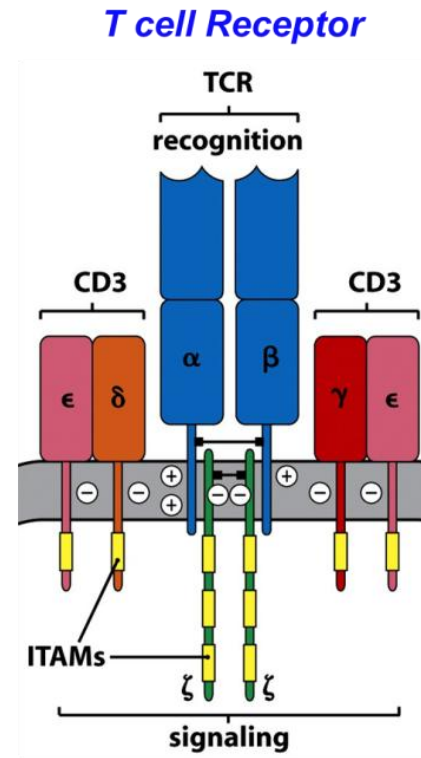
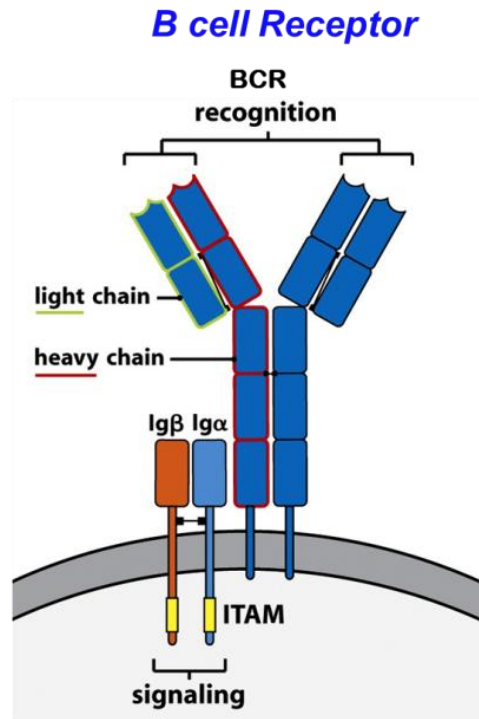


T Cells and Cytokines

Dr. Issa Abu-Dayyeh

T cell receptors

T Cell and B Cell Antigen Receptors (TCR and BCR)



Traditional T cell: $\alpha\beta$, Non traditional T cells: $\gamma\delta$

Traditional T cells ($\alpha\beta$)

Represent over 95% of circulating T cells.

Express either CD4 or CD8 co-receptor

The $\alpha\beta$ receptors of a traditional T cell recognize both the peptide and the MHC Molecule.

Nontraditional T cells

$\gamma\delta$ T cells:

Represent around 5% of circulating T cells.

Do not express CD4 or CD8 co-receptor

Most abundant in areas like the intestine, the uterus, and the tongue which are in contact with the outside world.

Less diverse than traditional T cells. Like the innate immune system, they can watch the front lines and are tuned to recognize invaders that enter at certain locations.

NKT cells:

Less than 0.5% of T cells, express **$\alpha\beta$ receptor** and NK receptors (NK1.1).
Repertoire of **$\alpha\beta$** receptors is limited and they recognize lipid antigens presented on CD1 molecules.

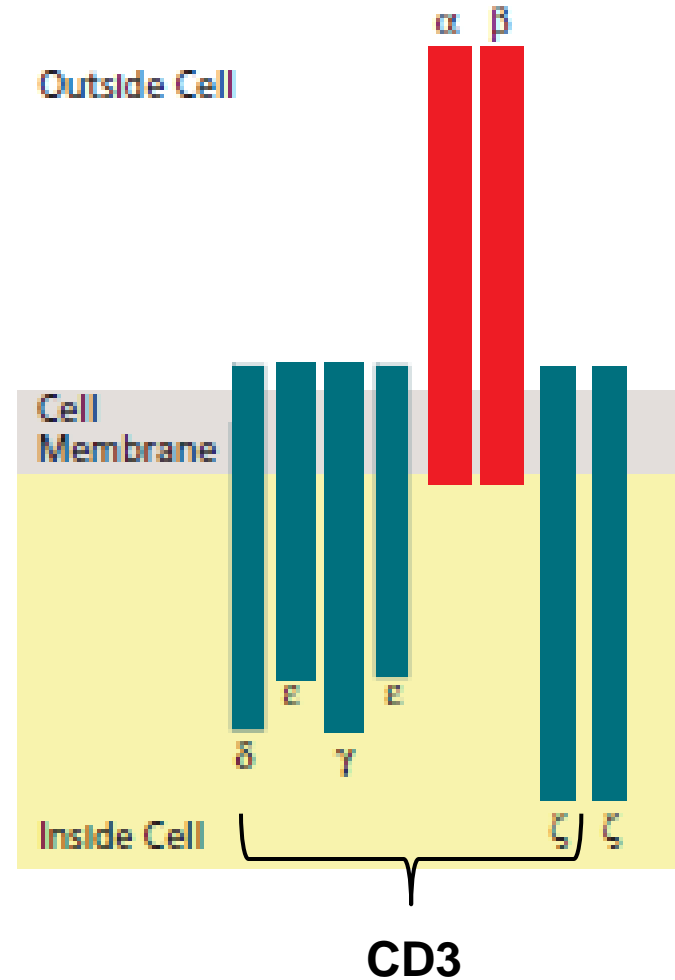
Signalling of T cell Receptors

Signaling by TCR involves clustering these Receptors together in one area of the T cell Surface

TCR is not an ON/OFF switch

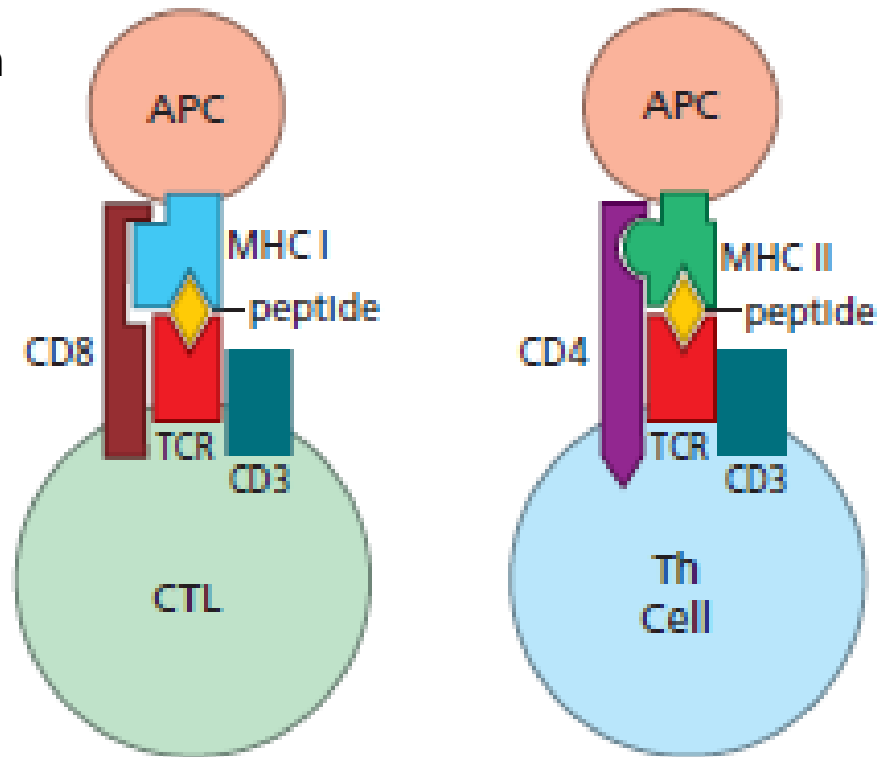
Sends versatile signals depending on how, when, and where it is triggered.

Ex: death, anergy, activation scenarios.



CD4 and CD8 co-receptors

- Main function is to focus the attention of Th cells and CTL on the proper MHC molecule.
- Signaling receptors
- Only loosely associated with the TCR/CD3 complex.
- Clips that stabilize the TCR/MHC-peptide interaction, thereby strengthening the signal sent by the TCR.



Signals sent: Help or kill!

Co-stimulation

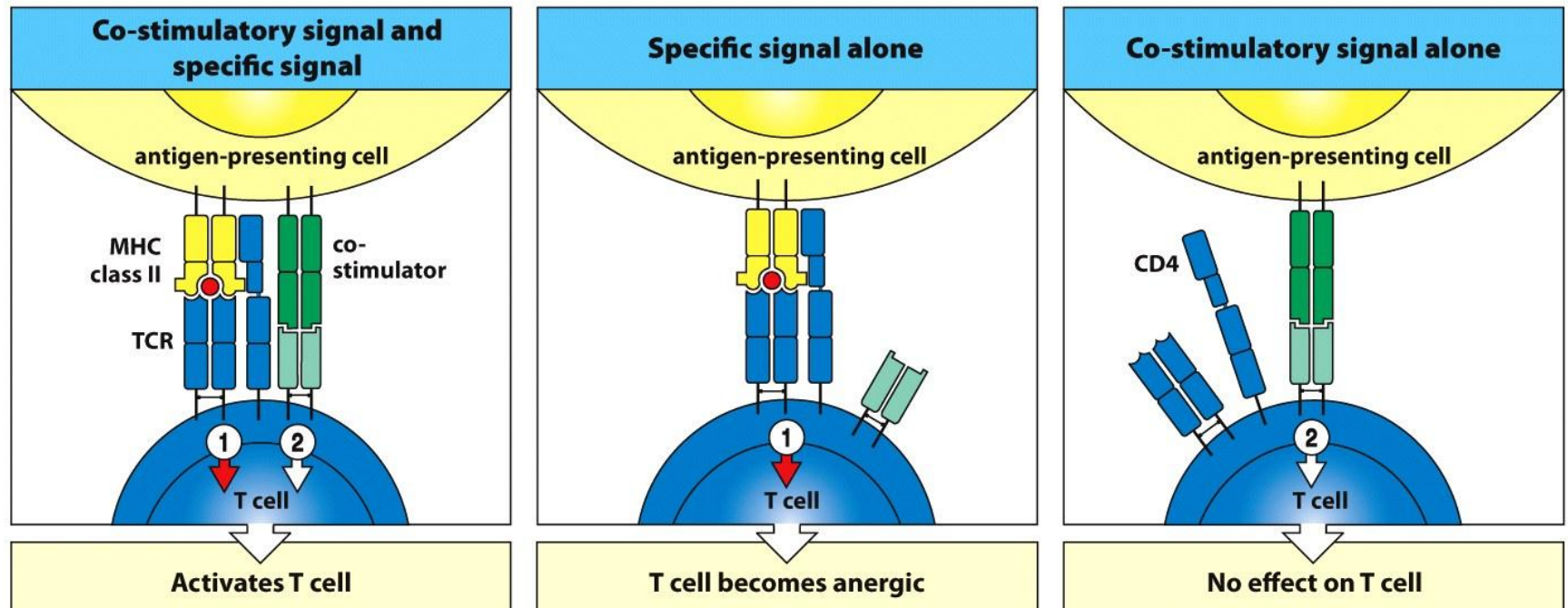


Figure 8.18 The Immune System, 3ed. (© Garland Science 2009)

Activates T cells and lowers the threshold number of TCRs needed to bind to antigen.

Best studied example: B7-1, B7-2, CD40 on APC and CD28, and CD40L on T cells.

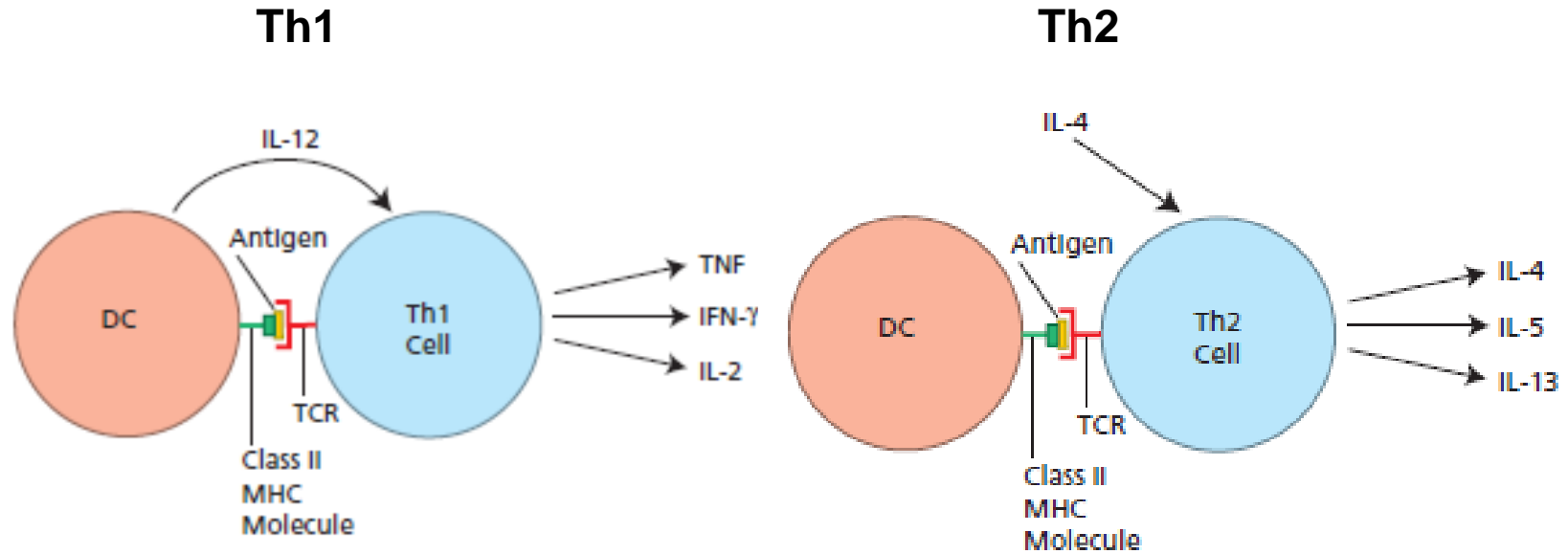
Thought to work through recruiting lipid rafts to the surface of T cells.

T cell activation

Sequence of events:

- 1- Adhesion molecules mediate weak binding between the Th cell and the APC while the TCRs engage their cognate antigen presented by the APC.
- 2- Receptor engagement strengthens the adhesion between the two cells, and up-regulates CD40L expression on Th cells.
- 3- CD40L then binds CD40 on APC and stimulates expression of MHC and co-stimulatory molecules on APC surface.
- 4- Co-stimulation provided by APC amplifies the `TCR engaged` signal, causing more efficient Th cell activation.
- 5- When activation is complete, cells disengage, and Th proliferates by secreting growth factors that bind to receptors that appear as a result of their activation.

Th Subsets



TNF and IFN- γ are potent M ϕ activators
Drive IgG3 class-switch.

Perfect package against viral and bacterial
attacks in blood and tissue.

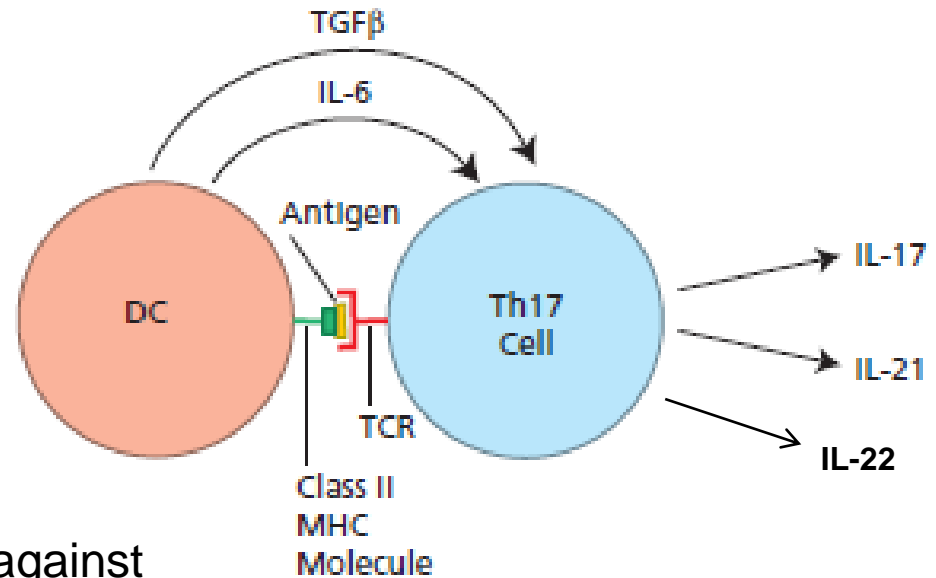
IL-2 stimulates the proliferation of CTLs, NK,
and Th cells themselves.

IL-4 drive an IgE switch and IL-5 an IgA
switch. IL-13 stimulates mucus secretion
in intestines.

Perfect package against parasites and
pathogenic bacteria of the digestive tract.

Initial IL-4 source remains unknown.

Th17 cells



Recent finding, thought to play a role against fungi and extracellular bacteria.

IL-21 induces Th17 proliferation

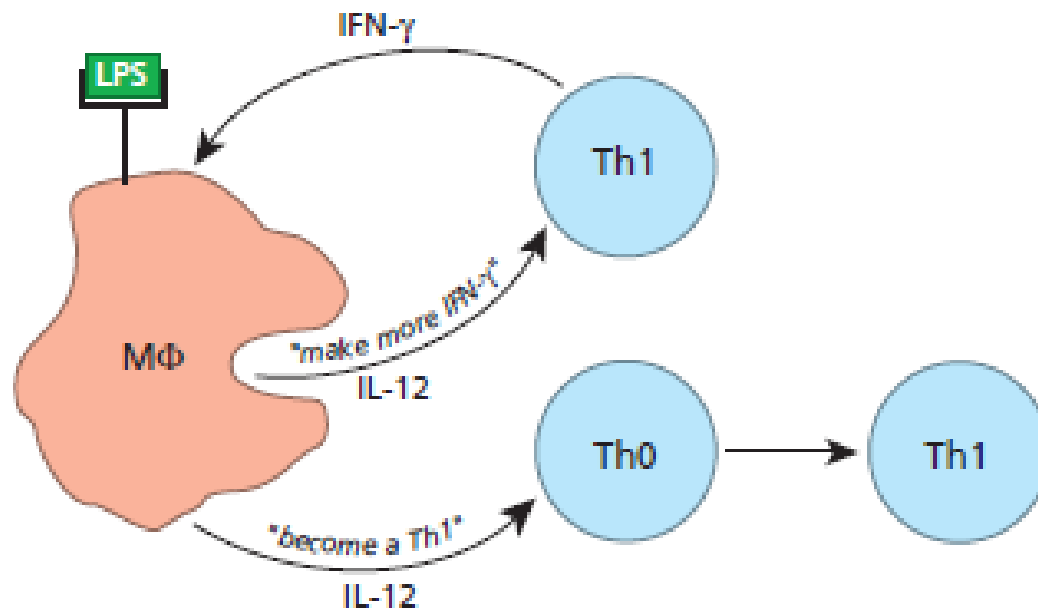
IL-17 recruits massive numbers of Neutrophils to site of infection.

IL-17 and IL-21 drive antibody classes that can opsonize fungi and bacteria and activate complement. (IgG1, IgG2, IgG3)

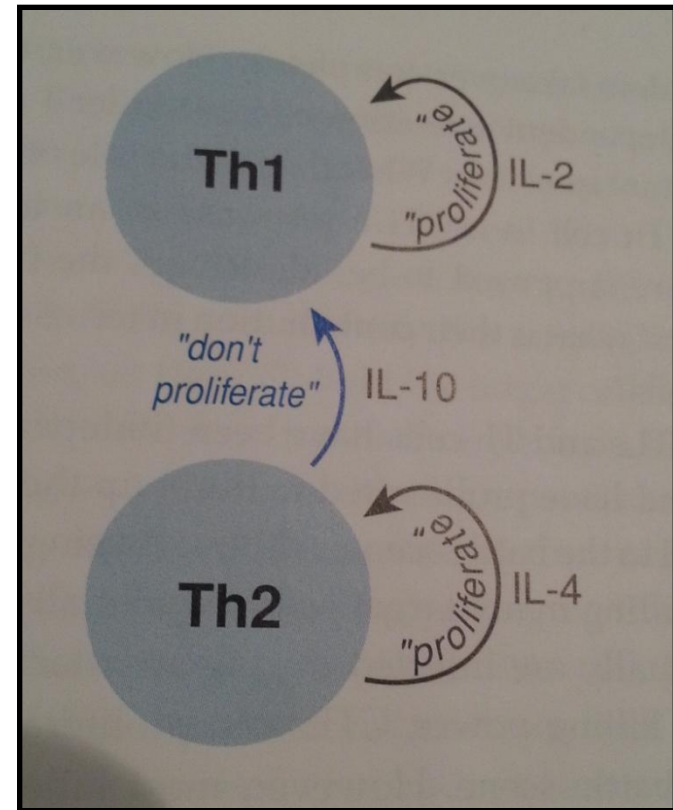
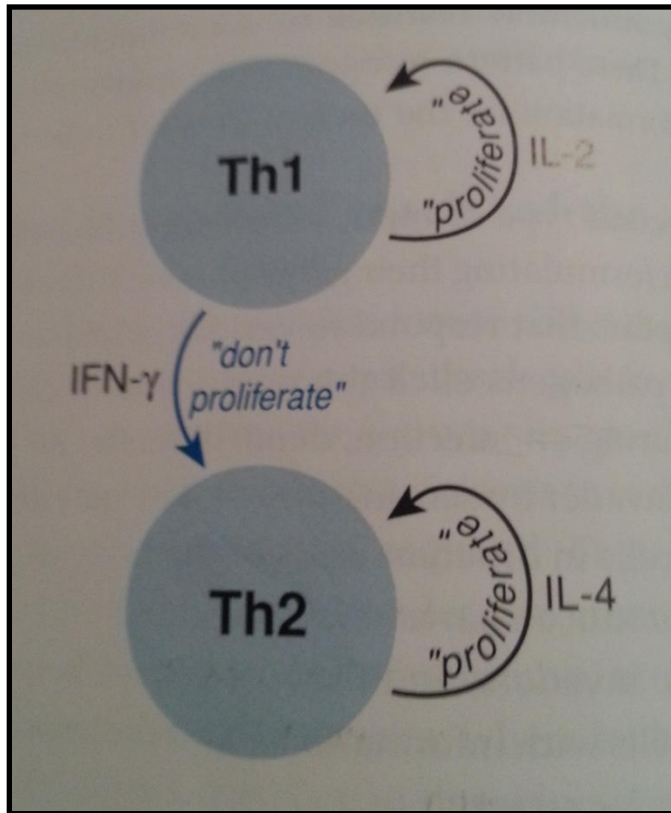
Th0 Cells

Some Th cells are activated by DCs and directed to different tissues without committing to a Th1 or Th2 profile.

Only when these cells arrive to tissue and do they commit to a profile based on the Cytokine milieu.

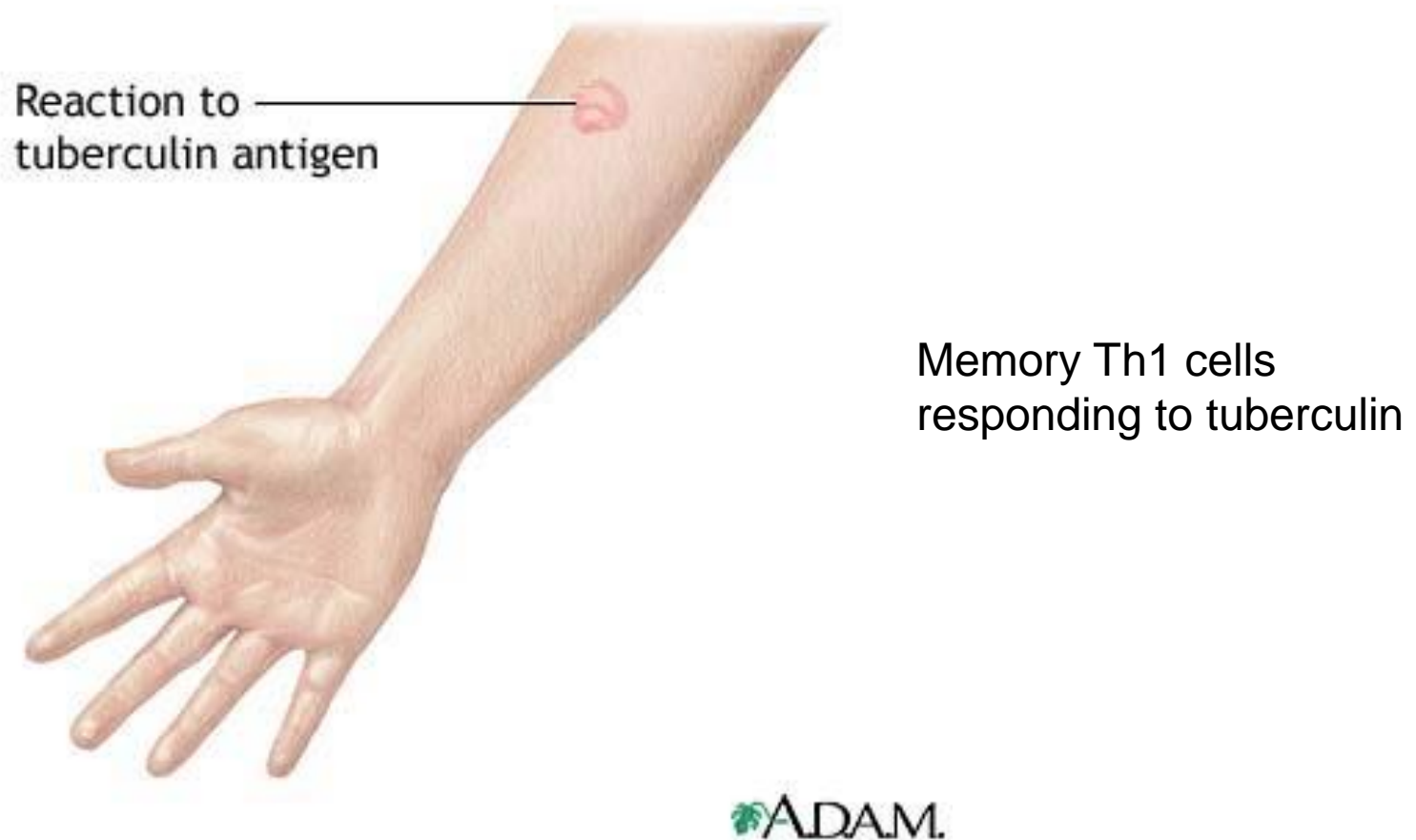


Profile ``lock-in``



Local effect!

Delayed Type Hypersensitivity

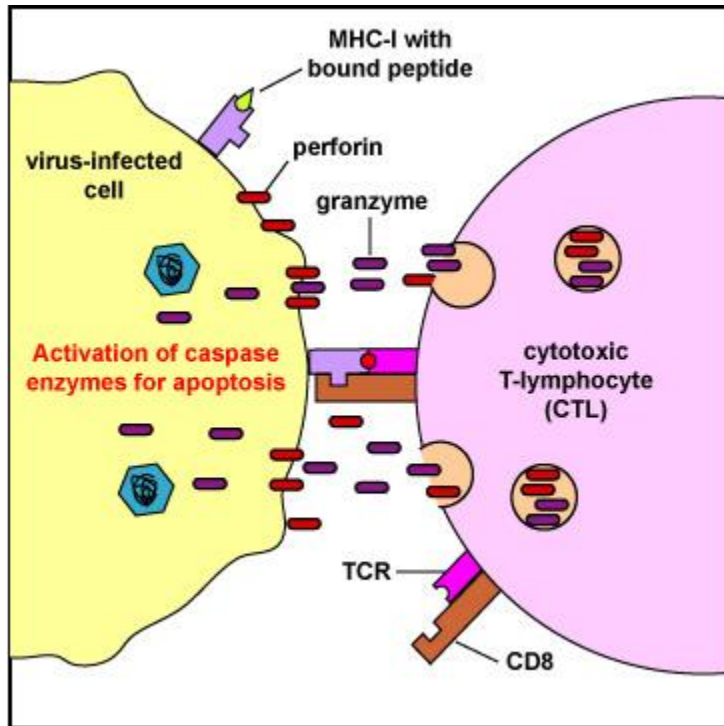


Disadvantages of tuberculin test?

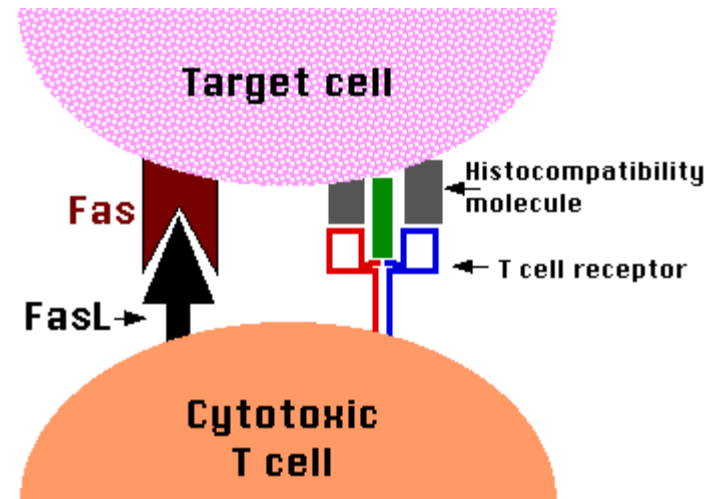
Quantiferon gold test?? Measure IFN- γ secreted by Th cells specific to TB.

How CTLs kill?

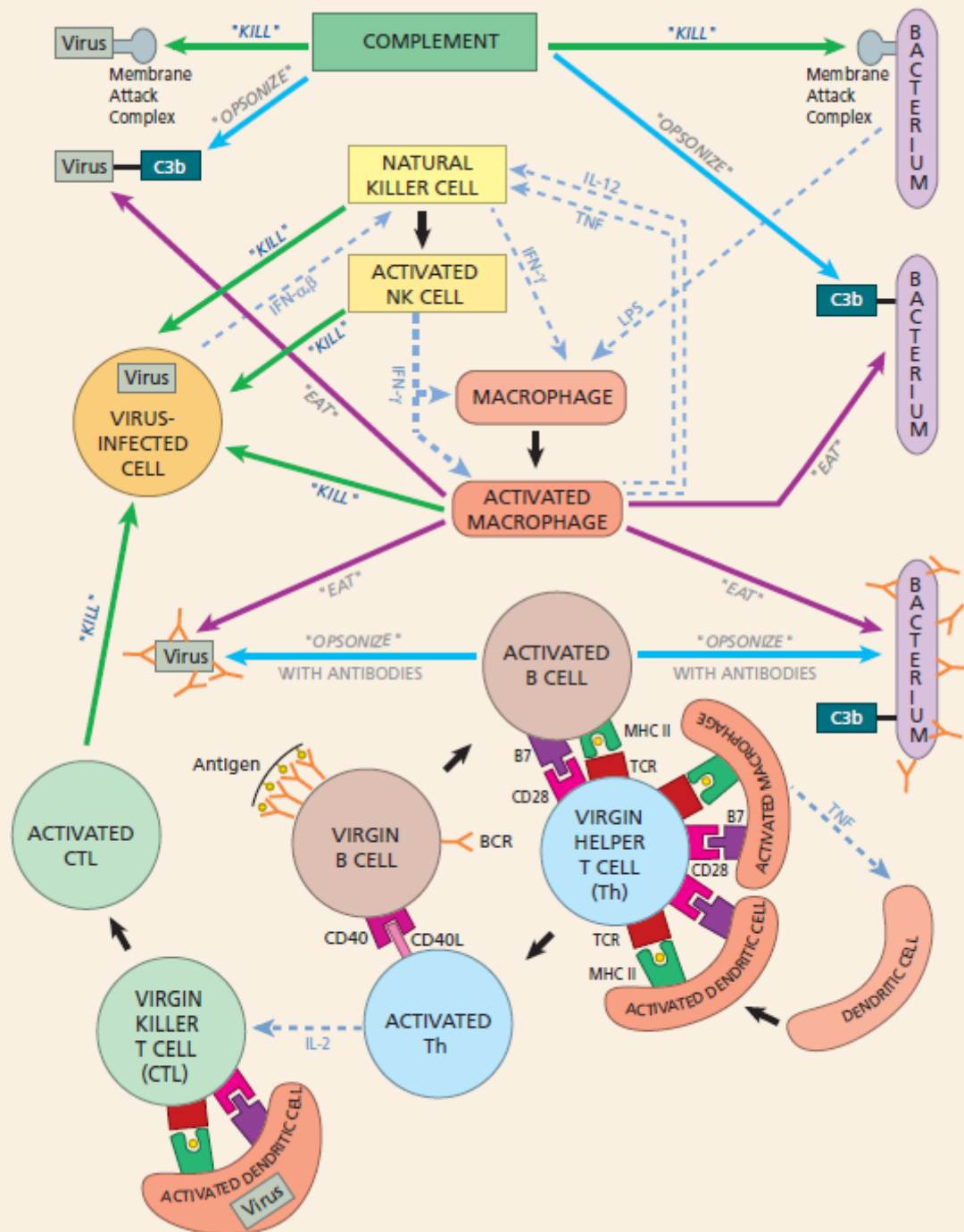
1- Perforin-Granzyme B



2- Fas-Fas-L interaction



One method by which cytotoxic T cells induce their targets (e.g., virus-infected cells) to commit suicide (apoptosis)



Thank you!

Questions???