Activity 1 - How does the immune system work?

The immune system did not evolve to stop humans carrying out organ transplants.

Instead we evolved it over millions of years to stop us being invaded and attacked by a variety of prokaryotic and eukaryotic pathogens. Some pathogens are microscopic ('microbes') and some are not (loosely called 'parasites').

So how does the immune system detect kill these invaders? Well, at first this may seem like a relatively simple thing to do – just send in some cells to find foreign stuff and neutralise or eat it! The problem comes with the word 'foreign'.

Remember that the body itself has thousands of genes many of which encode proteins which the immune system must not attack.

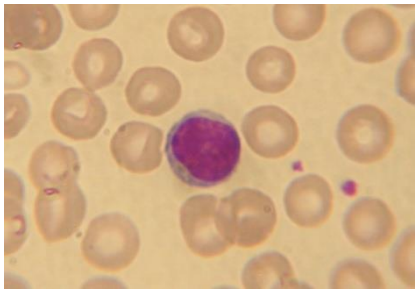
Sometimes your immune system does accidentally attack your own proteins, and the resulting illness is called an 'autoimmune disease':

http://www.healthline.com/health/autoimmune-disorders#Overview1

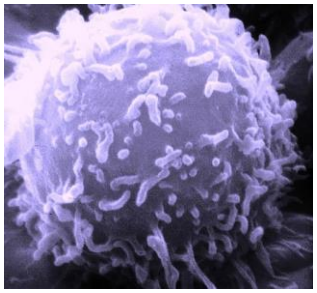
The central role of lymphocytes

Thus, distinguishing 'foreign' proteins from 'self' proteins is a major challenge of the immune system.

As you probably know, the central player in the acquired immune response (we'll briefly look at the 'innate' immune system later on) is a white blood cell: the lymphocyte. Lymphoctyes don't *look* very exciting through a light microscope, but they are slightly more interesting under scanning electron microscopy:



(Creative Commmons: https://en.wikipedia.org/wiki/Lymphocyte#/media/File:Lymphocyte2.jpg)



(Public domain: https://commons.wikimedia.org/wiki/File:SEM_Lymphocyte.jpg)

There are two main types of lymphocyte. All are made in the bone marrow, but while 'B-cells' mature there too, 'T-cells' migrate to an organ in the chest cavity called the 'thymus' where they mature.

*T-cells are named after the **T**hymus, but B-cells are not named after the **B**one marrow. Can you find out where the 'B' comes from? This is a veterinary, not a human medical question!*

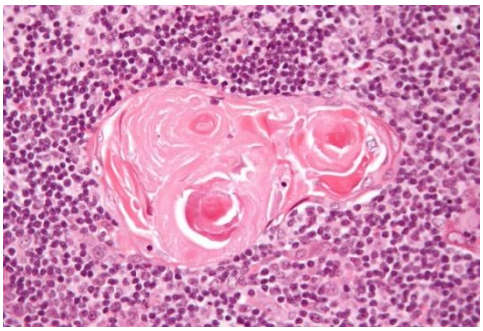
It is the T-lymphocytes which are the real key to the immune system.

Some of them (cytotoxic T-cells) will kill infected cells, but more important are the 'helper' T-cells because they coordinate the entire acquired immune system.

The vital job of the thymus

Considering most people don't even know the thymus exists, it is a staggeringly important organ.

As well as promoting the production and maturation of T-lymphocytes, the thymus also carefully 'educates' them. The thymus is made up of a strange mixture of tissues, expressing almost all the genes used anywhere in the body, and this explains its unusually messy, 'mixed' microscopic appearance:



(Creative Commons: https://en.wikipedia.org/wiki/Thymus#/media/File:Thymic_corpuscle.jpg)

The clever thing about the thymus is that any T-lymphocyte which recognises any of the proteins present in the thymus is *destroyed*. The effect of this is that any T-cell which might potentially attack the host's own cells is killed before it can ever become mature.

Thus, the only T-cells which escape the thymus to enter the blood and body tissues are the 'safe' ones, which do not recognise and attack the body's own tissues.

In other words, mature T-cells are the ultimate arbiters of what antigens are 'self', and mature T-cells should only attack foreign proteins – such as those made by pathogens.

Here are two articles about the elegant process of thymic 'education'. (Be aware when you read around this topic on the internet, that many sources state that the thymus regresses and has no further function in adulthood. This is wrong – it gets smaller, but it never stops working.)

http://study.com/academy/lesson/thymus-definition-functions-location.html

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1393761/

The thymus has in the past even been suggested to be more important than that:

http://www.nytimes.com/1982/01/26/science/mysterious-thymus-gland-may-hold-the-key-to-aging.html?pagewanted=all

A bit of trivia – can you find out where does the thymus get its name from? This is a botany question!

Another bit of trivia – veterinary this time. People sometimes eat animal thymuses. Can you find out what a butcher calls the thymus? Have you ever eaten it?

So how are immune responses initiated?

Once T-cells have left the thymus, they are ready to detect foreign molecules ('antigens') – usually proteins – and use them as a signpost which directs them to attack 'foreign' invaders.

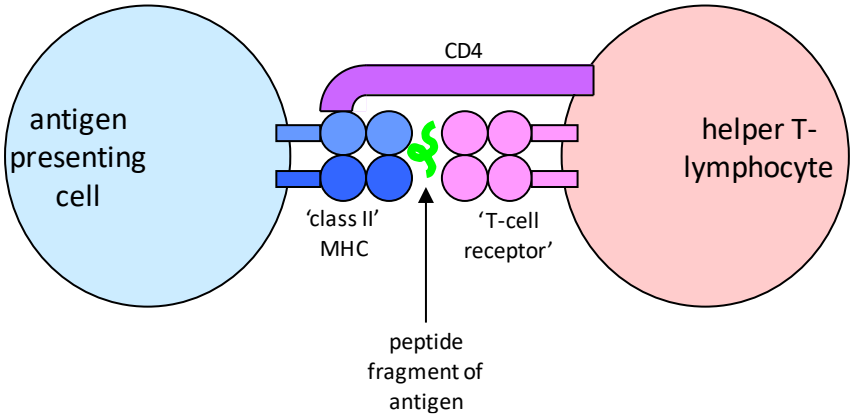
https://www.britannica.com/science/antigen

Of course, many T-cells will never encounter the antigens they are specifically programmed to detect, so they just sit there, in animals' lymph nodes, throughout life. However, just a few *will* detect their target antigen, and then they trigger an immune response…

'Helper' T-cells are at the core of this process, and without them the acquired immune response cannot take place.

They take part in one of the major inter-cellular interactions in the immune system – when specialised 'antigen presenting cells' (for example, macrophages) chop up foreign proteins into small peptides and 'serve them up' for helper T-cells to identify.

They are 'served up' on special presenting molecules called 'MHC' (you'll find out why in another resource), and another special molecule, rather boringly called 'CD4', makes sure the helper T-cell is bound to the correct MHC molecule.

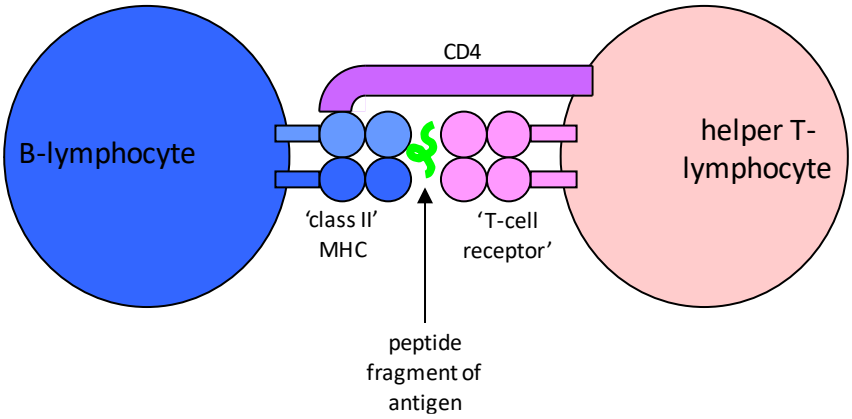


This may all look a bit complicated, but this cellular interaction is key to the power and specificity of the immune response.

Any helper T-cell activated in this way releases a barrage of chemicals which stimulates the proliferation and activity of almost every cell in the entire immune system – including itself!

So how does the acquired immune response destroy invading pathogens?

For example, the cell presenting the antigen may itself be a B-lymphocyte…

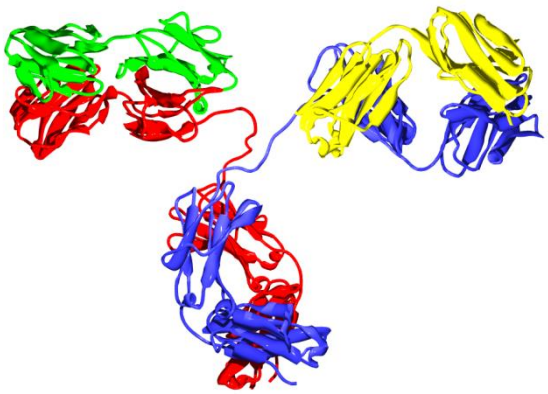


…and any B-cell stimulated in this way by a helper T-cell will proliferate, and its millions of descendants make antibodies.

Antibodies are large Y-shaped protein molecules (see below) which stick on to pathogens' proteins – either stopping them from working, or allowing other immune cells to find, attack or ingest them.

This antibody-based attack is called the 'humoral' acquired immune response.

http://biology.about.com/od/molecularbiology/ss/antibodies.htm



(public domain: https://en.wikipedia.org/wiki/Antibody#/media/File:Antibody_IgG2.png)

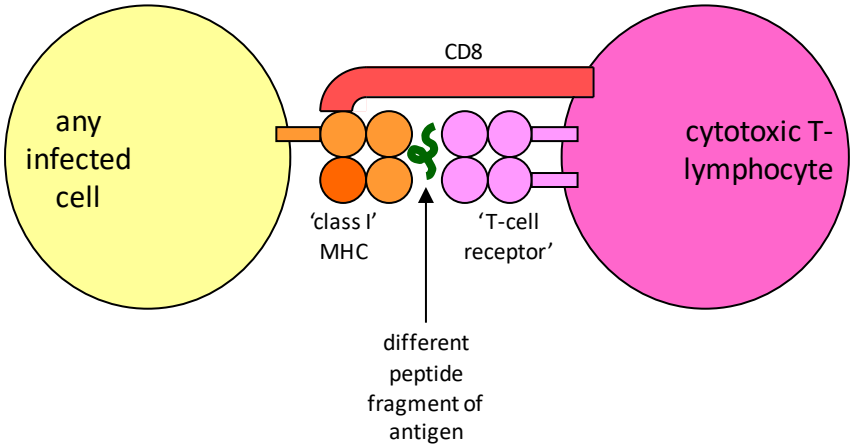
Alternatively, activated helper T-cells can also stimulate the proliferation of cytotoxic T-cells.

However to be fully activated, cytotoxic T-cells also undergo an inter-cellular interaction similar to the one which triggered the helper T-cells in the first place.

There is one major difference – almost all cells carry the ‘class I’ MHC molecules which can ‘serve up’ antigen fragments to cytotoxic T-cells (only certain cell types carry the ‘class II MHC’ which activates helper T-cells).

This gives cytotoxic T-cells the ability to kill just about *any* cell infected with the pathogen.

This attack process is the ‘cellular’ acquired immune response.



This attack process is the ‘cellular’ acquired immune response, and cytotoxic T-cells have several nasty ways to kill infected cells:

http://www.ncbi.nlm.nih.gov/books/NBK27101/

What about the 'innate' immune response?

This resource has mainly been about the acquired immune response – the systems which allows the body to respond to *any* foreign antigens, regardless of whether the individual, or even any member of its species, has ever encountered that pathogen before.

There is also an innate immune response. This is also extremely important, and works much faster, but it is much more limited. It is a set of varied, but unchanging responses to a limited set of antigens which animal species have evolved to recognise in the past.

Because any individual's innate immune system is 'pre-programmed' at birth and doesn't adapt to new antigens as life goes on, it is probably less important in the story of the immunology of pregnancy.

https://www.merckmanuals.com/home/immune-disorders/biology-of-the-immune-system/innate-immunity