2.1.4

# Humoral Immunity

Watch the video Adaptive Immunity Part 1 - Humoral Immunity

**Humoral immunity** refers to the production of antibodies, which are proteins that bind antigens and play an important role in fighting infections. Humoral immunity is the first branch of the adaptive immunity that we will go into. Adaptive immunity is split into the primary immune response and the secondary immune response. The primary immune response occurs when an antigen comes in contact with the immune system for the first time. The level of antibodies produced in reaction to this antigen reaches its peak in about 7-10 days. The secondary immune response occurs when you are exposed to the same antigen any time after the first exposure to the same antigen. This secondary response is much faster with the level of antibodies reaching its peak in 3-5 days.

How are antibodies against a specific antigen produced? First, an antigen must be exposed to an antigen presenting cell. The APC will phagocytose the antigen, degrade it into peptides, and express a fragment of the antigen on an MHC-II molecule. The APC will then travel to lymphatic tissue where it comes in contact with many T-cells. The APC then presents the antigen to naïve helper T-cells, which are T-cells that have differentiated in the thymus and undergone positive and negative selection but have not yet encountered a matching antigen in the periphery. One of the naïve helper T-cells will have a T-cell receptor that matches the antigen on the MHC-II. The T-cell will then bind to the MHC-II of the APC with its TCR. This bond is strengthened by co-receptors. CD4 is an important co-receptor found on helper T-cells while CD8 is a co-receptor found on cytotoxic T-cells. CD stands for “cluster of differentiation.” CD4 binds the MHC-II of the antigen presenting cell to the helper T-cell. Another cluster of differentiation that makes this binding possible is CD28 from the helper T-cell binding to the co-stimulatory molecule, B7, on the antigen presenting cell. After the binding of these receptors, co-receptors and co-stimulatory signals, the helper T-cell expresses cytokine receptors on its surface. The helper T-cell will then produce cytokines that bind to these receptors and cause an autocrine activation that brings about the proliferation of the helper T-cell. Now we have a helper T-cell that has encountered an antigen, been activated, and is proliferating.

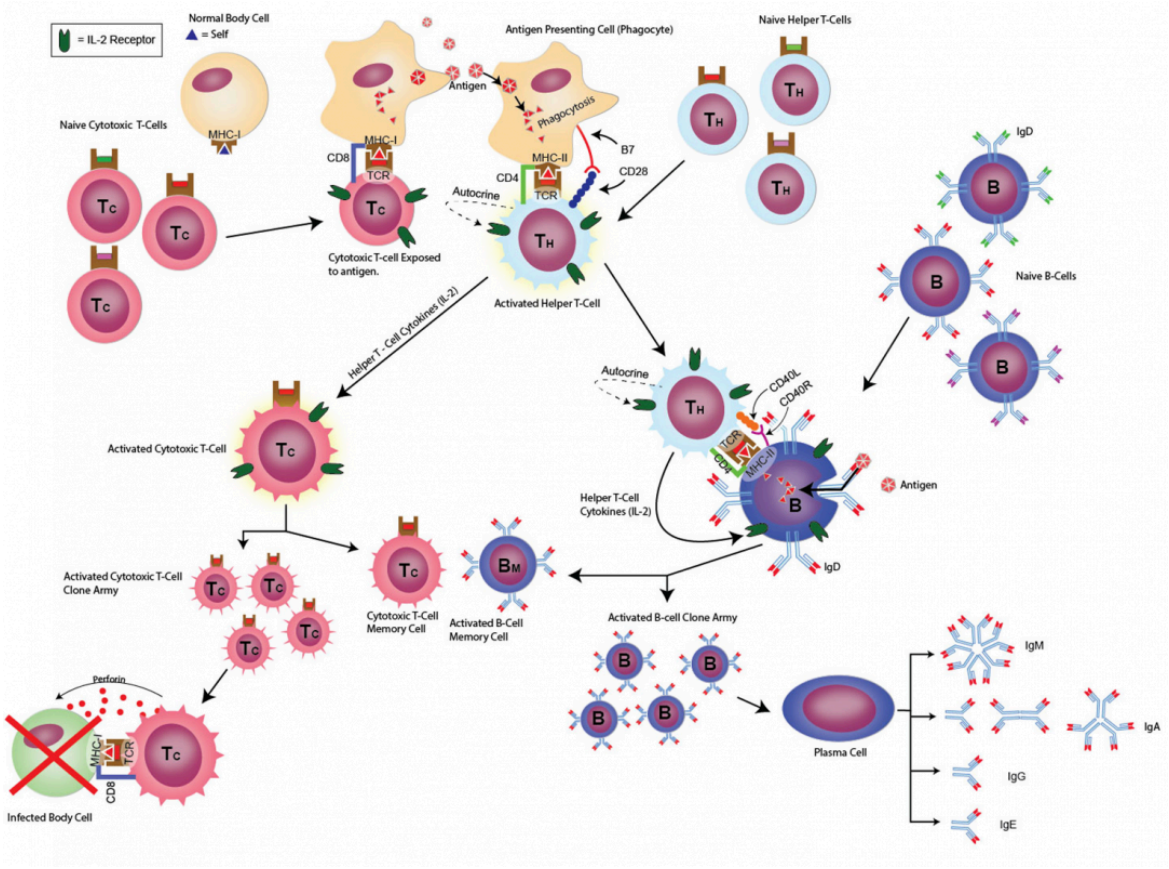
The activation of naïve B-cells is as follows. Naïve B-cells in the lymph nodes express IgD antibodies that serve as the B-cell receptor (BCR). In the first signal of activation, the BCR recognizes a particular antigen and uses receptor mediated endocytosis to bring it into the cell. Once inside the cell, the antigen is broken down into fragments and expressed on MHC-II molecules on the surface of the B-cell. The B-cell gets its second signal for activation from one of the proliferated helper T-cells that we discussed previously. The TCR of the helper T-cell will bind to the MHC-II molecule on the B-cell. This bond will be made stronger by CD4 and CD40L of the helper T-cell. After these bindings, the B-cell will express cytokine receptors for cytokines like IL-4, IL-5 and TGF-beta on its surface. The helper T-cells produce these cytokines and complete the activation of the B-cell. The activated B-cell then proliferates to form a clone army of identical activated B-cells. Some of these cells will become activated memory B-cells. If the body is exposed to this same antigen again, they will become plasma cells for antibody production.

Plasma cells are capable of making five different types of antibodies: **IgD, IgM, IgA, IgG** and **IgE**.

IgD is generally bound to the B-cell plasma membrane, although a small amount can be secreted into the plasma. IgD starts to be expressed as soon as a naïve B-cell leaves the bone marrow. It acts as a BCR to recognize antigens and

helps activate the B-cell. There is not a lot known about what IgD does as a unique and important function in the plasma. For this class, we will try to simply recall that IgD acts as a BCR in early (naïve) B-cells. After a B-cell is activated, IgM is also expressed which can bind to the cell membrane or be secreted. IgM is the first antibody to be produced by an activated B-cell. IgM is responsible for transfusion reactions in the ABO blood system.

Plasma cells will generally undergo an isotypes switch (meaning to switch to a different type of antibody production) depending on the cytokines that are being produced by the antigen presenting cells of any tissue and also the cytokines being secreted by specific types of T-helper cells. Isotype switching causes plasma cells to start producing IgA, IgG, or IgE. IgA is secreted from mucosal epithelia into tears, saliva, and mucous membranes of the lungs to combat microbes in the eyes, gastrointestinal tract, and respiratory tract. It is also found in breast milk and provides passive natural immunity benefits to an infant. IgG has the highest concentration of all the antibodies in the plasma and can cross the placenta to provide immune protection to the fetus and newborn until the antibodies degenerate after birth. IgE combats parasites and binds to mast cells and basophils to stimulate the inflammatory response. IgE is the major antibody in allergies.




**Adaptive Immune System Activation**

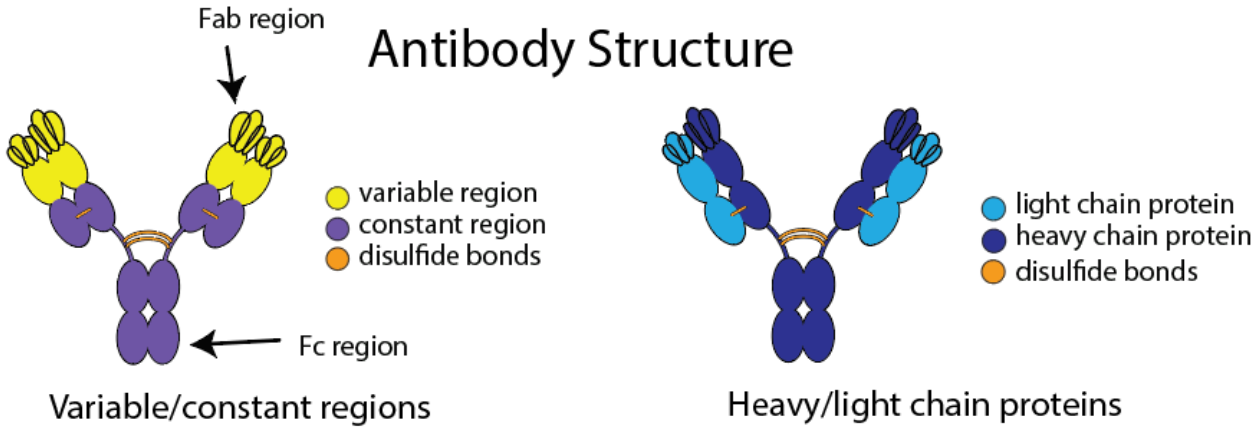
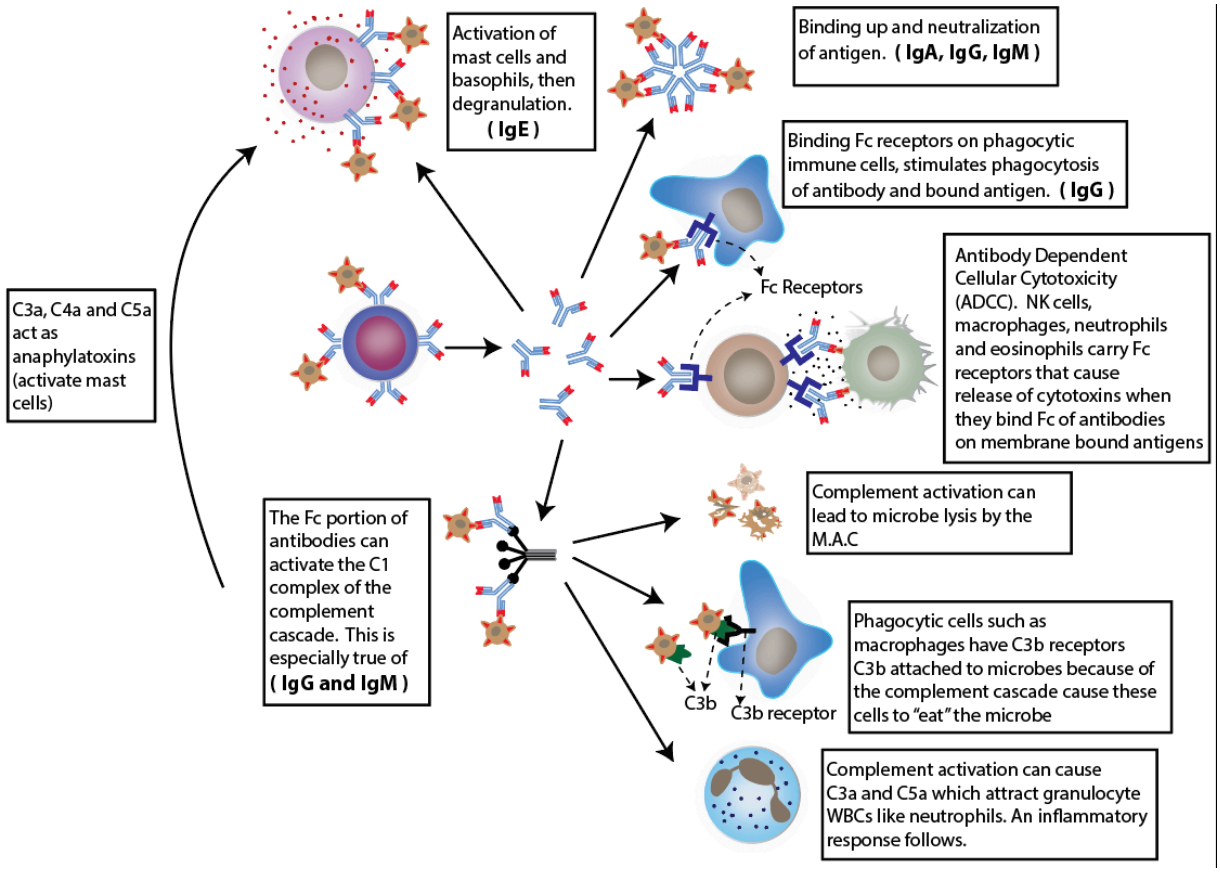



*Image by Mackenzie Call BYU-I W20*

Antibodies are made of protein chains bound together by disulfide bonds. There are two identical heavy chains and two identical light chains in an antibody. Functionally, the antibody can be split into two parts: the Fab and Fc regions. The Fab region binds to the antigen it is specific for and is variable between antibodies made by different plasma cells. The Fc region is constant (same between antibodies within a class) and binds to the Fc receptors found on immune cells. In other words, the Fc region is the same for all IgA antibodies, all IgG antibodies, and so on, but it is different between these classes. These two different regions allow for antibodies to interact with the antigens and then other components of the immune system. Now that we have an idea about how antibodies are constructed, let's discuss how they work and why they are so important. There are several direct and indirect immune mechanisms that are activated by antibodies.




**Various Antibody Actions**Image by JS BYU-I F13

The image above details how antibodies work within the immune system. It shows how IgE can activate and degranulate mast cells, resulting in histamine release that contributes to the inflammatory response. Antibodies can also simply bind up an antigen and prevent it from being toxic (if it is covered up by antibodies it cannot interact with our cells and harm them). Phagocytic cells have Fc receptors that bind to the Fc portion of antibodies. If a phagocyte comes upon antibodies bound to antigen the phagocyte will attach to the Fc portion of the antibody. This triggers a phagocytic event that causes the cell to engulf, consume, and destroy both the antibody and the antigen it is attached to. In this way, antibodies act to promote opsonization. Other non-phagocytic leukocytes can also have Fc receptors. When they bind the Fc portion of an antibody, they are triggered to release cytotoxins that can destroy any cell that antibodies might be bound to. This mechanism is called **antibody dependent cell-mediated cytotoxicity** or **ADCC**. This mechanism is effective for removing cells that don't belong, including damaged or cancerous cells. These cells express strange proteins capable of triggering a humoral immune response that creates antibodies against incorrect cellular membrane proteins.

Finally, as you have already learned, antibodies can trigger the complement system which will enhance inflammation, chemotaxis, opsonization, and the membrane attack complex.