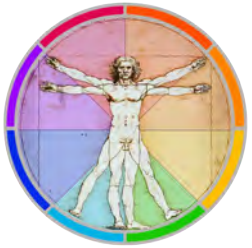
HUBS191 Lecture Material

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 37

L37: Insufficient or Overactive Immune Response

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Objectives to know that:

- Immune deficiencies can be inborn or induced by viruses (also by some medical treatments* or poor nutrition).
- The concept of tolerance to self-antigens. That Rheumatoid arthritis and type I diabetes are examples of immune cells attacking self cells (autoimmunity).
- The effector molecules (IgE) and cells (T cells, B cells and mast cells) involved in the allergic reaction.

e.g. *Chemotherapy / radiation therapy

Severe Combined Immunodeficiency (SCID)

- X-chromosome linked disease, therefore more common in XY-males. Note XX-females are ‘carriers’. Patients lack functional T cells and B cells.

Virus-induced immune suppression

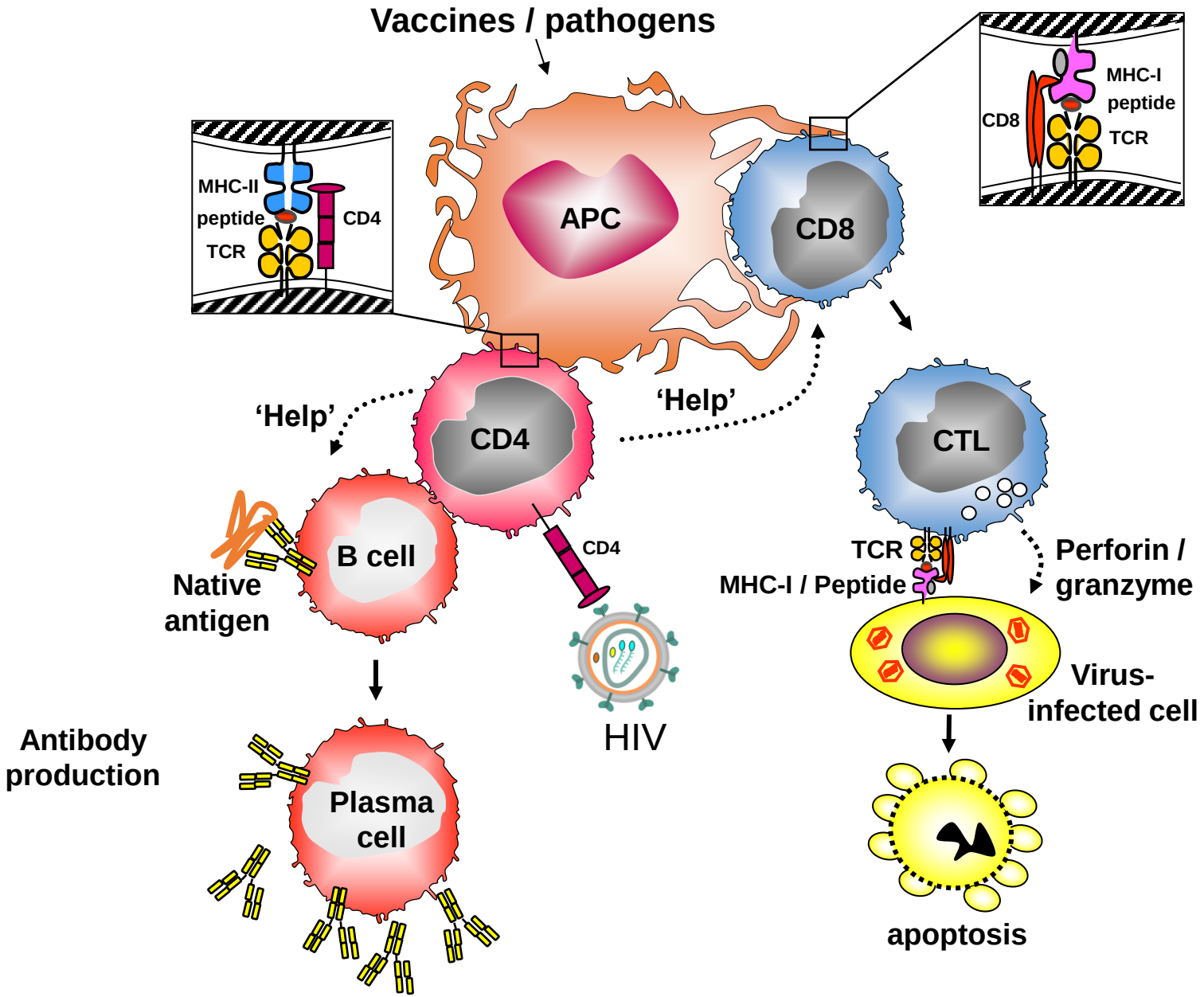
- Measles, HIV and many other viruses interfere with normal host immune system.

- HIV targets and can kill CD4 T cells.

- This leads to a diminished levels of CD4 T cells unable to provide “help” for antibody and cytotoxic responses.

Human immunodeficiency Virus (HIV)

- HIV-receptor is CD4 molecule on CD4 T cells
- Infection leads to loss of CD4 T cells
- CD4 T cells help both humoral (B cell / antibody) and cytotoxic responses,
- HIV infection impacts on immunity to microbes (fungi, bacterial and virus) and to cancer.


Vaccines / pathogens
MHC-II
peptide
TCR
CD4
APC
CD8
MHC-I
peptide
TCR
CD8
'Help'
'Help'
CD4
CTL
B cell
Native
antigen
CD4
HIV
TCR
MHC-I / Peptide
Perforin /
granzyme
Virus-
infected cell
Antibody
production
Plasma
cell
apoptosis

Autoimmune disease

- Normally prevented by host mechanisms of immune tolerance (next slide).

- Although the innate system can trigger autoimmunity or exacerbate (make worse) autoimmunity...

- Autoimmune attack is mediated by the adaptive immune response.

Immune tolerance

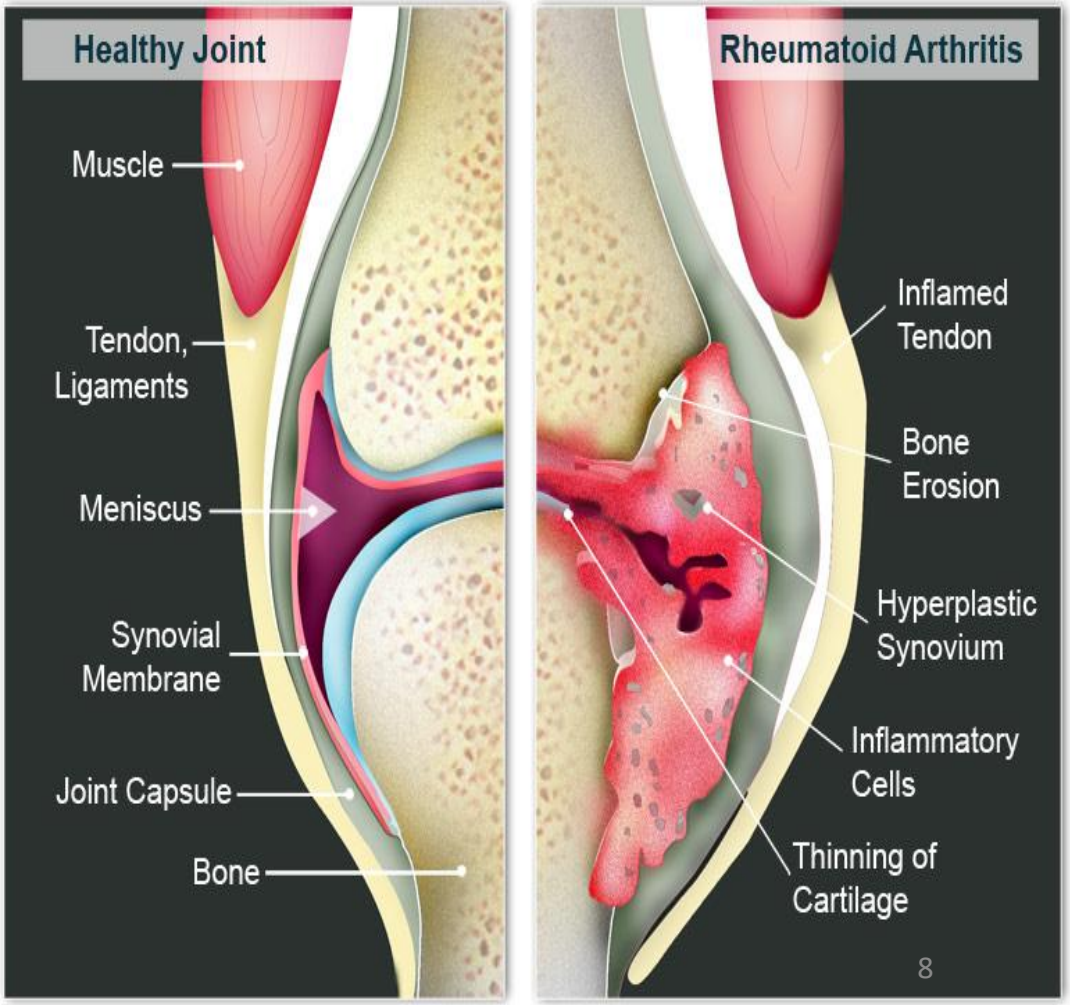
- Immune tolerance is critical to avoid autoimmunity.
- The thymus acts to delete autoreactive (self-reactive) T cells.
- In the periphery there are other mechanisms to ensure that autoreactive T and B cells are silenced.
- Failures (due to your genes or triggering infection) in immune tolerance can lead to autoimmunity.

Rheumatoid arthritis (RA) is a autoimmune disorder that primarily affects joints

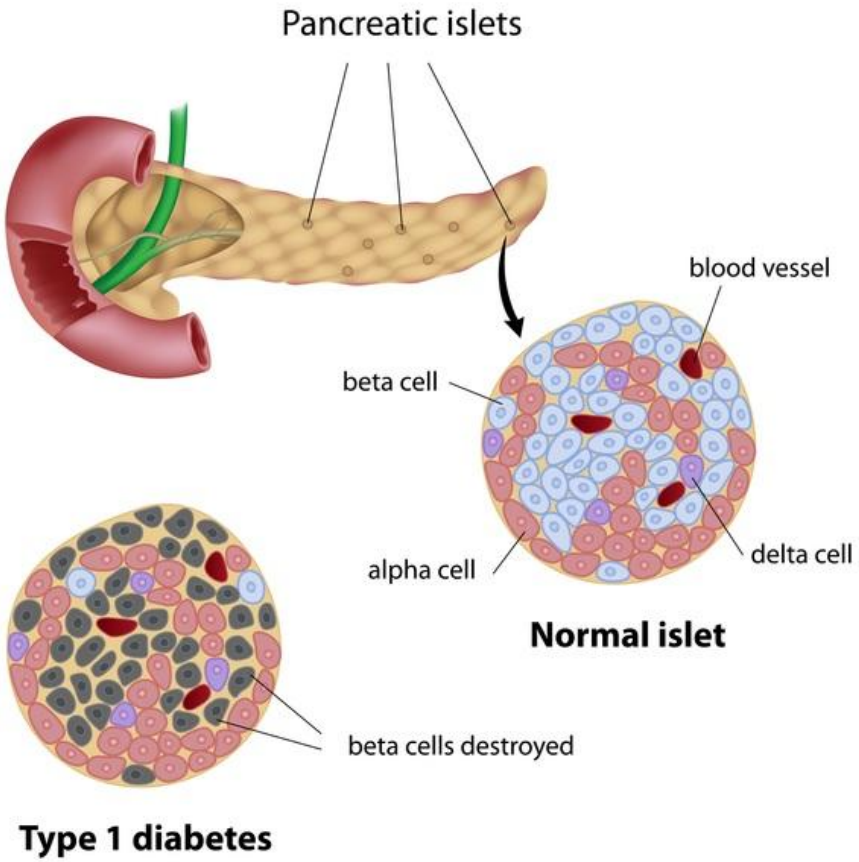
(an example of what happens when our immune cells attack self tissue)

Autoreactive T cells and B cells attack self-antigens present in the joints.

Affects ~1% of population. Often late onset in life.



Diabetes Type I:
Insulin beta-cells attacked. Other islet cells may escape autoimmune attack.



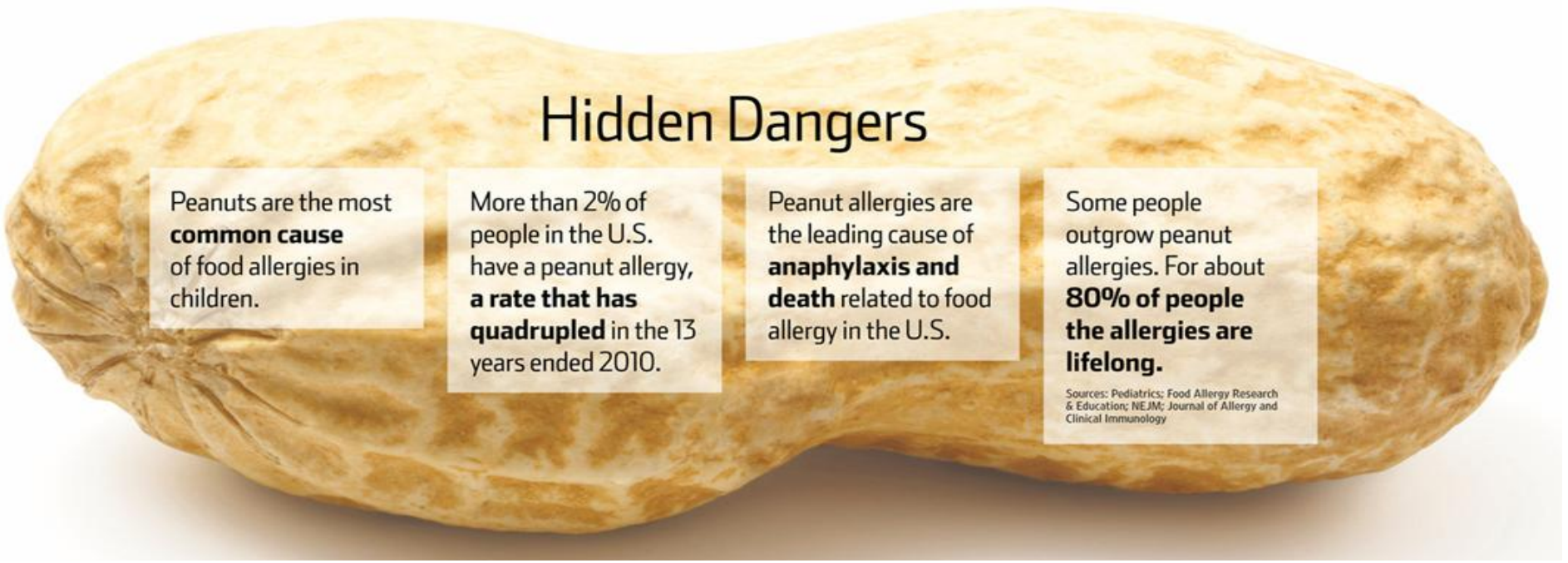
Allergic reactions

- ‘Allergens’ are the antigens that trigger allergy.
- Are normally ‘harmless’ environmental antigens: non-toxic plant, animal or other food materials.
- Chemicals can induce allergy (e.g. penicillin)
- Range of outcomes: from hay fever to systemic anaphylaxis

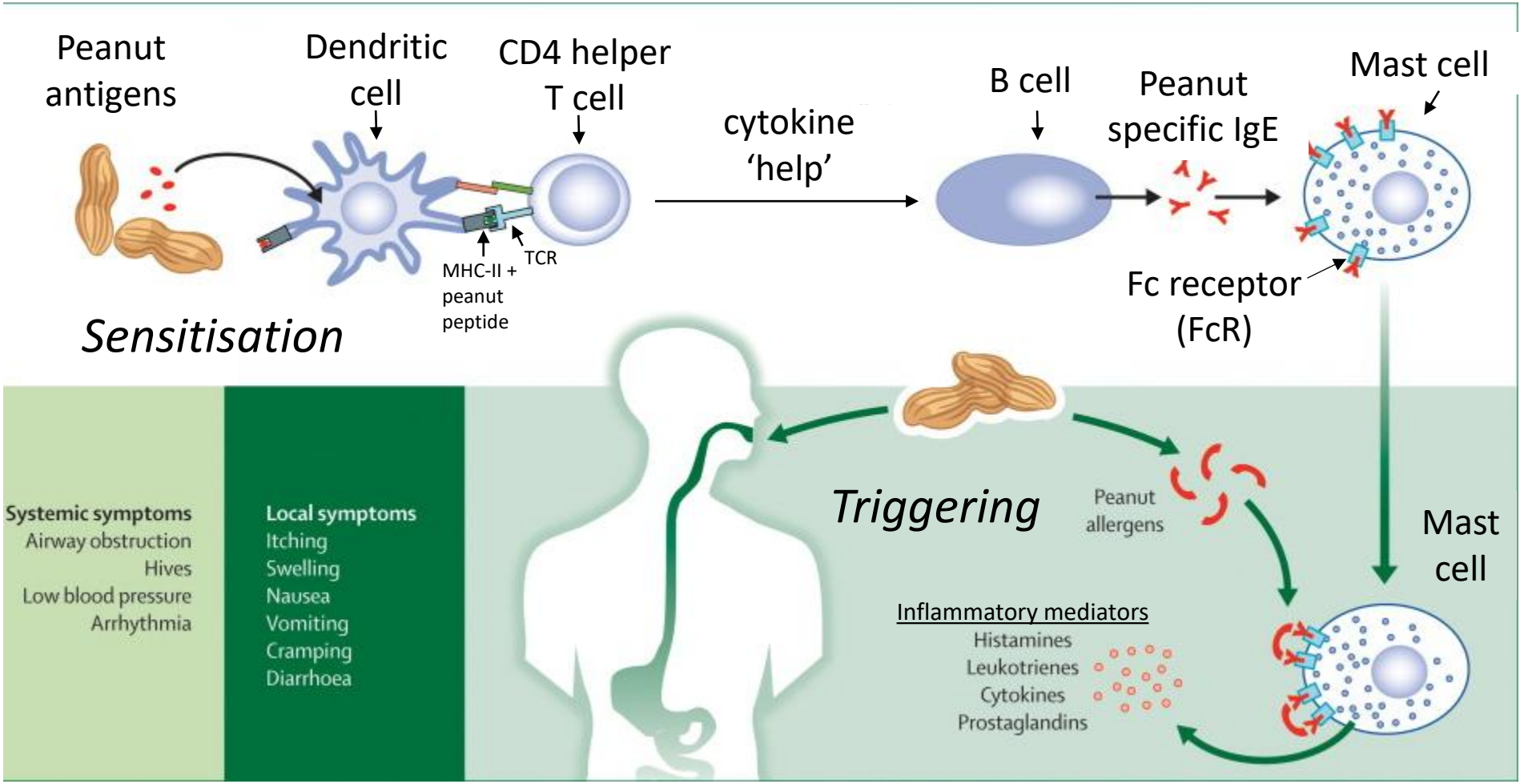
Allergic reactions: the effector response:

- DC present peptides from peanut proteins (allergens) to helper T cells
- Primed helper T cells activate B cells to secrete IgE
- Secreted IgE binds to mast cell receptors (FcR)
- Binding of peanut proteins to FcR on mast cells triggers mast cell degranulation and release of histamine and other inflammatory mediators

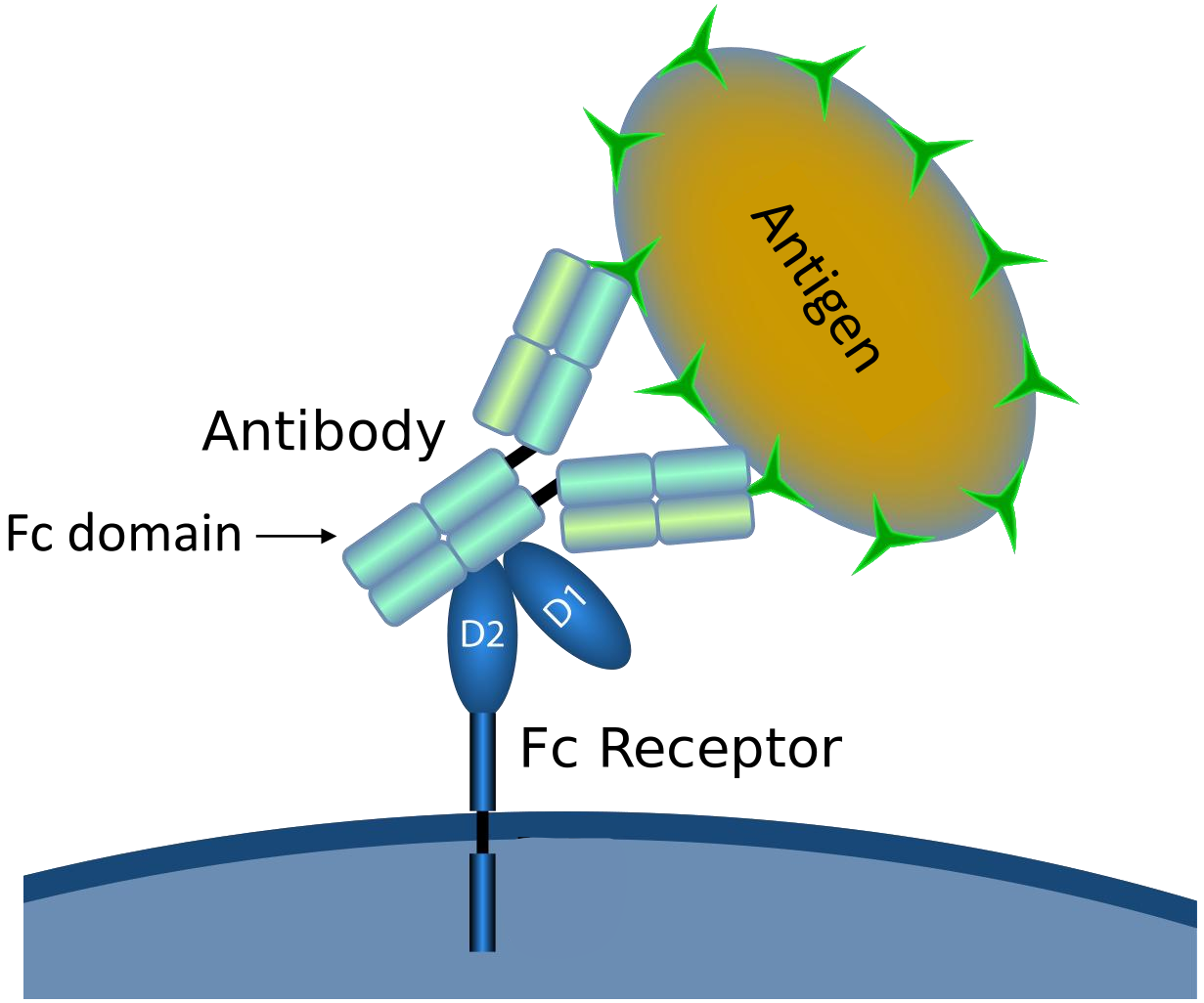
Peanut allergies



1. DC takes up peanut antigens and activates CD4 helper cell.
2. CD4 T cells provide help for B cells that form IgE secreting plasma cells.
3. IgE binds to Fc receptors on mast cells.
4. Peanut allergens trigger (via IgE / FcR) mast cells to release histamines and other inflammatory mediators.

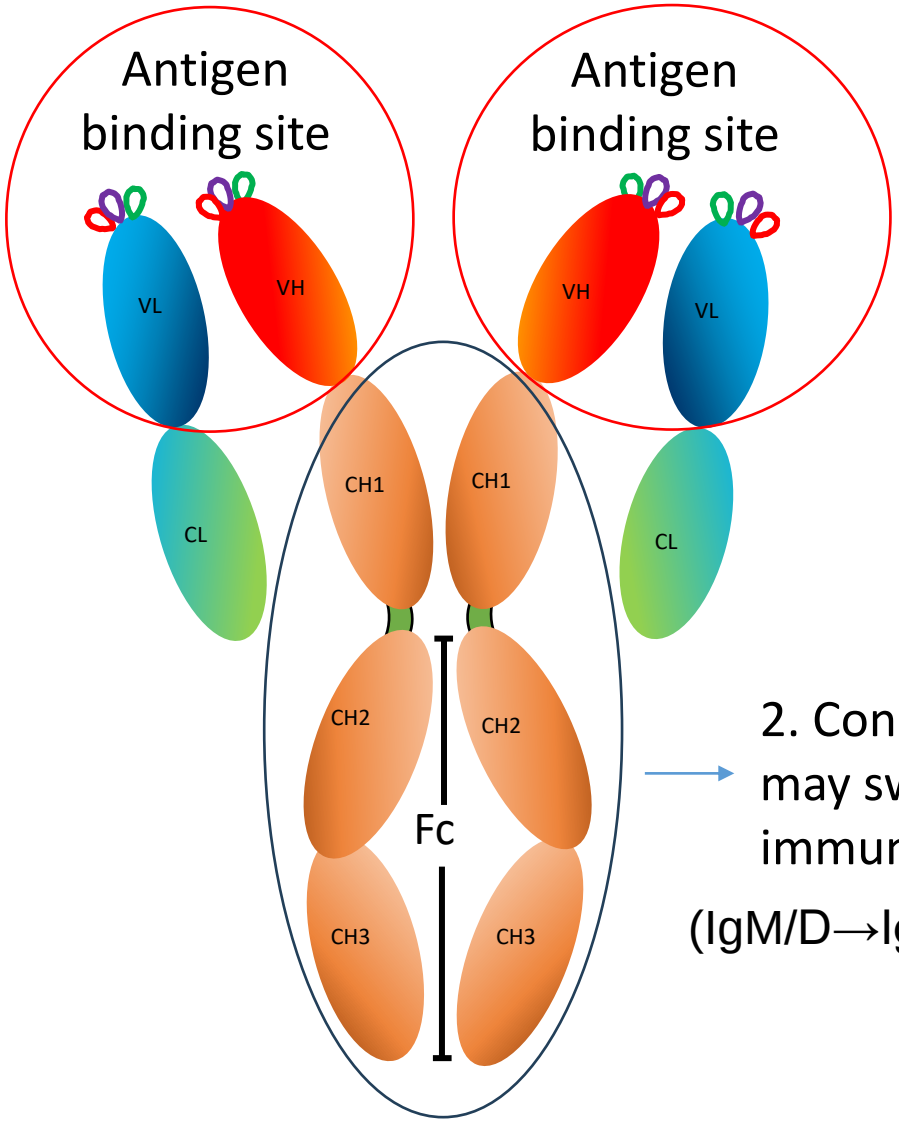


Fc receptors (FcR) bind to the Fc domain (on constant region) of antibody. FcR facilitate a number functions, including phagocytosis and mast cell activation (see previous slide).



Order of events for changes in antibody structure

1. Rearranged in bone marrow (during generation of diversity)



2. Constant region may switch during immune response.

(IgM/D→IgG→IgA→IgE)

HIV targets:

(A) CD2 positive cells

(B) CD4 positive cells

(C) CD8 positive cells

(D) CD16 positive cells

Severe combined immunodeficiency (SCID) results in a loss of:

(A) Neutrophils

(B) Dendritic cells

(C) Bone marrow stem cells

(D) T cells and B cells

Severe combined immunodeficiency (SCID) is:

(A) inborn / genetic / inherited

(B) caused by malnutrition and stress

(C) due to HIV or measles virus infection

(D) a possible cause of autoimmunity

Severe combined immunodeficiency (SCID) is more common in biological males because it is:

(A) an organ specific endocrine disorder

(B) a multi-organ metabolic disorder

(C) y-linked

(D) x-linked

Rheumatoid arthritis is a disease affecting primarily the:

(A) Kidneys

(B) Joints

(C) Pancreas

(D) Gut

Autoimmune disorders result from a breakdown of:

(A) Cytotoxic cell function

(B) Antibody production

(C) Immune tolerance

(D) Effector cell function

The following is true of the development of allergy:

(A) CD8 cytotoxic T cells are responsible for allergic inflammation

(B) T cells stimulate histamine release from mast cells

(C) Dendritic cells activate allergen-specific T cells

(D) Allergy is only induced by food substances

Diabetes Type I is due to destruction of islet:

(A) Alpha cells by B cells

(B) Beta cells by T cells

(C) Gamma cells by T cells

(D) Theta cells by T cells

Diabetes Type I results in a loss of production of:

(A) somatostatin

(B) somatotropin

(C) glucagon

(D) insulin

The percent of people in the US with peanut allergy is approximately:

(A) 0.002%

(B) 0.02%

(C) 0.2%

(D) 2%

Immune tolerance is critical to avoid autoimmunity. An example of immune tolerance is:

(A) Neutrophils dying to form becoming pus-cells

(B) Virus-infected cells being destroyed by cytotoxic T cells in the skin

(C) Autoreactive, immature T cells (thymocytes) being deleted in the thymus upon recognition of self-peptide in the context of MHC.

(D) B cells stimulated to produced antibodies reacting the synovial membranes

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