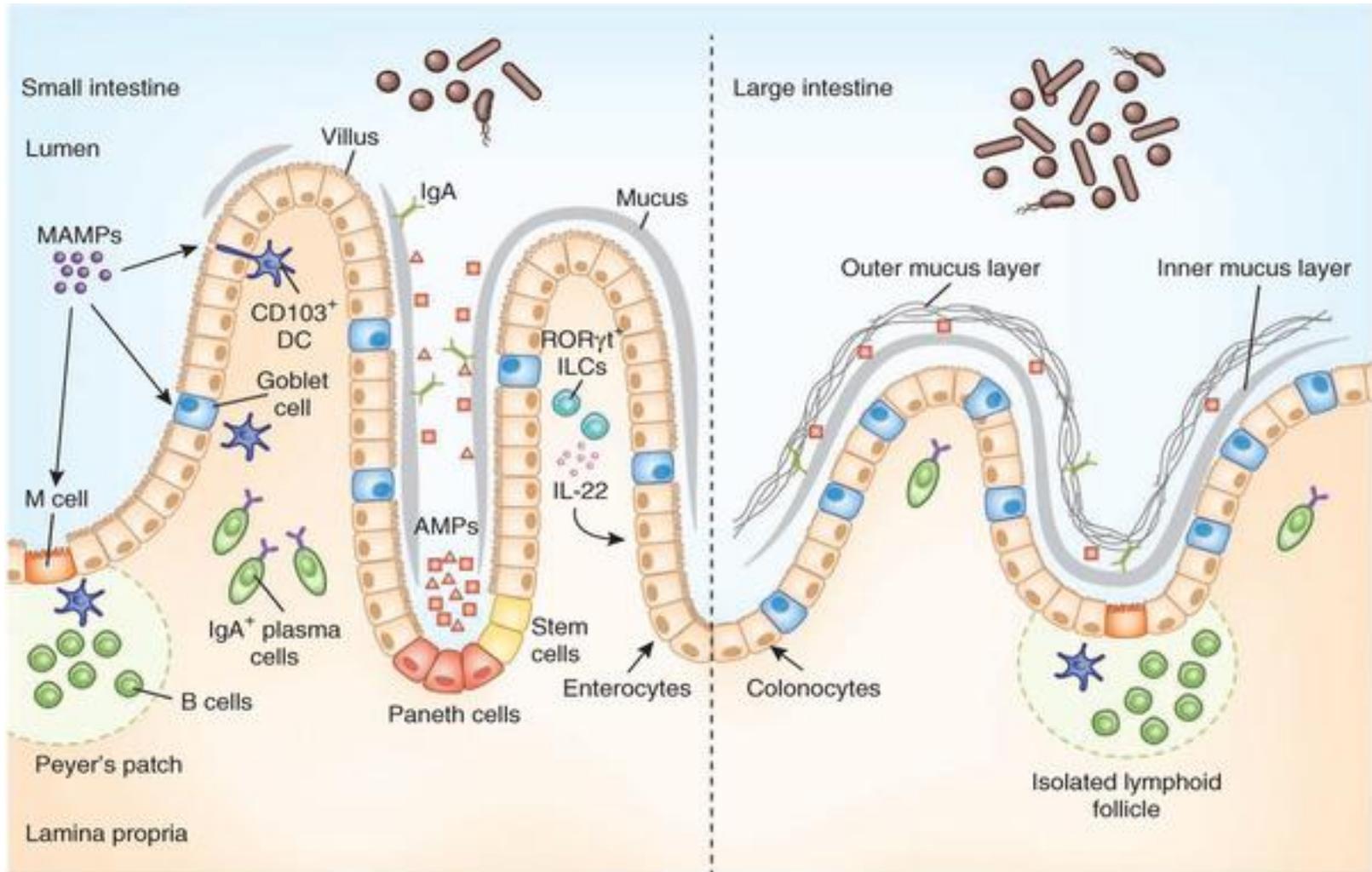


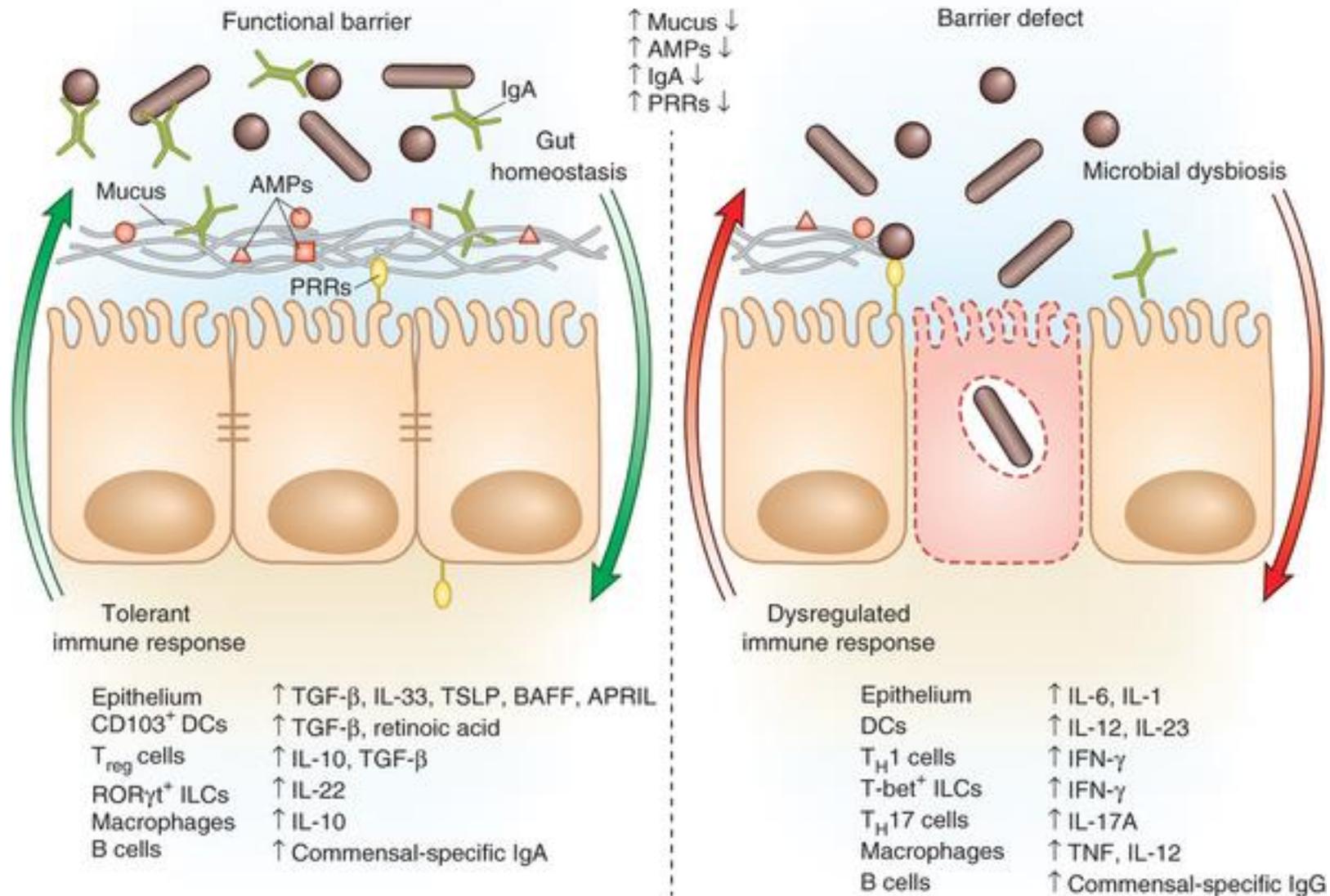
Restraining the immune system

Dr. Issa Abu-Dayyeh

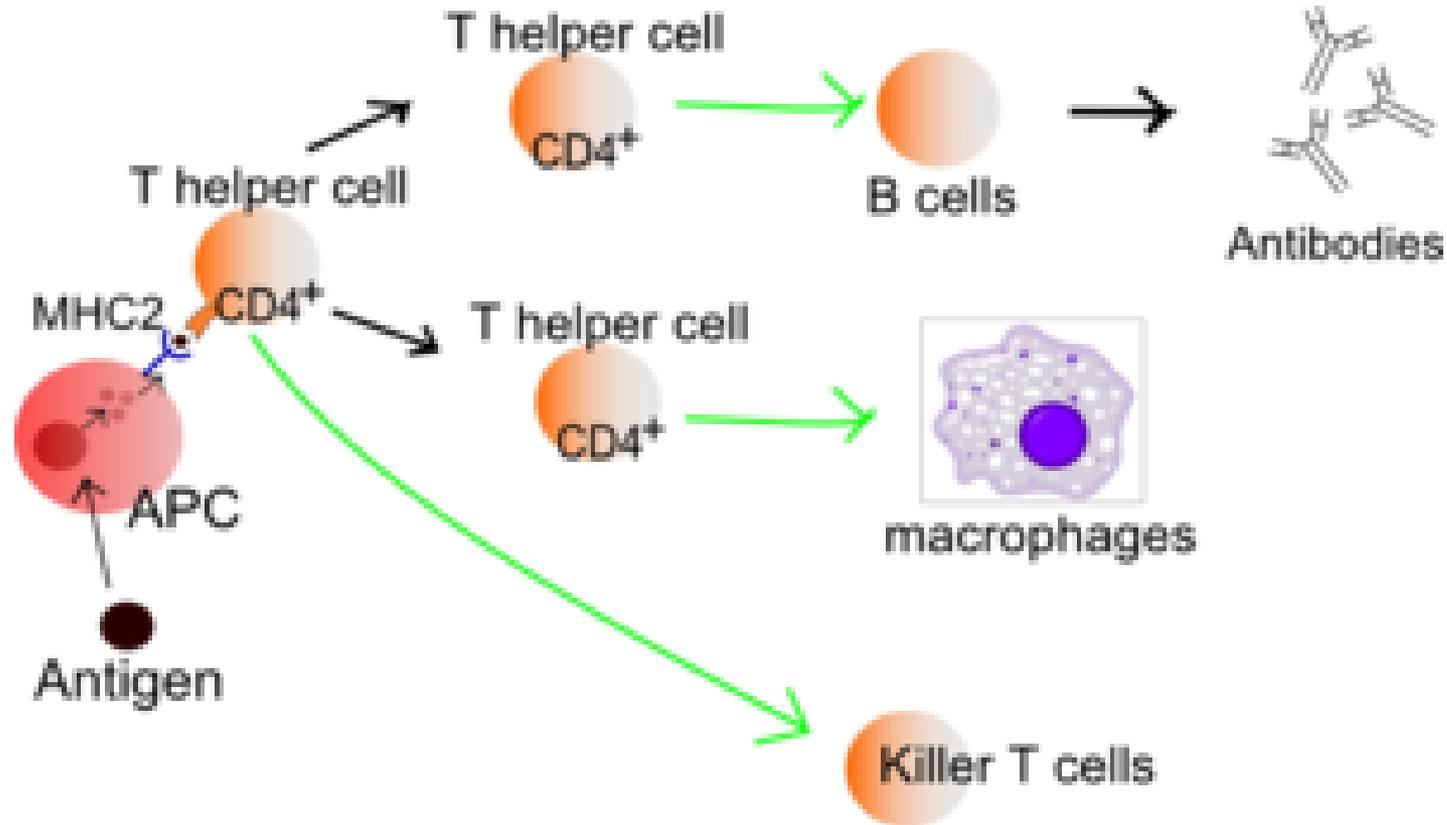
Intestines and commensal bacteria



When things go wrong!

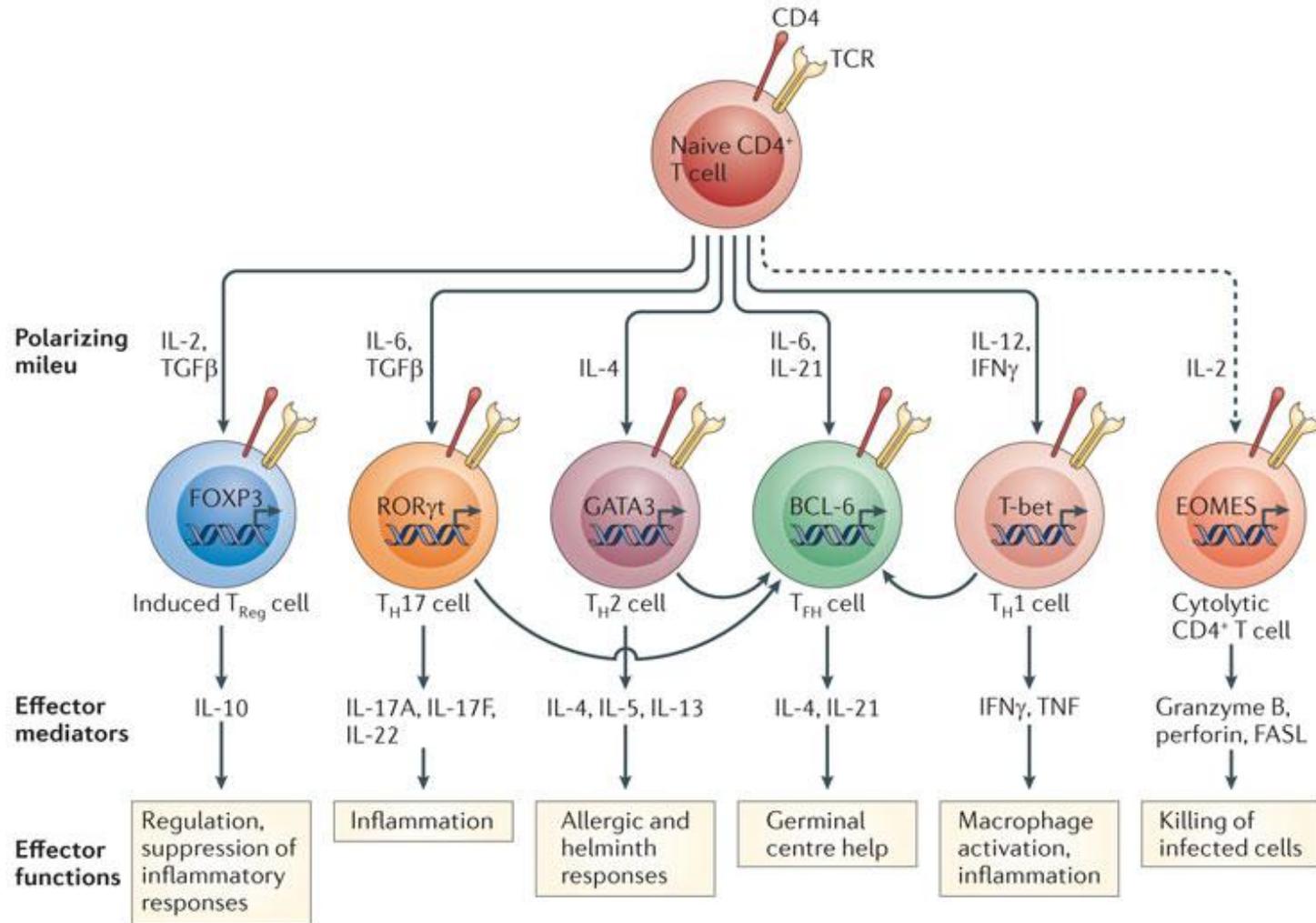


Immune activation, then what?

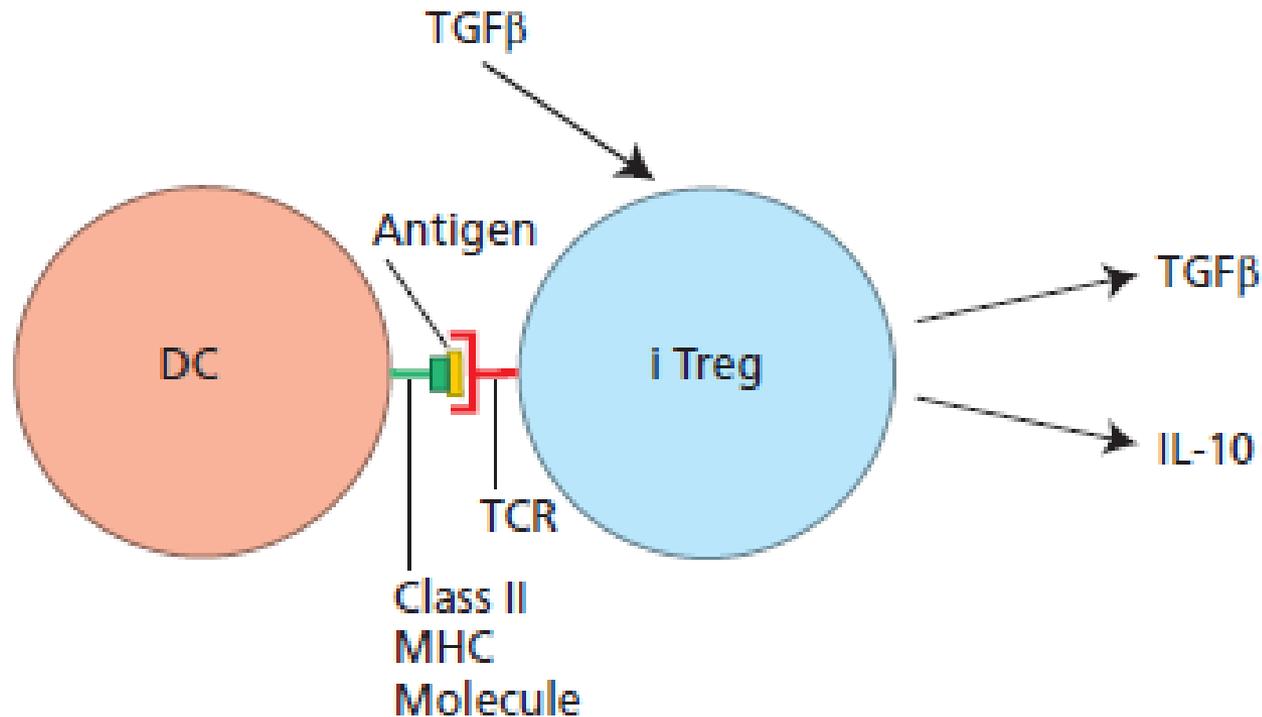


Ending the immune activation or else?

Th (CD4 cells)



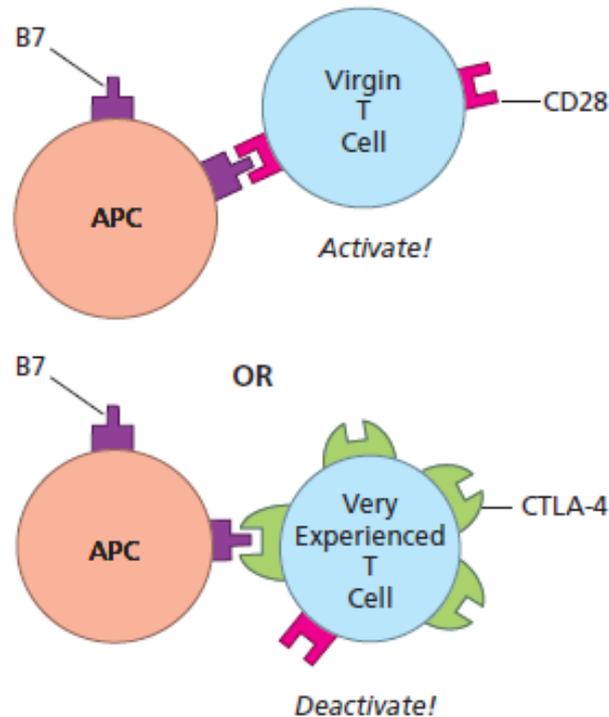
Inducible T regulatory cells (iTregs)



Deactivating the system

As foreign antigen is eliminated, the level of activation of both the innate and adaptive Systems decreases.

Binding of B7 molecules on APCs to CTLA-4 receptor on T cell, inactivates it.



Has much higher affinity to B7
Compared to CD28

CD28 vs. CTLA-4

Early in an infection, B7 binds to CD28 and acts as a co-stimulator.
Then after the battle has been raging for a while, B7 binds mainly to CTLA-4,
Making it harder for these T cells to be reactivated, and helping to shut down the
adaptive immune response.

Other inhibitory receptors on T cells exist; example PD-1

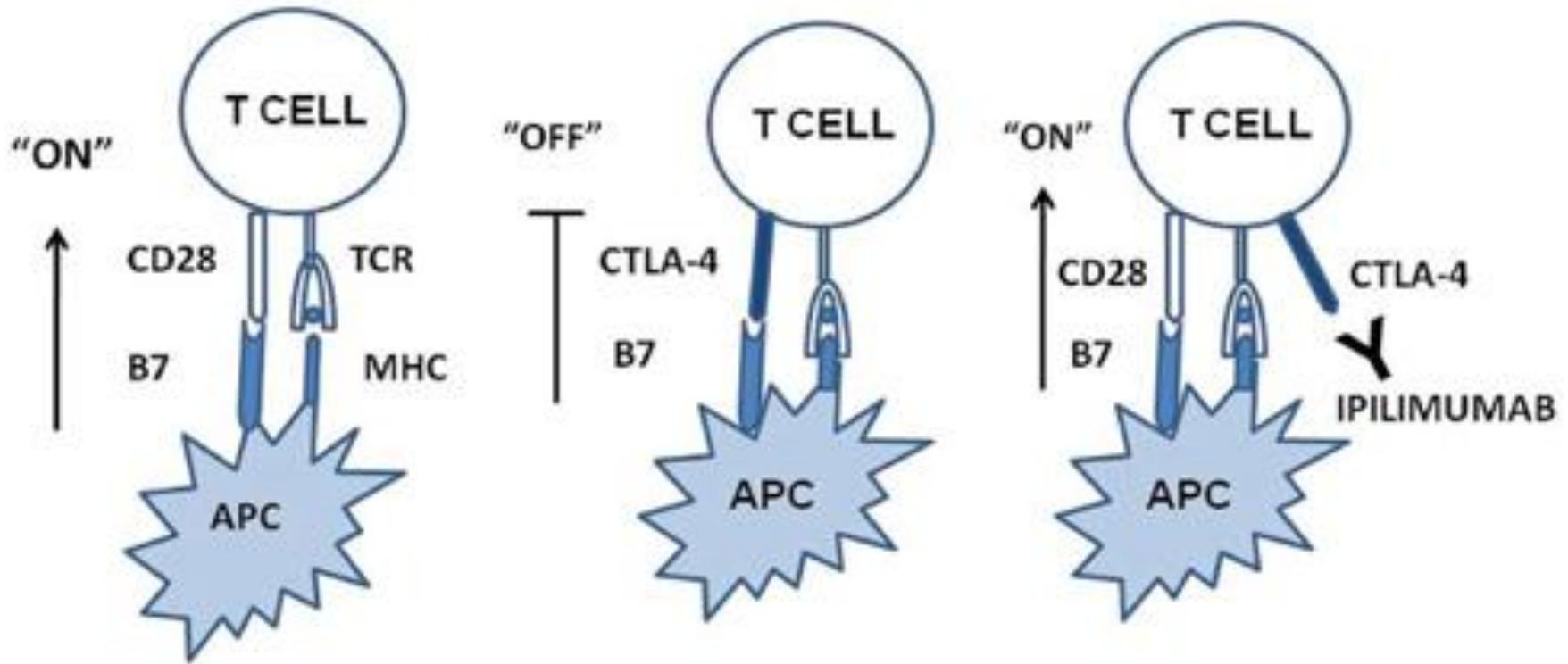
Are inhibitory receptors good or bad?

Depends!

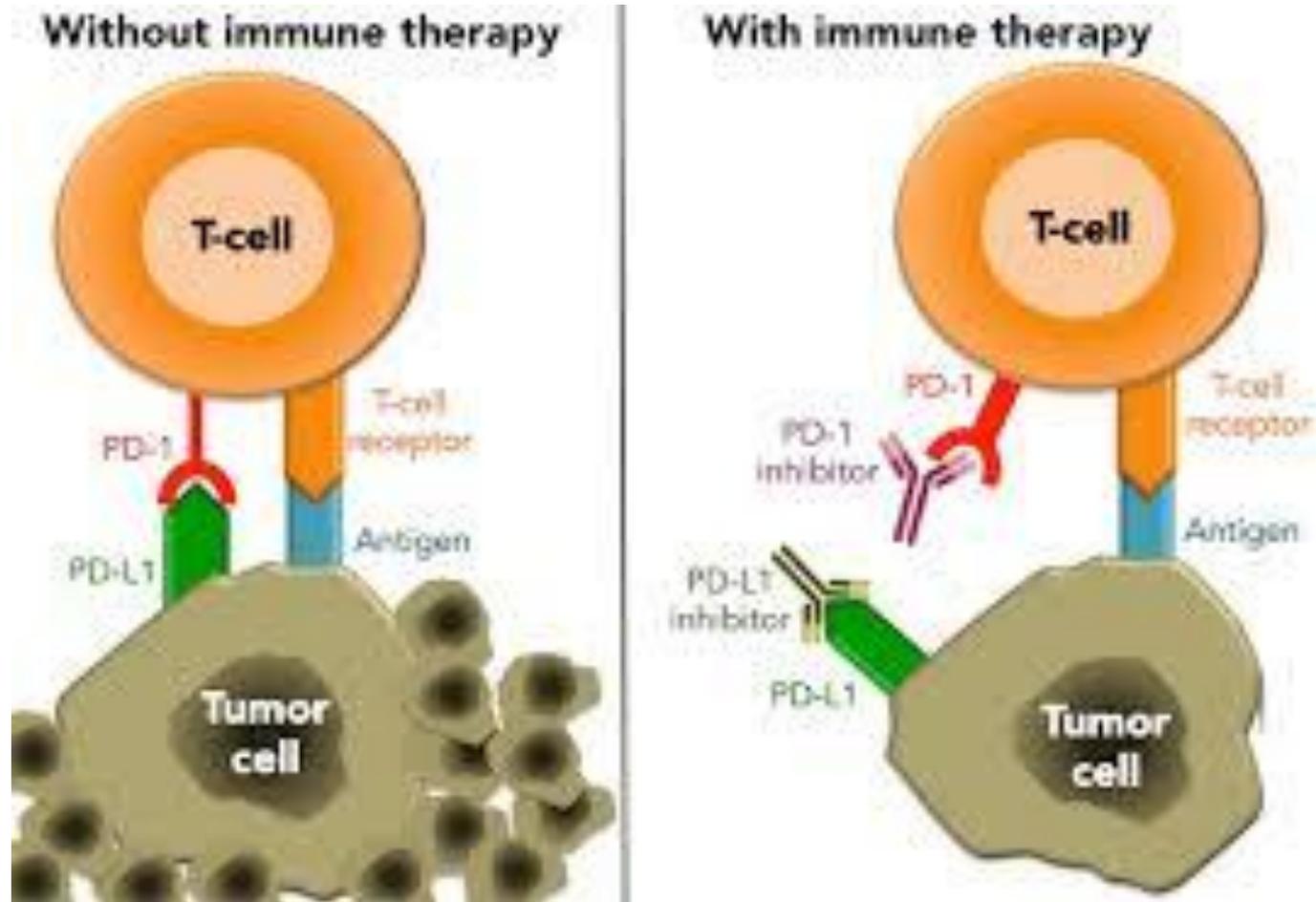
Good in ending immune response and avoiding autoimmune disease

Can be bad in Cancer control and cause treatment failure!

CTLA-4 targeted Immunotherapy



PD-1 targetted Immunotherapy



Life is short!

Neutrophils live for few days only.

Half-life of NK cells is about a week.

Less NK= less IFN- γ = less M ϕ activation

DCs live for about a week after arriving to lymph node.

Less APC activity= less Th and B cell activity

Plasma cells die after about 5 days.

Antibodies have a short life too (IgG half-life is longest= 3 weeks)

Immune response can end relatively fast and invader-specific antibodies drop fast

Exhaustion

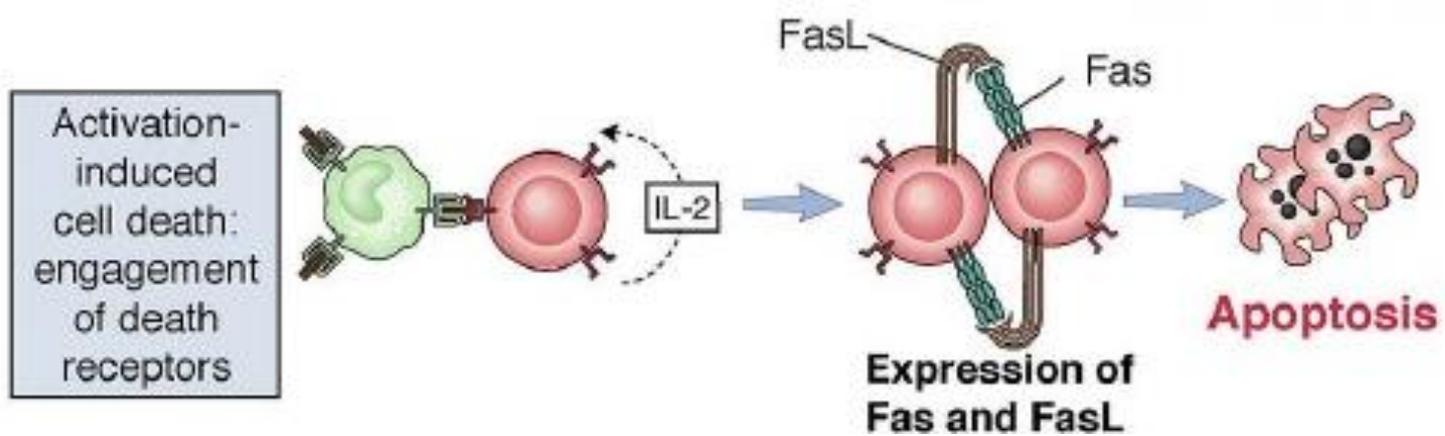
Although DCs, NK, and plasma cells have a short life, T cells don't, They actually Live long. How do we get rid of the big number of activated T cells??

Activation-Induced Cell death (AICD)

Activated T cells are sensitive to FasL-Fas Interactions, so they can help each other Commit suicide.

AICD eliminates T cells which have been repeatedly activated, and makes room for New T cells that can protect us from the next microbes which might try to harm us.

Activation-Induced Cell Death (AICD)



Summary

The immune system uses several tolerogenic mechanisms to avoid unnecessary stimulation of the immune system. Ex: T-regs

Disappearance of foreign antigen upon end of infection is the first step to end an immune response

The short life of many immune components help end an immune response quickly
ex: Neutrophils, NK cells, and plasma cells

The presence of negative immune regulators help inactivate T cells
Ex: CTLA-4 and PD-1

Exhaustion and killing by AICD helps eliminate repetitively activated T cells

All of the above help reset the system to be ready for the next attack!



?Any question