Specific Immune Response

The specific Immune response is divided into two branches; the Humoral response and the Cell Mediated response. These two response are controlled by Antigen presenting cells (APC) and T-helper cells (T<sub>h</sub>).

A. The Humoral response
   A) Targets extracellular antigens
   B) The effector cells are B-cells that Differentiate into Plasma cells
   C) Marks target cells for destruction with secreted antibodies from Plasma cells.

B. Cell Mediated Response (overview)
   A) Targets intracellular antigens, cancerous tumors, and tissue transplants.
   B) The effector cells are T-cytotoxic cells(T<sub>c</sub>) that differentiate into Cytotoxic T-lymphocytes (CTL)
   C) CTLs kill infected host cells by releasing perforin molecules into the plasma membranes of these cells which cause cytolysis.

C. APC and T<sub>h</sub> cells.
   A) T<sub>h</sub> cells produce Interleukin-2 (IL-2). IL-2 from T<sub>h</sub> cells causes T<sub>c</sub> cells to proliferate and differentiate into CTLs and B-cells to proliferate and differentiate into Plasma cells.
   B) APC cells present antigen to T<sub>h</sub> cells. This activates T<sub>h</sub> cells causing them to release IL-2.

II The cell mediated response. (In detail)
A) The cell mediated response is controlled or initiated by the non-specific immune response. This is true because APC stimulate T<sub>h</sub>-cells to produce IL-2
   1. Macrophages of the non-specific immune response phagocytose pathogens, process the antigens and display the antigens in the context of an MHC II molecule. These phagocytes are now APCs that are able to stimulate T<sub>h</sub> cells.
   2. APCs move to the lymph node via the lymphatic vessels. In the lymph node they come in contact with the T<sub>h</sub> cells.
   3. An APC will stimulate the appropriate T<sub>h</sub> cell to produce IL-2. This stimulation is accomplished when the T<sub>h</sub> cell receives two different signals from the APC; a primary signal and a co-stimulatory signal.
      1. Primary signal occurs when the T<sub>h</sub> cell binds with its T-cell receptor (TCR) to the APC MHC II/antigen complex. The primary signal causes Interleukin-2 receptors (IL-2R) to appear on the surface of the T<sub>h</sub>-cells.
      2. Co-stimulatory signal occurs when the T<sub>h</sub>-cell binds with its surface CD28 receptor to the APC s B7 protein. This signal in conjunction with the primary signal stimulates the T<sub>h</sub>-cell to produce and secrete IL-2.
      3. IL-2 produced by the T<sub>h</sub>-cell binds to the IL-2R on the plasma membrane of the T<sub>h</sub>-cell. This signals the T<sub>h</sub>-cell to proliferate.
4. The new $T_h$-cell clones are all active and produce IL-2.

B  Activation of the $T_c$-cell
1. Following macrophages into the inflamed region are lymphocytes. One type of lymphocyte is the $T_c$-cell which monitor intracellular infections.
2. If the pathogens are growing intracellularly proteins or antigens from the pathogens will be displayed on the outside of the infected host cell in the context of an MHC-I molecule.
3. The Primary signal for the $T_c$-cell: At the site of infection, A $T_c$-cell that is specific for the antigen will bind to the MHC-I antigen complex with its TCR. This is the primary signal. The primary signal causes IL-2R to appear on the outside of the plasma membrane and we now say the $T_c$-cell is activated.

III  The Humoral response
A) B-cells differentiate into Plasma and Memory cells
1. B-cells enter site of infection and bind extracellular antigen with B-cell receptors (BCR)
2. Receptors pull in extracellular antigens in a process referred to as receptor mediated endocytosis.
3. Extracellular antigen is digested and processed in B-cell vacuole and presented in MHC II molecule on the outside plasma membrane of B-cell. Thus the B-cell becomes an APC.
4. B-cell migrates to the lymph node where it comes in contact with a $T_h$-cell specific for its MHC/ antigen complex.
5. Primary signal: $T_h$-cell binds MHC/ antigen complex with its TCR. This is the primary signal which causes IL-2R to appear on both the $T_h$-cell and the B-cell.
6. Co-stimulatory signal: The CD40L protein on the $T_h$-cell binds to the CD40R on the B-cell. This co-stimulatory signal causes IL-2 to be secreted from to $T_h$-cell.
7. IL-2 binds to the receptors on the $T_h$-cell and causes the $T_h$-cell to proliferate.
8. IL-2 binds to B-cell IL-2 R and causes the B-cell to differentiate into Plasma cells and Memory cells. IL-2 also causes the proliferation of these cells.
9. Memory cells do not react right away but are held in reserve for later infections. The secondary response that is carried out by memory cells is different in 3 ways.
   1. Memory cells produce antibodies that bind with greater affinity to their antigens than the antibodies produced in the initial response.
   2. The response time is much vaster than the primary response
   3. A greater number of antibodies are produced.

B) Antibodies function in 6 ways to protect the body
1. Agglutination: Enhances phagocytosis and reduces number of infectious units to be dealt with
2. **Opsonization**: Coating antigen with antibody enhances phagocytosis
3. **Neutralization**: blocks adhesion of bacteria and viruses to mucosa. Also blocks active site of toxin
4. **Activation of complement**
5. **Increases inflammation** through the byproducts of the complement system (C5a and C3a)
6. **Antibody dependant cell mediated cytotoxicity**: Antibodies attached to target cell cause destruction by non specific immune system cells.

C) Structure of an Antibody
1. Antibody composed of two heavy chains and two light chains. These chains bind together to make a Y shaped molecule. See figure 17.5.
2. The two sections located at the ends of Y s arms are called variable (V) regions. The variable region is structurally identical for all antibodies synthesized by a particular plasma cell. The Antibodies from each plasma cell however are different or unique from all other antibodies produced by other plasma cell.
3. The stem of the antibody molecule as well as the lower portion of the arms called constant (c) regions. There are 5 major types of C regions which correspond to the 5 different classes of antibodies. All plasma cells in the body are producing one of these classes of antibodies. A particular plasma cell may switch the particular class of Antibody that it is producing in order to fight an infection in a different way.
4. The structure of Antibodies may be described by the way they are cut and digested by proteases. The proteases cut the stem region about 2/3rds the way up. The stem portion is referred to as the **FC region** and the Y portion with the top third of the stem is referred to as the **Fab region**. The FC region often acts as the receptor for phagocytes during opsonization or Antibody dependant cell mediated cytotoxicity. The FC region contains the antigen binding region.
5. The five classes of Antibodies include the following
   1. IgM
   2. IgD
   3. IgG
   4. IgE
   5. IgA