Immunology course / 2017

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LECTURES 1: an overview of the immune system

Definitions:

-Immunity is the protection against infection

***Immune system** is the cells and molecules responsible for defending the body against pathogens

*The immune system can be divided into: innate and specific immune systems

Innate immunity= فطري، أساسي = natural = native immunity = composed of cells and proteins always present to fight microbes, they act immediately in response to infections and it doesn't need previous sensitization

Innate immunity is composed of:

1. Epithelial barriers: skin, respiratory and gastrointestinal epithelium.. These prevent entry of microbes

2. Phagocytic leukocytes: macrophages and neutrophils

3. Natural killer cells

4. Complement system proteins

Innate immunity acts quickly and can act against any pathogen, If it's not enough , then the adaptive immune system is stimulated

Adaptive immunity = specific = acquired immunity. Adaptive immunity is normally silent (خلايا نائمة) and is activated when there an infections.

Composed of lymphocytes (B and T lymphocytes) and their products

Each B or T cell responds to a specific antigen. B cells recognize antigens by antibodies .T cell recognize antigens by receptors

What's an antigen? مستضد

So: the immune system recognizes antigens, what are antigens?

Antigen is a molecule that can induce an immune response. It can be peptides, polysaccharides or lipids. They have to be foreign to the body (non-self)

There are millions of antigens present on pathogens that can cause harm to our bodies. *Adaptive immunity is specific*. So each antigen is recognized by one B or T cell .This means we *need millions of receptor types* to recognize these antigens! Each receptor on a B or a T lymphocyte is encoded by a gene.

We don't have enough genes to encode for the estimated 100 million receptors needed on B cells alone!!! Human cells have 25000 genes only.

How to solve this mystery?

Susumu Tonegawa is a Japanese scientist who received the Noble Prize in 1987, for his discovery of the genetic mechanism that produces antibody diversity.

Antibody diversity means the ability of our B lymphocytes to produce huge number (100 million) of antibodies, which are structurally different, so each antibody recognizes one antigen in a lock and key manner

Note that DNA in each cell in our bodies is the same. However in B cells, as the cells mature *DNA changes so it can produce these different AB*

This means in each mature B cell there are some DNA differences that are responsible for the different AB produced

Antibody structure:

To understand how changes in DNA can cause this antibody diversity, let's first talk about the structure of antibodies.

Antibodies are made up of two pairs of two different proteins; Heavy chain Hc and the light chain Lc. Each immunoglobulin has two regions Fab and Fc region. The Fab region are the hands that bind the antigen, whereas the Fc is the tail that can bind to a phagocyte or other cells..

The specific structure of the Fc region gives the AB its class: IgG, IgM, IgA ,IgD, IgE (MAGED)

Mix and match 10,000 heavy chains with 10,000 heavy chain and we can get the needed 100 million antibody structured needed to fight all possible antigens.

Within the chromosomes encoding heavy chains there are multiple copies of DNA molecule (gene segments) called V,D,J,C segments. Each of these segments has several copies and each copy is slightly different : for example there are 40 different V , 25 different D and so on.

B cells mix and match these segments to create the desired diversity. This process is called modular design (see figure below) This is similar to creating countless numbers of proteins by mixing and matching 20 amino acids ,or to creating countless words by mixing the letters of the alphabet

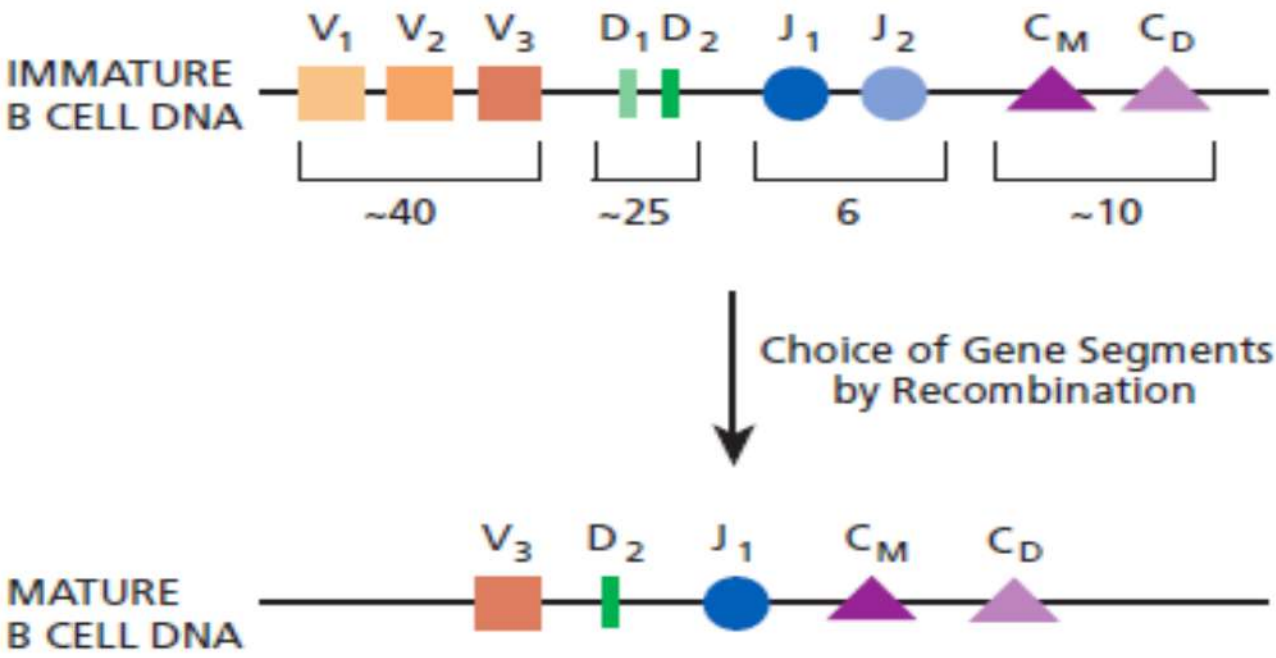
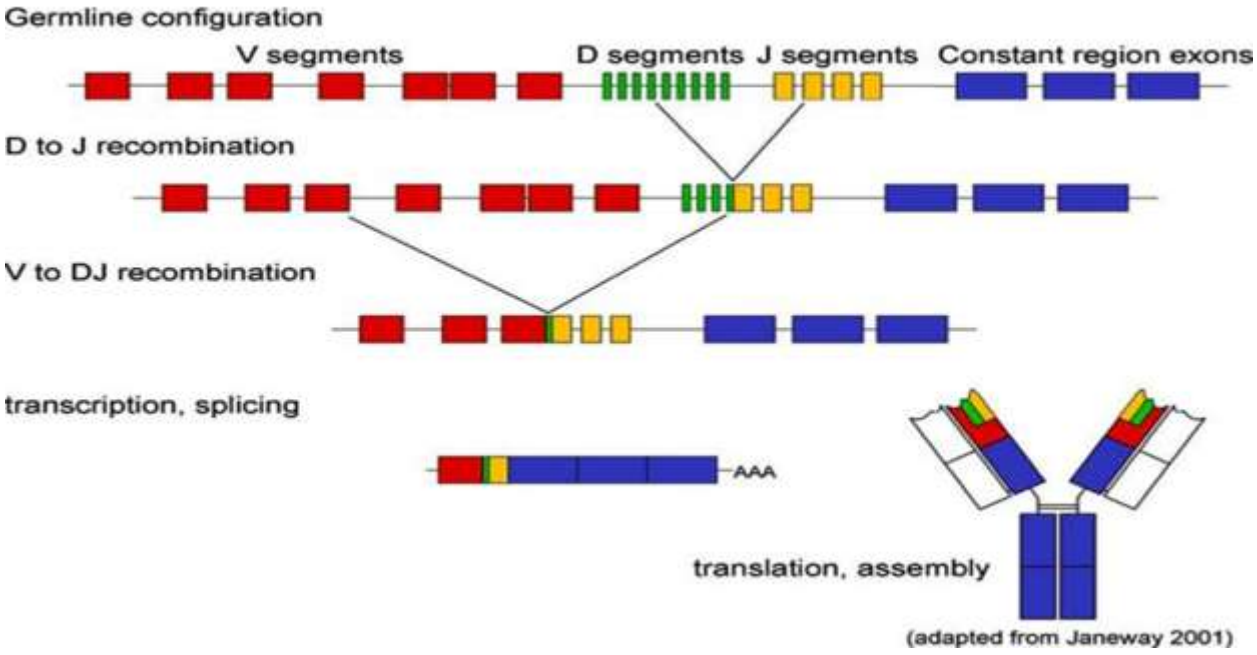
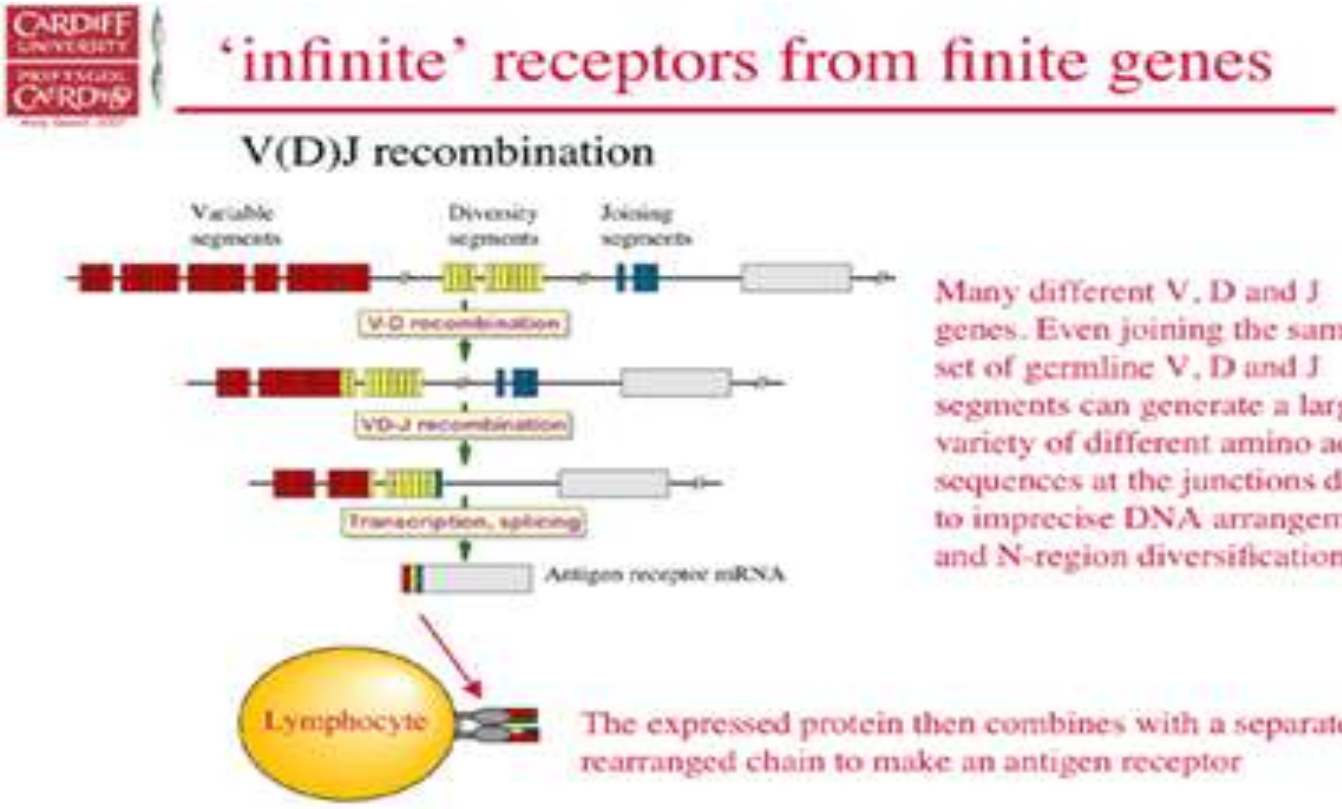


Figure 5: V(D)J Recombination





Ok: so we solved the antibody diversity issue. But note that we have 3 billion B cells in our blood. These produce 100 million AB type. This means there are **30 B cells per antigen**. If the body encounters an antigen, its army against this antigen is only 30 cells! This is not enough!

We need more and more cells of that clone that produces the specific antibody to the invading pathogen, this occurs through proliferation of this B cell able to produce this antibody. This process of proliferation is called: Clonal expansion.

CLONAL EXPANSION

The needed clone of cells is made on demand. After the mix and match process, a small amount of these modules(AB) are produced, expressed on the surface as B cell receptors These receptors fish (wait) for the cognate antigen(the specific antigen they will fight, the complementary one) .When they catch the antigen they divide and proliferate .They produce AB to the antigen. These antibodies go to the circulation .One B cell can produce 2000 AB per second! . **Note that B cells mature at this stage and become plasma cells. The plasma cells produce the AB**

So now we have loads of one B cell clone specific to the invader (the specific antigen)

When the battle ends, we don't need this clone. It will become a burden on the blood.. So they die by apoptosis

However, some of them survive and become memory cells.. So if the same antigen is encountered again they are ready and clonal proliferation can be quicker and more efficient.

HOW DO ANTIBODIES GET RID OF THE PATHOGEN

Antibodies don't kill. They tag the invader = opsonization = German word meaning prepare for eating. They tag by the fab region leaving the fc to be recognized by macrophages

PROBLEMS WITH ANTIBODIES:

If virus goes into cell cannot be stopped by antibodies and here come the function of T killer cells. We have 300 billion T cells. T cells have receptors TCR which have great diversity… same mechanisms like B cells

There are three types of T cells

1. Killer T cells :kill pathogens

2. Helper : secrete cytokines

3. Regulator: regulates the immune system so it does not over react.

Differences between B and T lymphocytes:

	B cells	T cells
Maturation site	Bone marrow	Thymus
Antigens recognized	Any organic molecule	proteins
Antigen recognition	Recognize directly	presented

Differences between innate and specific immunity:

Innate defends **non-specifically** and buys time for adaptive immune system to kick in if needed.

- Innate immune system decides which cells should respond, where, and when!
- The innate immune system rules!

SUMMARY

-Immune system defends us against pathogens

-It does so by the innate immunity first which acts quickly and is not specific

-Innate immunity includes: epithelial barriers, phagocytes and complement system

-If innate is unable to get rid of the pathogen , the specific immune system is activated

-Specific immunity includes B and T lymphocytes.

-B lymphocytes recognize any organic antigen by their receptors

-B cell receptors are antibodies present on the cell surface T cells recognize peptide antigens by their T cell receptors

-Both B and T need a huge diversity of their receptors in order to recognize all possible antigens

-This diversity is obtained by modular design where there is DNA recombination of the receptors' genes

-The needed clone to a certain antigen proliferates: clonal expansion

- Once recognized, the pathogens are eliminated by several mechanisms.

-Once the pathogen is eliminated the proliferated lymphocytes die by apoptosis

-Some cells survive as memory cells

SO: that was just a quick overview. Details of the processes mentioned here will be discussed in the coming lectures.