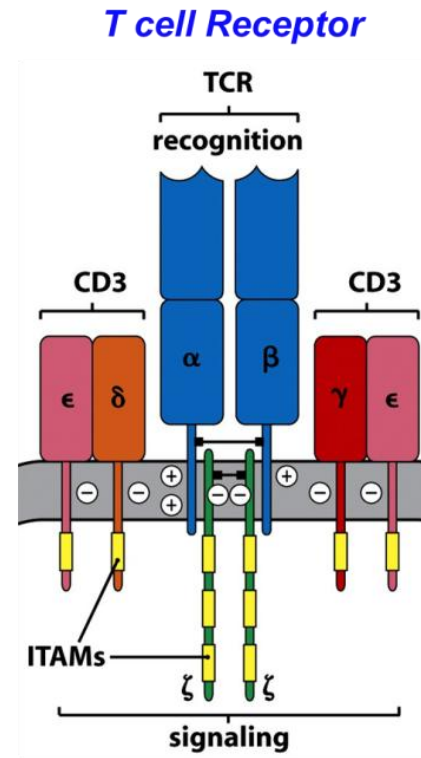
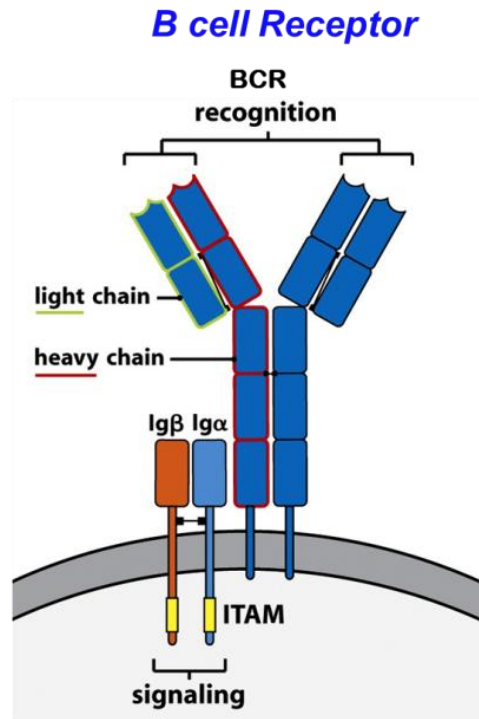


T Cells and Cytokines

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.

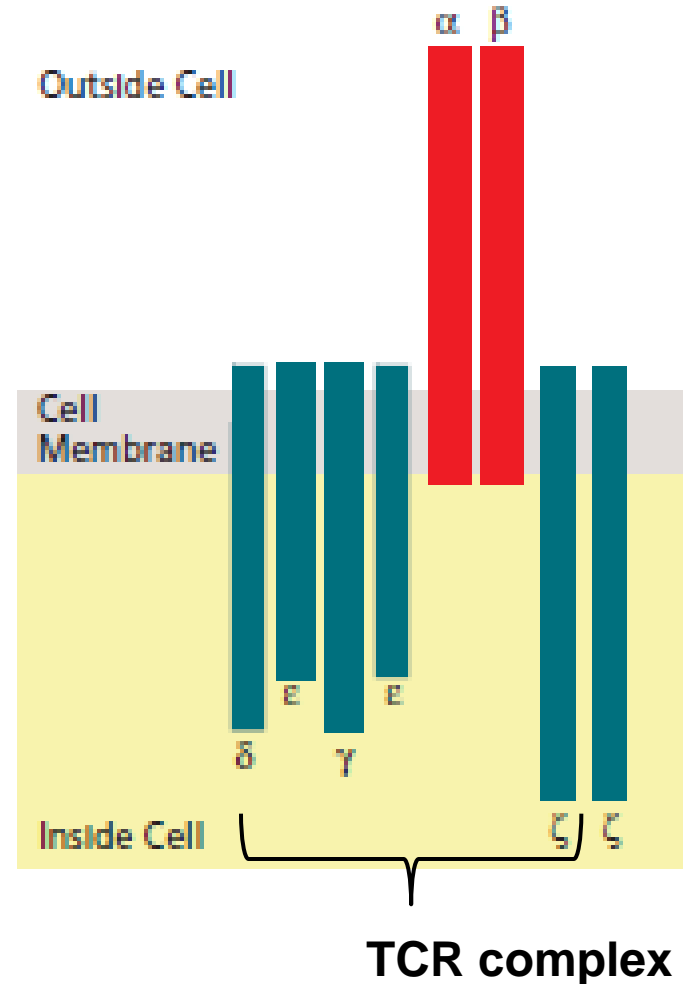
Signalling of T cell Receptors

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

TCR is not an ON/OFF switch

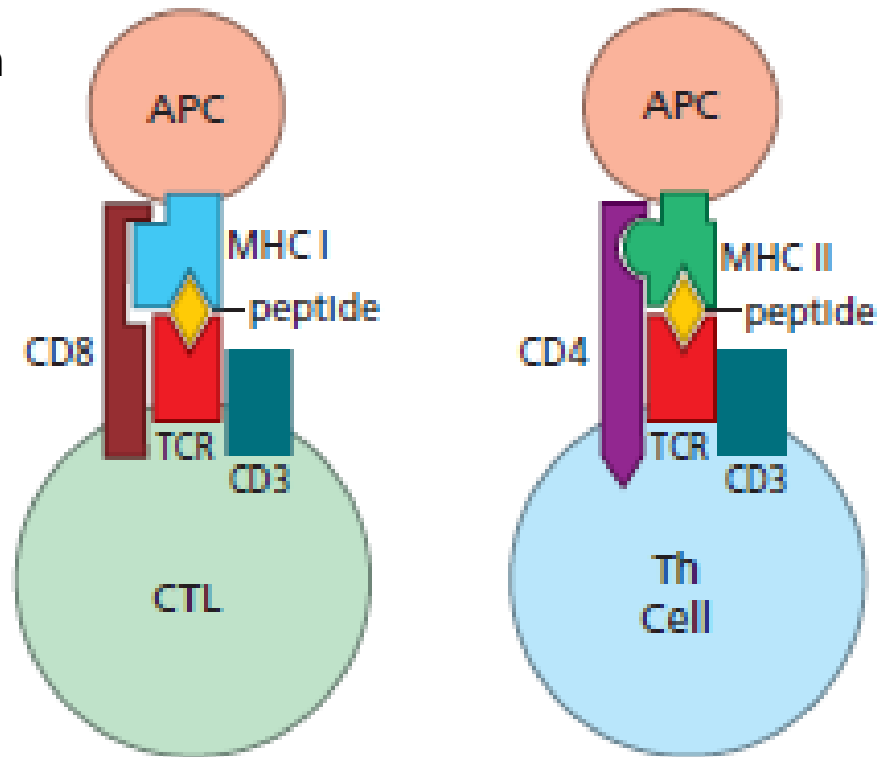
Sends versatile signals depending on how, when, and where it is triggered.

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

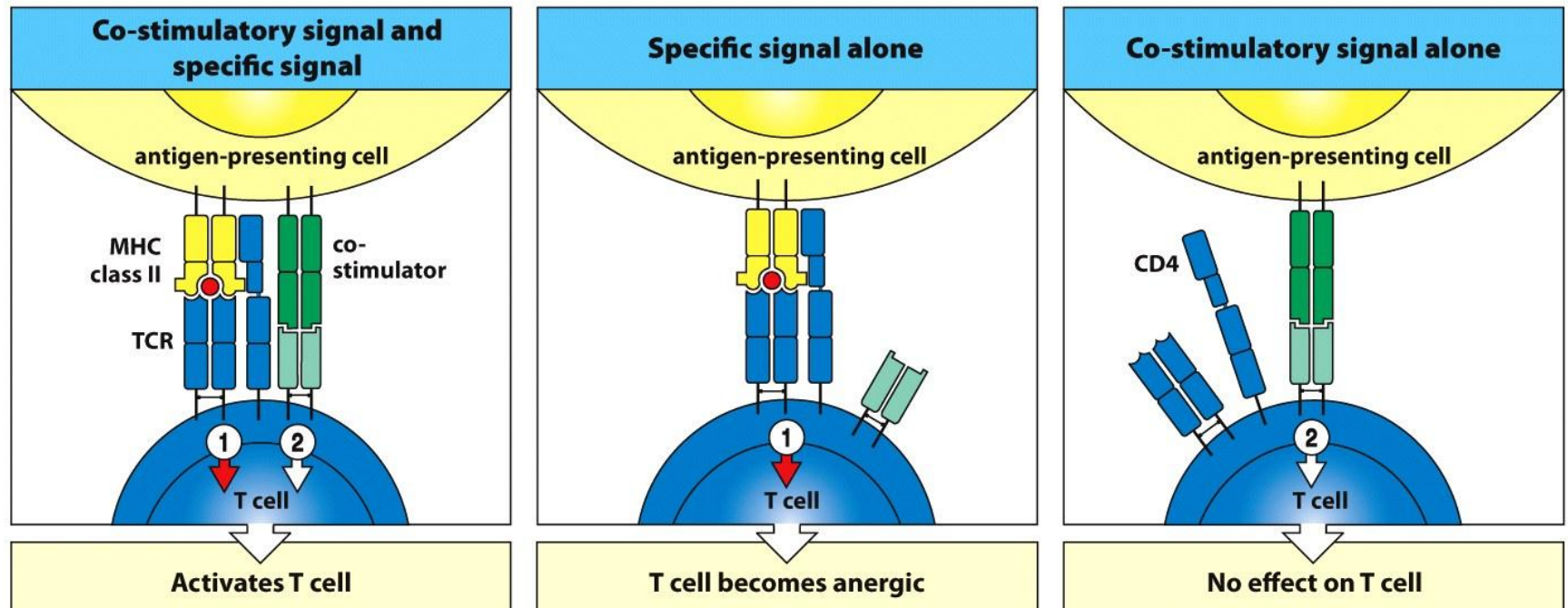


Figure 8.18 The Immune System, 3ed. (© Garland Science 2009)

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.

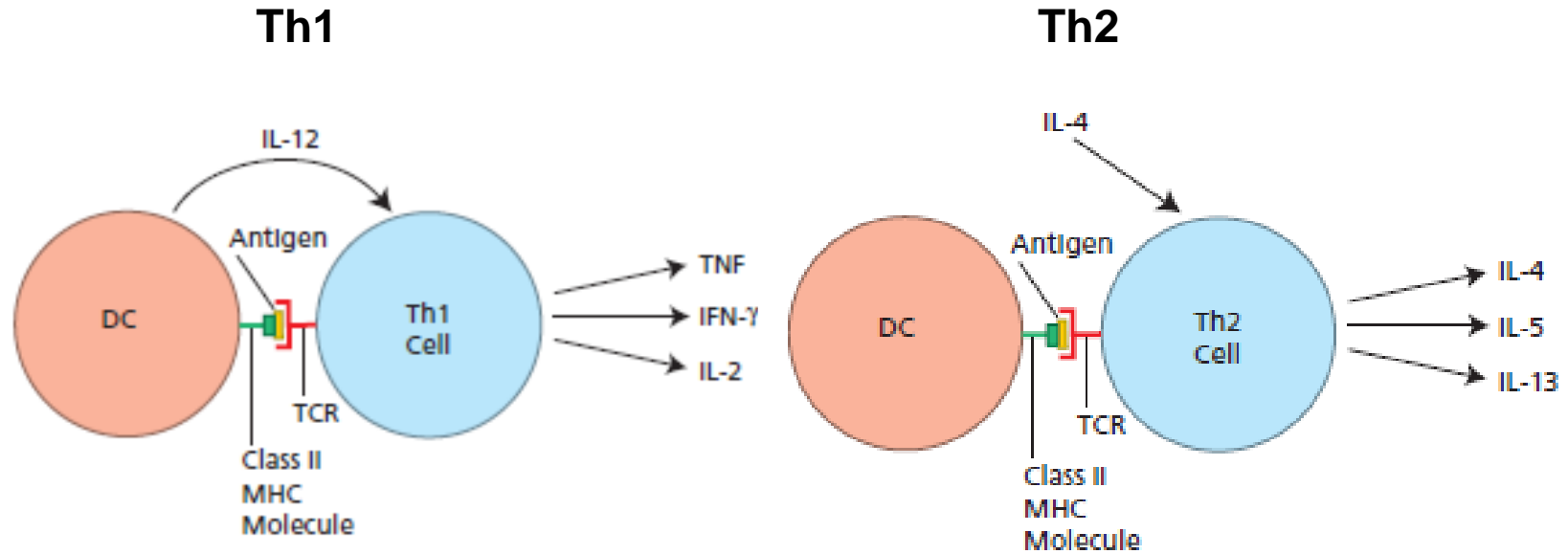
Thought to work through recruiting lipid rafts to the surface of T cells.

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.

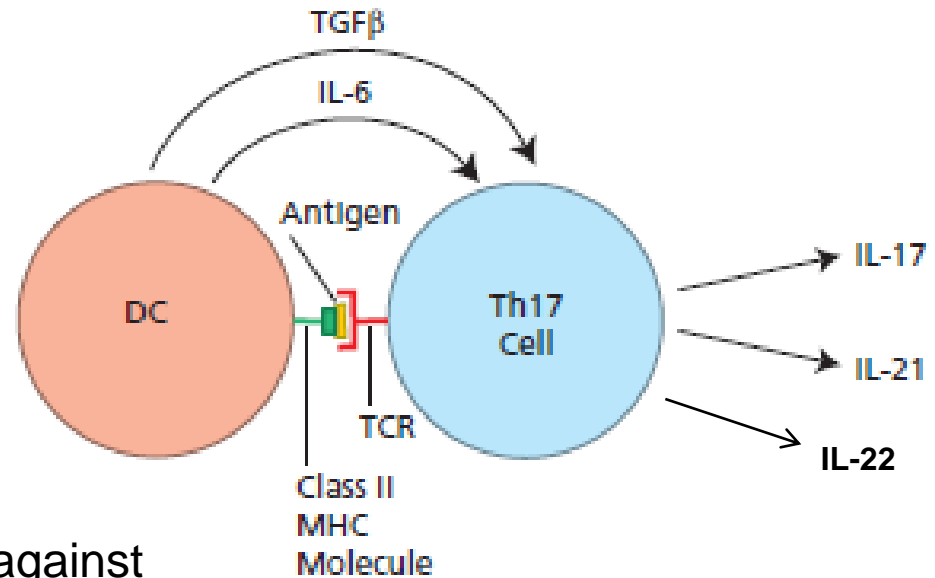
IL-2 stimulates the proliferation of CTLs, NK,
and Th cells themselves.

IL-4 drive an IgE switch and IL-5 an IgA
Switch/eosinophil activation. IL-4/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/ stimulate B cells in germinal centres.

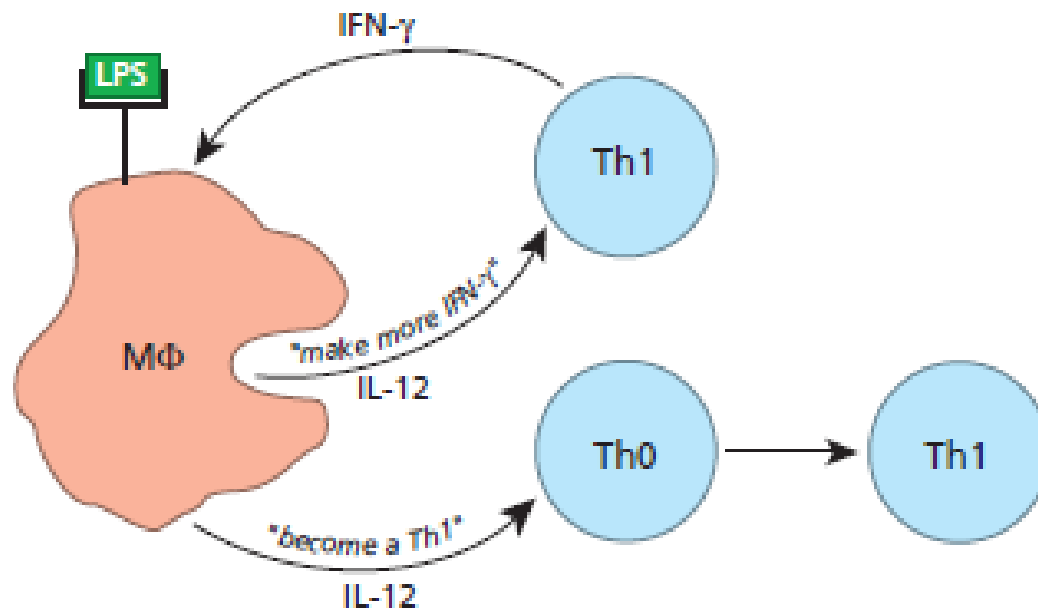
IL-17 recruits massive numbers of Neutrophils to site of infection/ Stimulates production of antimicrobial substances (ex: Defensins)

IL-22 stimulates production of antimicrobial peptides and serves to maintain epithelial Barrier integrity.

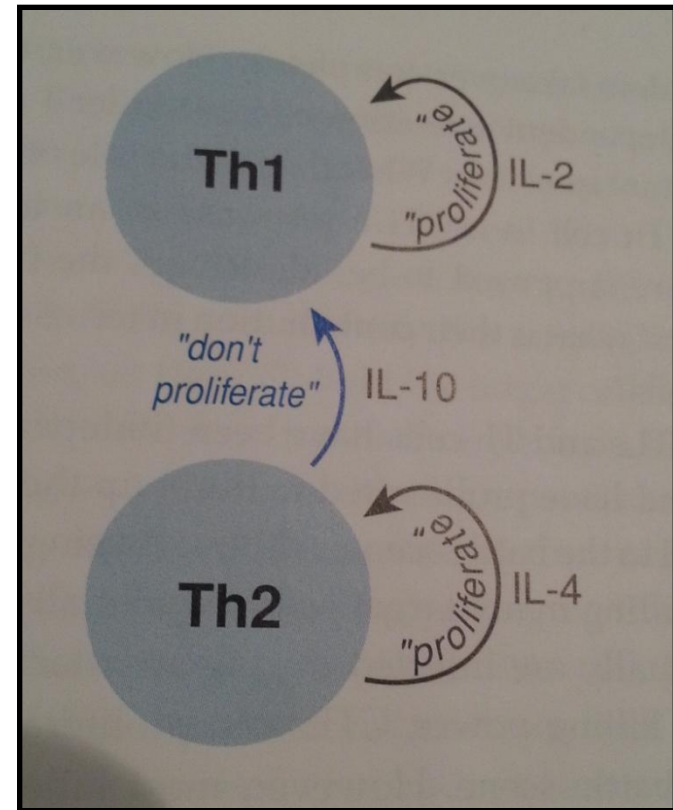
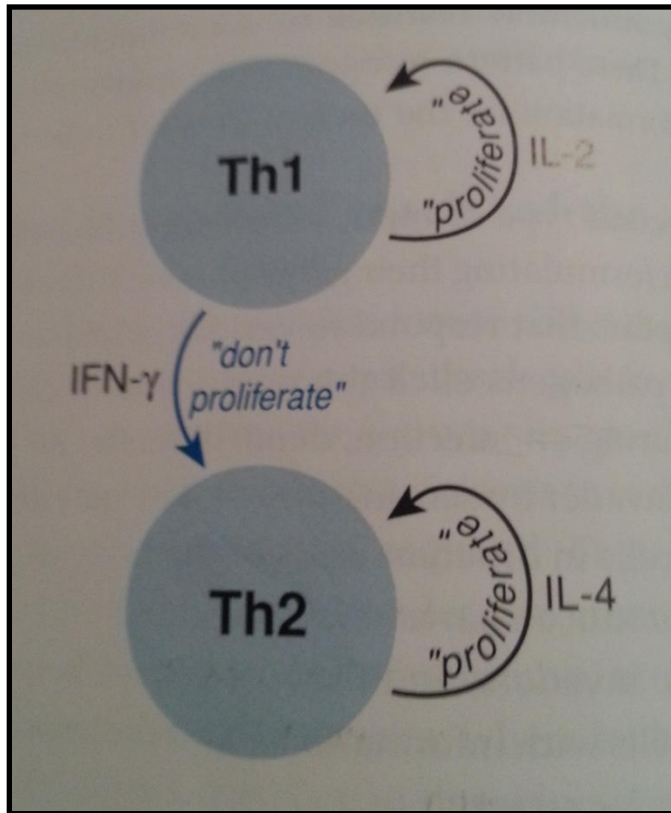
Th0 Cells

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.

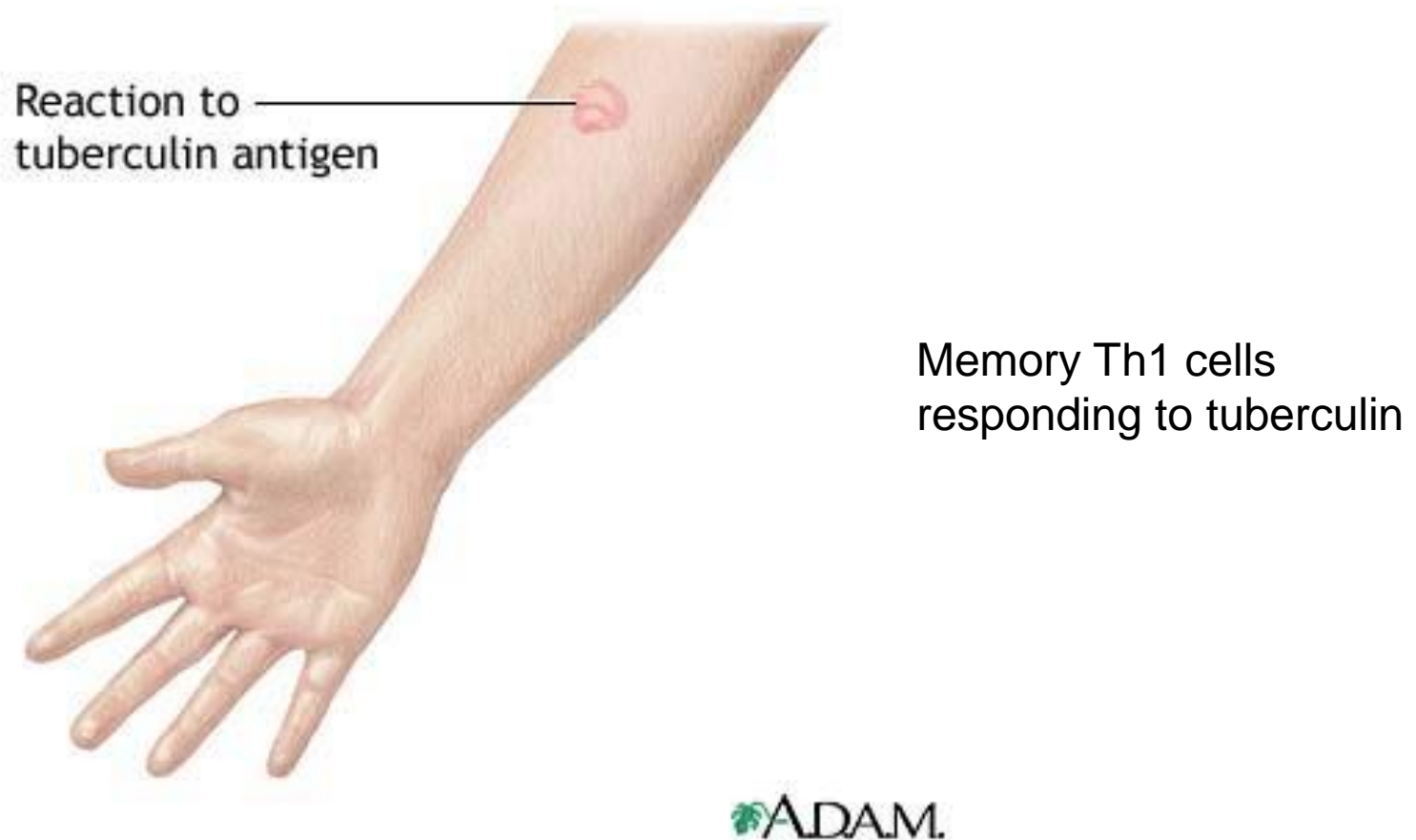


Profile ``lock-in``



Local effect!

Delayed Type Hypersensitivity

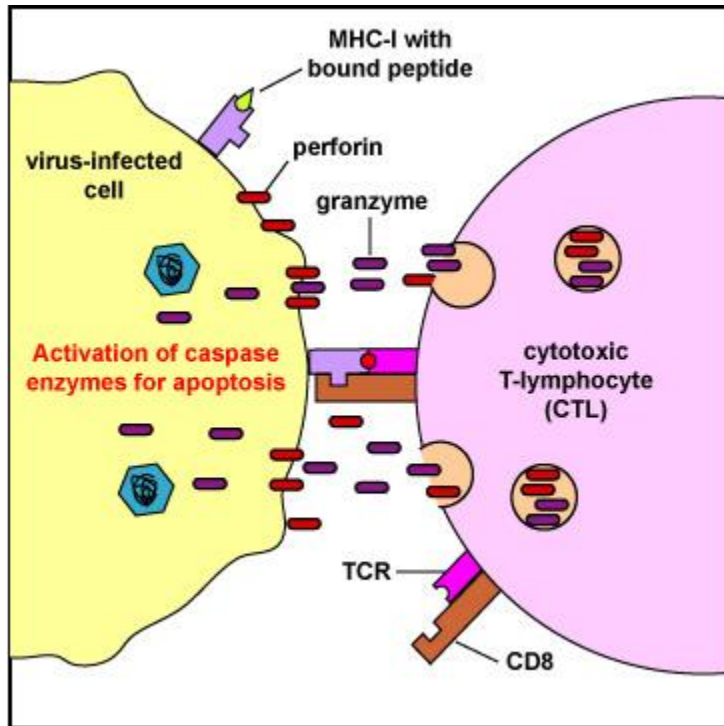


Disadvantages of tuberculin test?

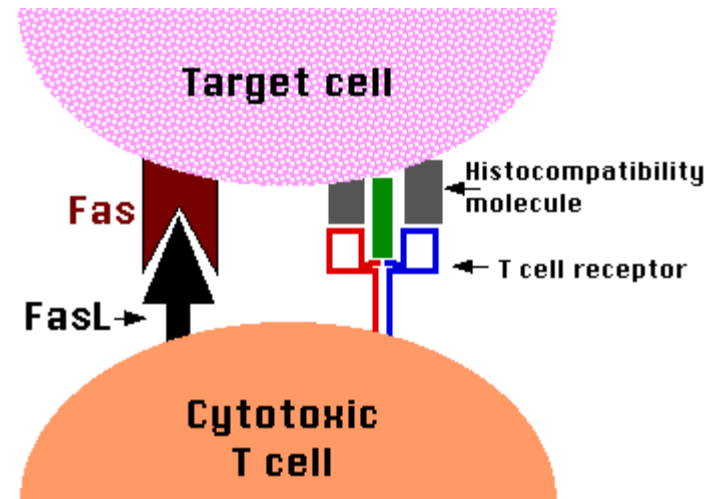
Quantiferon gold test?? Measure IFN- γ secreted by Th cells specific to TB.

How CTLs kill?

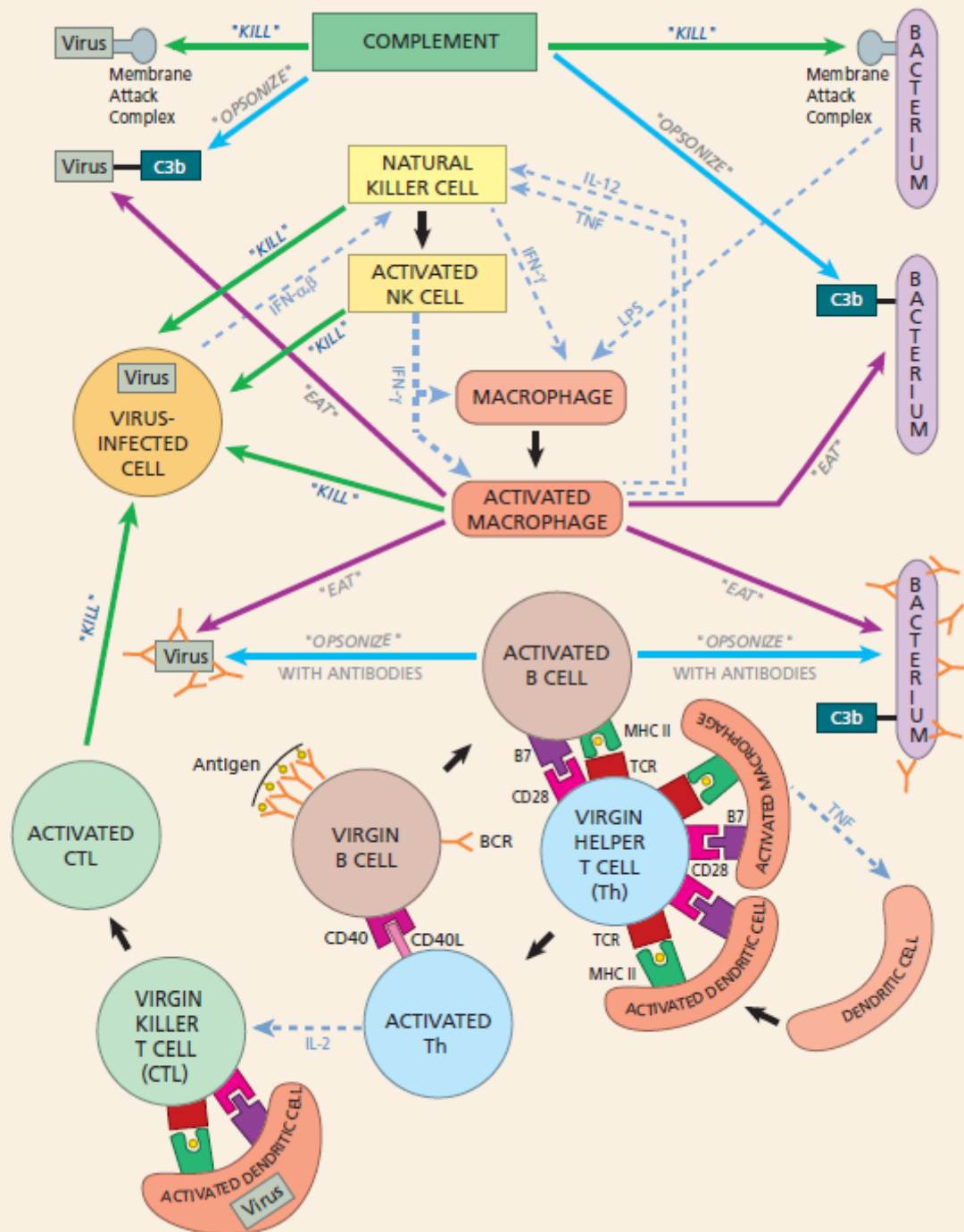
1- Perforin-Granzyme B



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???