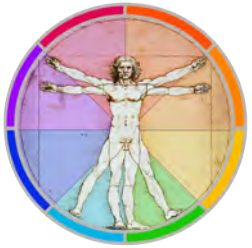
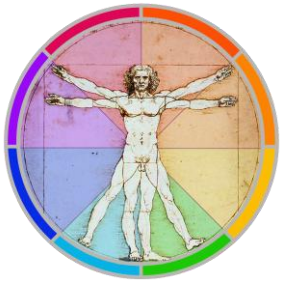
HUBS191 Lecture Material

This pre-lecture material is to help you prepare for the lecture and to assist your note-taking within the lecture, it is NOT a substitute for the lecture !



Please note that although every effort is made to ensure this pre-lecture material corresponds to the live-lecture there may be differences / additions.



HUBS191
Lecture 38

The immune response to infection – a wrap up

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New Zealand

Microbiology & Immunology
Te Tari Moromoroiti me te Ārai Mate

Objectives

- to integrate knowledge of how innate and adaptive immunity work together to protect our body from infection and disease:
- how adaptive immune response destroys viruses and bacteria with cells and antibody
- understand the basic components of a vaccine and how these work to prime the adaptive immune response

Readings: Marieb 10e; “Humoral” &"Cellular immunity" p792-819

Examinable L37 material:

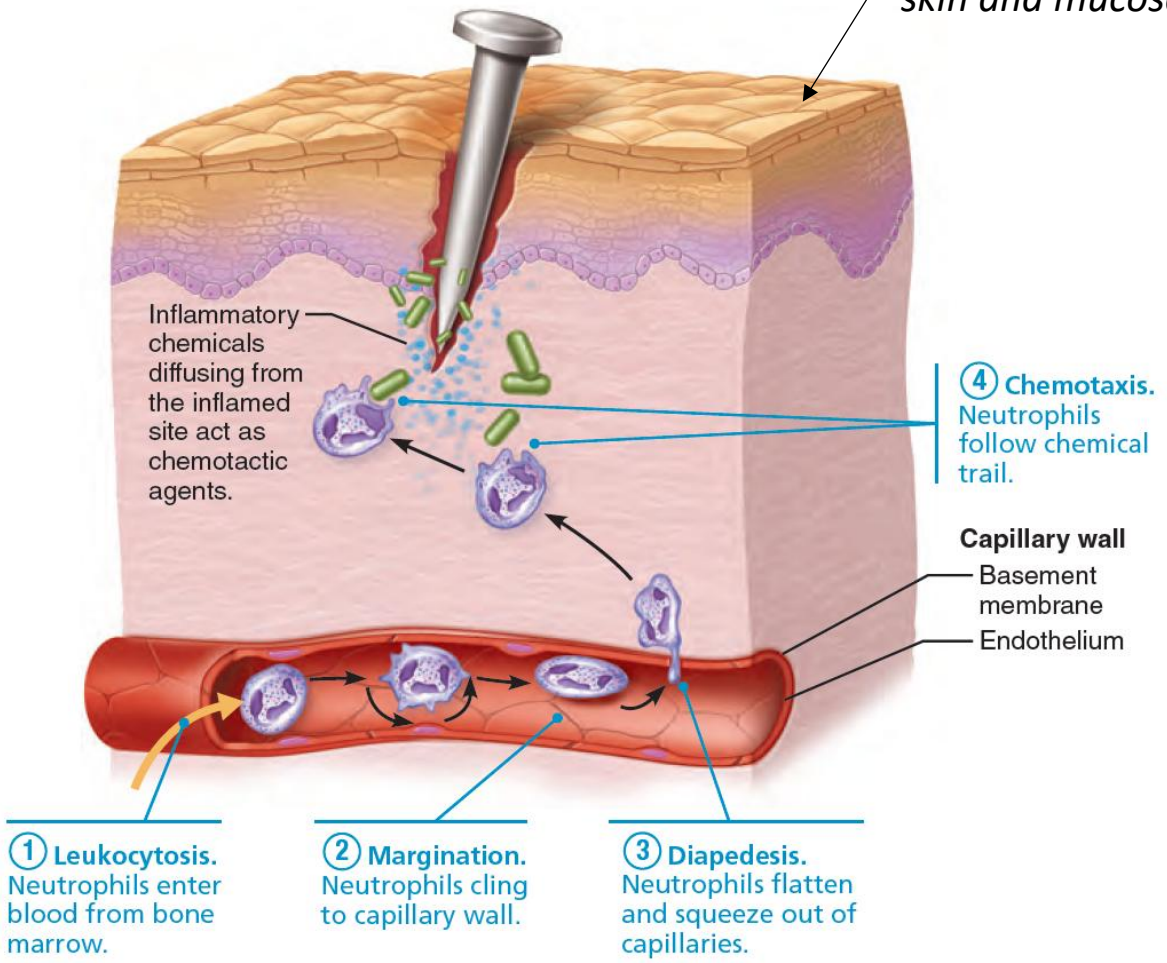
- The cause/s of autoimmune disease (loss of immune tolerance and infection as a trigger) and give examples of autoimmune diseases.

- Immunodeficiency and its causes: genetic (e.g. SCID), infection related (e.g. virus: measles and HIV), environmental (malnutrition) or treatment-related (chemotherapy).

What happens if bacteria make it past our first defences?

Phagocyte mobilisation. Marieb p797

Example of physical barrier: constant replacement of cells (shared property of skin and mucosa).

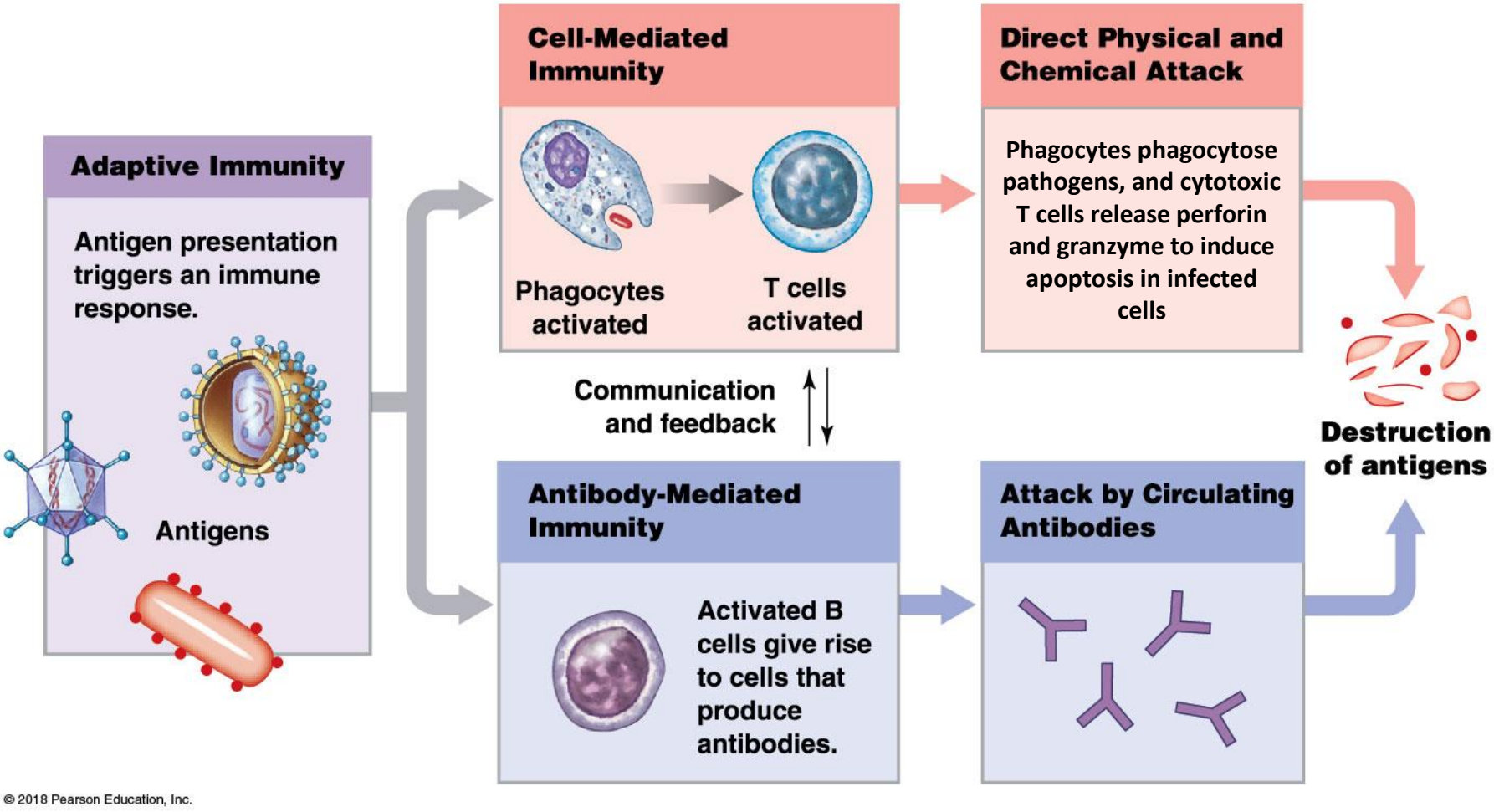


Inflammation makes capillaries leaky. Neutrophils squeeze out of leaky capillaries and enter tissue.

Neutrophils are attracted to the site of infection by chemicals released from damaged / infected cells, or associated leucocytes (especially macrophages)

Bacteria are phagocytosed. Lysosomal enzymes (e.g. acid hydrolases) in the phagolysosome kill the bacteria.

Immunity to pathogens is usually a combination of cell mediated immunity and antibody production

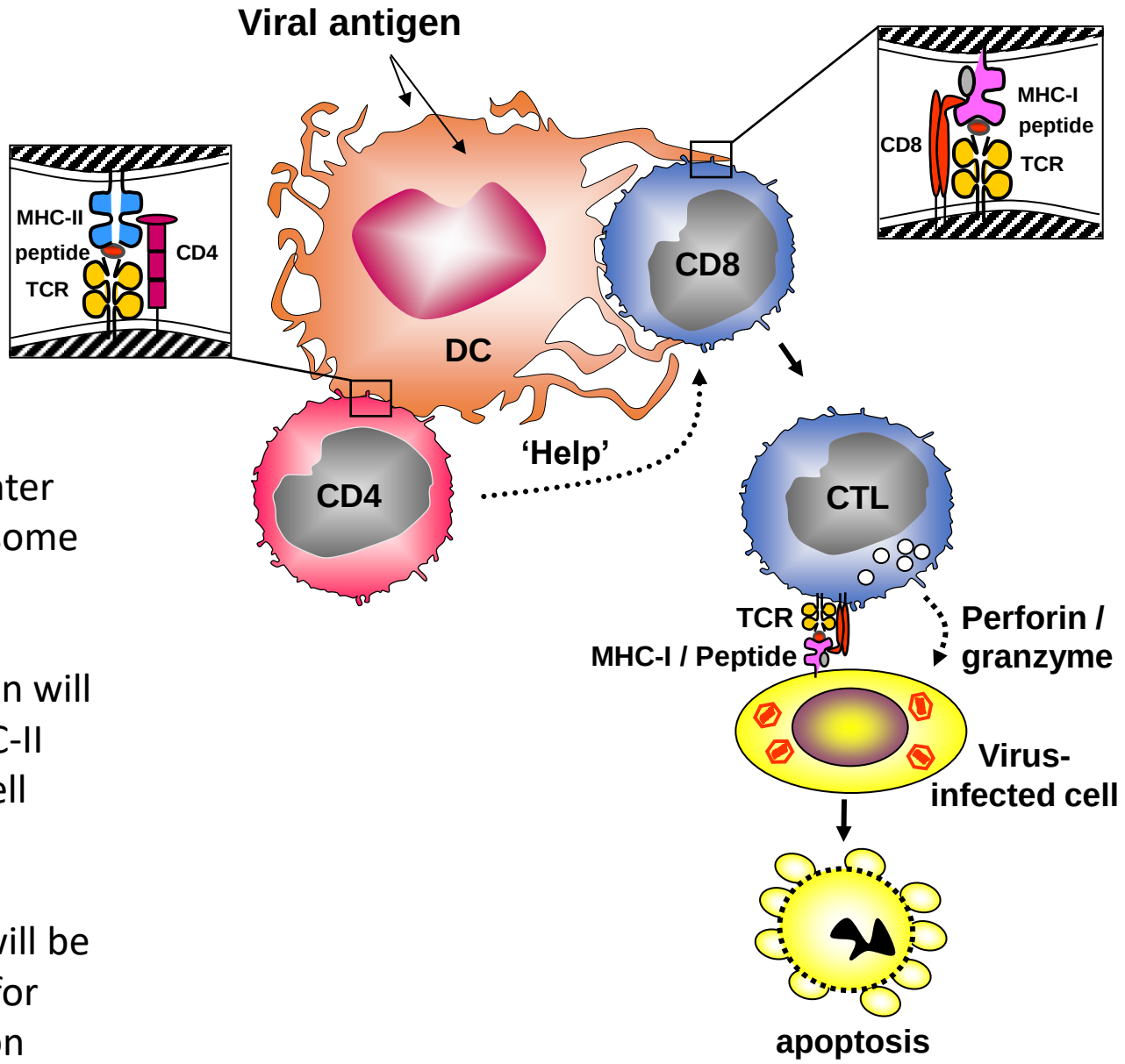


e.g. Optimal anti-viral immune responses require CD4 T cells, CD8 T cells and B cells (for antibody production – especially neutralising IgG)

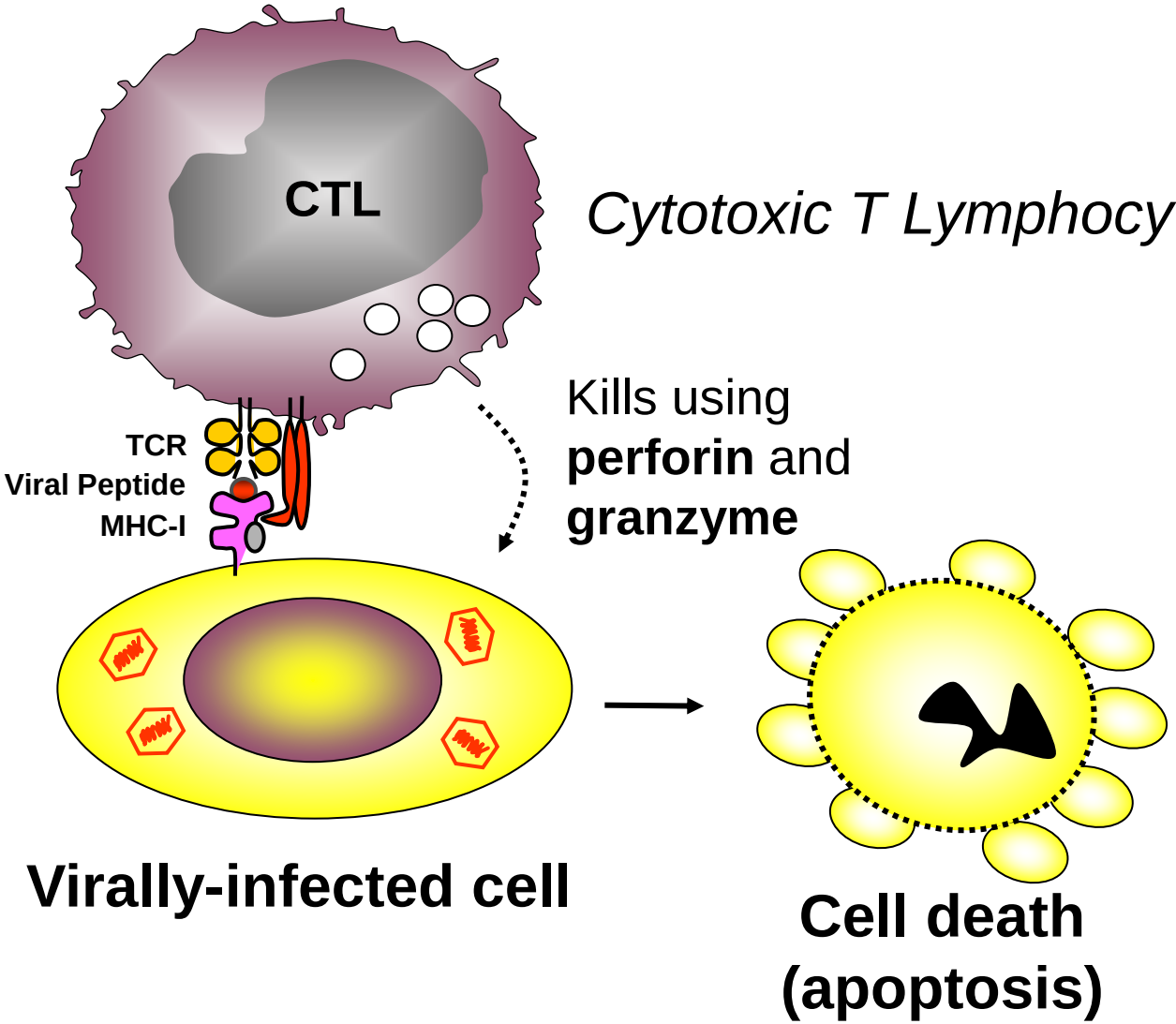
Viral proteins can enter both the phagolysosome and cytosol of DC:

- Phagosomal antigen will be loaded onto MHC-II for CD4 (helper) T cell stimulation

- Cytosolic antigen will be loaded onto MHC-I for CD8 T cell stimulation



CTL kill virus infected cells using perforin and granzyme

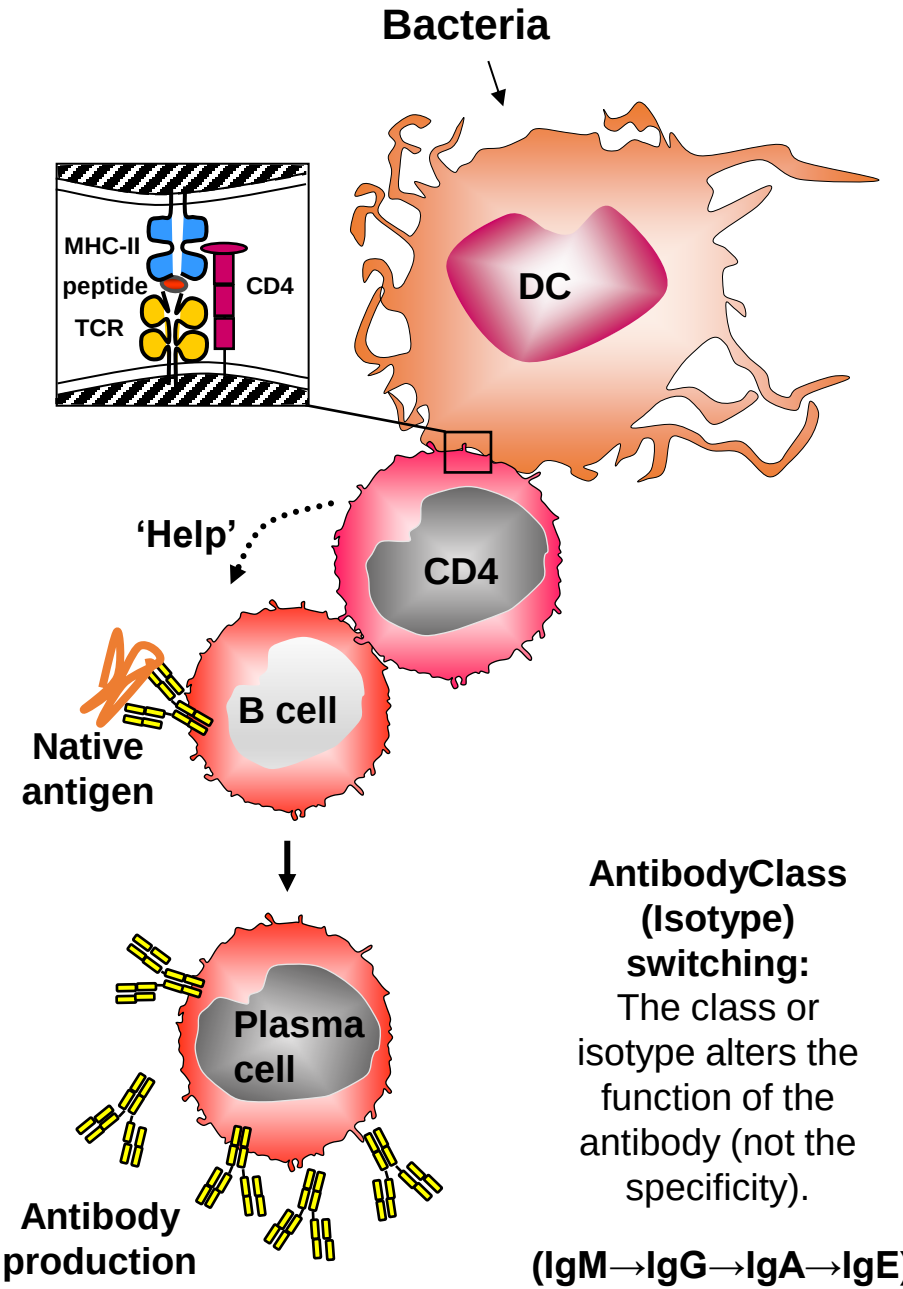


Bacterial proteins enter the phagolysosome of DC:

Phagosomal antigen will be loaded onto MHC-II for CD4 (helper) T cell stimulation

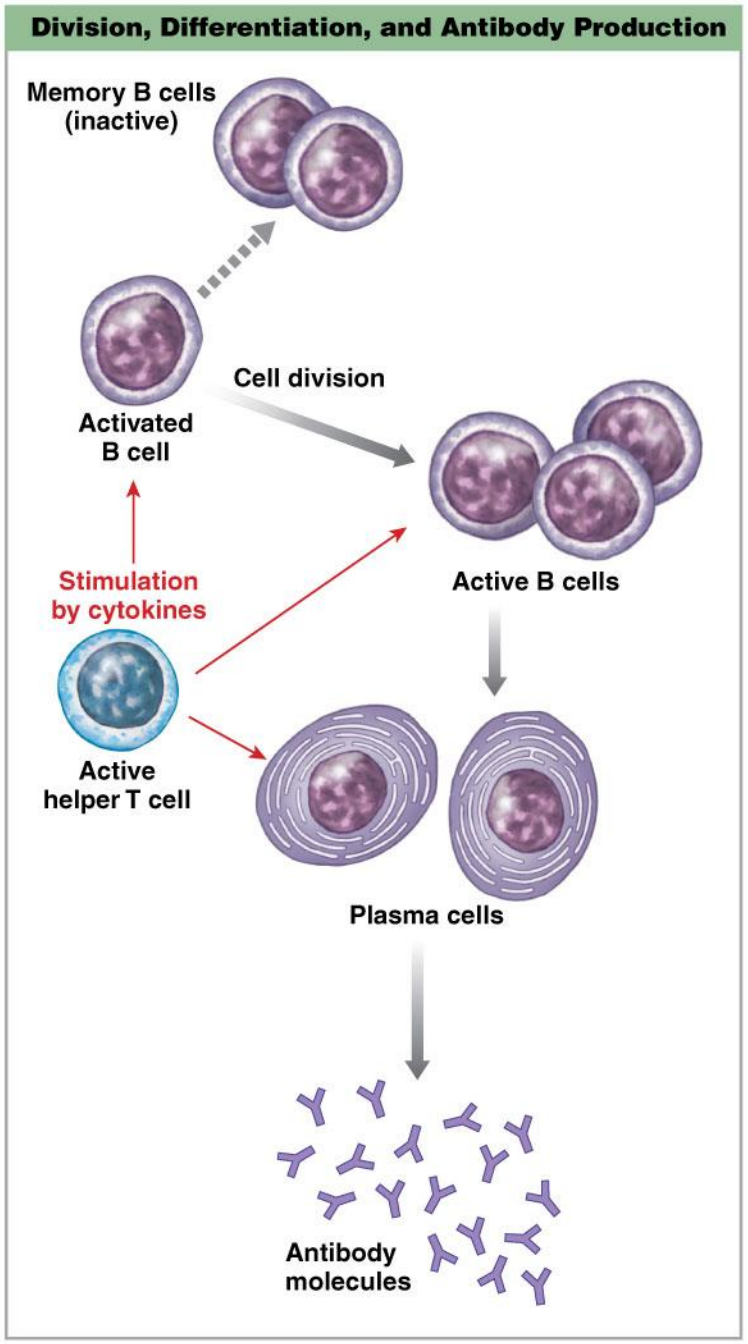
Helper T cells stimulate B cells to make antibody.

Only B cells that recognise antigen are activated.



AntibodyClass (Isotype) switching: The class or isotype alters the function of the antibody (not the specificity).

(IgM→IgG→IgA→IgE)



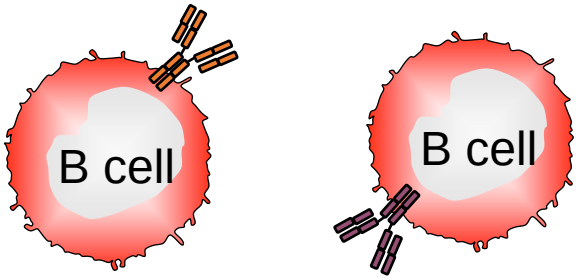
Activated B cells divide and differentiate into plasma cells that secrete antibody, as well forming a separate population of memory B cells.

At the second encounter with antigen, Memory B cells are more numerous and are rapidly stimulated by antigen to become plasma cells.

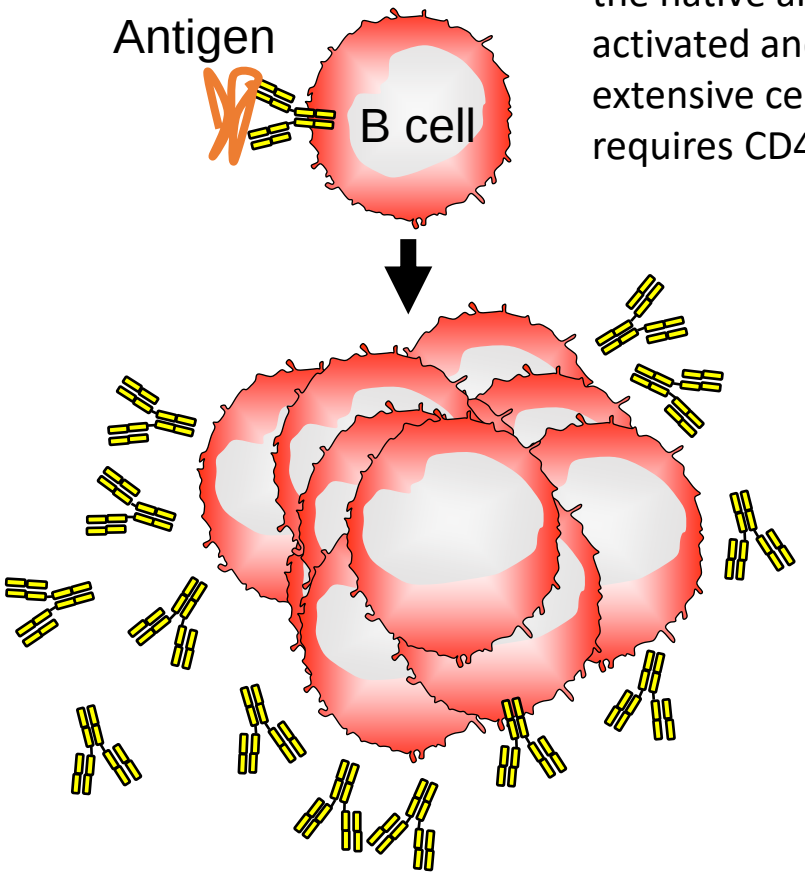
Secondary immune responses are characterised by the predominance of class-switched antibodies: IgG, IgA and IgE

Clonal selection:

Selective expansion of lymphocytes that interact with antigen

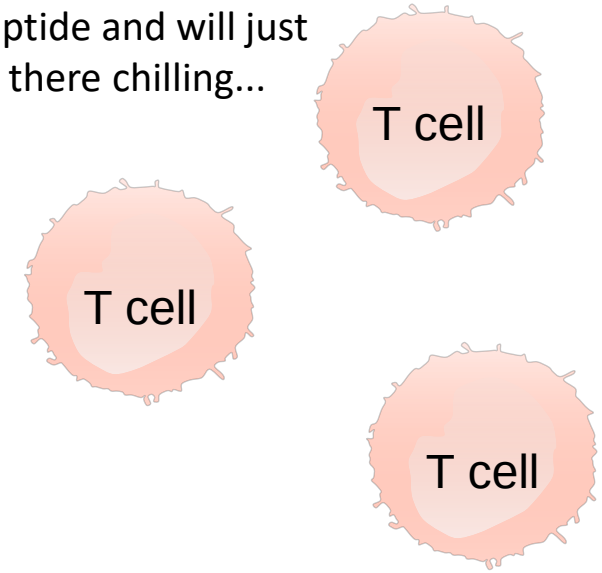


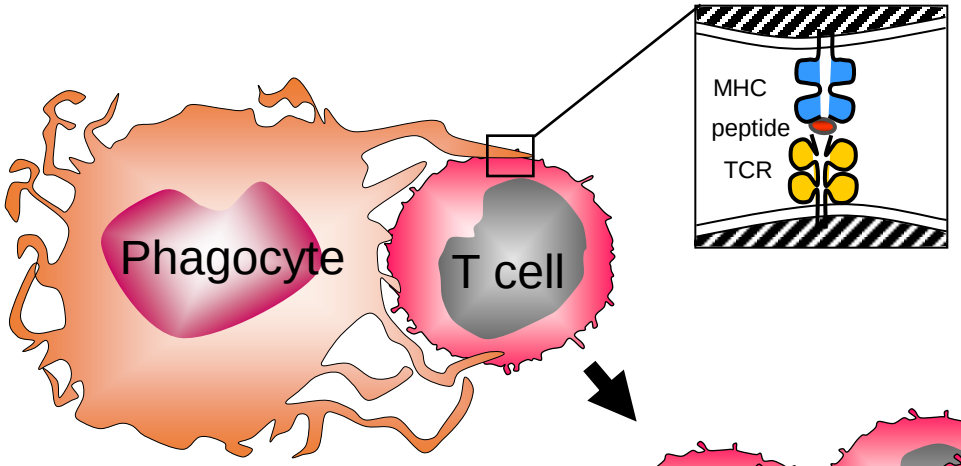
These B cells are not specific for the native antigen and will just sit there chilling...



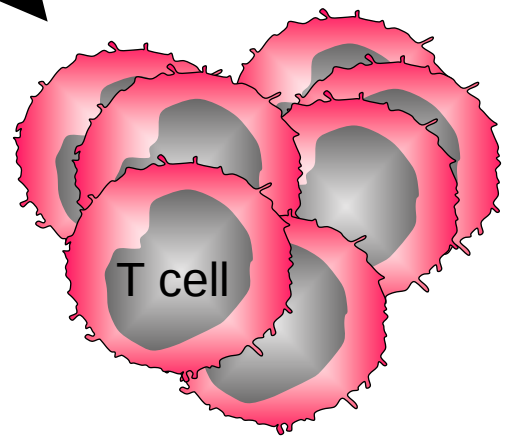
This B cell is specific for the native antigen. It is activated and undergoes extensive cell division (also requires CD4 T cell help).

These T cells are not specific for the peptide and will just sit there chilling...





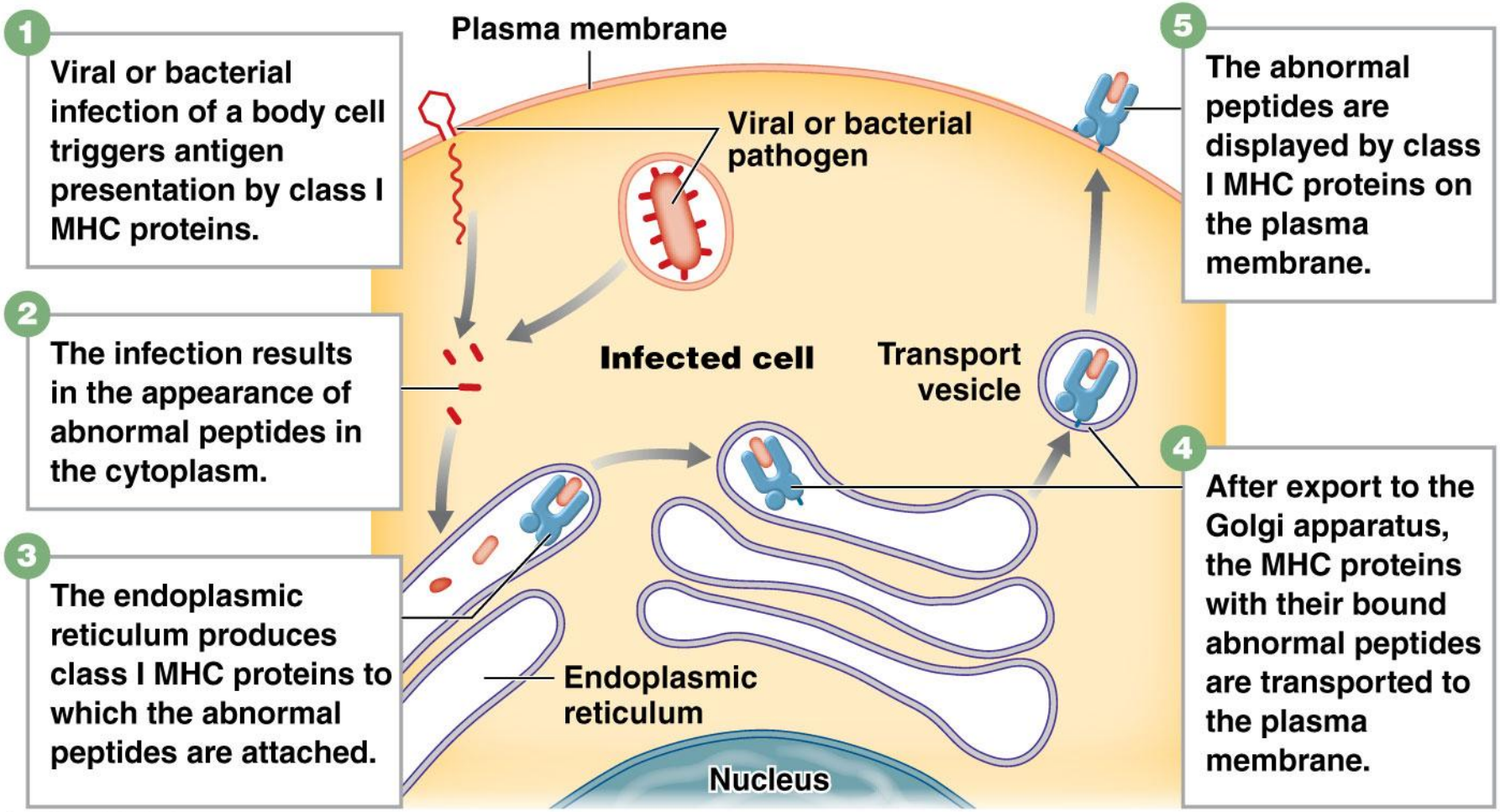
This T cell is specific for the peptide. It is activated and undergoes extensive cell division.



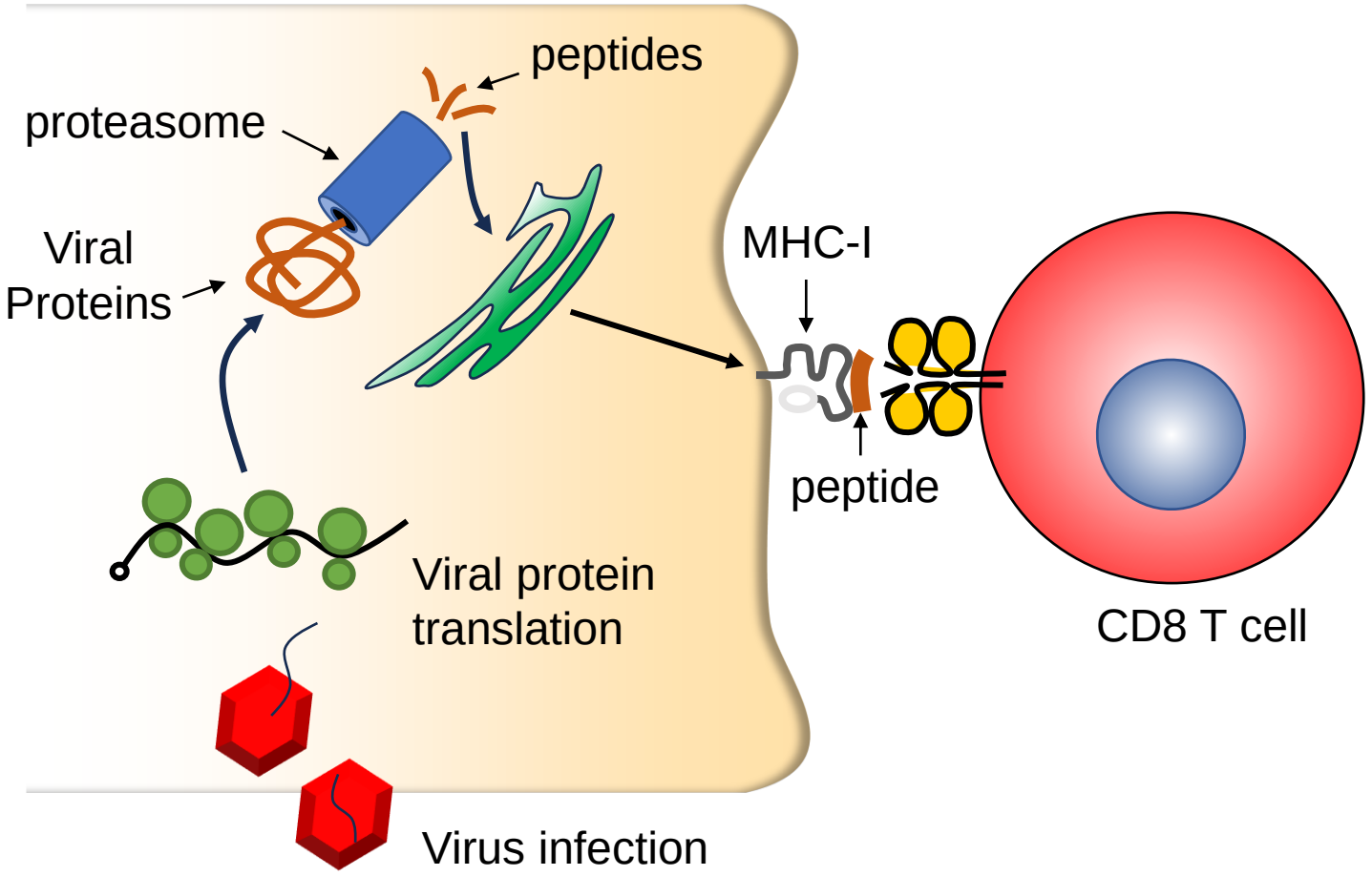
Clonal selection:

Selective expansion of lymphocytes that interact with antigen

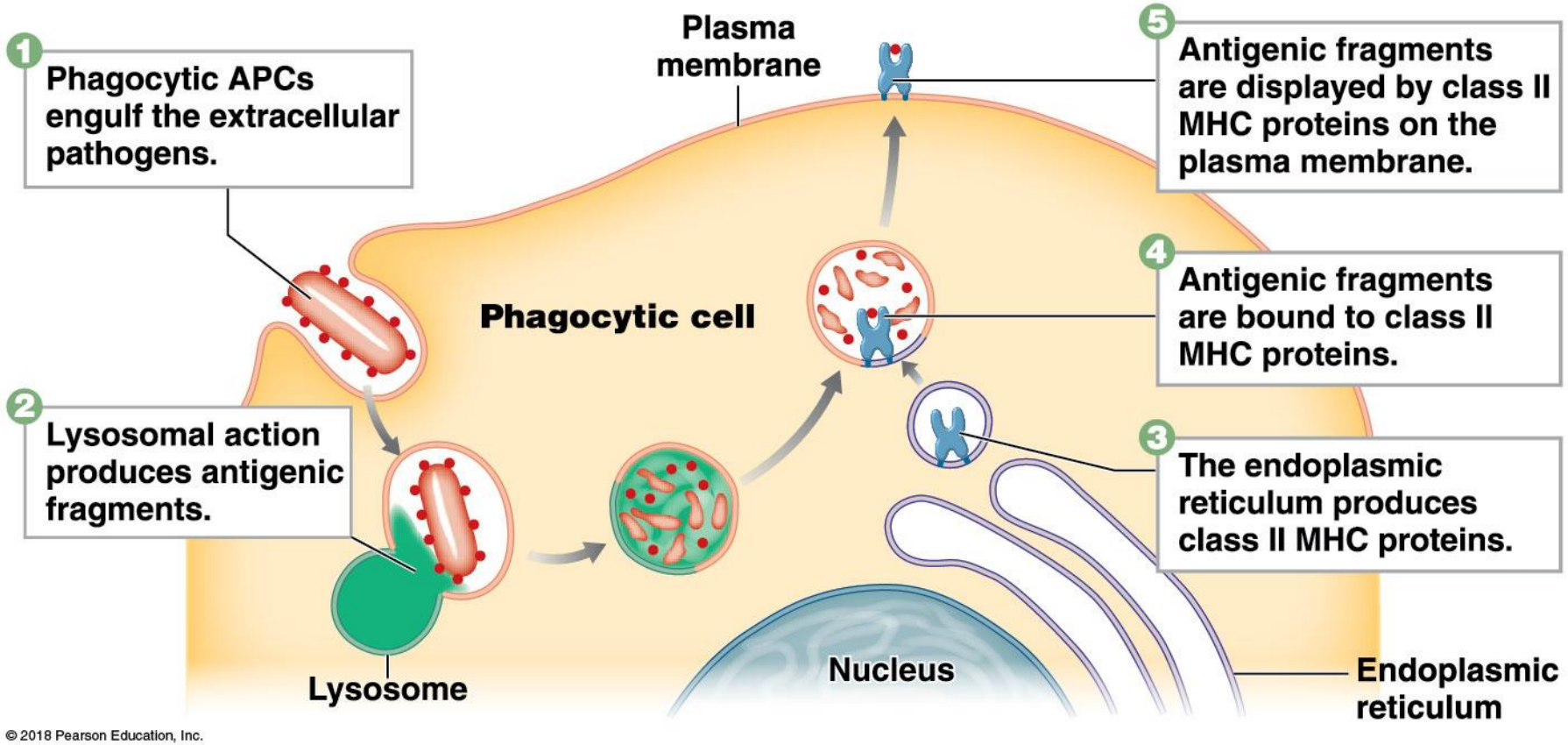
MHC-I loading with peptide



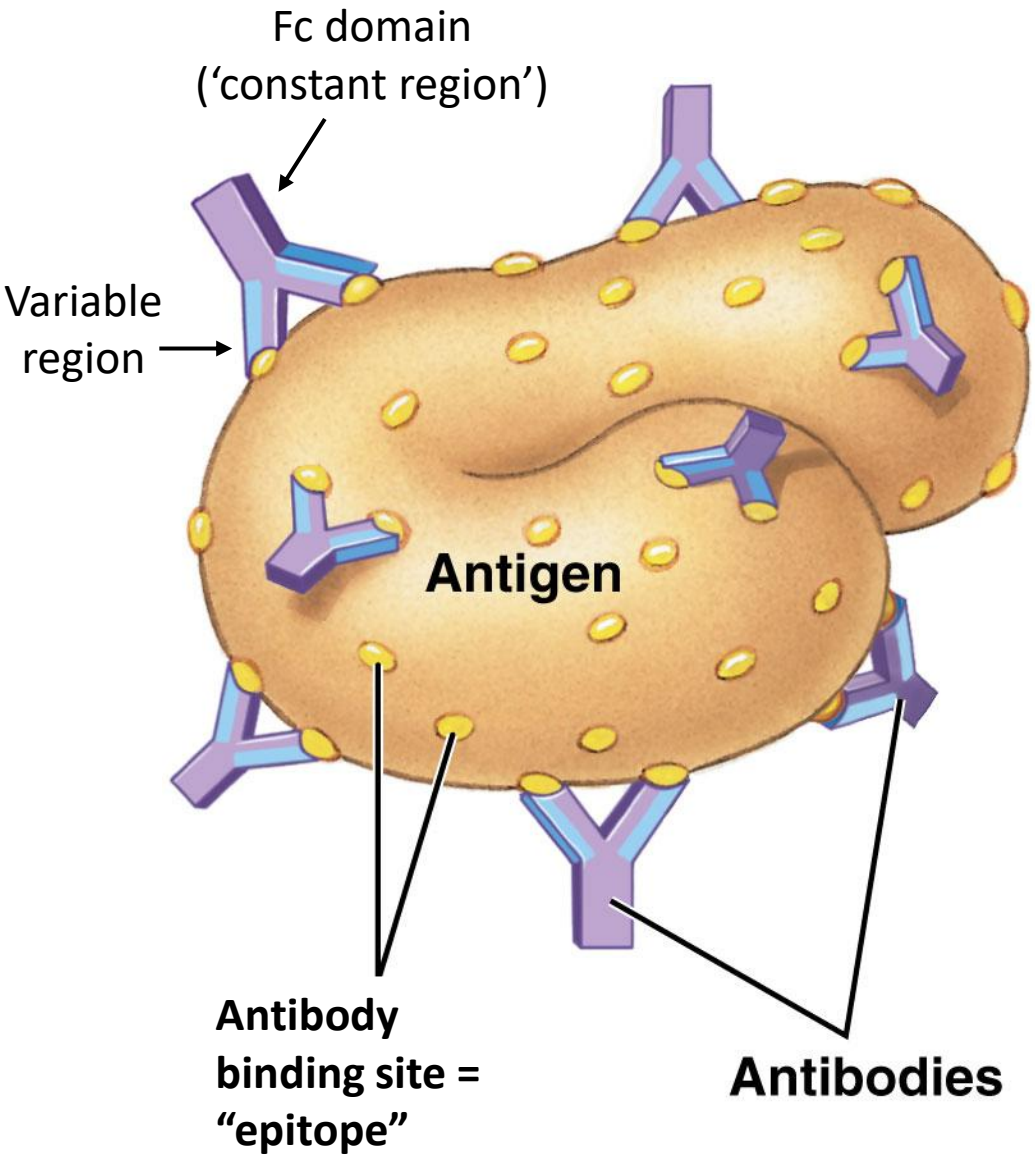
The ‘proteasome’ degrades cytoplasmic proteins to peptides.



MHC-II loading with peptide



Antibodies binding to defined regions (antibody binding sites) on a larger structure

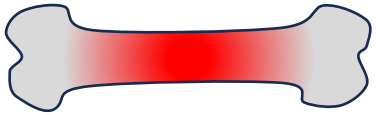


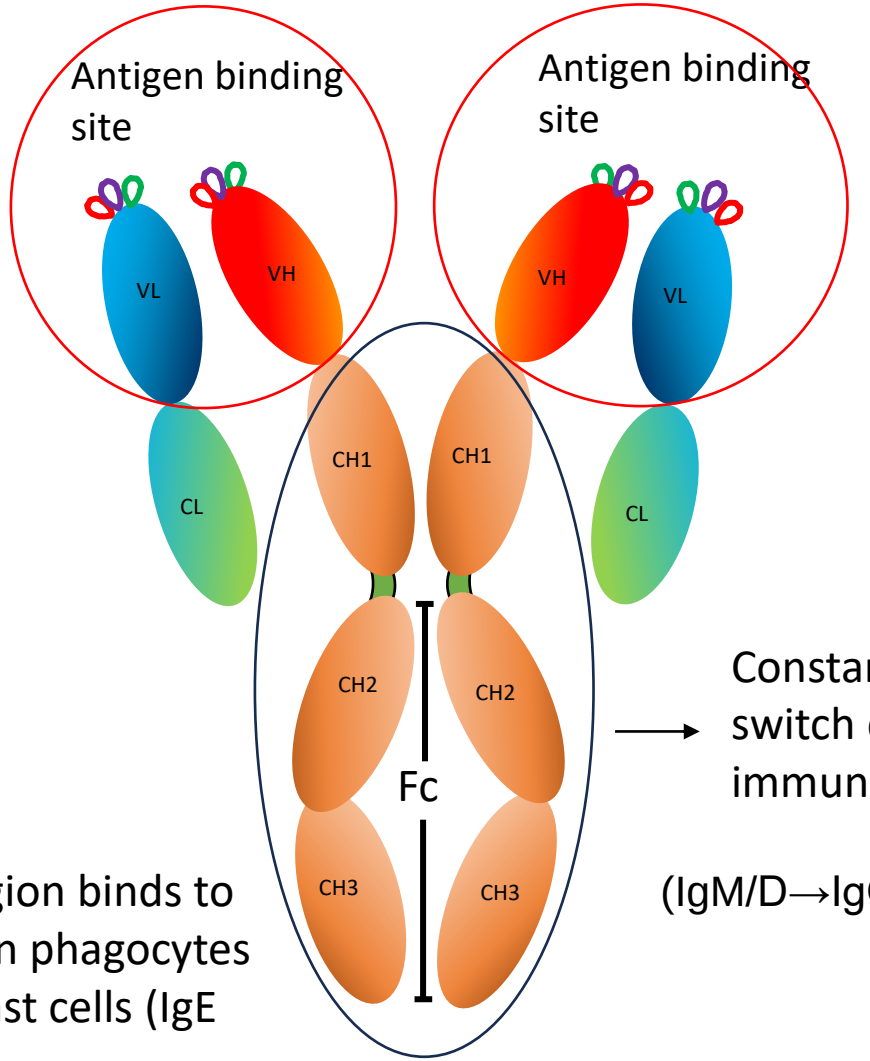
Antibodies bind native antigens. Several different antibodies may target a single type of microbe.

The term native antigen means that the antigen does not have to be processed to peptide (or in context of MHC).

Antibodies can recognise just about any structure!

Rearranged in bone marrow (during generation of diversity)





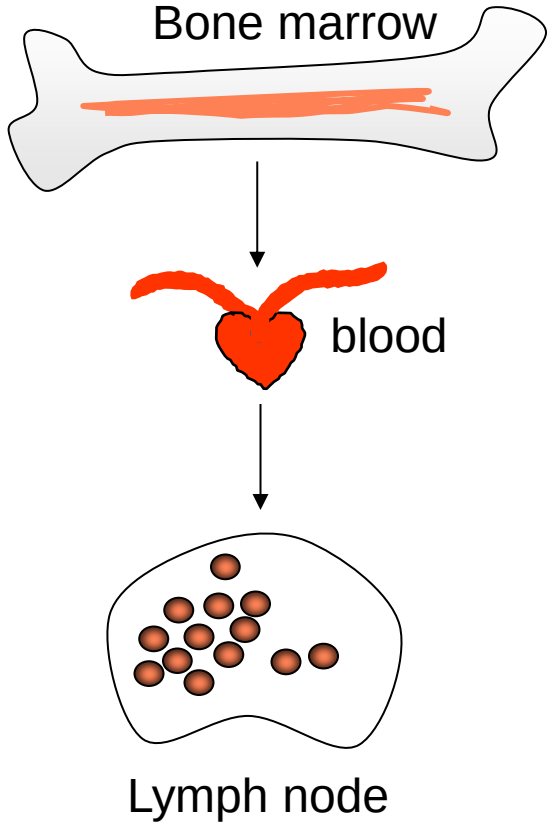
Constant region may switch during immune response.

(IgM/D→IgG→IgA→IgE)

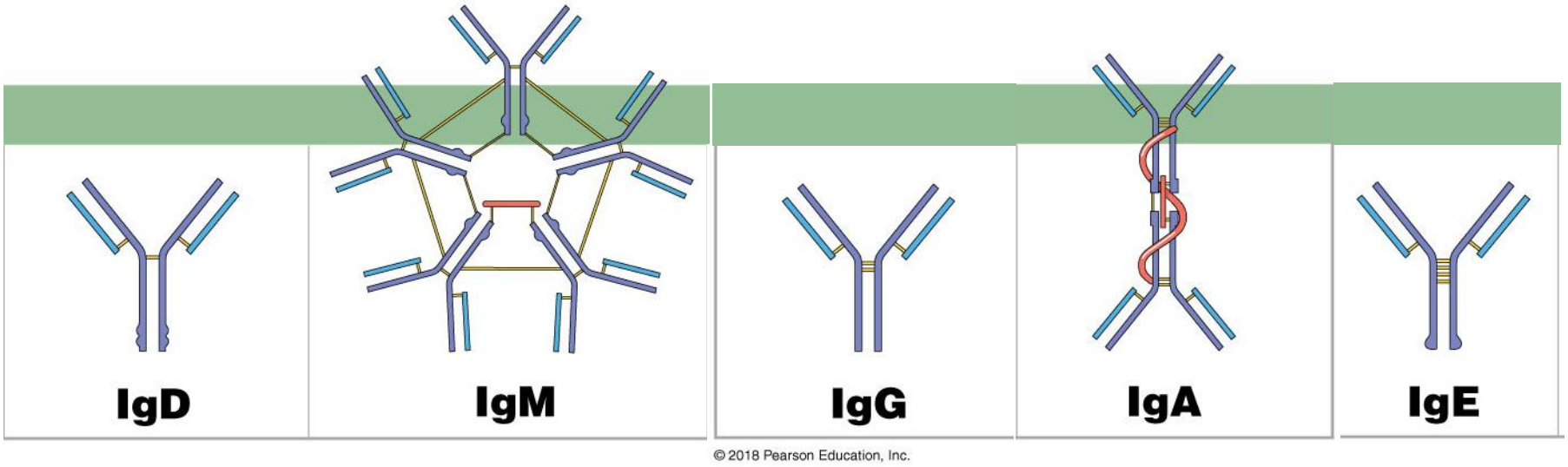
Fc region binds to FcR on phagocytes or mast cells (IgE only)

B cell receptor (BCR) gene rearrangement

Isotype switching (during immune response)



Isotypes of antibody: during the immune response, B cells can genetically the switch the heavy chain to change class (isotype). This does not change the antibody-specificity, but does change the function of the antibody.



IgD	IgM	IgG	IgA	IgE
Signalling Function Only	Classical activation Of complement	Crosses placenta / Neutralisation	Mucosal protection	Targets parasites / Allergic response

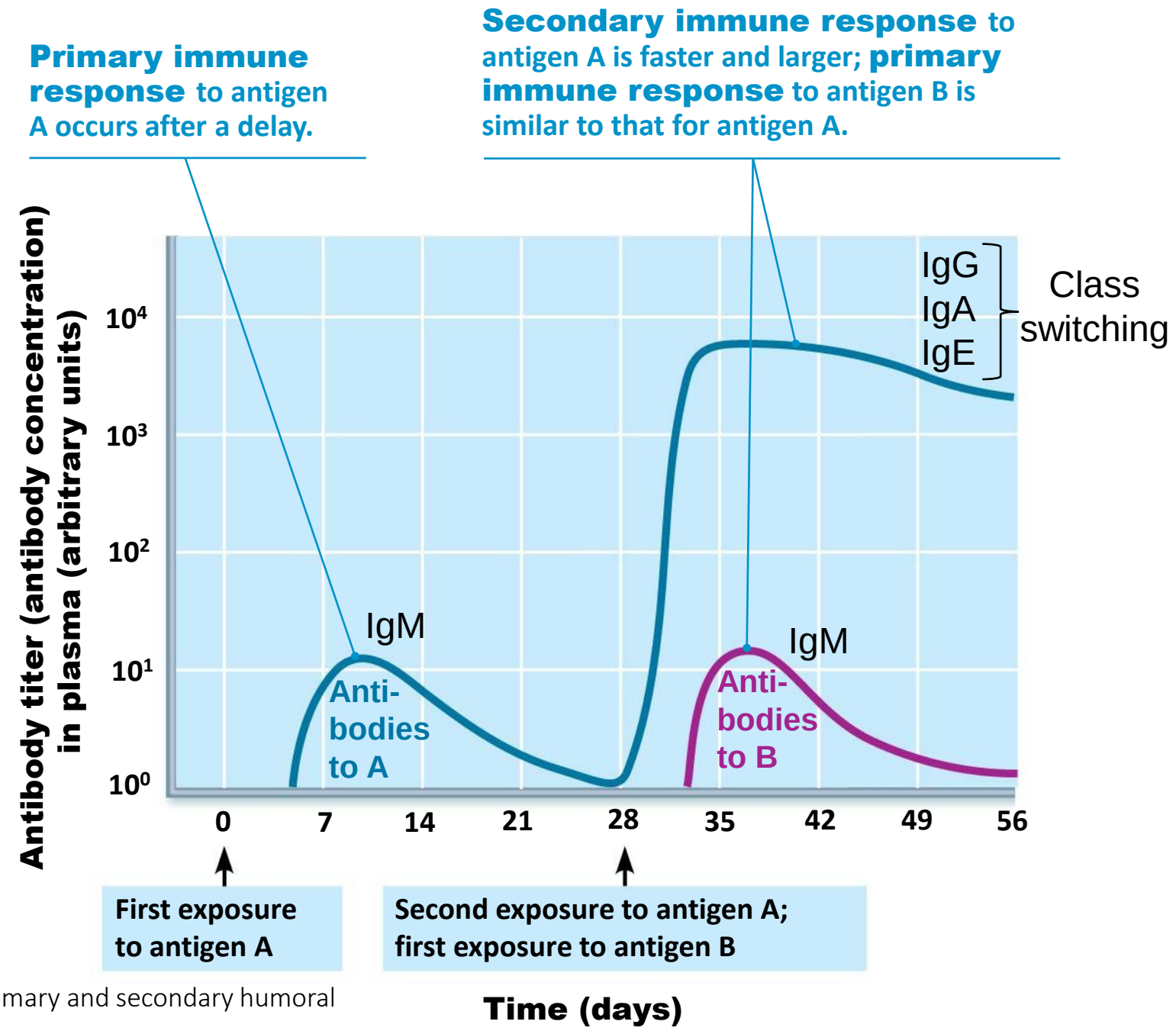


Figure 21.12 Primary and secondary humoral responses.

Primary vs. secondary immune response: Formation of antibody classes and lymphocyte differentiation state.

Antibodies

Class-switched antibodies

	IgM / IgD	IgG	IgA	IgE
Primary	+++	-/+	-/+	-/+
Secondary	+	+++	++	+

T and B lymphocytes

	Activated & Memory T cells	Activated & Memory B cells
Primary	+	+
Secondary	+++	+++

Vaccines save lives
Examples:

- Live attenuated: Mumps, Measles, Rubella, Polio-Sabin
- Killed: Polio-Salk, some SARS-CoV2 and some influenza vaccines
- Sub-unit protein: tetanus, SARS-CoV2
- Sub-unit mRNA: SARS-CoV2 (e.g. Pfizer or Moderna vaccine

‘Adjuvants’ usually required for sub-unit vaccines

- Adjuvants are immune stimulants added to vaccines that enhance the activation of antigen presenting cells (APC).

- For example, the mRNA SARS-2 vaccine is intrinsically adjuvanted: the lipid-encapsulated mRNA is immunostimulatory.

- RNA can stimulate Toll-like receptors (L33)

Where can microbiology and immunology take you?

Where do our graduates go?

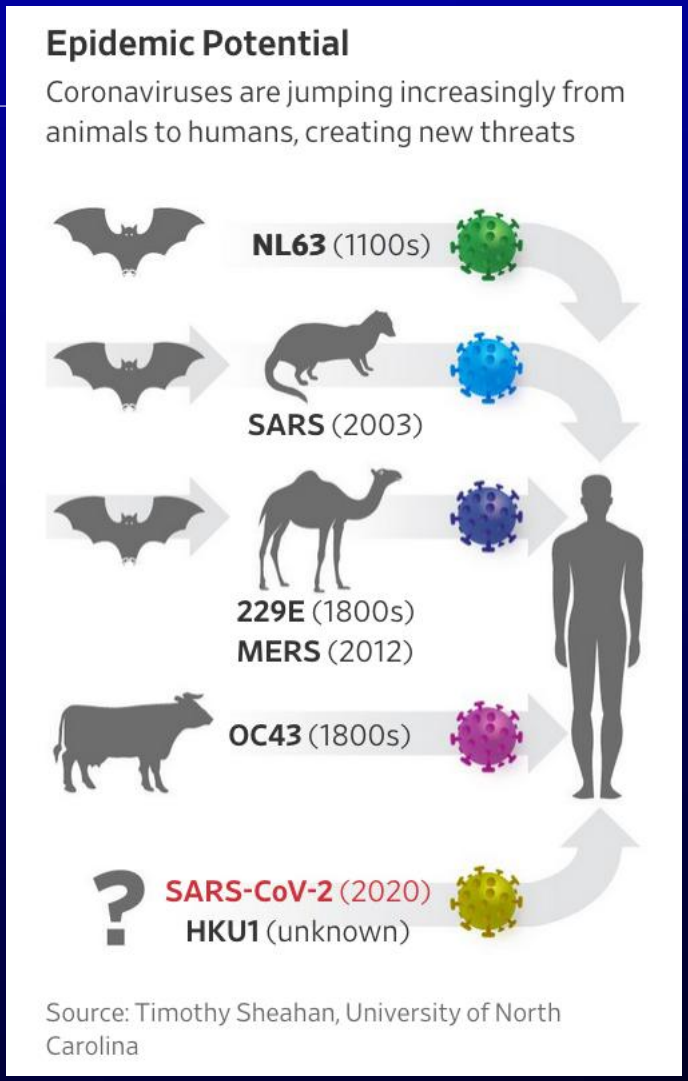
A modern-day explorer:
Prof Jemma Geoghegan

“Prime Ministers Emerging Scientist Prize & Prime Ministers Science communication Prize”

Where did the virus come from?

Horseshoe bat
Rhinolophus affinis

Malayan pangolin
(*Manis javanica*)



Where to start?

BSc Major in Microbiology at Otago

First year:

CELS 191 Cell and Molecular Biology

HUBS 191 Human Body Systems 1

CHEM 191 / 111: The Chemical Basis of Biology and Human Health

Second year:

MICR 221 Microbes to Medicine

MICR 223 Infection and Immunity

GENE 221 Microbial Genetics

Four required for major / two for minor:

MICR 332 Health Microbiology

MICR 334 Advanced Immunology

MICR 335 Molecular Microbiology

MICR 337 Virology

Plus an option for > B-average students:

MICR 360 Special Topics

Dr. Richard Webby (Microbiology & Immunology graduate).

Now: Director of *World Health Organisation Collaborating Centre on the Ecology of Influenza Virus.*

"In addition to the very social atmosphere of the Microbiology & Immunology dept., the training I received from the department is unequalled amongst my peers at St Jude and has put me in a great position to pursue a successful career in academic science."

https://www.stjude.org/directory/w/richard-webby.html

Clonal selection is the:

(A) selective expansion of lymphocytes able to recognise antigen.

(B) generation of diversity in the bone marrow and thymus

(C) Stimulation of cells with a single Toll-like receptor.

(D) the same as class switching / isotype switching

B cells progress to plasma cell and memory cell stage after:

(A) Receiving CD4 T cell help (cytokines) .

(B) Recognising antigen through their B cell receptor (BCR).

(C) Recognising antigen through their B cell receptor (BCR) AND after receiving CD4 T cell help (cytokines).

(D) Binding antigen-MHC-II presented by a dendritic cell.

In dendritic cells, viral antigens normally access which location/s:

A) the cytosol

B) the phagolysosome

C) The cytosol and the phagolysome

D) the nucleus

To progress to CTL, naive CD8 T cells require which signal/s:

A) recognition of MHC-I / peptide

B) help provided by CD4 T cells

C) recognition of MHC-I / peptide and help provided by CD4 T cells

D) apoptotic signals

CD8 CTL recognize virus infected cells (and cancer cells) via:

A) MHC-I / peptide

B) MHC-II / peptide

C) help provided by CD4 T cells

D) bound antibody or complement

Adjuvants:

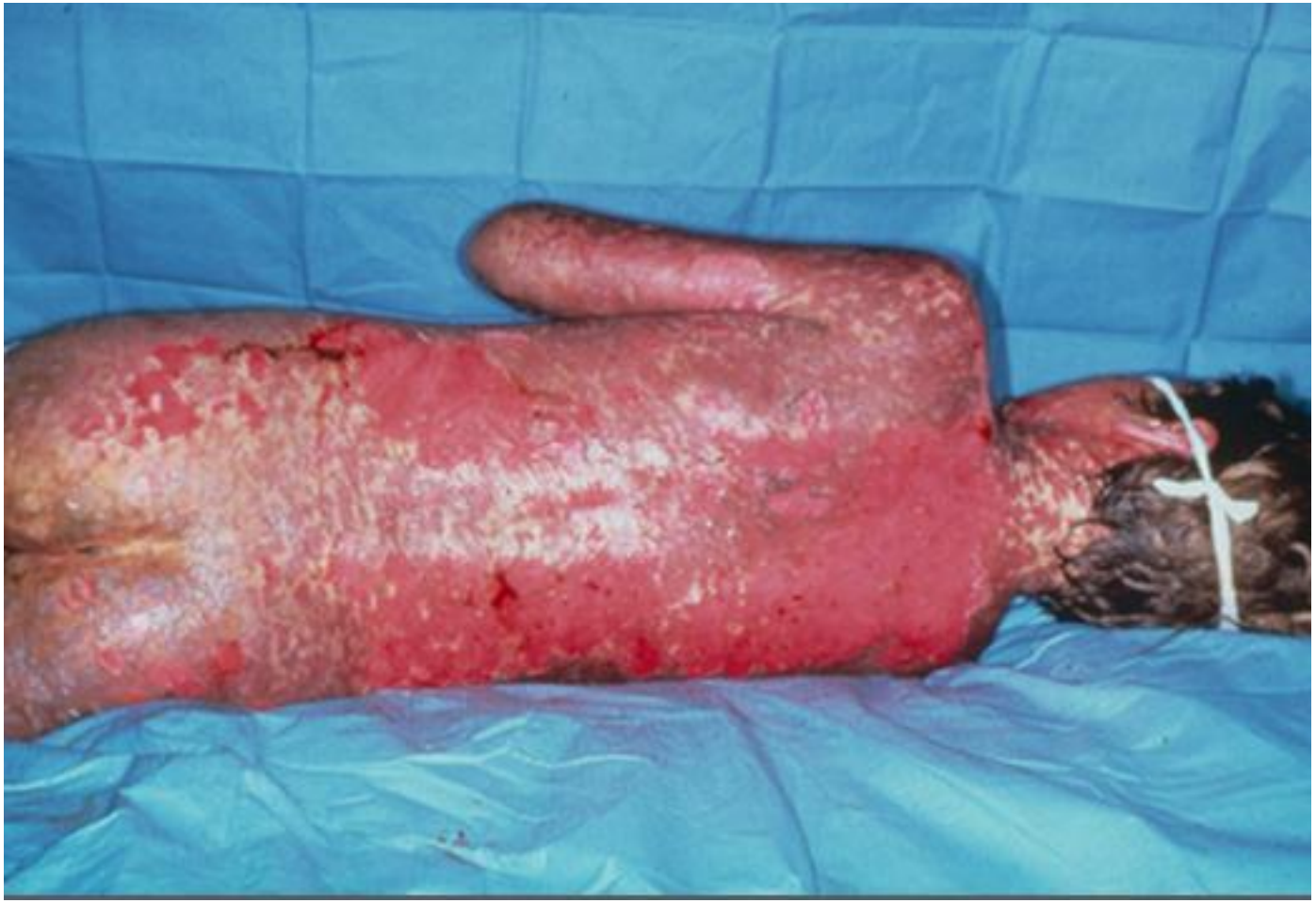
(A) Increase the stability of vaccines.

(B) Enhance the activation of antigen presenting cells

(C) are peptides that stimulate the T cell response

(D) Prevent auto-reaction of vaccines

A patient was administered penicillin for a minor skin infection. Two days later the same patient was admitted with a severe skin reaction.



http://reference.medscape.com/features/slideshow/allergic-reactions

What is your diagnosis?

(A) a widespread skin infection caused by penicillin resistant bacteria

(B) autoimmune reaction triggered by the infection

(C) A hypersensitivity reaction to penicillin mediated by IgE

(D) an immune deficiency reaction triggered by penicillin facilitated bacterial infection

Cytotoxic T lymphocytes (CTL) kill by releasing:

(A) the membrane attack complex

(B) granzyme and perforin

(C) C3b

(D) the T cell receptor

Vaccination would be successful in sea urchins (T / F)

Sharks possess essentially the same immune system* as mammals (T / F)

**T cells, B cells, MHC etc…*

HUBS191