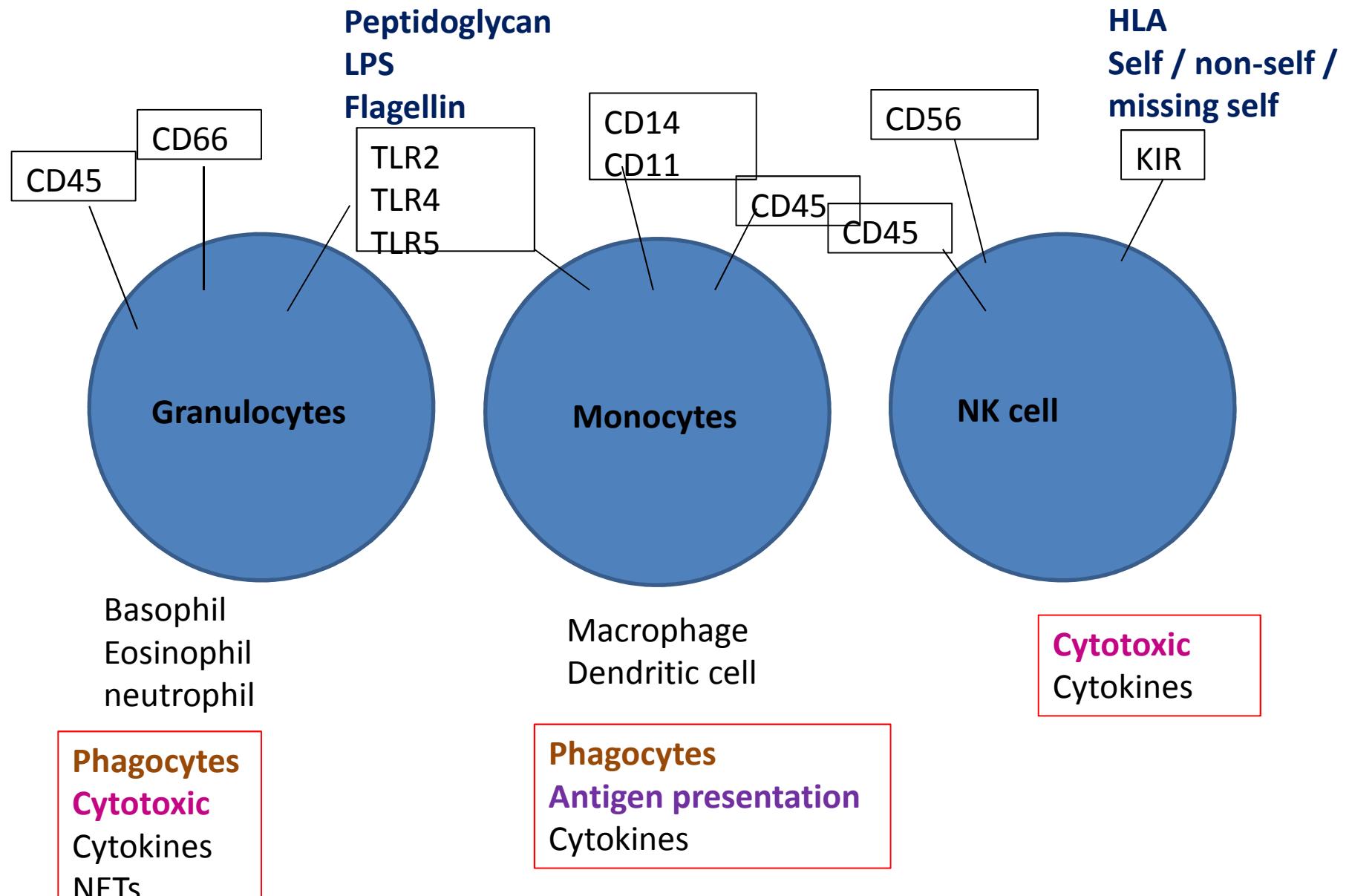


Summary of innate cells, their surface markers and surface receptors, ligands and function



Adaptive immunity

Today's learning objectives

- Adaptive immunity

Adaptive cell types and their surface markers

TCR and BCR, structures, similarities

Antigen and epitope

HLA class I and II

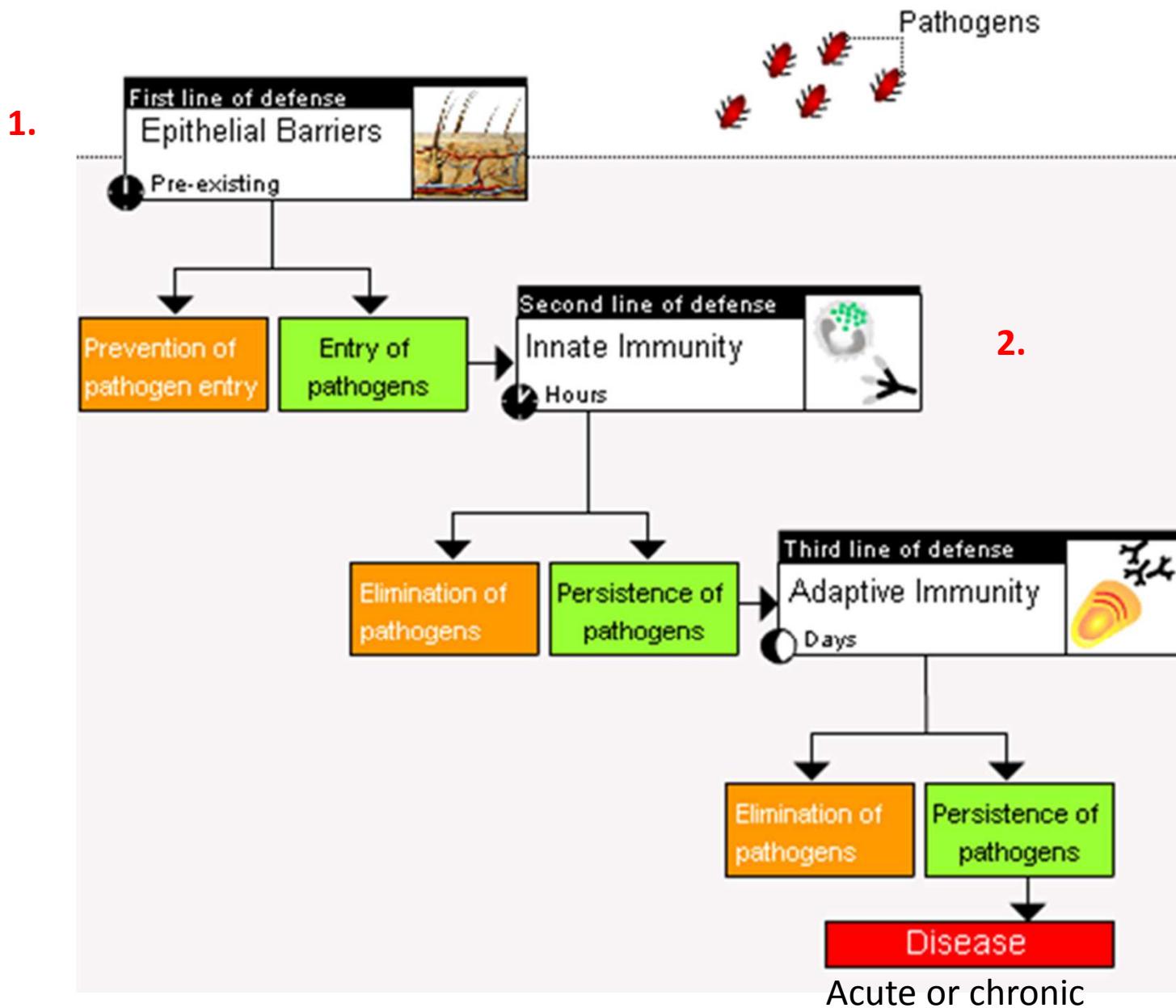
Functions of activated CD8+ T cells

Memory

Adaptive immunology

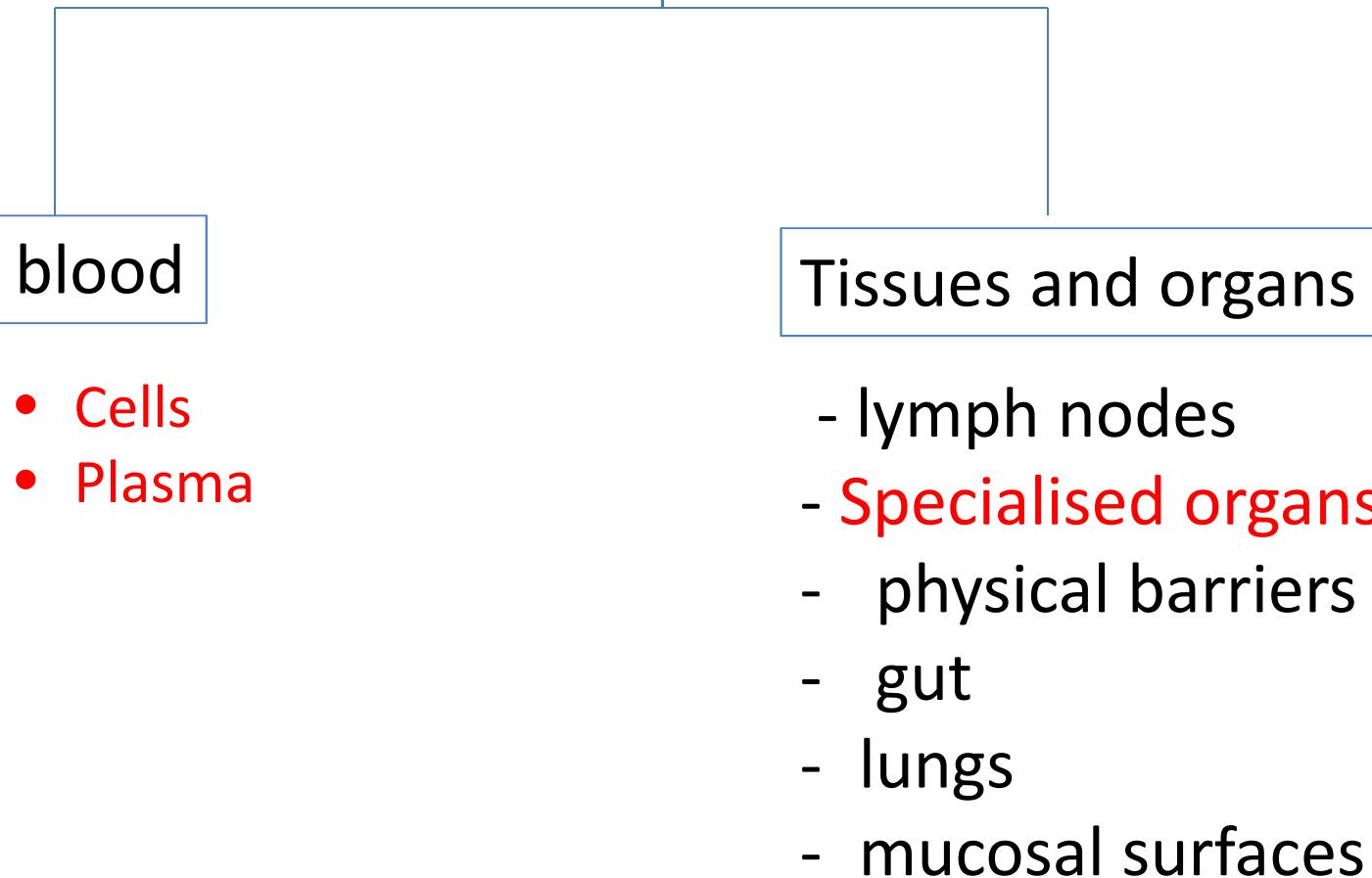
- B cells and T cells
- TCR , BCR and antibodies
- Antigens and epitopes
- HLA class I and II
- Antigen presentation to cells, T cell immune synapses
- Naïve vs activated cells
- General T and B cell responses to activation :
 - Clonal proliferation
 - Differentiation
 - memory
- CD8+ T cell activation and effector response

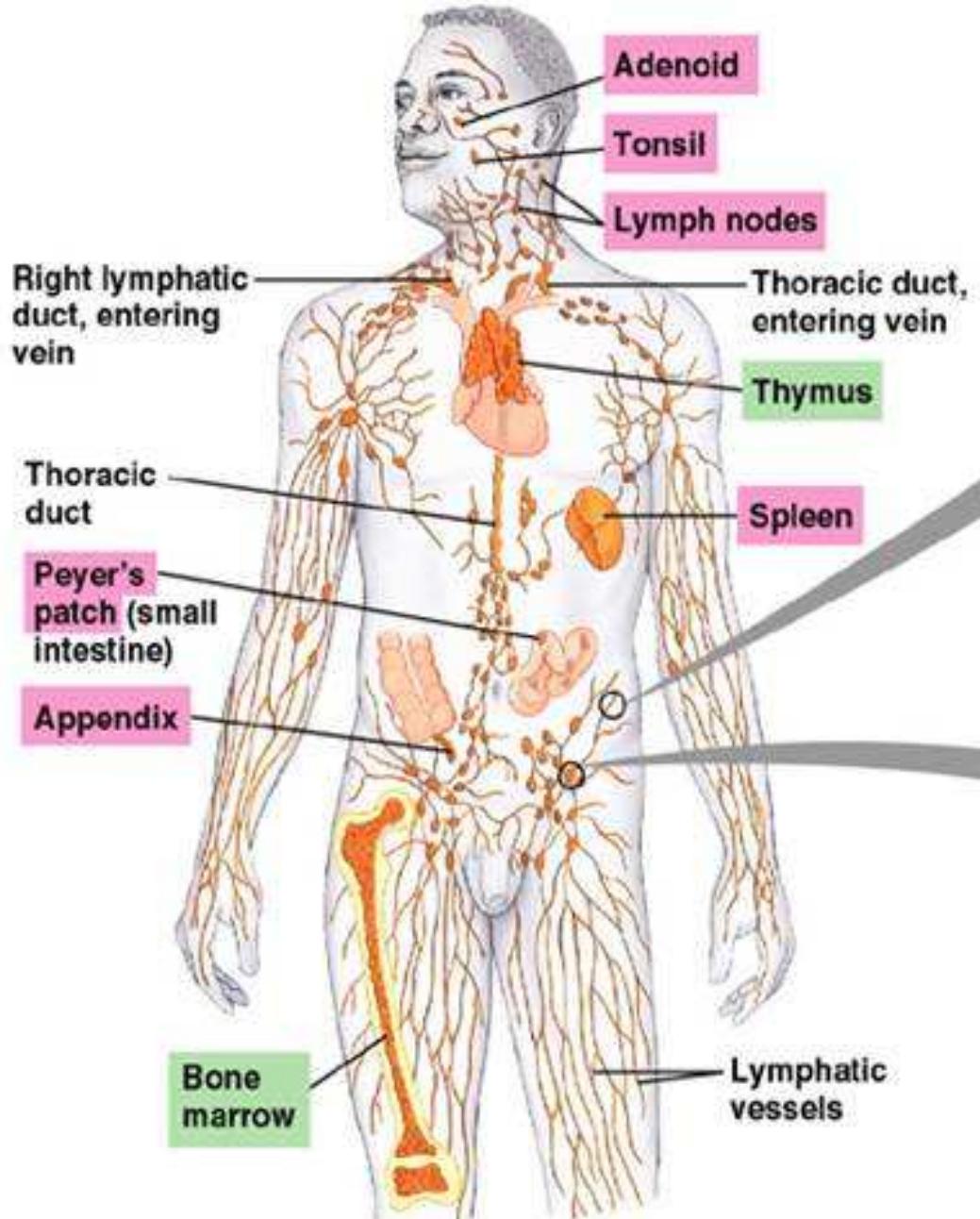
» Three lines of defense



	ADAPTIVE
What it recognises	Very specific - recognises particular pieces of particular pathogens
Receptors	Very large variety
How fast it reacts	Takes some time to develop (days) (unless memory response)
Memory?	yes - increased response on next exposure
In which species it is found	Only jawed vertebrates
components	<u>Cells:</u> B and T cells <u>Humoral:</u> antibodies

Which parts of the body house the adaptive immune system?





(a)

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Specialised Lymphoid tissues and organs all over the body

MALT= mucosa-associated lymphoid tissue (under mucosal surfaces)

BALT = Bronchus-associated lymphoid tissue (lungs)

GALT = gut -associated lymphoid tissue (digestive tract)

Spleen: where adaptive immune responses are initiated i.e. where innate and adaptive cells meet

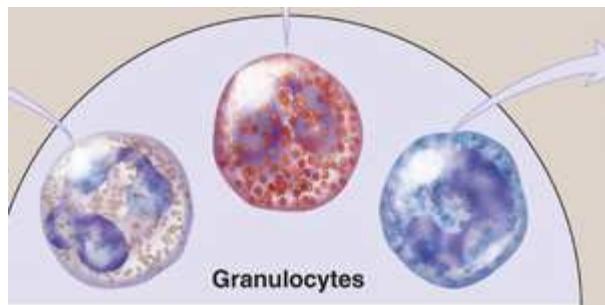
Bone marrow: where B and T cells are produced and where B cells mature

Thymus: where T cells mature

Leukocytes (white blood cells)

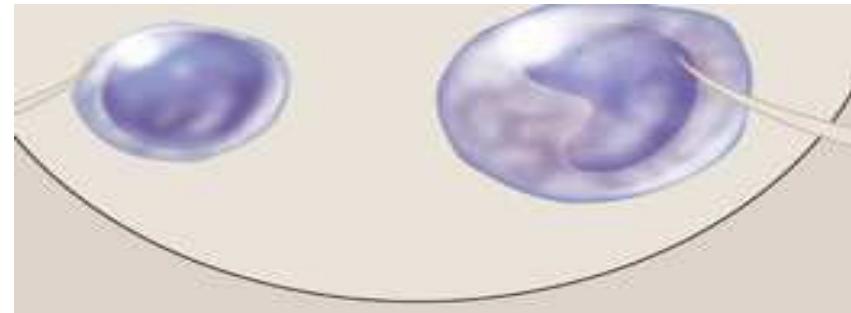
INNATE
ADAPTIVE

Granulocytes



- Neutrophils
- basophils
- eosinophils

lymphocytes



- T cells
- B cells
- NK cells

monocytes

- Monocytes
- (develop into macrophages and dendritic cells in tissue)

Adaptive immune system - part 1: cells

Cells of the adaptive immune system include

1. T cells (develop in the Thymus); subtypes include:
 - CD4+ T cells or T helper cells
 - CD8+ T cells or cytotoxic T cells
 - Regulatory T cells
 - Memory T cells

2. B cells (develop in Bone marrow); subtypes include:
 - Plasma cells
 - Memory B cells

Adaptive immune system - part 1: cells

Recognising T and B cells

Cell type	Surface marker
T cells	CD3+, T cell receptor (TCR)
T helper cells	CD4+
Cytotoxic T cells	CD8+
Regulatory T cells	CD4+, CD25+
B cells	CD19+ CD20+ , B cell receptor (BCR)
Activated T and B cells	CD38+

Adaptive immunity:

Humoral immunity vs.

cell-based immunity

- Immune response which involves antibodies
- Mediated by B cells
- Against extracellular pathogens
- Immune response which does NOT involve antibodies; uses cytokines, cytotoxicity and T cells / macrophages
- Mediated by T cells
- Against intracellular pathogens

Adaptive immunity:

Primary immune response vs secondary immune response

- Adaptive response the first time the body encounters a pathogen
- No existing memory B or T cells
- Up to 2 weeks to respond (slow)
- Adaptive response the second or next time the body encounters the same pathogen
- A memory response
- Uses memory B or T cells
- Responds within days (fast) and bigger / stronger response

2 approaches to pathogen recognition

INNATE

Look for a pattern

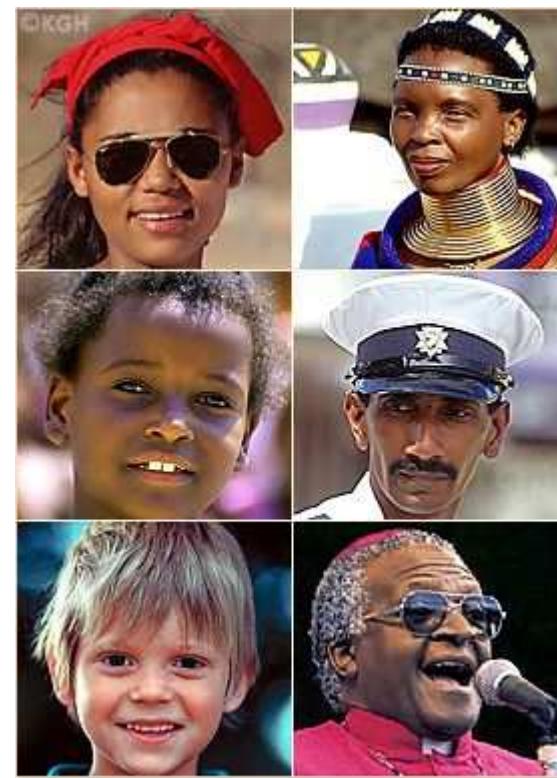
Use pattern recognition receptors (PRR)



ADAPTIVE

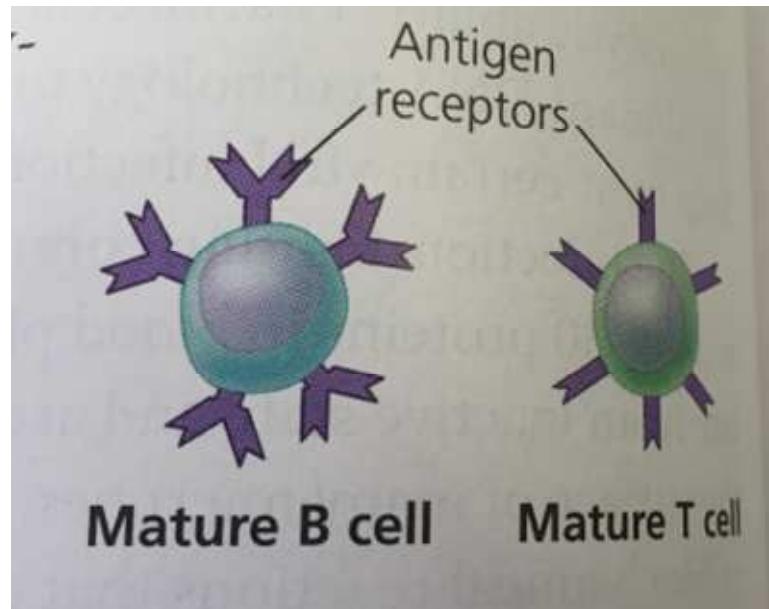
Look for particular details

HOW?
What receptors?



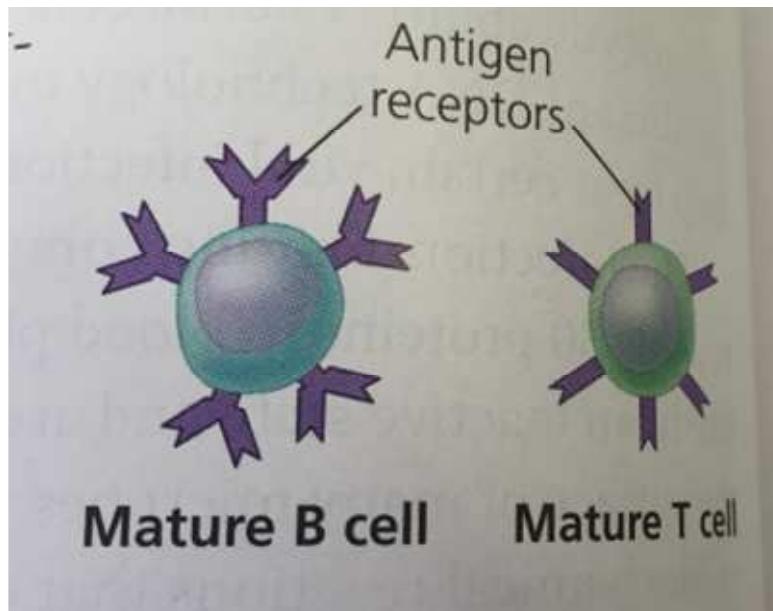
How does the adaptive immune system recognise specific pathogens?

- Special receptors on the surface of the T and B cells
- Called the **T cell receptor (TCR)** and the **B cell receptor (BCR)**



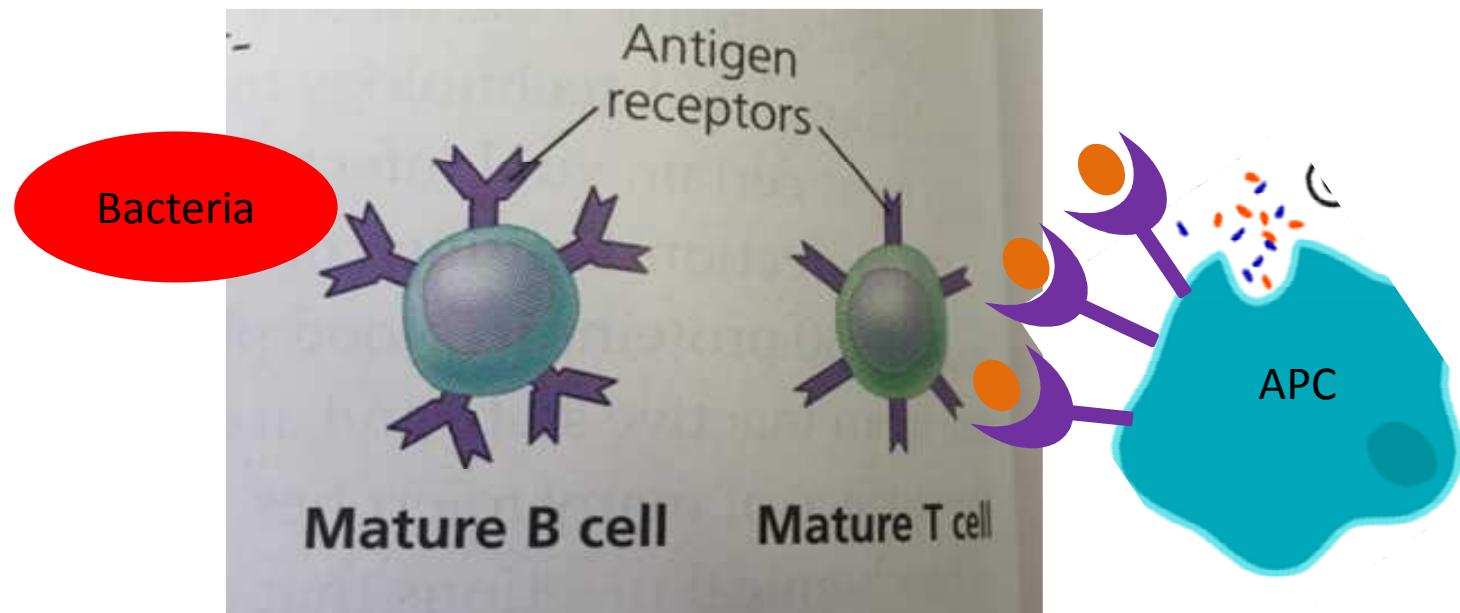
How does the adaptive immune system recognise specific pathogens?

- T cell receptor (TCR) and the B cell receptor (BCR)
- Your body has billions of different types of TCRs and BCRs (i.e. billion types of T and B cells), so can recognise many different bits of pathogens
- **All the antigen receptors on a single B or T cell are identical**
- each B or T cell has a different specificity



How does the adaptive immune system recognise specific pathogens?

- T cell receptor (TCR) and the B cell receptor (BCR)
- B cells and BCR can recognise free pathogen
- T cells and TCR can only recognise bits of pathogen displayed by HLA on antigen presenting cells



B cell receptors

- Y shaped molecule attached to B cell membrane
- Two chains: heavy (blue) and light (red)
- Chains joined by a disulfide bridge
- Each chain has a constant region and a variable region
- together the H and L variable regions form an antigen-binding site

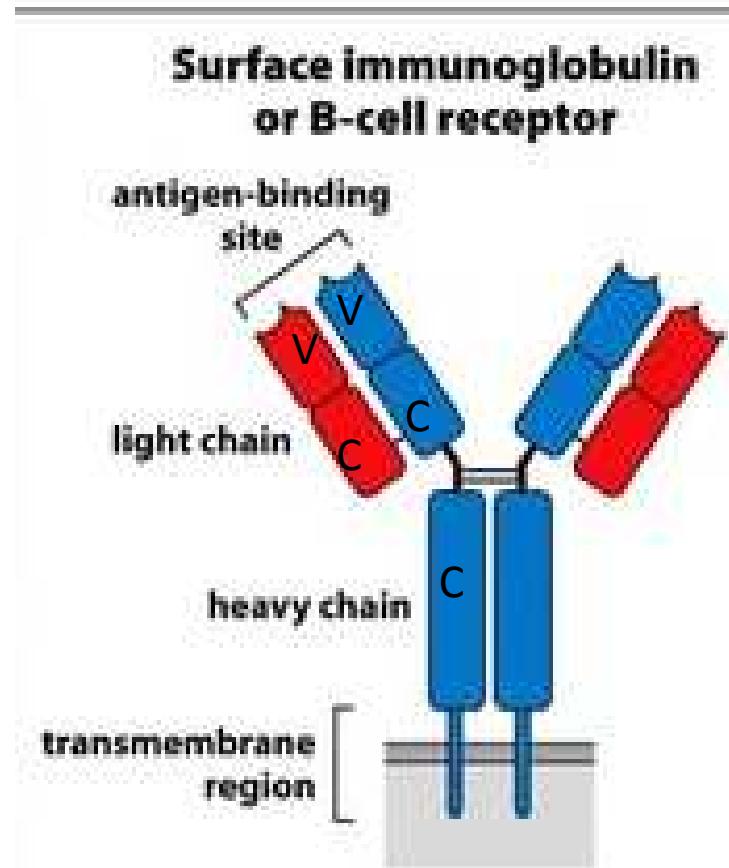
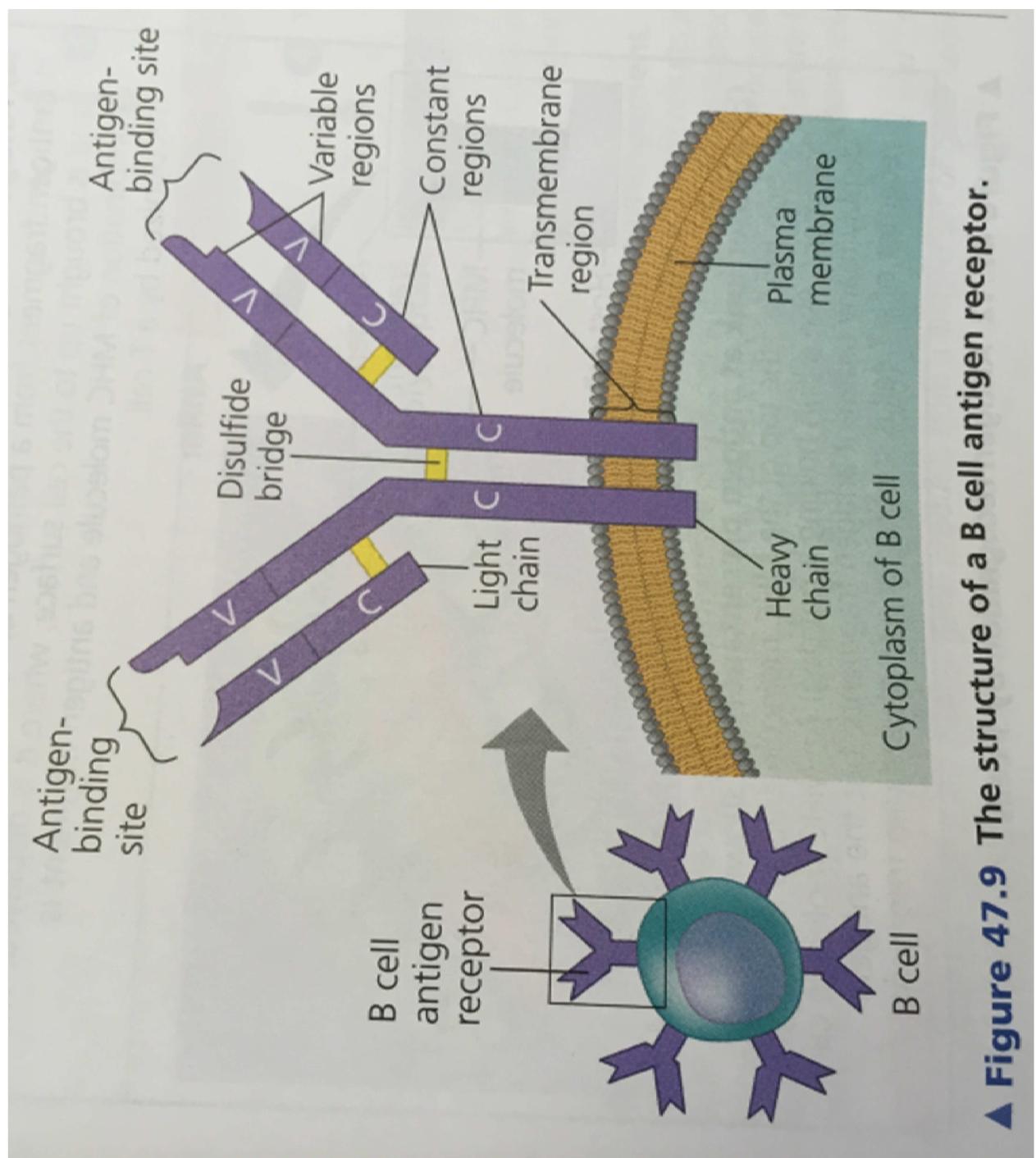


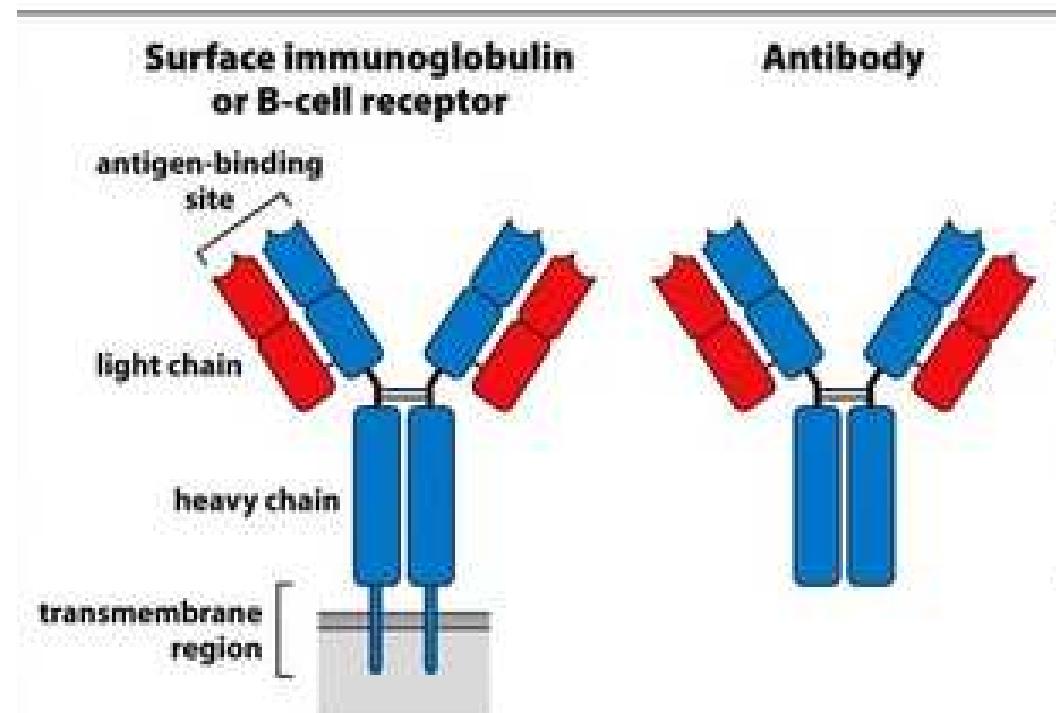
Figure 3.1 The Immune System, 3rd. (© Garland Science 2008)



▲ **Figure 47.9** The structure of a B cell antigen receptor.

B cell receptors

- BCR are nearly exactly the same thing as **antibodies (immunoglobulins)**
- BCR are attached to B cell membranes whereas antibodies are secreted into the plasma
- binding of a pathogen to a specific BCR causes the B cell to start secreting that same antibody
- Antibodies have the same antigen specificity as the B cell that produced them



T cell receptors

- attached to T cell membrane
- Two chains: alpha and beta
- chains joined by a disulfide bridge
- Each chain has a constant region and a variable region
- together the two variable regions form an antigen-binding site

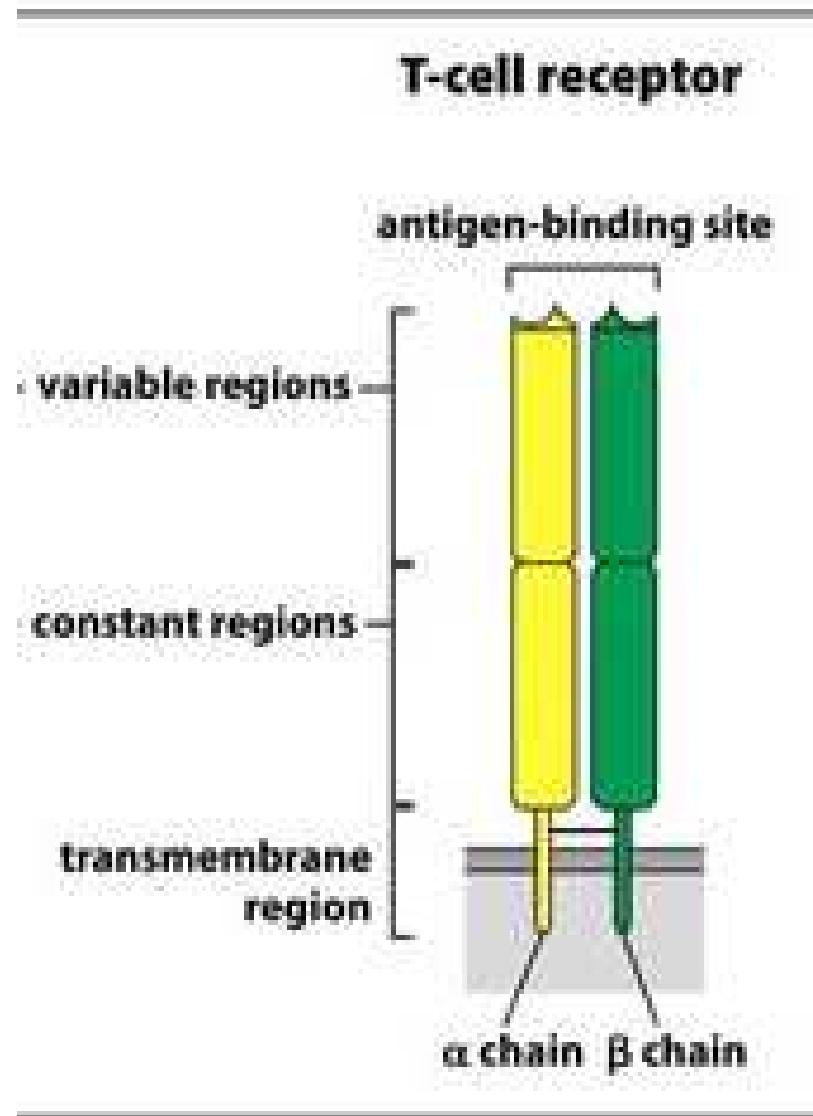
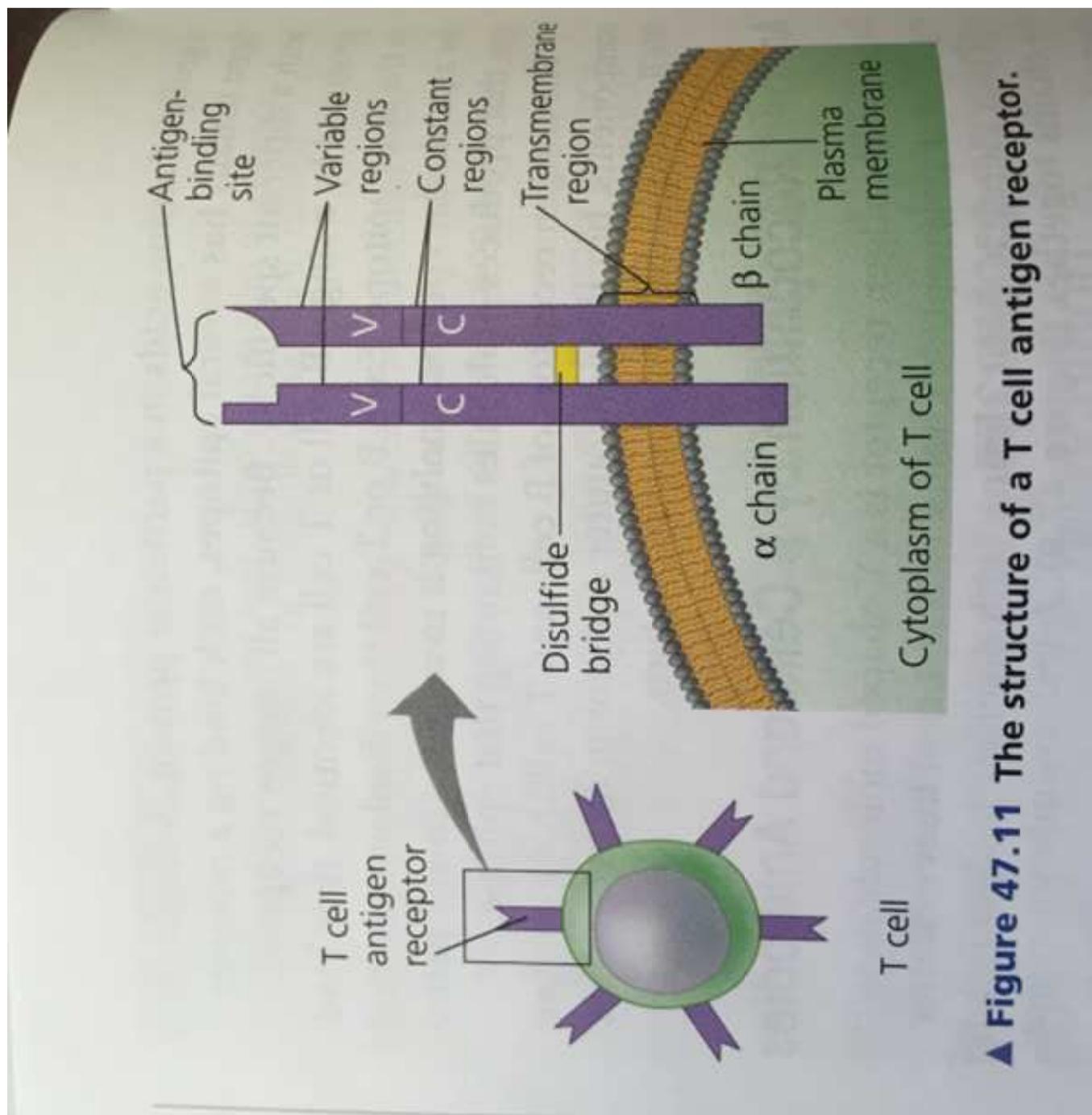


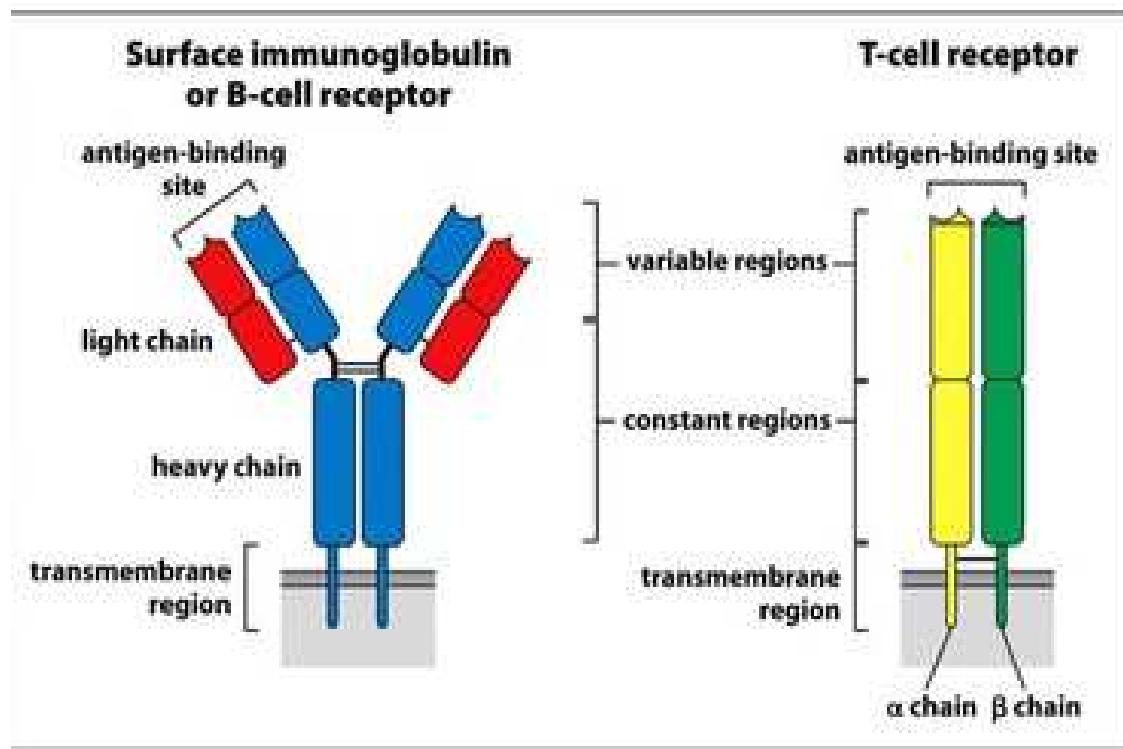
Fig 47.11



▲ Figure 47.11 The structure of a T cell antigen receptor.

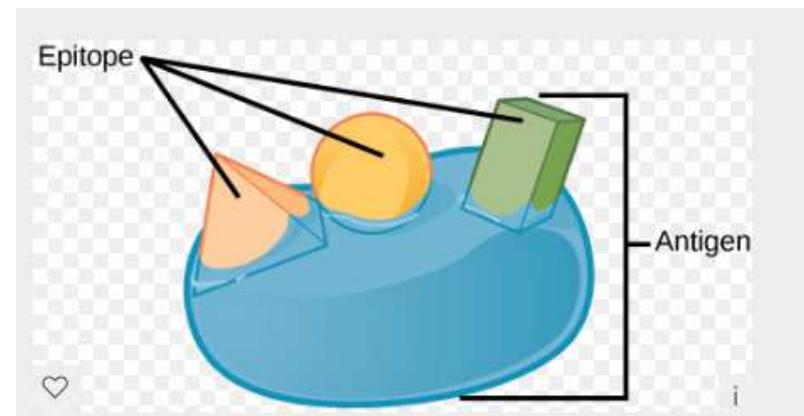
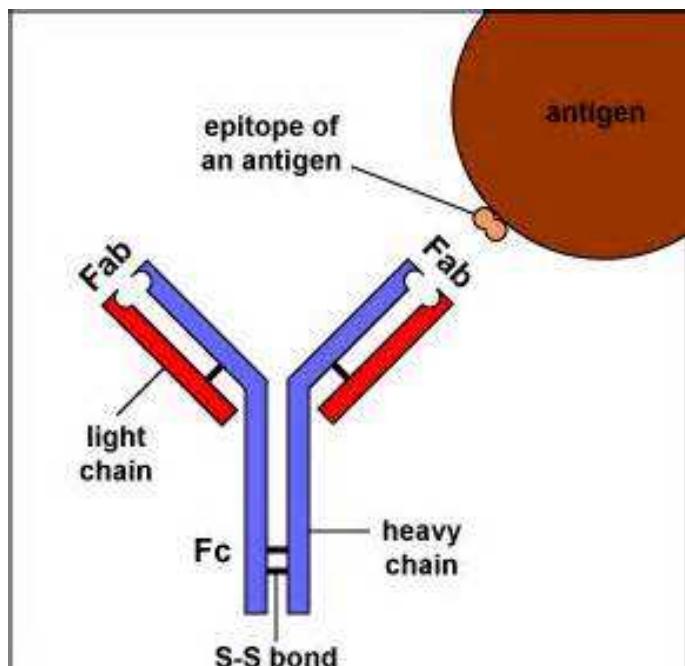
TCR vs BCR

- Both BCR and TCR are dimers
 - TCR has α and β chains
 - BCR has 2 chains, each divided into heavy and light sections
- each chain has variable and constant regions
- The combined variable region (at free end of chains) is where the bit of pathogen (antigen) binds



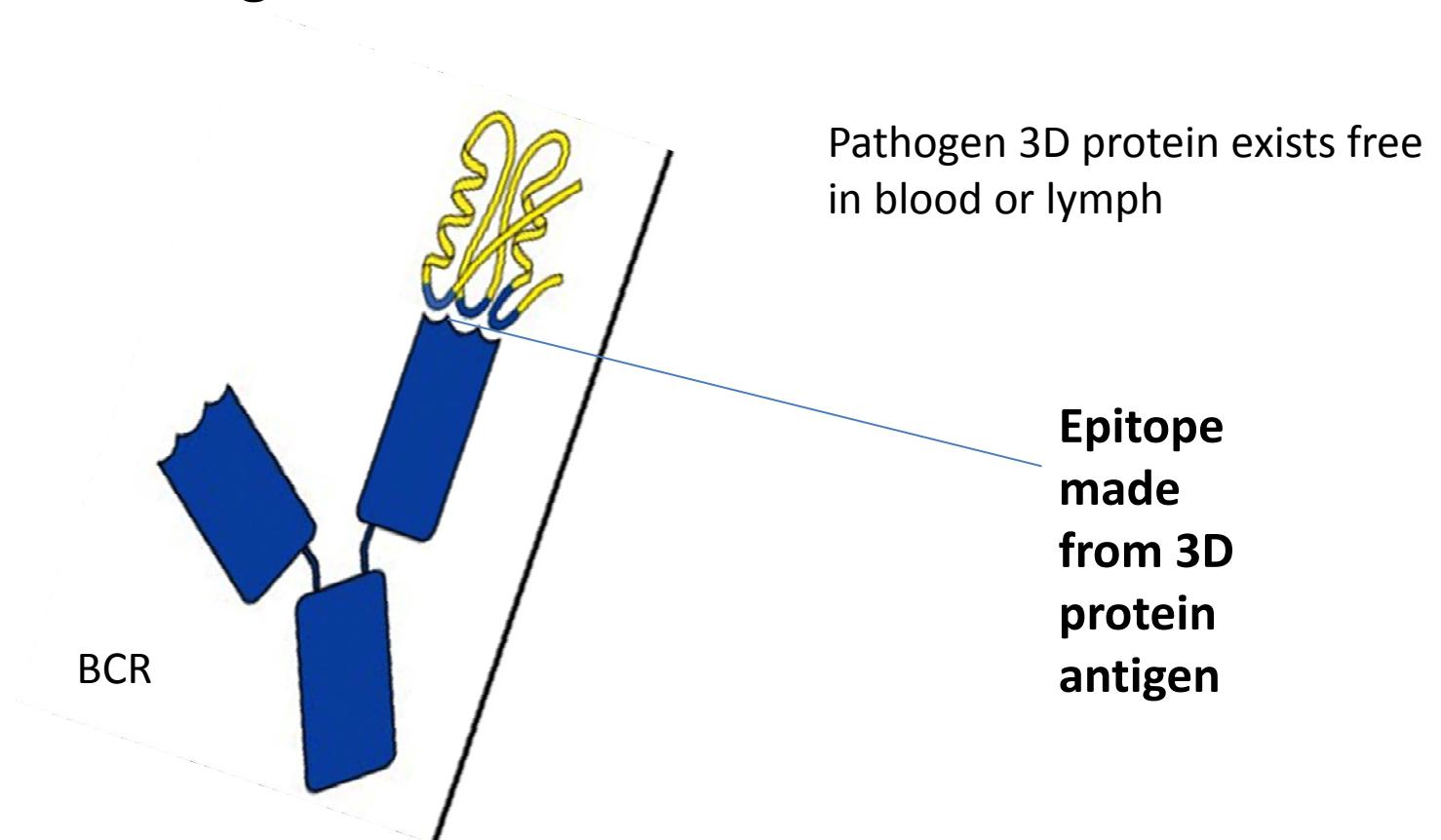
Antigens

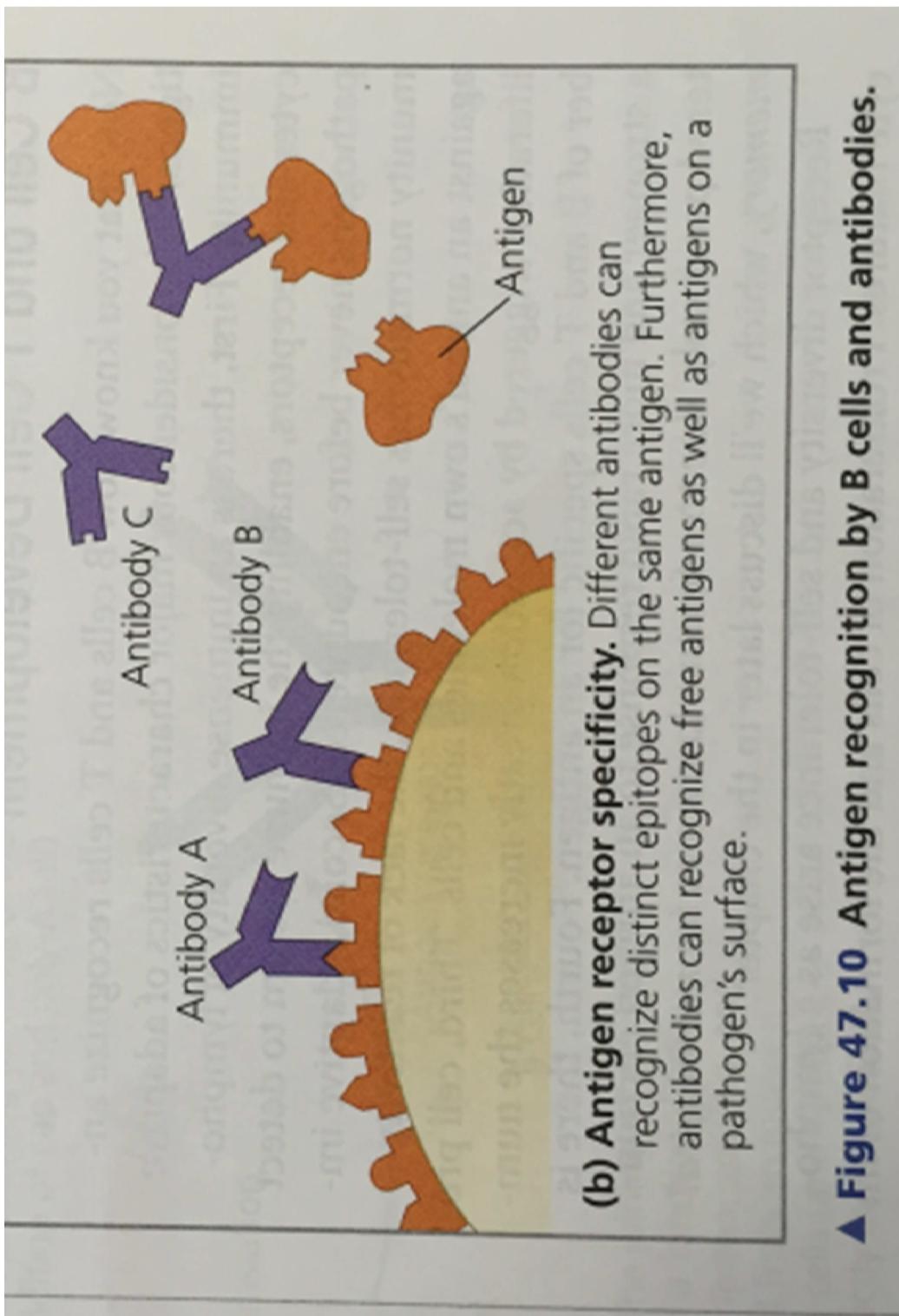
- Small pieces of pathogens called **antigens** : these are what will induce an immune response
- Antigens are usually small pieces of **protein or polysaccharide** from the pathogen
- The even smaller part of the antigen that actually binds to the receptor is called the **epitope** (an antigen fragment)
- One antigen can have several epitopes
- Each **receptor is very specific** and **recognises a specific epitope**



Antigens and BCR

- B cell receptors bind antigens that are bits of **protein folded into their native 3D configuration**

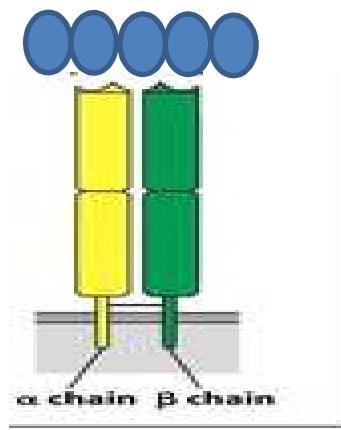




▲ **Figure 47.10** Antigen recognition by B cells and antibodies.

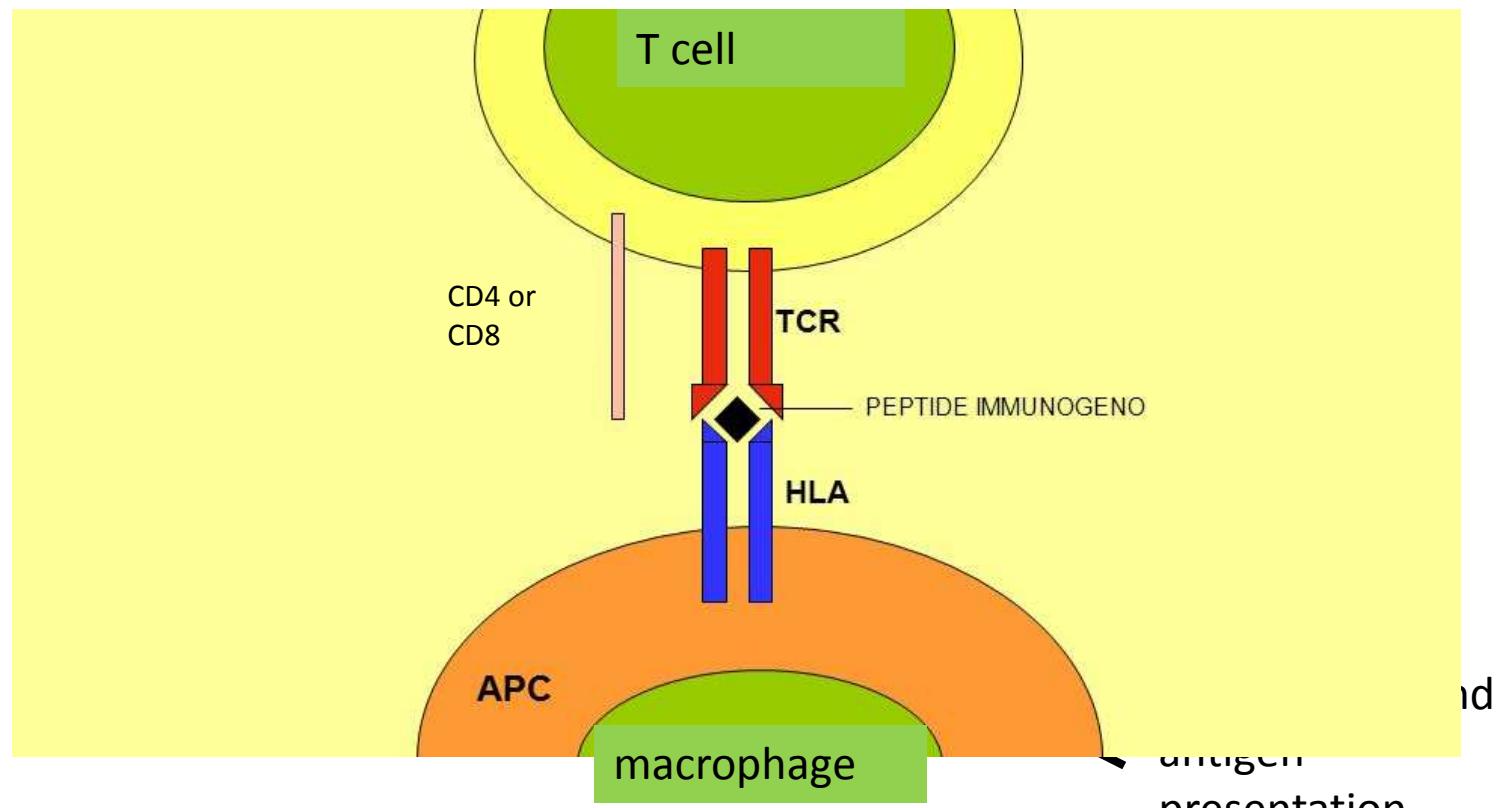
Antigens and TCR

- T cell receptors bind antigens that are **linear peptides (chain of amino acids)**

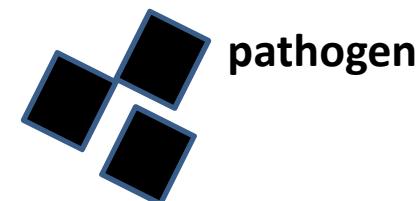


- However there are no free linear pathogen peptides floating around for TCR to bind
- pathogen linear peptides come from phagocytosis and antigen presentation
- Pathogen peptides are always presented by MHC molecules on the surface of innate antigen presenting cells

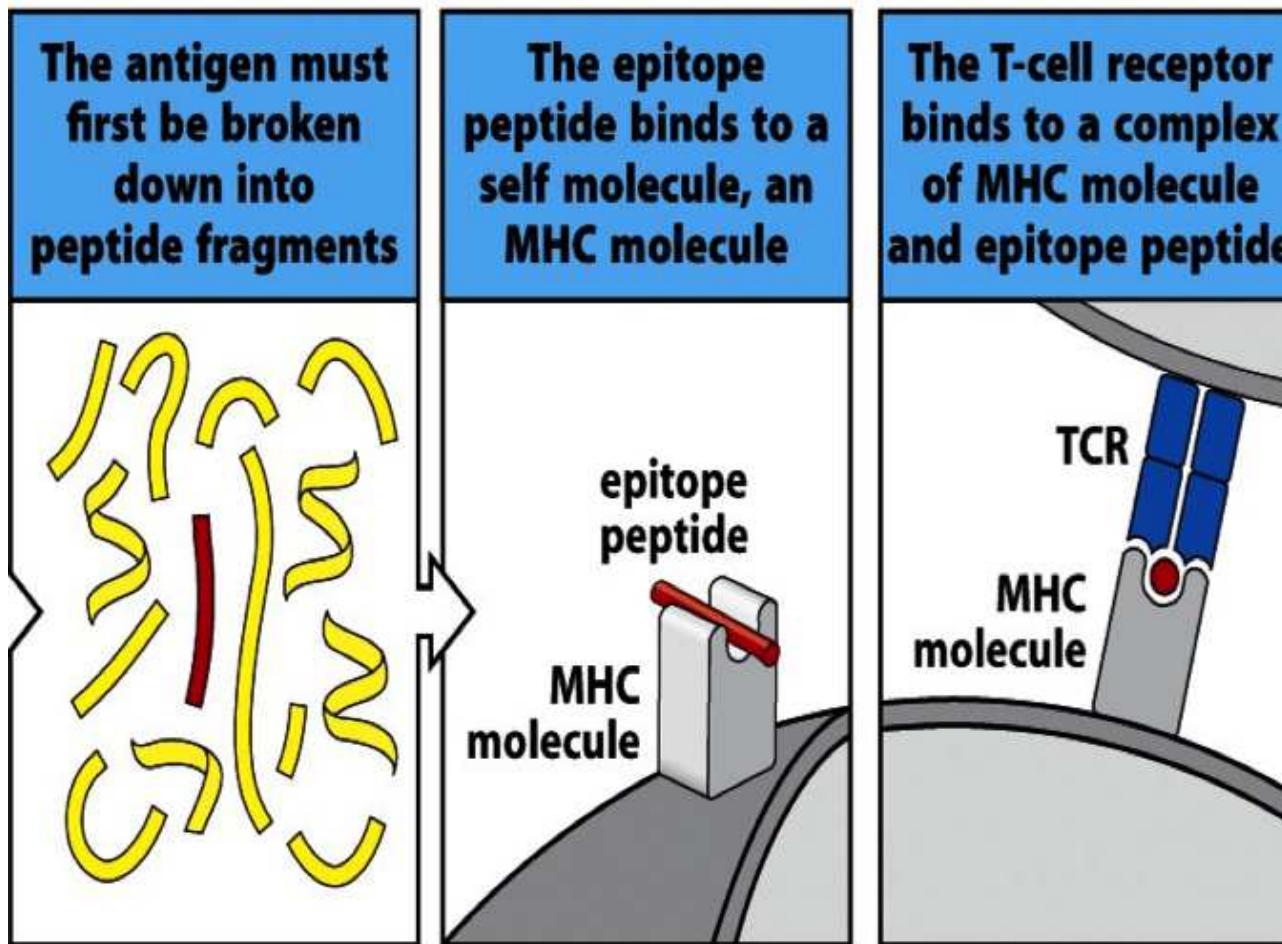
antigens are presented to TCR on T cell, via MHC (HLA) on innate antigen presenting cells

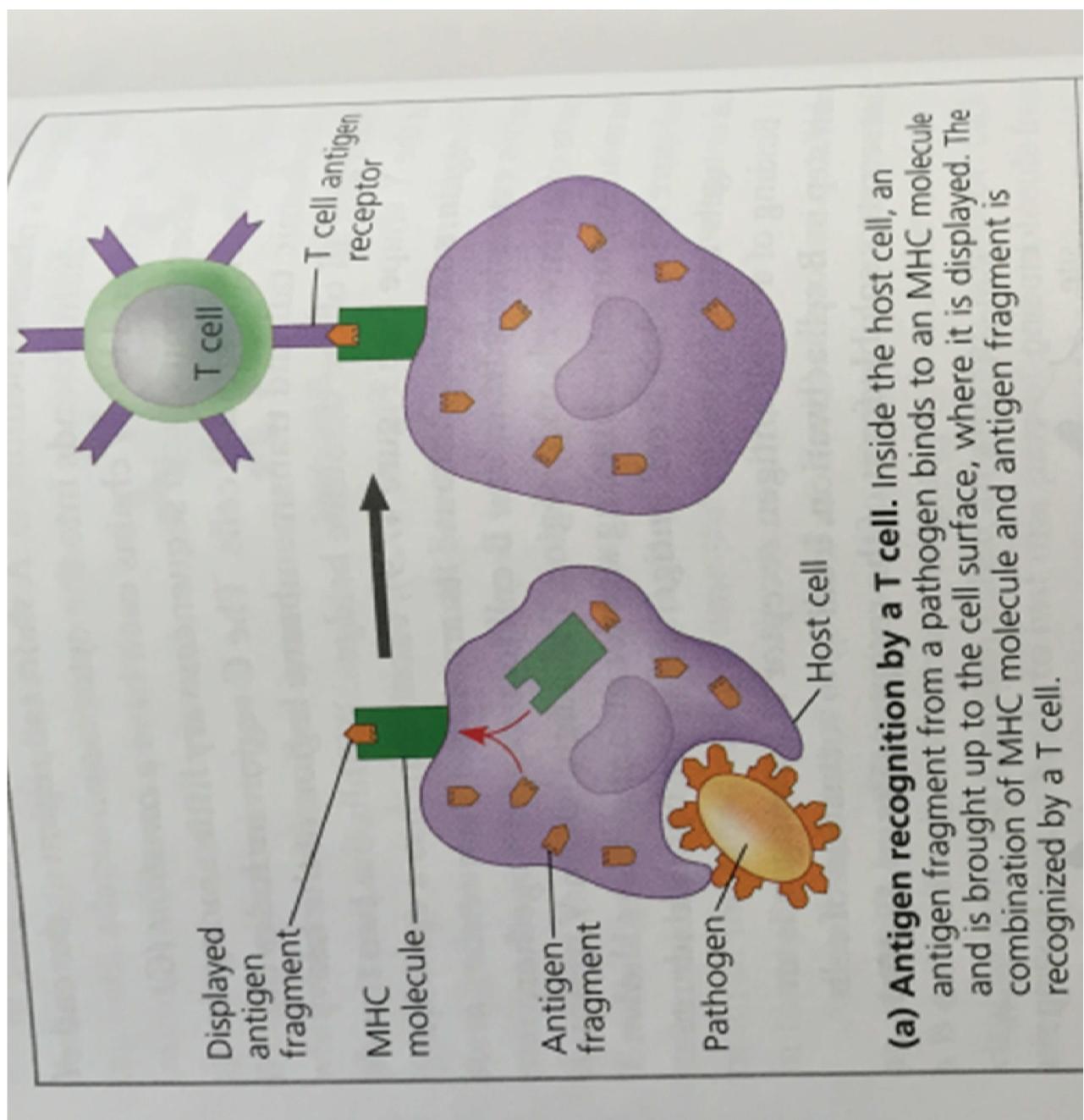


(an immune synapse
With 2 cell types interacting)

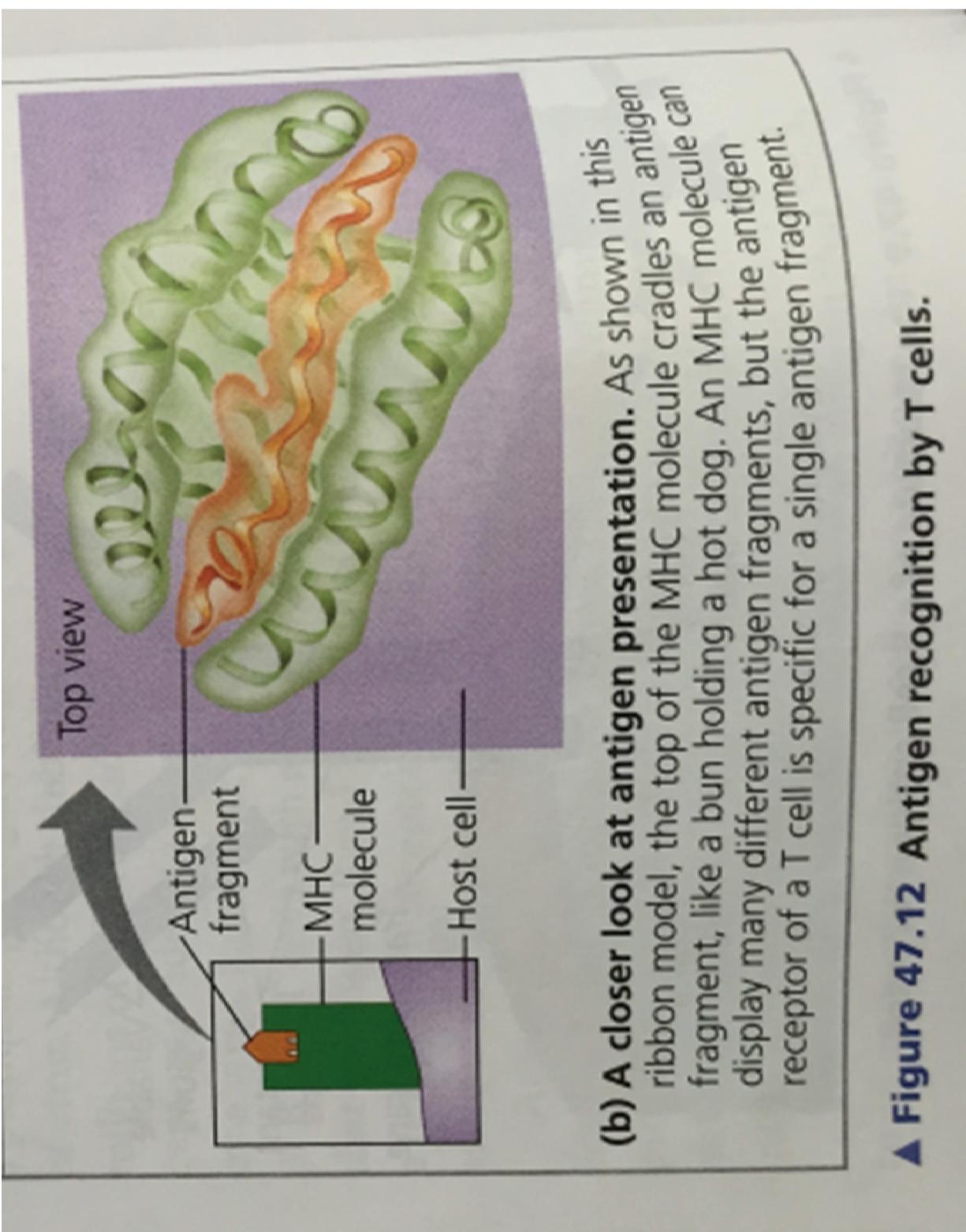


**Pathogen peptides that bind to TCR come from
phagocytosis and antigen presentation on the surface
of innate cells**





(a) Antigen recognition by a T cell. Inside the host cell, an antigen fragment from a pathogen binds to an MHC molecule and is brought up to the cell surface, where it is displayed. The combination of MHC molecule and antigen fragment is recognized by a T cell.



Check your understanding

1. Draw a TCR and a BCR
2. What is the difference between an antigen and an epitope?
3. Draw an immune synapse between a T cell and an innate antigen presenting cell.
4. What is the main difference between NK cell response to HLA and T cell response to HLA ?

T and B cell response after antigen binds to TCR / BCR: An overview

- Antigen-specific T or B cells with exactly the right TCR / BCR for a particular pathogen epitope are rare
- Before they match their matching antigen, they are called “**naive**” cells
- After they meet their matching antigen via HLA presentation , they respond by becoming “**activated**”
- Other signals may be required in order to fully activate T or B cells

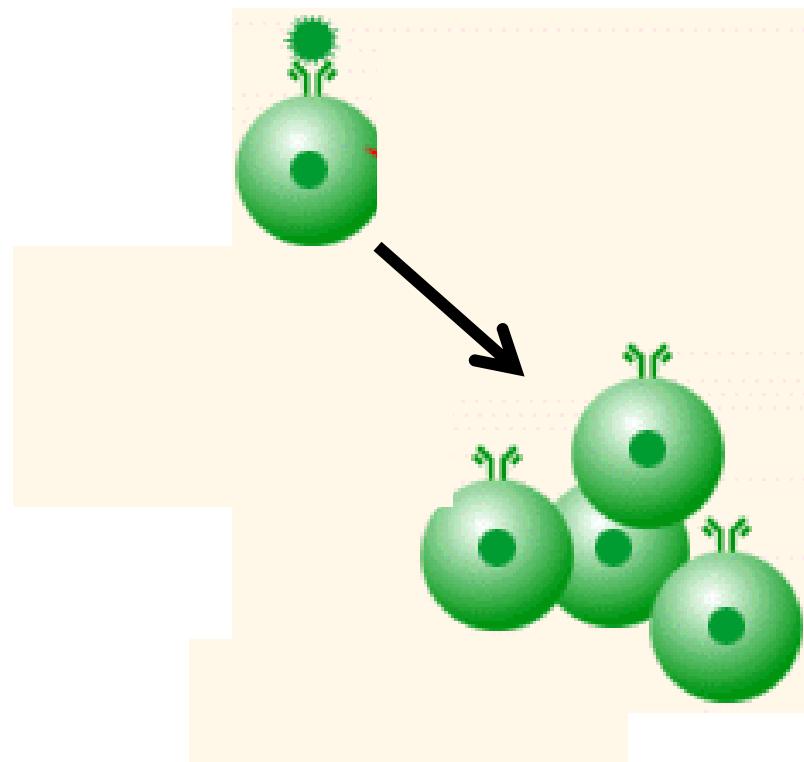
T and B cell response after antigen binds to TCR / BCR: An overview

After they meet their matching antigen , they respond by becoming “activated”

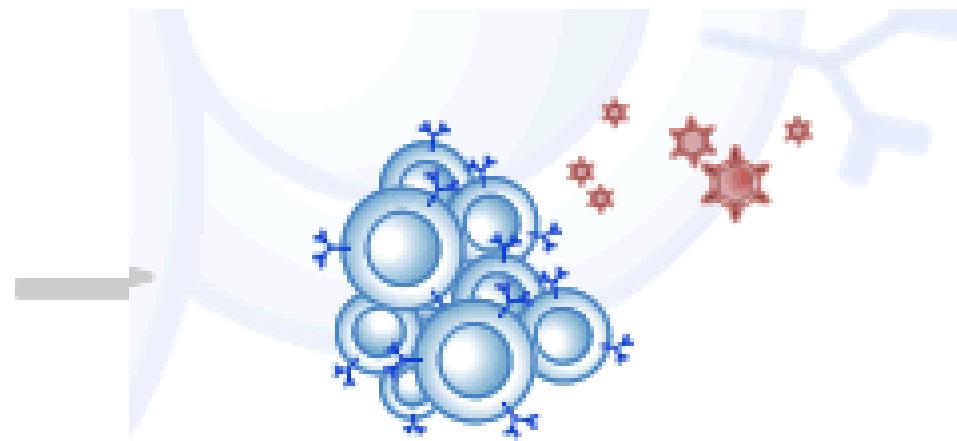
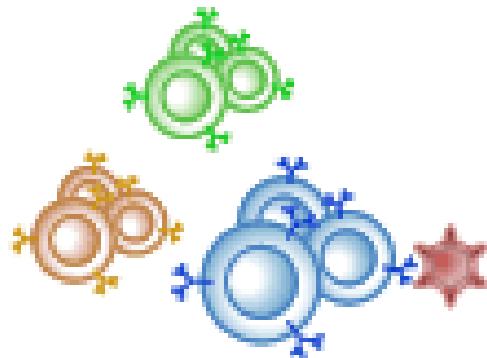
- Activated T and B cells do several things:
 1. They proliferate (clones of themselves)
 2. They differentiate into effector and memory cells.
 3. Differentiated effector cells perform their specific functions .
T cells produce a cell-mediated response
B cells produce a humoral response
 4. They produce cytokines

T and B cell response after antigen binds to TCR / BCR: An overview

- After naïve T or B cells meet their matching antigen , they respond by creating an “army” of identical T or B cells with exactly the same TCR/ BCR and same epitope specificity
- This is called **clonal proliferation**



T and B cell response after antigen binds to TCR / BCR: An overview



Each color represents an identical group of naive B cells that is capable of recognizing and responding to a single antigen. Thus, each group represents a "clone."

Activated cells proliferate, keeping pace with the proliferation of microbes. This is called "clonal expansion".

Reset

Show all

T and B cell response after antigen binds to TCR / BCR: An overview

- The next thing that happens is that the clonal cells differentiate (turn into different subtypes with different functions)
- Some of the T and B cells are effector cells; they need to “fight” and perform specific effector functions immediately
- Some of the T and B cells become memory cells: they will live for along time and “remember” that they have seen this antigen before. If they meet the same antigen again, they can very quickly proliferate again.

T and B cell response after antigen binds to TCR / BCR: An overview

- What T cells differentiate into :
 - Memory T cells (CD8 or CD4)
 - Effector T cells: CD8 Cytotoxic or CD4 helper functions
- When B cells differentiate :
 - Memory B cells
 - Effectors are plasma cells (which make lots of antibodies)

After activation, naïve T cells differentiate into effector and memory T cells

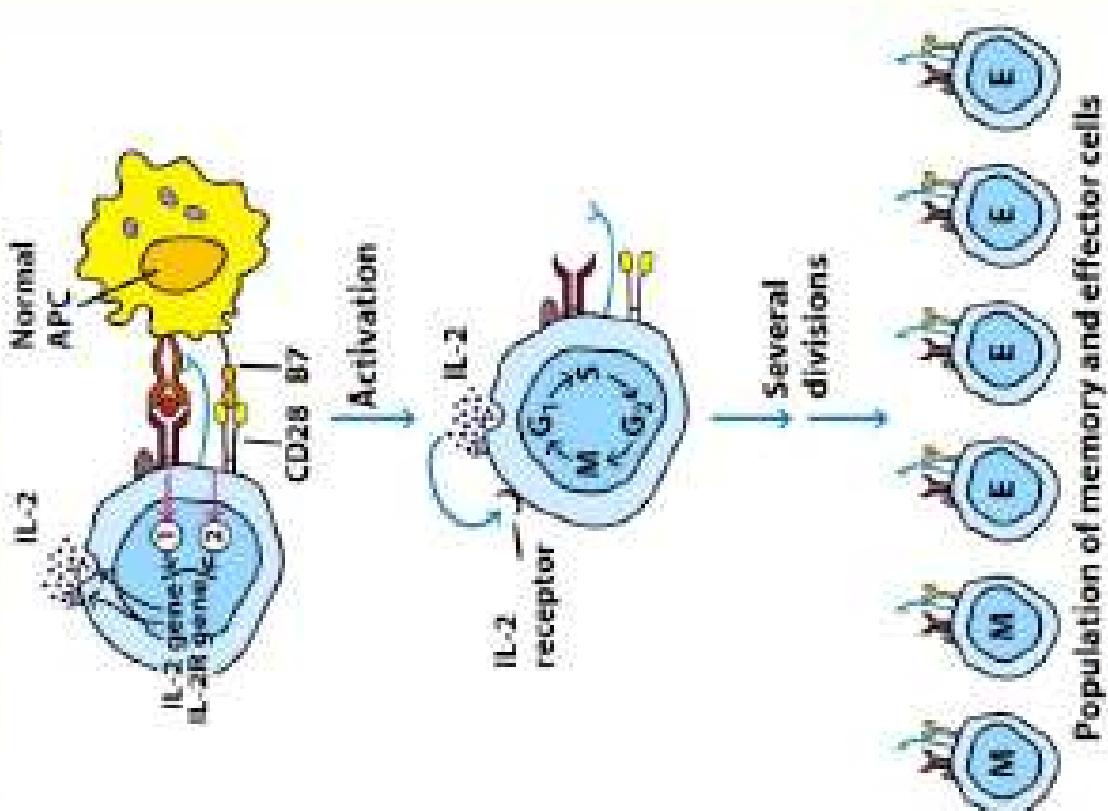
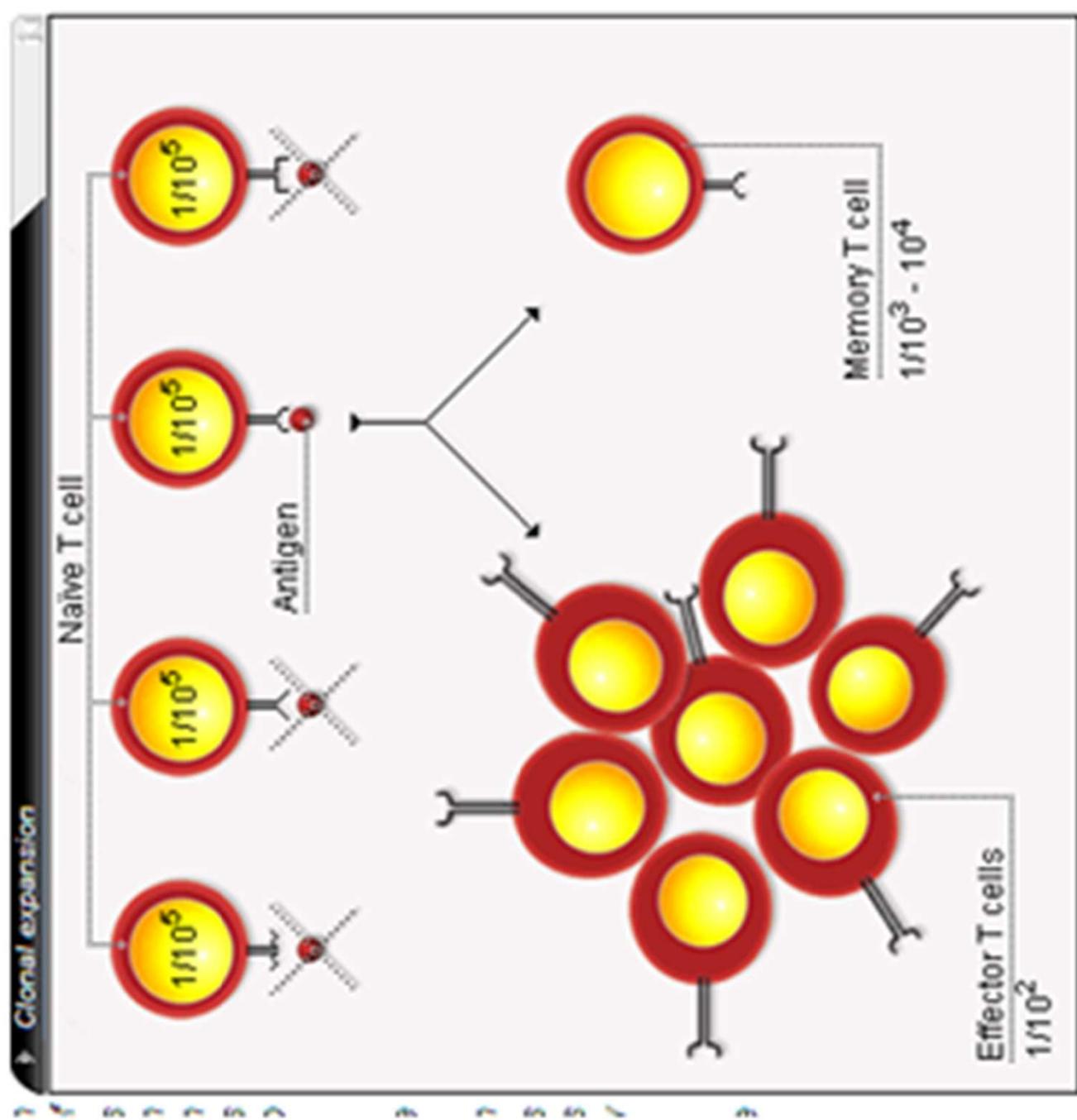
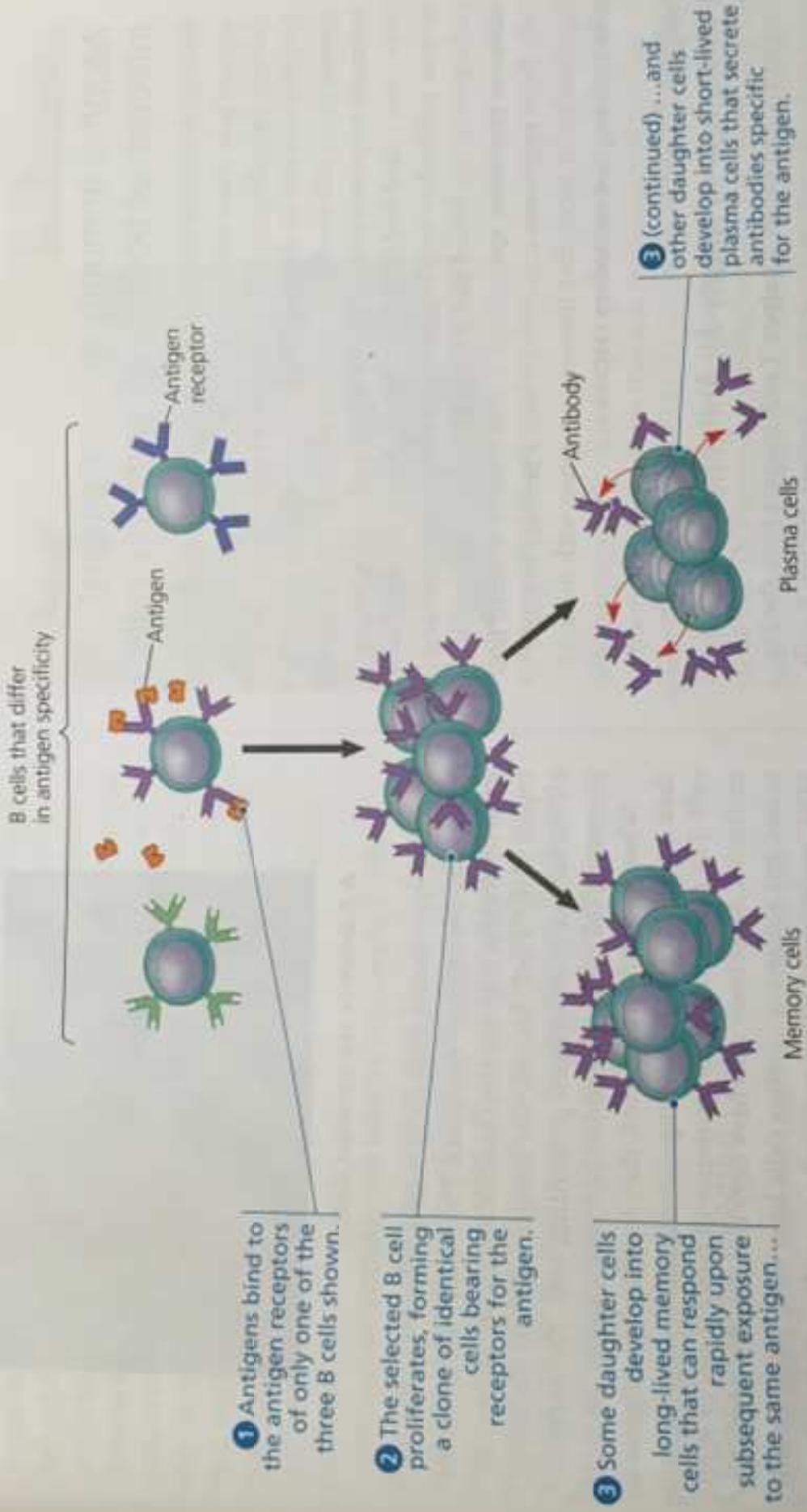


Figure 10-17



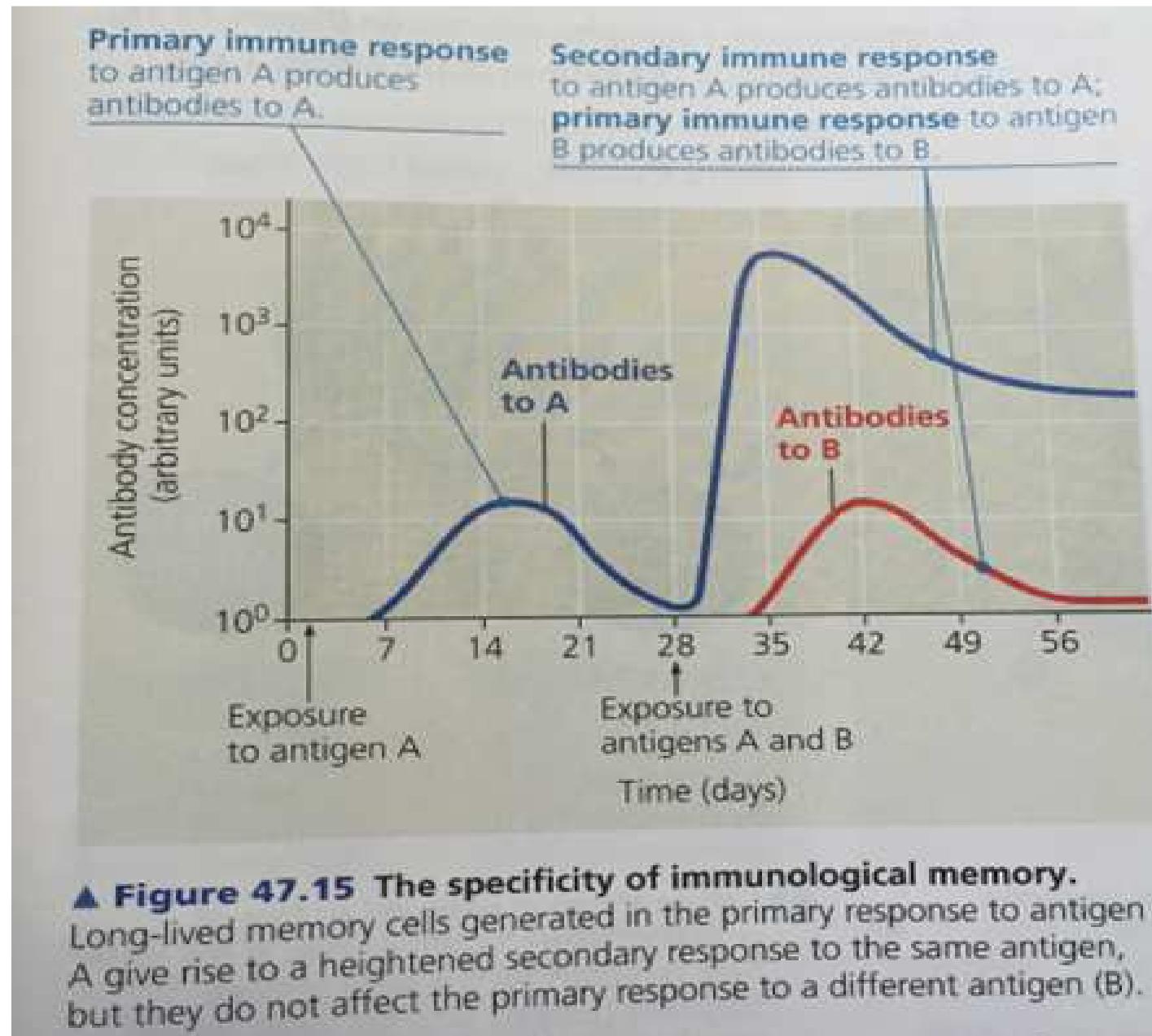


▲ **Figure 47.14** Clonal selection of B cells.

What is immunological memory?

- This is a property of the adaptive immune response (T and B cells)
- It refers to differences in the immune response seen when the T or B cell encounters an antigen for the first time, compared to its response on any subsequent exposure to the same antigen
- First encounter: **primary immune response**
- Next encounters: **secondary immune response**
- The next time, the response is **faster, stronger and lasts longer.**
- E.g. first time, adaptive response takes 10-17 days to peak
- Next time, the same response takes only 2-7 days
- Relies on **special B and T memory cells : rapidly** respond to form thousands of clonal effector cells
- Basis of **vaccination**

What is immunological memory?



T and B cell response after antigen binds to TCR / BCR: An overview

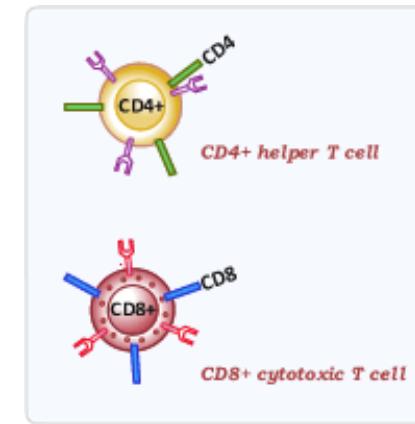
1. Activation
2. Proliferation
3. Differentiation: effector and memory cells
4. Cell-mediated or humoral responses

...we will now look at T and B cell activation, response
and function in more detail.....

T cell activation, response and function

Remember that there are 2 main types of T cells:

- Cytotoxic CD8+ T cells
- Helper CD4+ T cells



There are also 2 types of HLA (MHC) molecules

- HLA class I
- HLA class II

They have

- similar but slightly different structure
- similar but slightly different functions

Both types bind antigens and present them to T cells

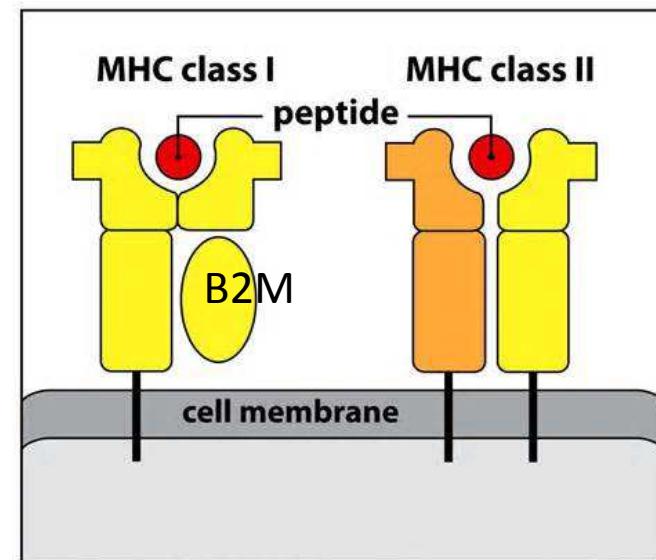
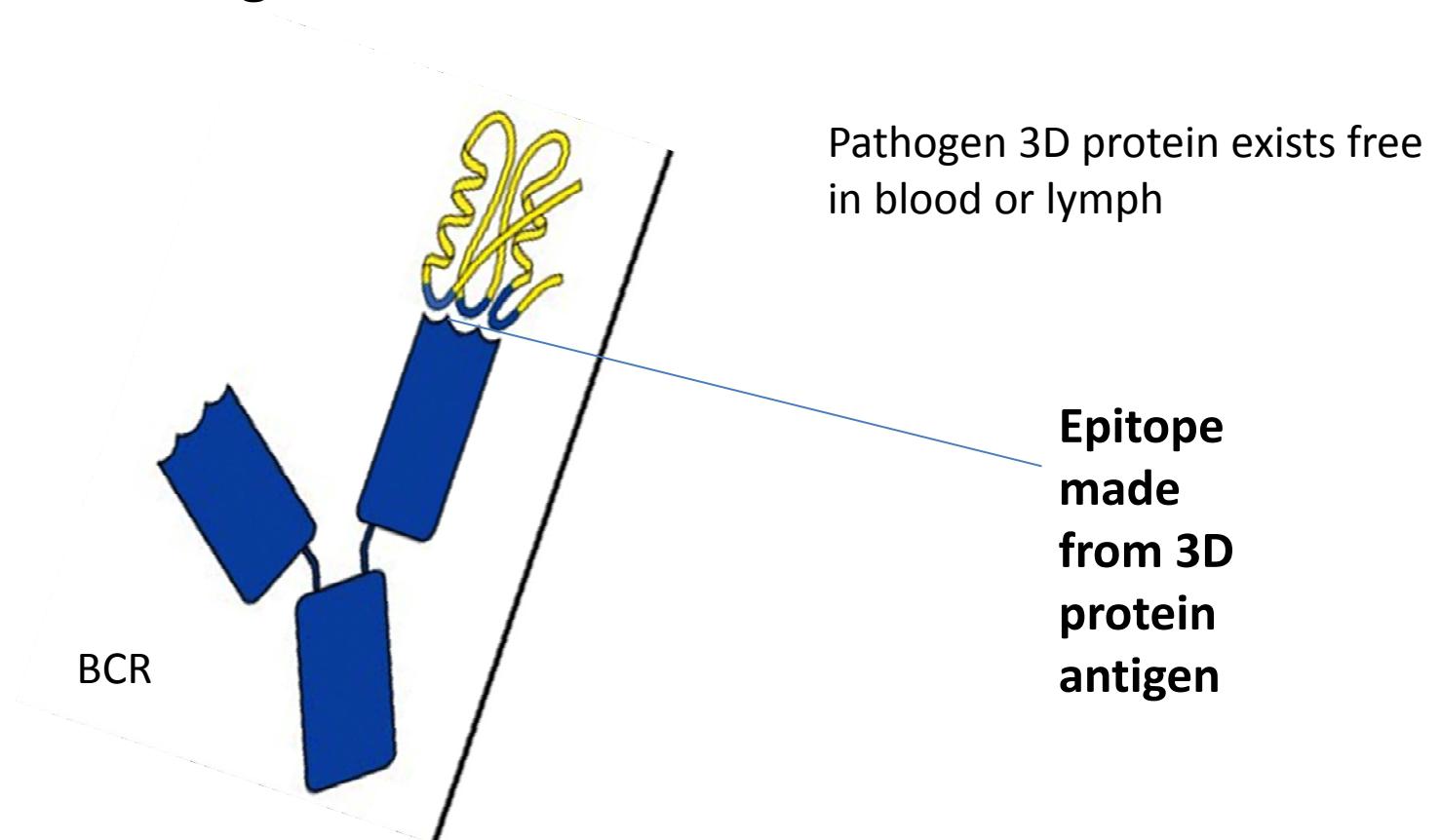


Figure 3.8 The Immune System, 3ed. (© Garland Science 2009)

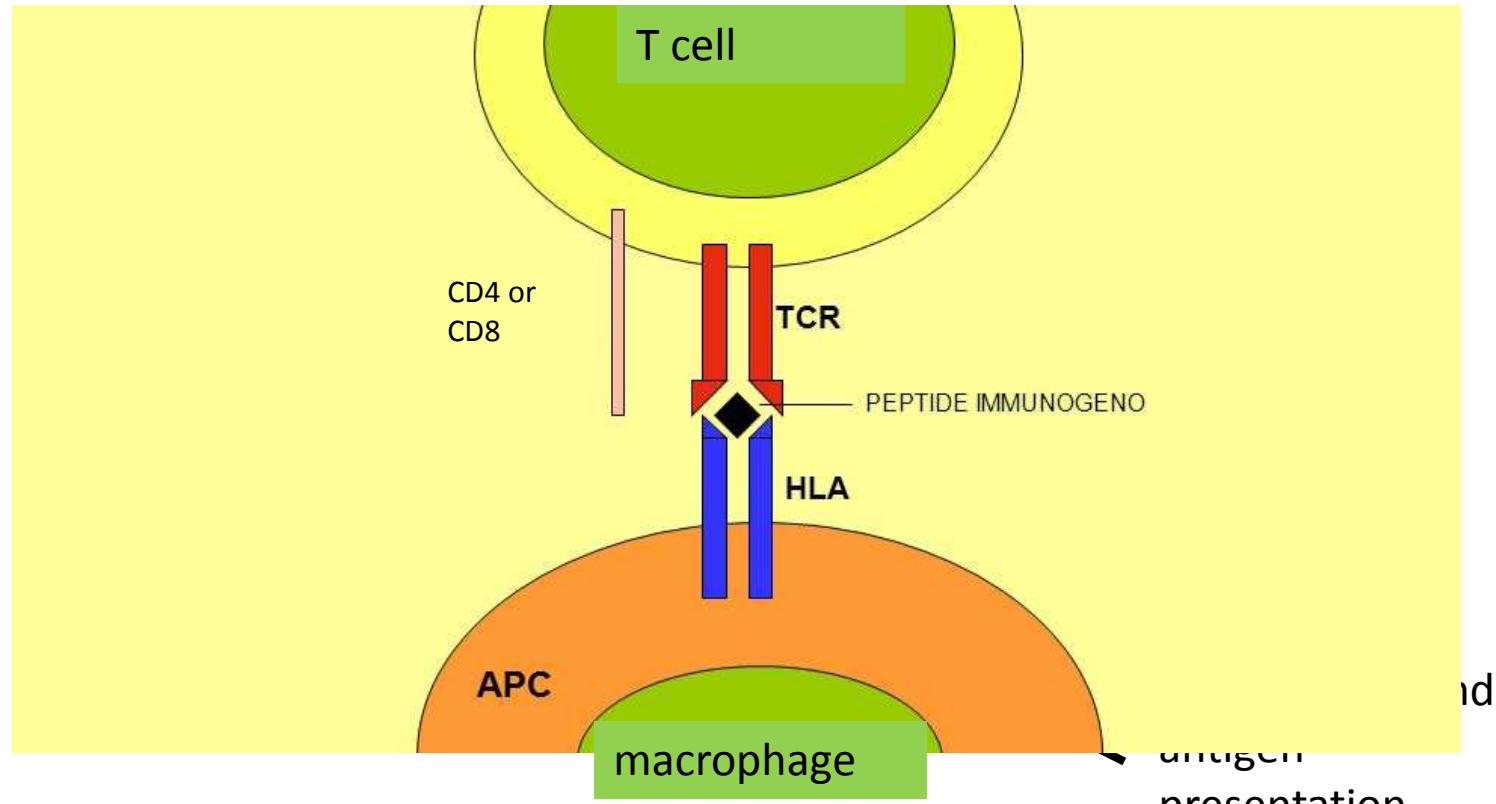
	MHC I 	MHC II 
Located in which cell types?	ALL nucleated cells in the body 	ONLY antigen presenting cells: - dendritic cells - macrophages - B cells 
Presents antigens from which cellular compartment?	From within the cytosol Antigens from intracellular pathogens e.g. viruses	From within vesicles Antigens from extracellular pathogens e.g. bacteria
Recognized primarily by receptors on which type of T cell?	CD8+ cytotoxic T cells	CD4+ helper T cells

Antigens and BCR

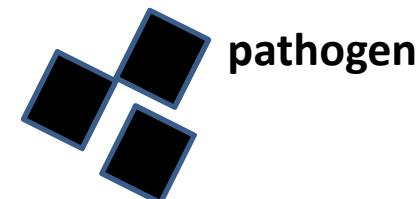
- B cell receptors bind antigens that are bits of **protein folded into their native 3D configuration**



antigens are presented to TCR on T cell, via MHC (HLA) on innate antigen presenting cells



(an immune synapse
With 2 cell types interacting)



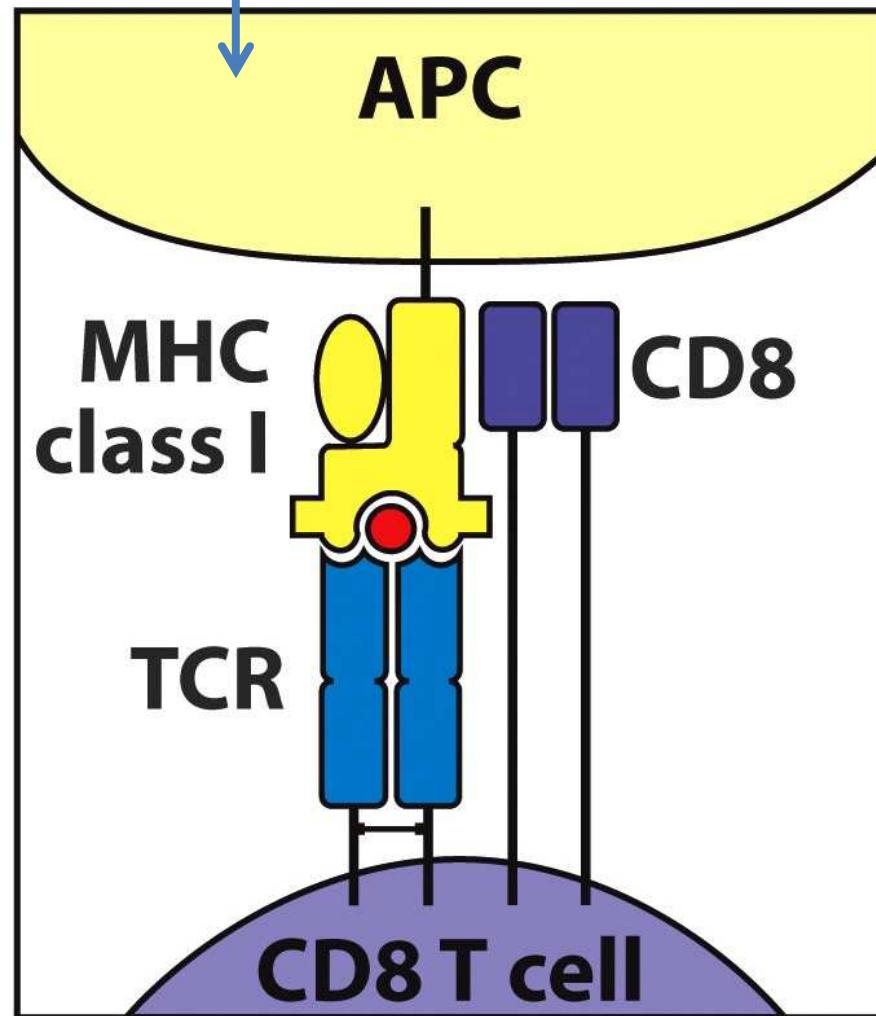
	MHC I 	MHC II 
Located in which cell types?	ALL nucleated cells in the body 	ONLY antigen presenting cells: - dendritic cells - macrophages - B cells 
Presents antigens from which cellular compartment?	From within the cytosol Antigens from intracellular pathogens e.g. viruses	From within vesicles Antigens from extracellular pathogens e.g. bacteria
Recognized primarily by receptors on which type of T cell?	CD8+ cytotoxic T cells	CD4+ helper T cells

T cell activation, response and function

Both types of T cells are activated by antigen presented on HLA on antigen presenting cells

- HLA class I presents viral peptides to CD8+ T cells
- HLA class II presents bacterial peptides to CD4+ T cells
- The TCR of the T cells interacts with the HLA /antigen

Viral peptides
usually by infection



Bacterial peptides usually
by phagocytosis

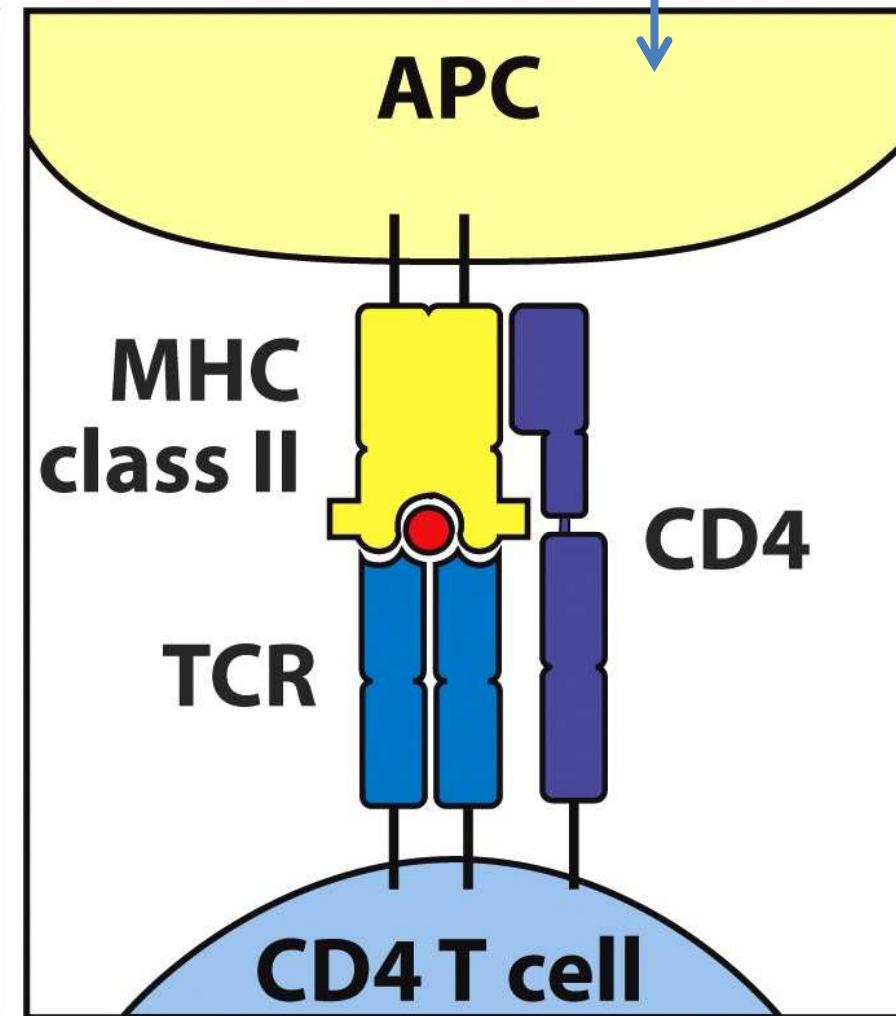
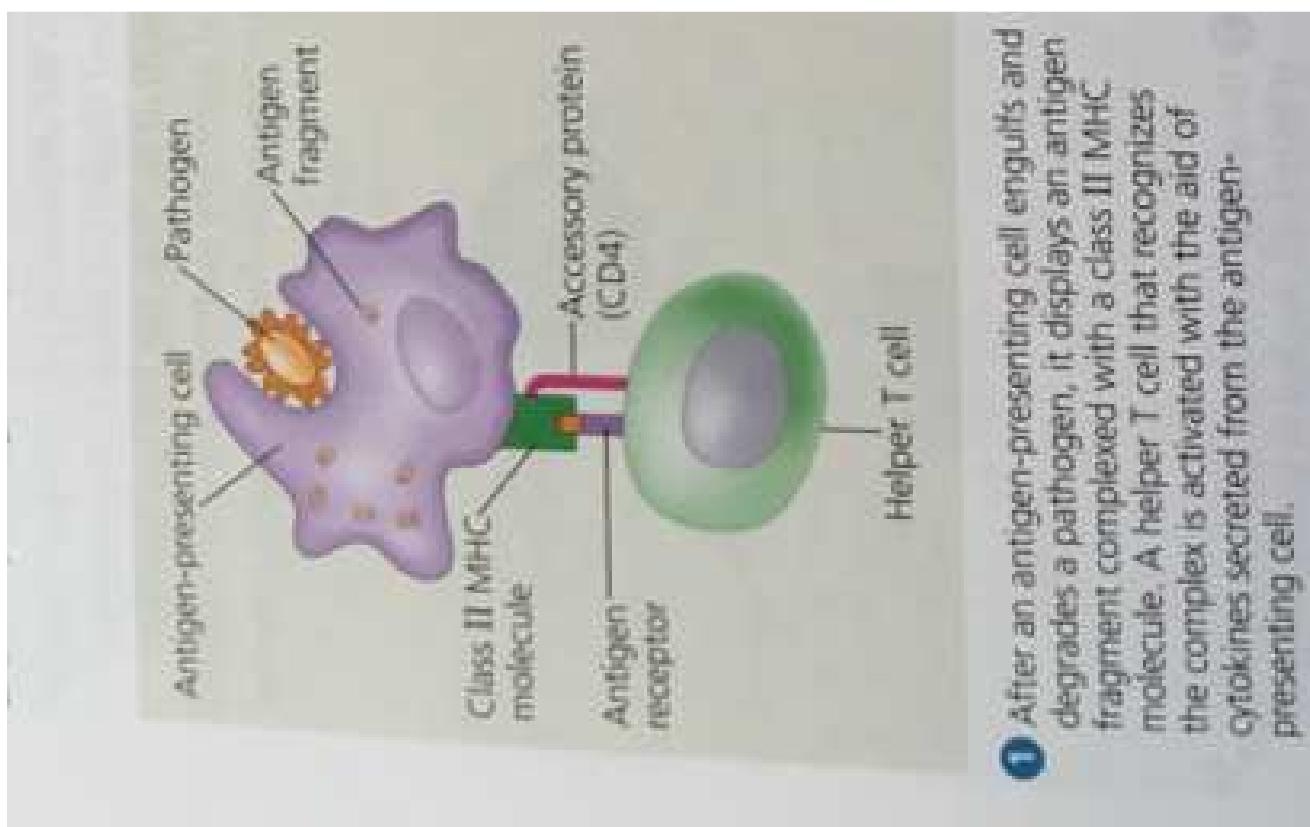
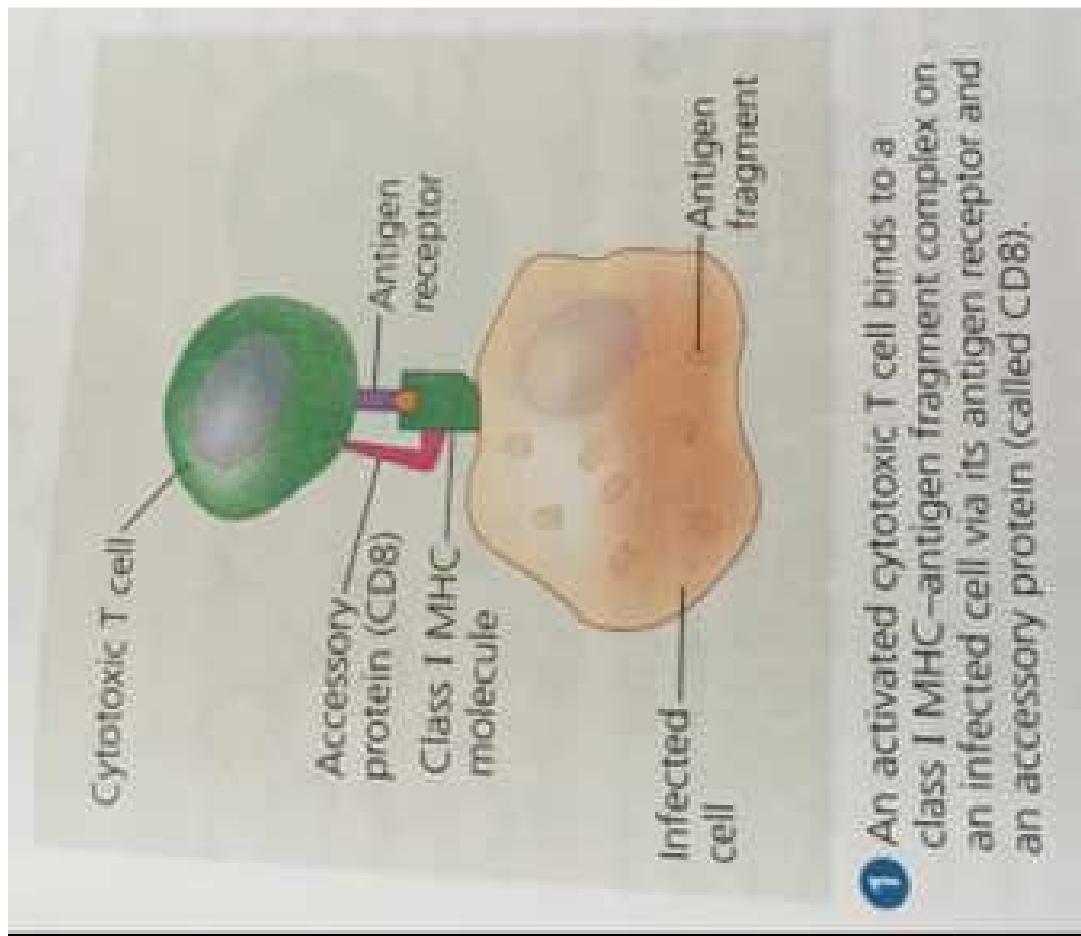


Figure 3.9 The Immune System, 3ed. (© Garland Science 2009)



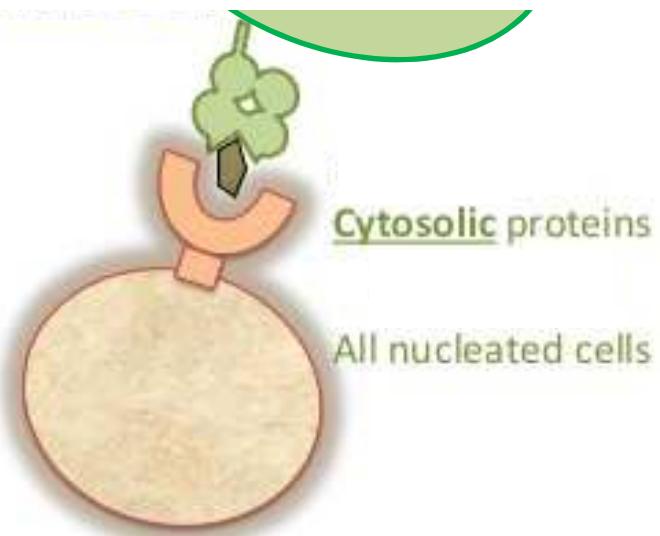
- After an antigen-presenting cell engulfs and degrades a pathogen, it displays an antigen fragment complexed with a class II MHC molecule. A helper T cell that recognizes the complex is activated with the aid of cytokines secreted from the antigen-presenting cell.



- An activated cytotoxic T cell binds to a class I MHC–antigen fragment complex on an infected cell via its antigen receptor and an accessory protein (called CD8).

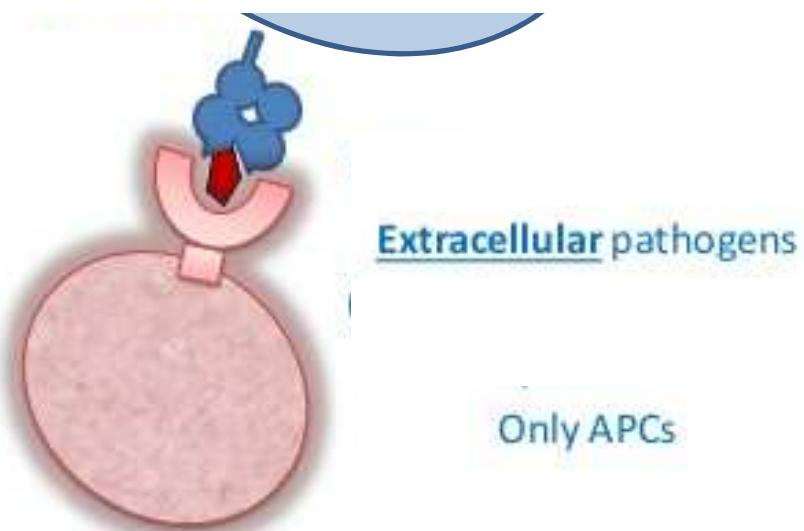
2 flavors of HLA

HLA class I on all cells



CD8+ Cytotoxic T cell

HLA class II on APC only



CD4 T helper cell

T cells recognise Intracellular pathogens and extracellular pathogens

Virus / intracellular

- infect innate cell or phagocytosis by innate cell
- displayed on surface by HLA class I
- recognised by TCR of CD8+ cytotoxic T cells

Bacteria / extracellular / helminths

- phagocytosis by innate cell
- displayed on surface by HLA class II
- recognised by TCR of CD4+ helper T cells

CD8+ T cells response to activation

1. Proliferation
2. Differentiation into
 1. effector CTL (cytotoxic T lymphocytes)
 2. memory T cells
3. Produce cytokines e.g. IL-2
4. When the effector CTL synapse with an infected cell , **they release toxic proteins / granules to lyse the infected cell (cytolysis) ; induce target cell death (apoptosis)**
E.g. perforin, granzymes

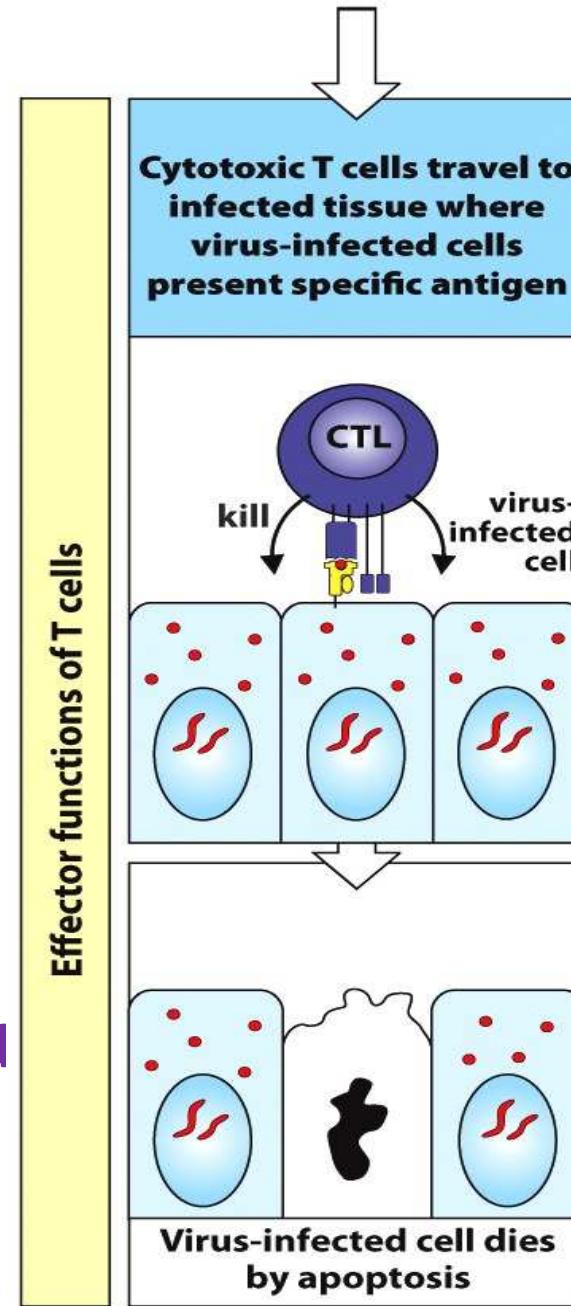
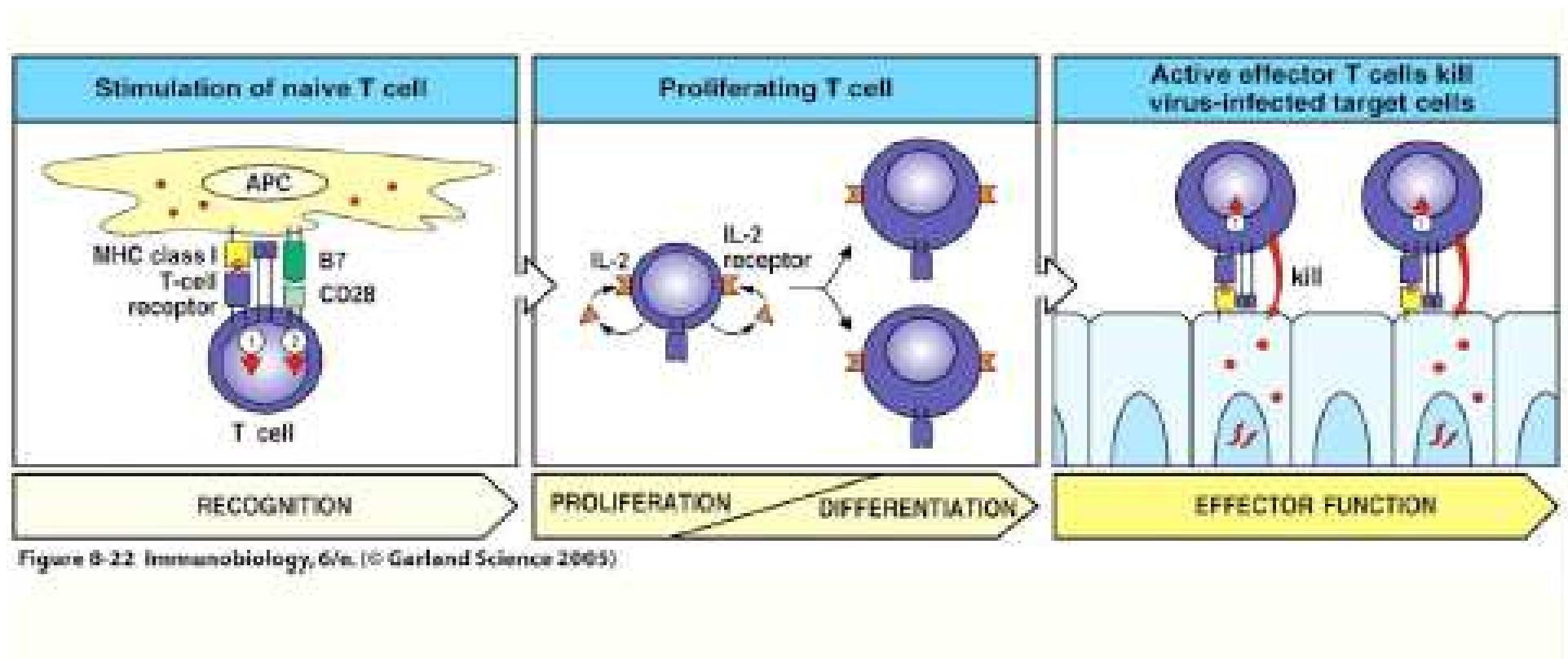
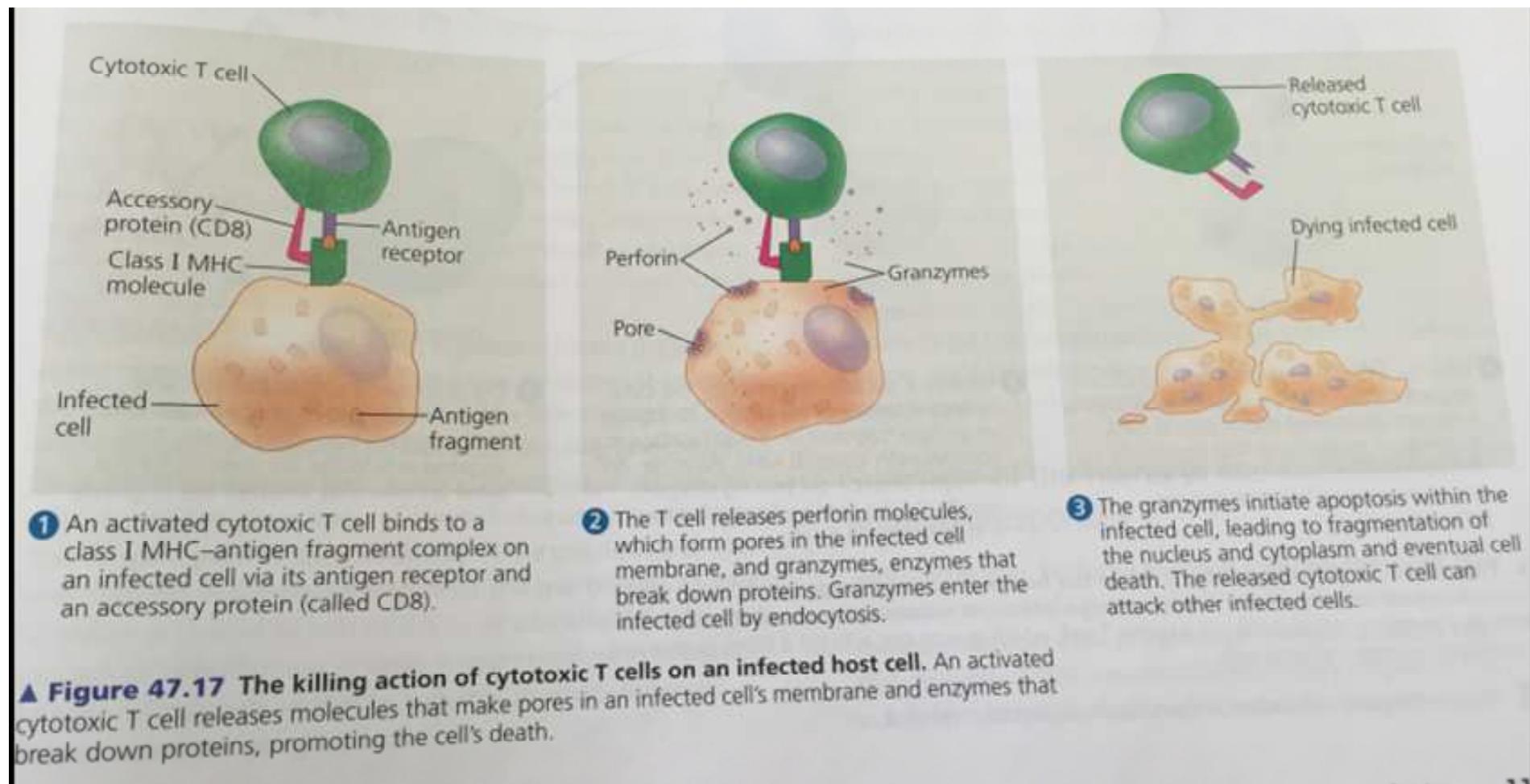


Figure 8.39 part 2 of 2 The Immune System, 1

CD8+ T cells response to activation



CD8+ T cells response to activation



Check your understanding

1. What is the difference between naive and activated lymphocytes?
2. Generally what happens after T or B cells are activated?
3. What is the difference between HLA class I and class II?
4. How do CTL cause cytolysis of infected cells?
5. What type of pathogen stimulates a CD8 + T cell response? A CD4+ T cell response?

How many types of cell synapses have we learnt about so far?

