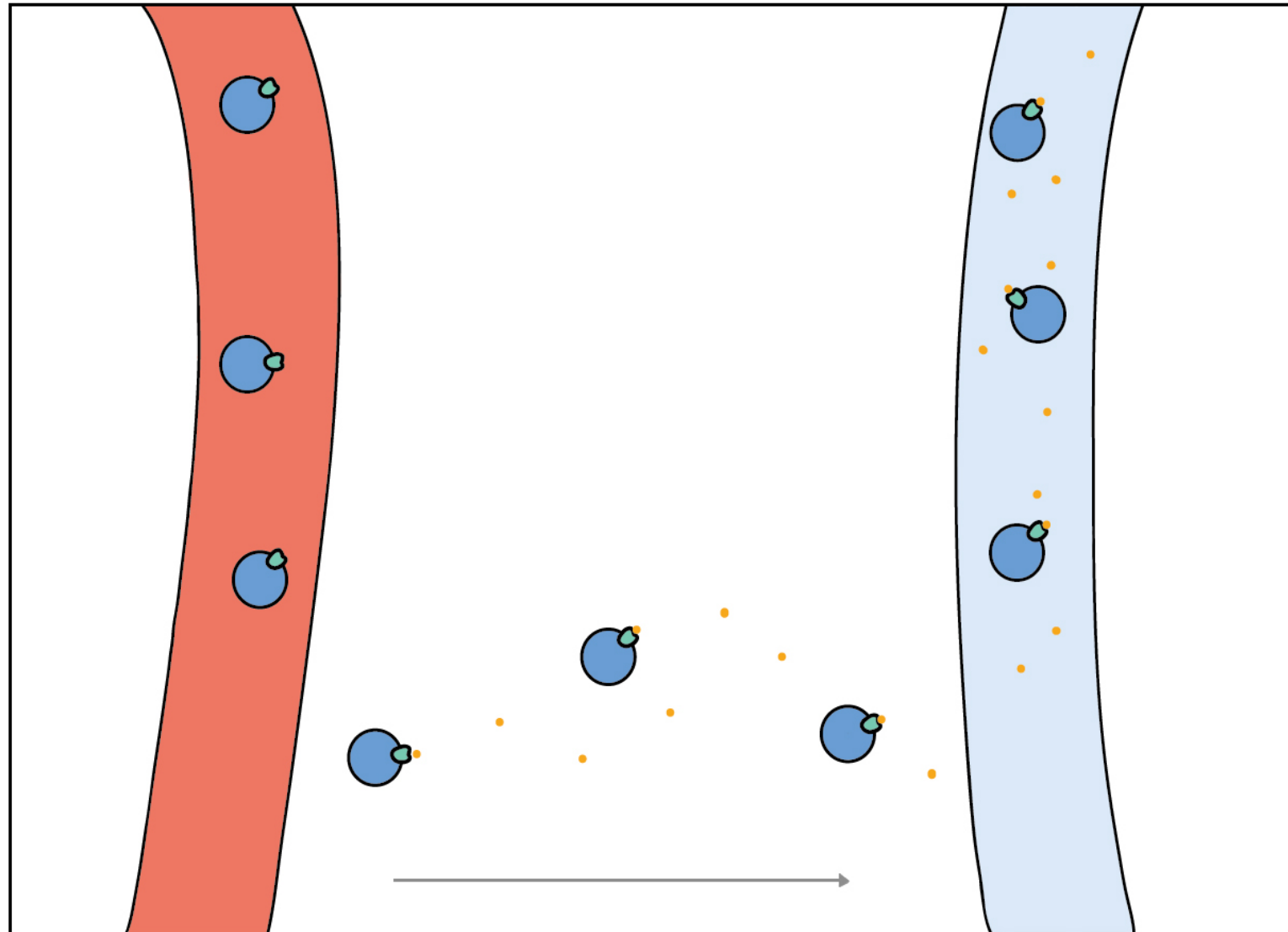
Sphingosine 1 phosphate 1 (S1P1)

S1PR1 on cell surface
S1P1 gradient guides T
cells
Out of SLO's.

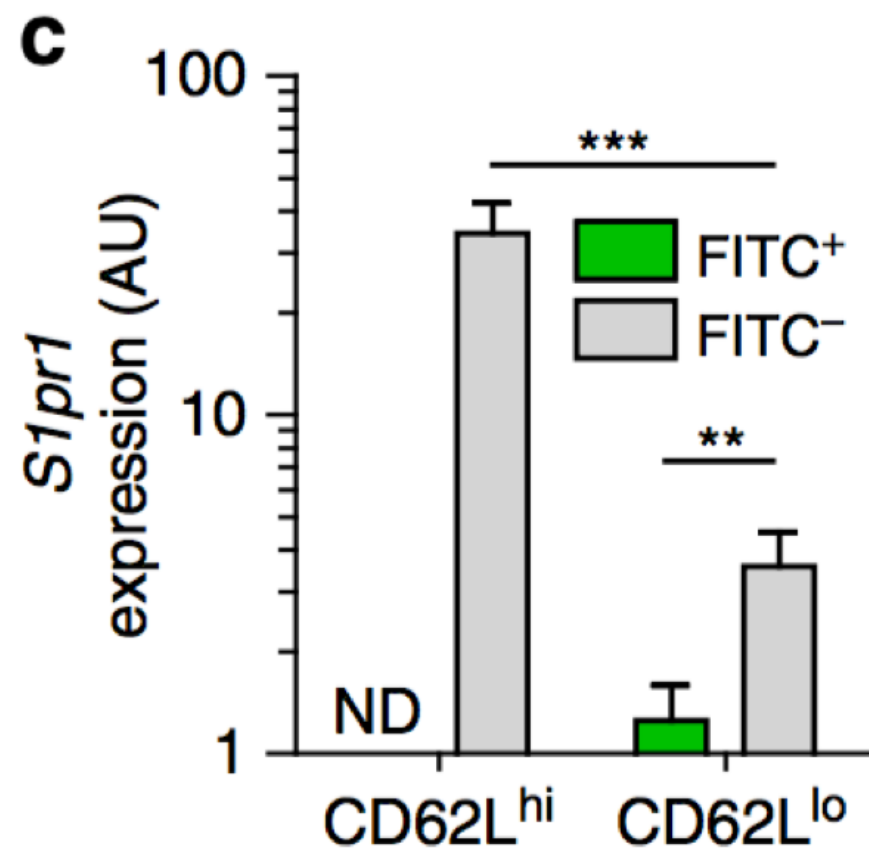
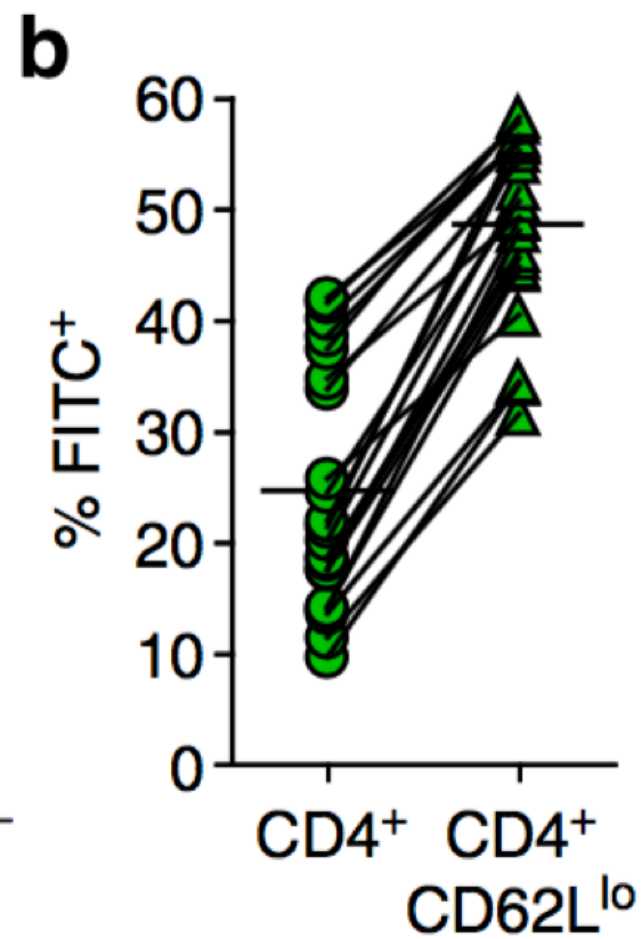
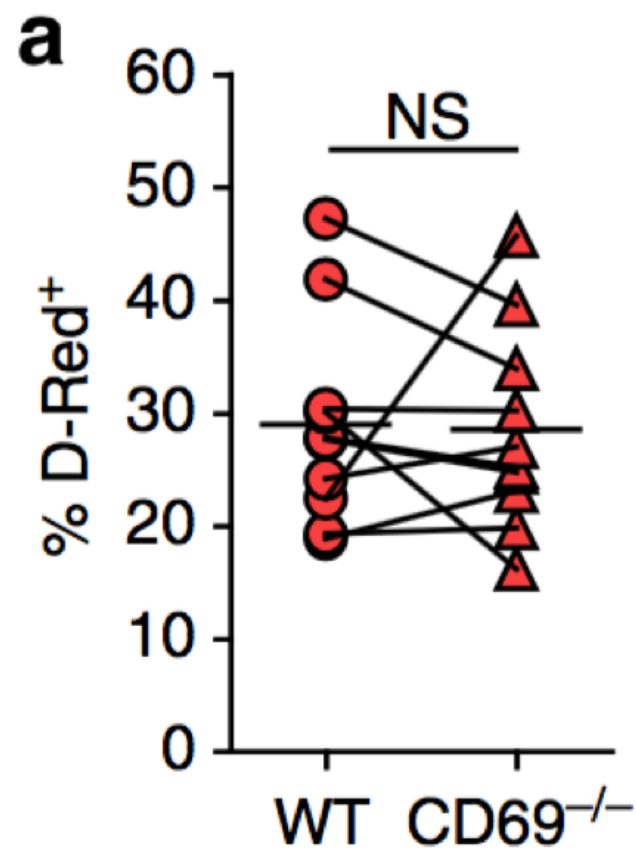
Most resident cells in PP
were CD69^{hi}.

CD69 on cell surface binds
to S1PR1 – emigration ?

WT/CD69 / mixed H2B-
Dendra2 BM chimeras



- Blood
- Lymph
- T cell
- S1P1 Receptor
- S1P1



T cell receptor

Are T cells generated in every PP and become resident?

Seed CD4⁺ memory/effector T cells other PP's?

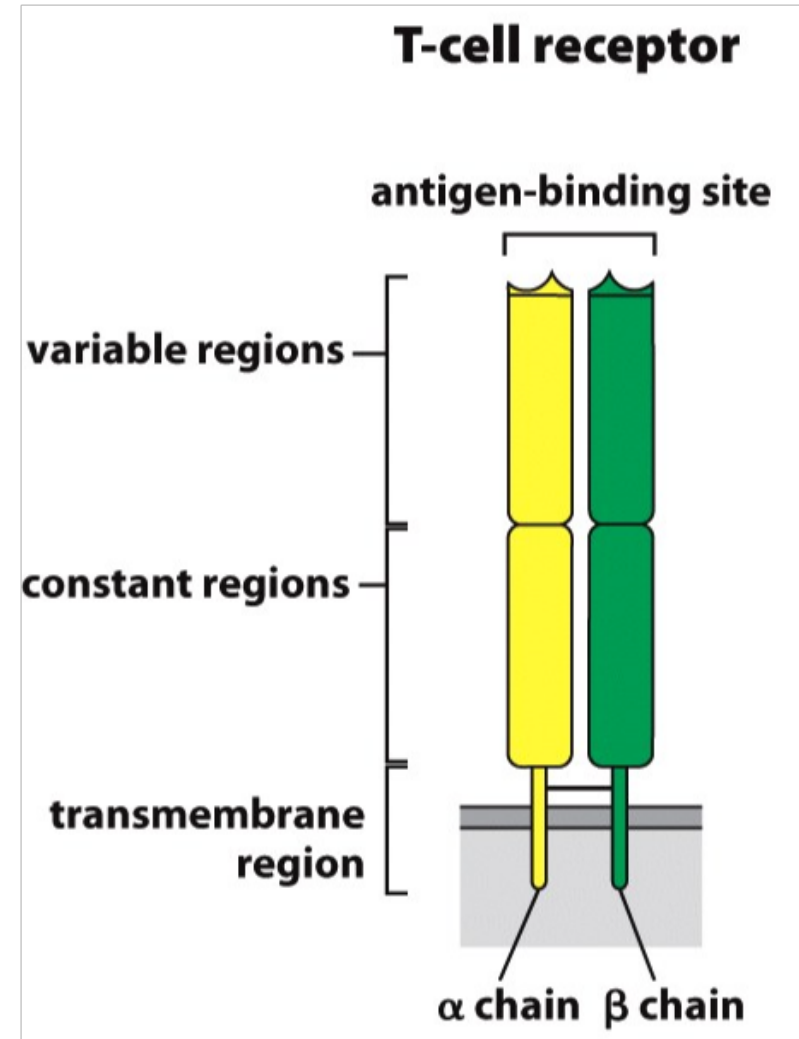
T cell receptor analysis.

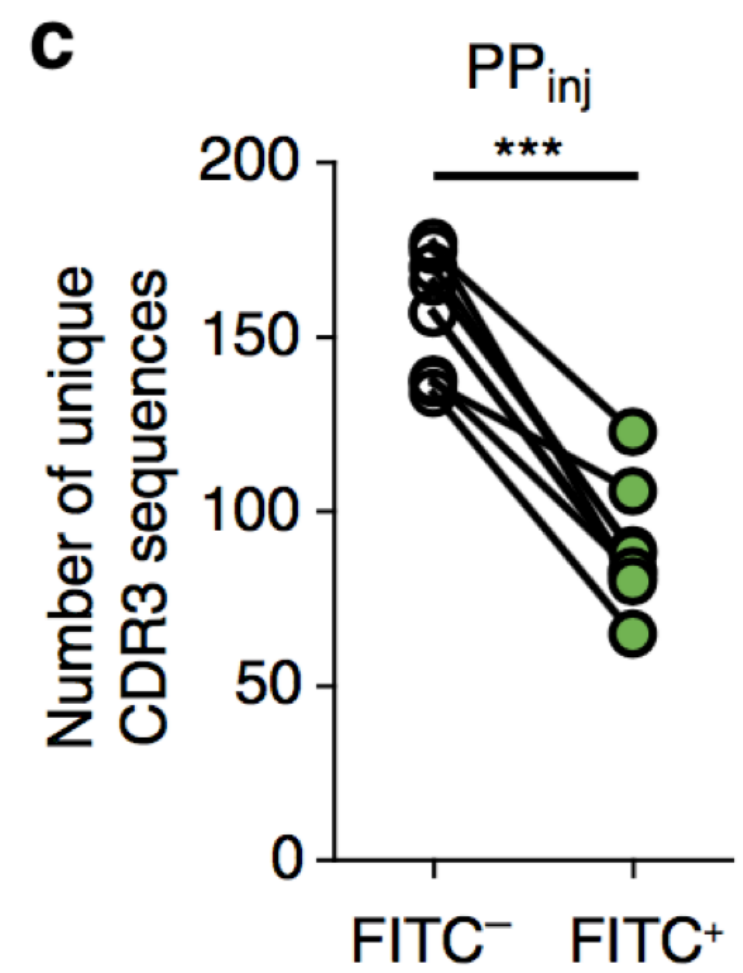
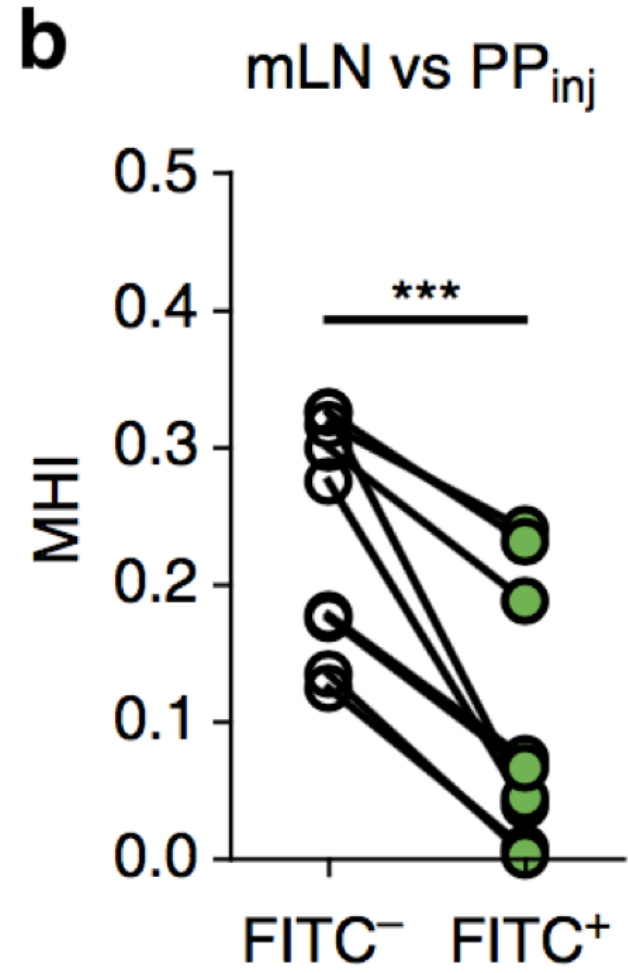
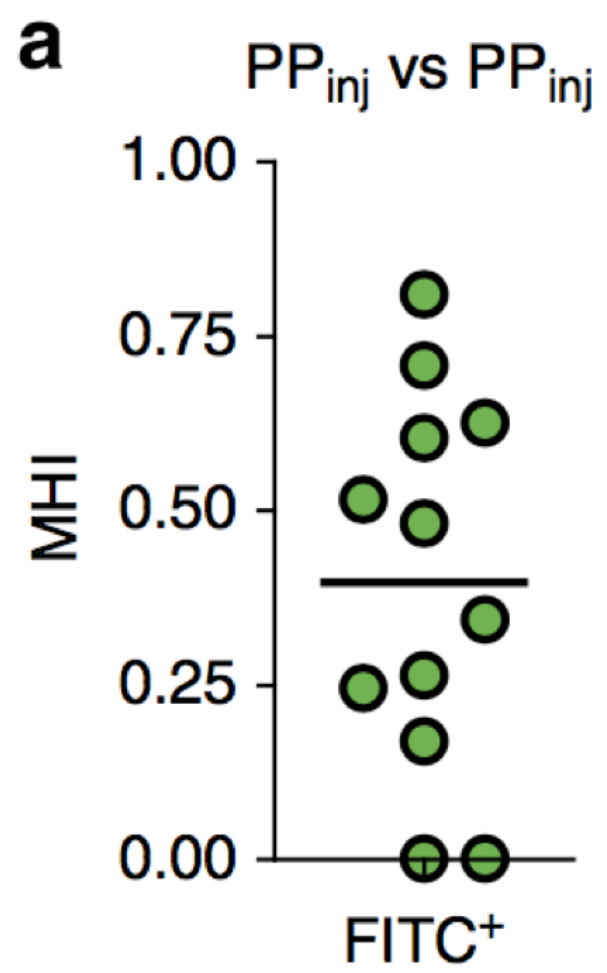
Va8 (TRAV12) family

Morisita–Horn index (MHI)

1.0 – 100% similarity

0.0 – 0% similarity





RAG-sufficient OT-II transgenic mice

Most CD4⁺ T cells express the OT-II TCR.

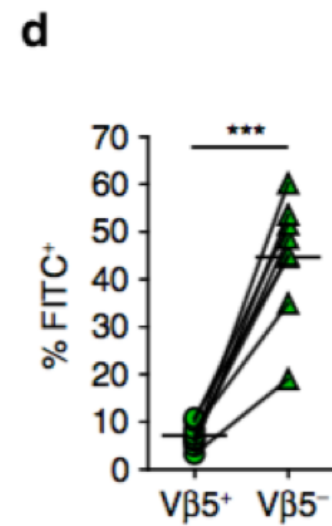
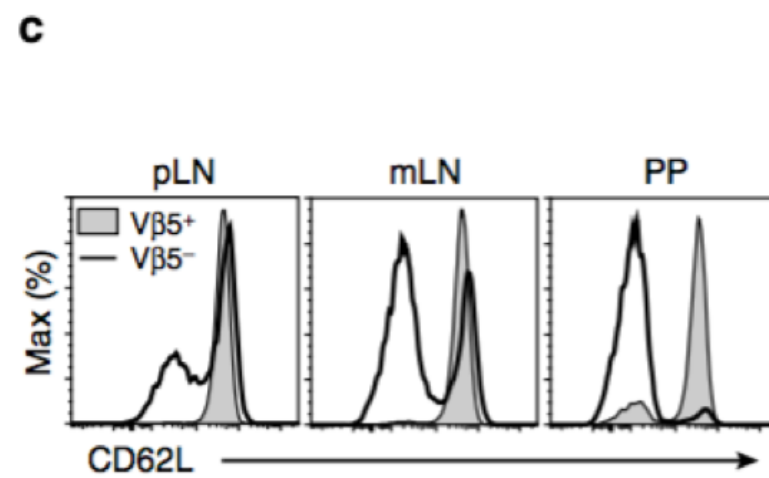
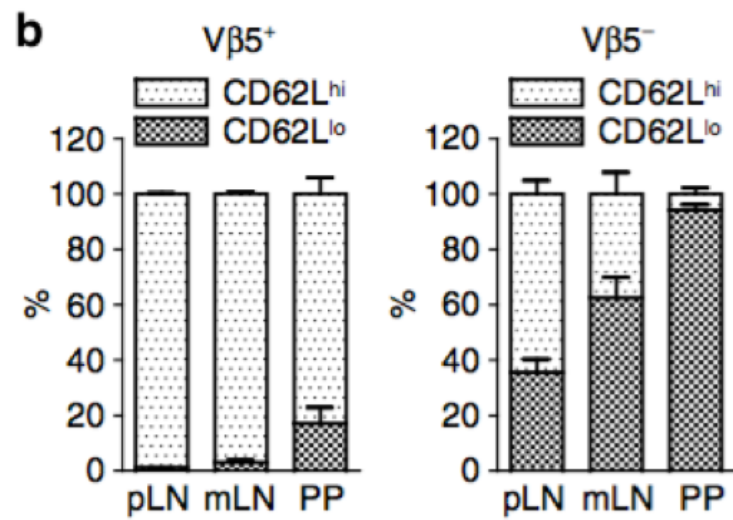
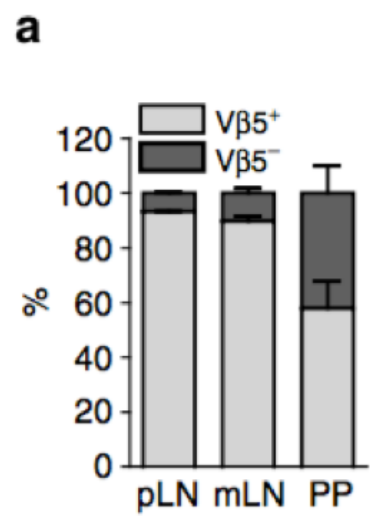
Consists of Va2 and Vb5 chains .

Specific for Ovalbumin (OVA).

Some CD4⁺ T cells express other TCR's.

- Endogenous recombination events.





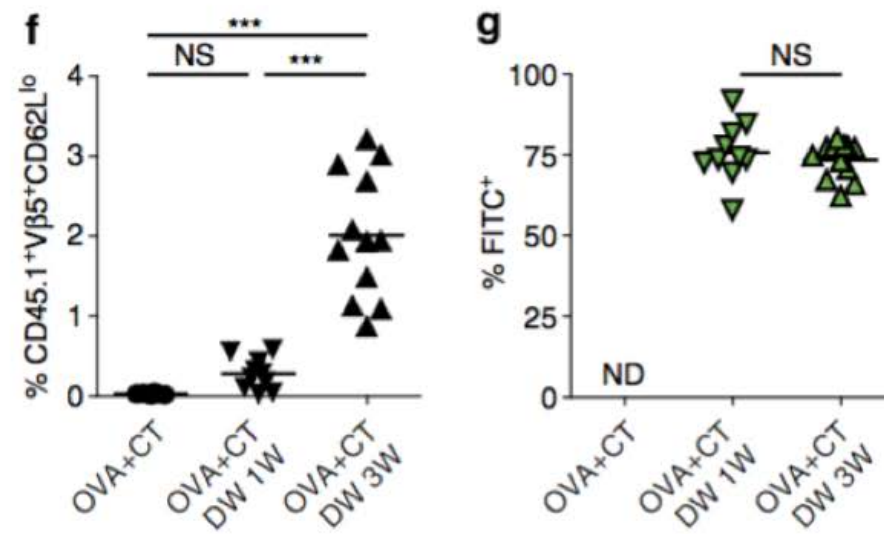
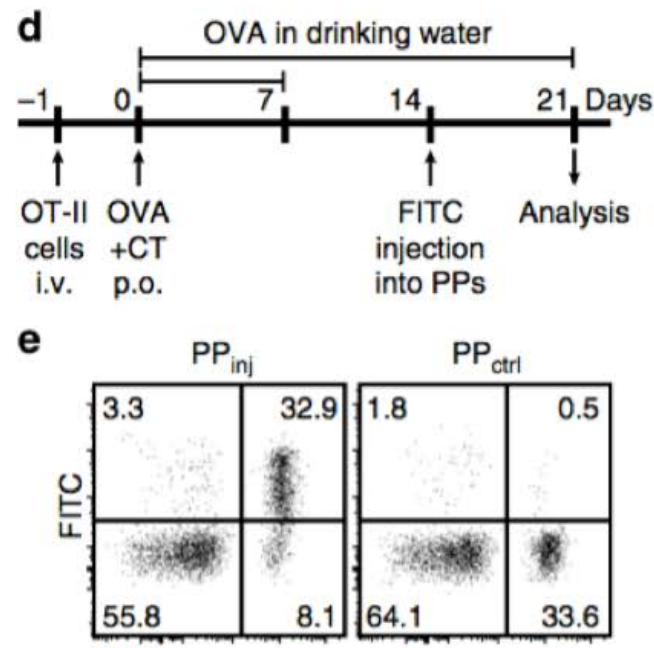
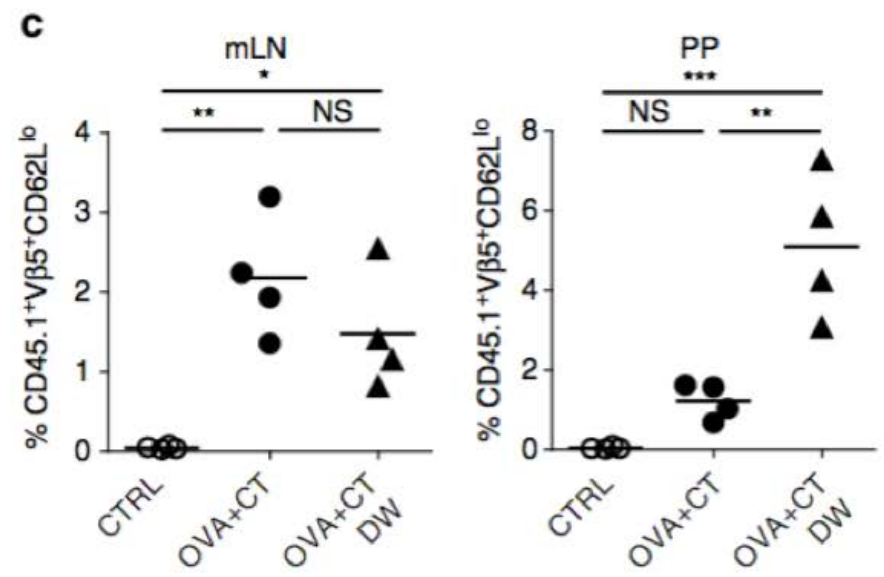
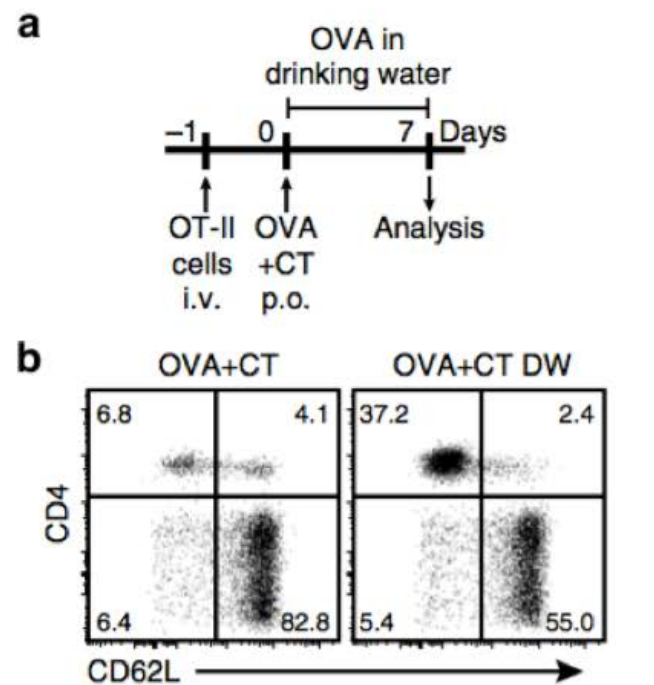
TCR signaling is important for resident T cell generation

Generation of resident OT-II in PP's.

Adoptive transfer of congenially marked (CD45.1⁺) OT-II cells

WT mice immunized with OVA + cholera toxin





Conclusion

TEM cells are CD62L^{lo} CCR7⁻ - home to non-lymphoid tissues

TCM cells are CD62L^{hi} CCR7⁺ - circulate through lymphoid tissues

First evidence of antigen-experienced CD4⁺ T cells retained in lymphoid tissues.

Phenotype - CD62L^{lo} - make up to 50% of effector/memory.

Reside for 7 days.

...longer duration?

