Lecture 6: Introduction to MHC and T-cells.

Suggested Reading - Chapter 9

Key terms: MHC I, MHC II, T_H, T_C, b7, CD28

Antigen Presentation:

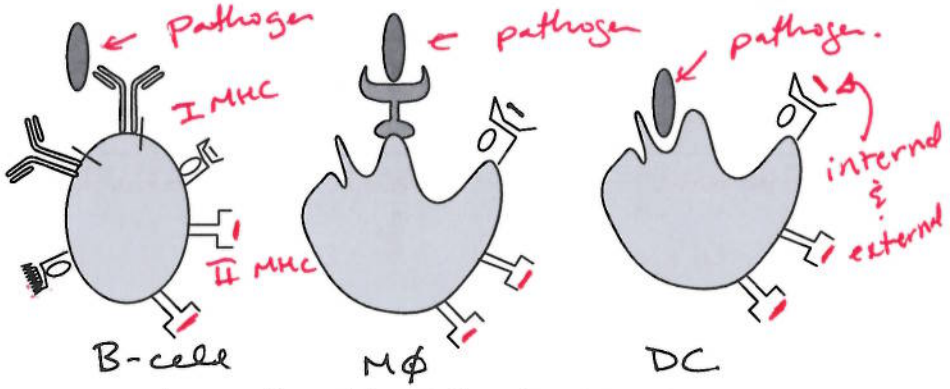
External Antigens:

1. Antigens captured by proAPCs (*professional* antigen presenting cells)

Cell type	Location	Receptor for Endocytosis	Typical infectious agent.
Macrophage	Tissue + Lymph nodes	CR, Fc	extracellular
Dendritic Cell	Tissue → Lymph node	" , phagocytosis	bacteria
B-cell	Lymph node.	BCR	virus

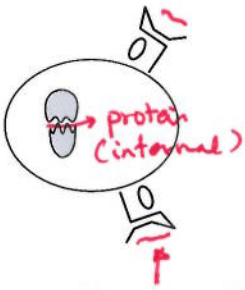
Pro APC

2. Antigen processed by enzymes in primary & secondary granules, lysosome.
3. Peptides from antigen presented on class II MHC (DC can also present on class I, this is cross-presentation)
4. Specific interaction with T-cell receptor (TCR) on T_H-cells.
5. Activation of T_H- cells, followed by response of presenting cell to cytokines from T_H cells.



Internal Antigens (all cells)

1. Presentation of internally synthesized peptides on class I MHC.
2. Activation of T_C cells.
3. Development into T_{CTL} (cytotoxic T lymphocytes)



Sample of all proteins made in the cell

Major Histocompatibility Complex (MHC):

Genetics:

- Multiple genes coding for a large number of homologous proteins.
- All genes expressed.
- Large number of alleles in the population (immunological individuality)

Structure-Function

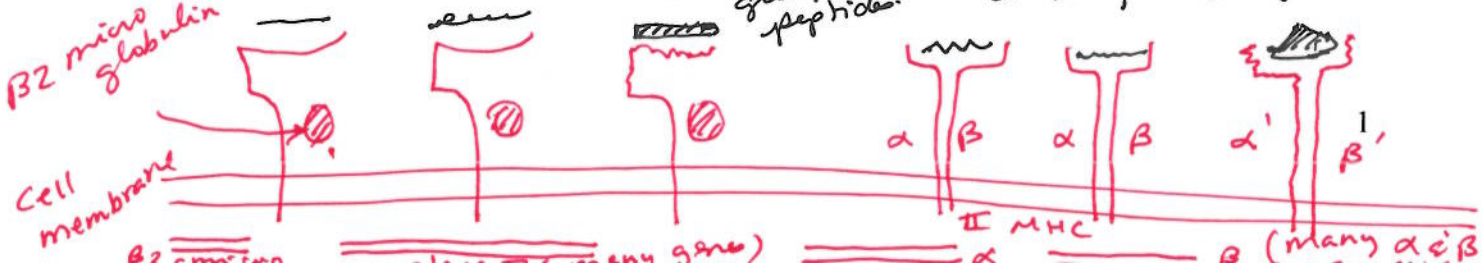
- Bind peptides with *low* specificity, length from 8-9 (MHC I) or longer (MHC II).
- Both foreign and self-peptides are presented **indiscriminately**.
- Only ***foreign*** peptides presented by ***self*-MHC** elicit an immune response (under normal conditions).

	Class I - MHC	Class II - MHC
Found on:	All cells	"Professional" Antigen-presenting cells (macrophage, dendritic, B-cell)
Peptides presented:	Internally synthesized (except for dendritic cells)	Outside of cell, via phagocytosis or receptor mediated endocytosis.
Recognized by:		

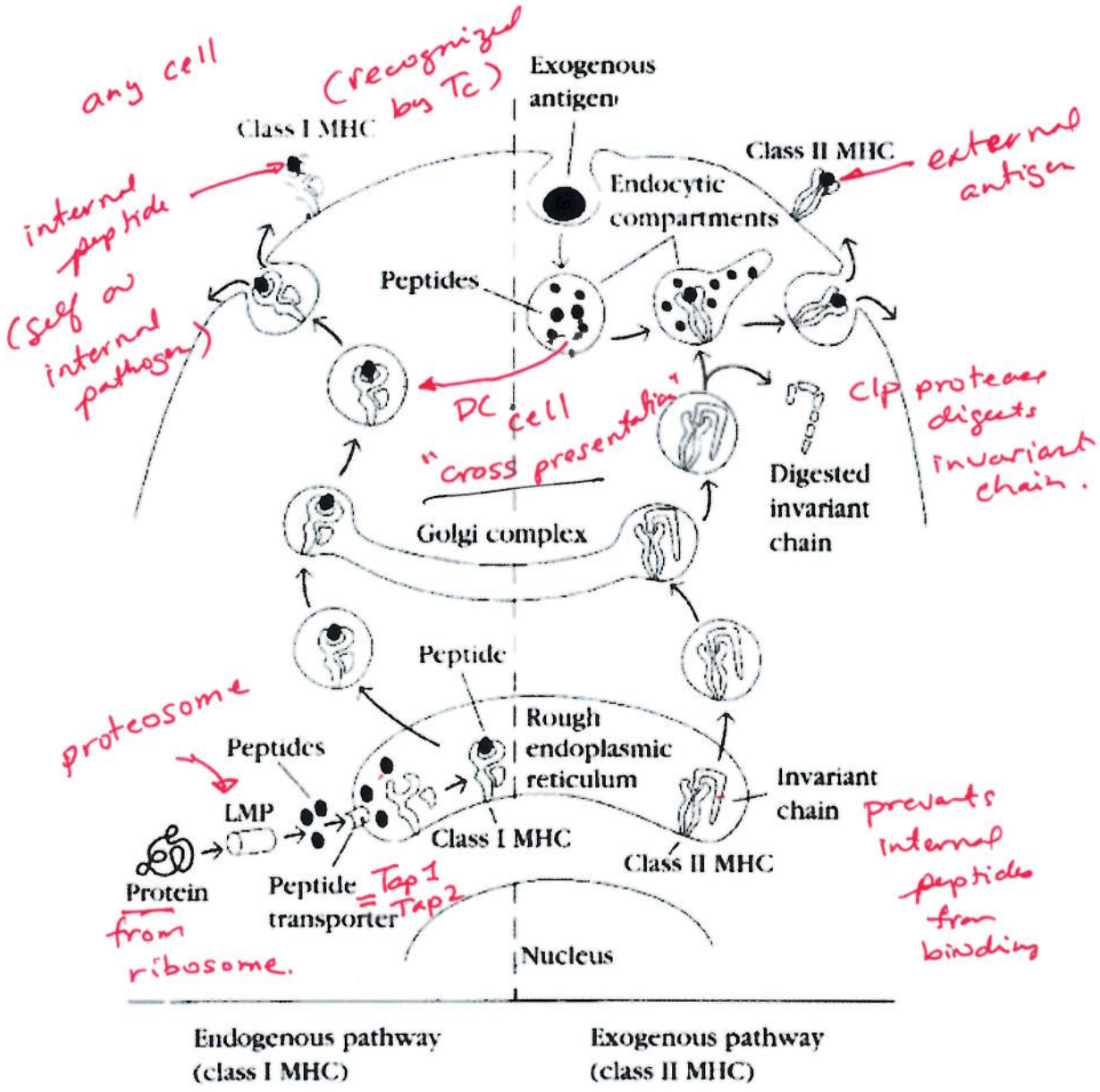
diff peptides presented by same MHC

diff MHC present diff group of peptides.

many alleles for class I & II ∴ each individual has a unique set of MHCs



Antigen Presentation Pathways (Left – all cells. Right – proAPCs)



Important players:

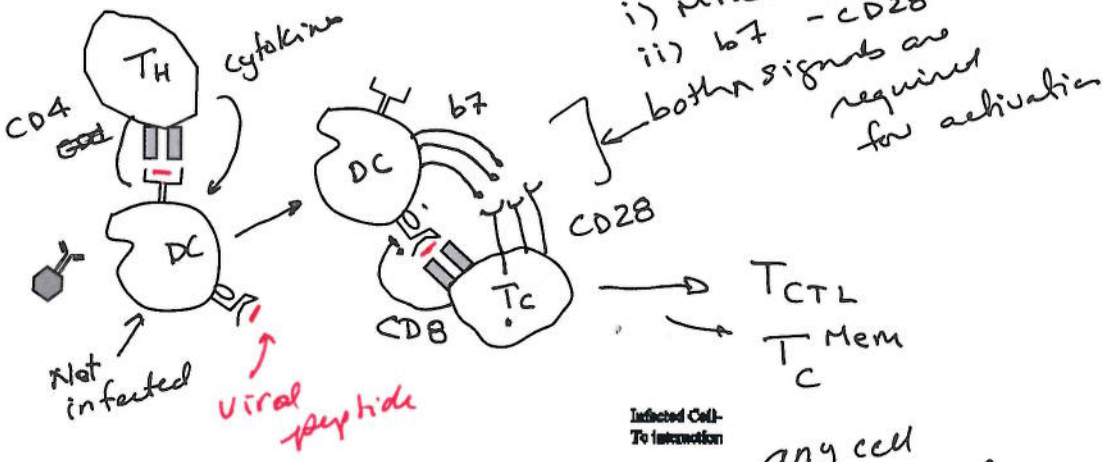
- Ribosome
- Proteasome (LMP)
- Tap1&2 (transporter)
- Invariant chain
- Clp protease

Cross presentation (DC & to a minor extent macrophage): Presentation of antigens acquired from outside the cell on class I MHC.

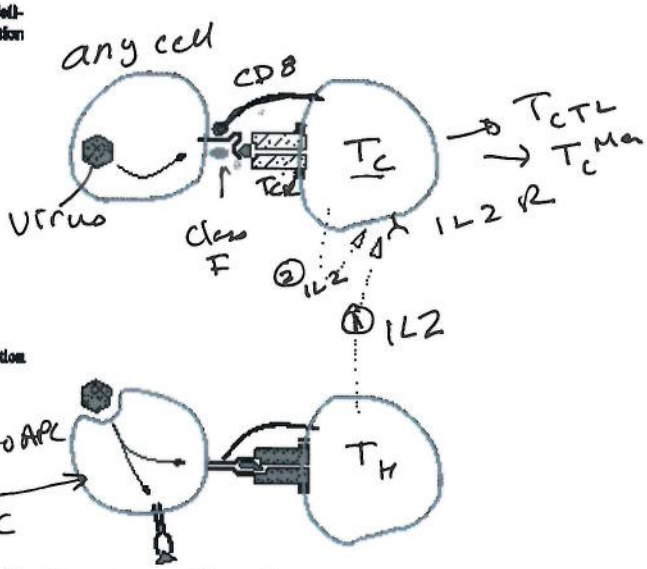
Activation of naïve T_C cells:

i) Directly by activated *DC* cells via class I MHC antigen presentation.

- DC cells become are activated (*licensed*) by T_H stimulation via class II presentation.
- Activated DC cells have high levels of B7 (a constimulatory molecule), which interacts with CD28 on the T-cell.
- Cross-presentation allows DCs to present externally acquired antigens on class I MHC, as if they were generated internally.



ii) By IL2 released by T_H cells that have be activated by **any** *pro*APC (macrophage, B-cell, DC). This allows **any** infected cell to activate T_C cells via MHC I.



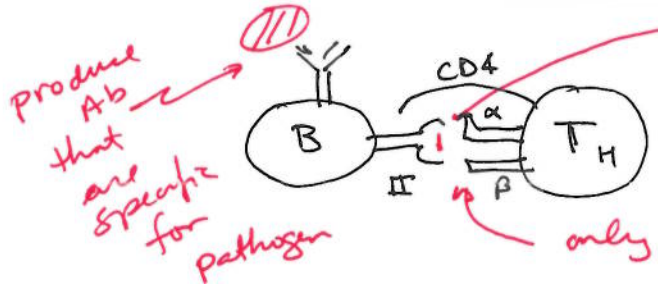
Activation of memory T_c cells – Any cell presenting the appropriate antigen on class I MHC can activate memory T_C cells.

Killing of Infected cells by T_{CTL}:

- Trigger – activation by foreign antigen on class I MHC.
- Mechanism - identical to NK cells. Perforin & granzymes, FasL

Summary: MHC, BCR, TCR.

	MHC	B-cell Receptor	T-cell Receptor
Diversity on a single cell:	High	Zero - homogeneous	Zero - homogeneous
Diversity in an individual:	Zero (all cells are the same with an individual)	10^8 different B-cells	10^{12} different T-cells
Diversity in population:	Very high (many alleles)	Very low	Very low
Specificity for ligand.	Low	Very high	Very high



Draw a B-cell being activated by a T-cell. Your diagram should show the relevant cell-surface molecules on each cell type.