

Sensory Systems II

1. The protein that binds the retinal in each of these is similar to the opsin of rod cells (40% identity). Color blindness (usually in males) arises due to recombination between related red and green receptor genes on the X chromosome.
2. Hearing arises as a result of signaling in the ear arising from hair cell micromanipulation (movement) arising from sound waves. Tipping of the cells causes little "tethers" to pull open ion channels that initiate a nerve signal.
3. Touch is the least understood sense. There are receptors for pressure, temperature and other sensations. Touch receptors can be linked to pain centers called nociceptors located in the spinal cord and brain. Interestingly, the compound capsaicin, which causes hot sensations in the mouth stimulates the same nociceptors.
4. The capsaicin receptor is a transmembrane protein. This protein contains a pore that opens to allow calcium ions in when capsaicin binds, thus initiating a nerve signal. Mice lacking the capsaicin receptor do not respond at all to capsaicin. Similarly, birds do not contain coding for a capsaicin receptor and are completely immune to it.

Immune System

This information is provided for all of you who love learning.

1. The immune system contains the innate immunity system and the adaptive immunity system.
2. The innate system uses a Toll-like receptor that binds to the PAMP lipopolysaccharide structure on the surface of Gram negative bacteria.
3. The adaptive immune system system contains two major groups of lymphocytes (immune system cells), B cells and T cells. B cells are involved in the production of antibodies and T cells are involved in both cellular killing, as well as stimulation of the B cells.
4. Immunoglobulin G (IgG) is one of five major antibody classes made by the B lymphocytes of the humoral immune system (cellular immune system described below). IgG is the most abundant antibody in the blood serum. Others include IgA (in mucus), IgM (early responder), IgD (function uncertain), and IgE (parasite protection).
5. The structure of antibodies has several common features. First, they are composed of two sets of Heavy (H) and light (L) chains arranged in a Y shape. Both the H and L chains have constant and variable regions. The variable regions of the H and L chains are adjacent to each other and the variation in these regions are responsible for antibody diversity (10^8 different shapes). The different classes of antibodies vary in the H chains in the constant region.
6. Molecules bound by antibodies are called antigens. Specific structural regions of an antigen bound by an antibody are called epitopes.
7. IgM antibodies are the first responders of the humoral immune system.

8. Antibody diversity arises from recombination of DNA sequences and splicing of mRNA sequences for coding for the variable regions of H and L chains.
9. For the light chains, the coding sequences are on human chromosome 2 and involve three protein domains - V, J, and C regions. V is the variable portion, J is the portion that joins the V to the C, which is the constant region. Mixing and matching of domains by recombination generates tremendous diversity - over 1000 antibodies per base pair of the human genome.
10. In H chains (chromosome 14), recombination occurs between segments V, D, J and C. Recombination within the constant regions of the H chains can result in "class switching" in which a desired variable segment is swapped among to the various segments to put the binding site onto regions to make IgG, IgE, etc.
11. The result of recombination and an error-prone replication in B cells means that the cells of the immune system have slightly different DNA sequences than the DNAs of all the other cells of the body. Splicing is the third factor contributing to increasing antibody diversity.
12. B cells with exposed antibodies are activated when clustering/aggregating of ITAM containing proteins occurs as a result of multiple antibody binding. This initiates a series of phosphorylations of the tyrosines on the ITAMs that stimulates a kinase called Syk to phosphorylate a transcription factor and cause a cellular response. The cellular response includes stimulating proliferation of that particular B cell.
13. T cells are part of the cellular immune system that acts to 1) induce apoptosis in infected cells (Cytotoxic T cells) or 2) to stimulate B lymphocyte production/action (Helper T cells).
14. Cytotoxic T cells act by binding to foreign peptides presented on Class I Major Histocompatibility Complexes (MHC) the surface of infected cells. Any cell of the body can be infected and possesses MHC I complexes. The foreign peptides make it to the surface of cells by action of protease action on cytosolic proteins from the infecting agent. The peptides are shuttled the endoplasmic reticulum, placed on MHC Class I proteins and the placed on the cell surface. Thus, infected cells are 'flagged' in this way as being infected.
15. Cytotoxic T cells have a receptor with extracellular proteins with variable binding domains. CD8 binds the constant region of MHC I and if the variable binding domain binds a foreign peptide, phosphorylation of ITAMs occurs (as in B cells), stimulating a kinase (ZAP-70) that phosphorylates target proteins. Subsequently, the cytotoxic T cell stimulated in this way releases perforin (channel forming protein) that binds to the infected cell and provides entry for the granzyme proteases. These enzymes invade the infected cell and stimulate it to go through apoptosis, breaking down the proteins and nucleic acids inside in the process.
16. Helper T cells (targets for HIV) act by binding to B lymphocytes presenting foreign peptides that they have internalized as a result of antibody binding. These are presented using a different group (Class II) of MHC. Class II MHC complexes (I also call them MHC II complexes) are present only on immune system cells and are used to flag immune system cells that have bound an antibody.
17. Helper T cells have a receptor, like the cytotoxic T cells along with ITAMs. When Helper T cells recognize a foreign peptide being presented by a B cell, it stimulates the Helper T cell to secrete cytokines that bind to a cytokine receptor on the surface of the B cell. This stimulates the B cell to grow, divide, and also secrete soluble forms of the antibody on its surface. It is this process that results in the proliferation of B cells targeting a common antigen.
18. Note that the Helper T cell protein that recognizes the constant region of Class II MHC is called CD4.

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Last, it has been a great term, folks. I have enjoyed getting to know you and wish you the best on the final and numerous future successes. This will be the last time I will teach this class for a few years, so you have been a great one to finish on.

Kevin