Lecture 9: Organ systems, Primary and Secondary  
Organ Systems – Immuno-surveillance & Enhanced Probability of Rare Events

1. Primary organs:
   - Bone Marrow: Responsible for initial development of T cells and maturation of B cells. Only B cells that express an intact immunoglobulin that recognizes foreign molecules are allowed to leave the bone marrow. B-cells that recognize self are either destroyed or are non-functional.
   - Thymus: Responsible for maturation of the T cells. Only T-cells that can recognize foreign peptides in complex with self MHC are allowed to leave the thymus. All others are destroyed.

2. Circulation Though the Lymphatic System.
   - A naive lymphocyte in the blood will enter the lymphatic system 2-12 hours after it is released from the bone marrow or thymus. Passage across the endothelial wall similar to that used by neutrophils in inflammation, except a different cytokine/cytokine receptor is used.
   - Approximately 3x10^11 lymphatic cells flow through the system on a given day.
   - A similar number are processed through the spleen.
   - This high flux of cells insures that a foreign antigen will meet the appropriate B and T cells within a short period of time.
   - If the naive lymphocyte does not encounter an antigen to which it can bind, it dies in a few days.
   - Memory lymphocytes (B, T_H, and T_C) cells circulate for years to decades.

FIGURE 3.23 Diagram of lymphocyte recirculation through the blood (purple) and lymph capillaries (gray) to the major organs of the lymphatic system.
3 Secondary organs:
The secondary organs of the immune system serve two purposes:
- First, they trap foreign material. This trapped material is processed by dendritic cells as well as other antigen presenting cells, such as macrophages.
- Second, they provide a high density of B- and T-cells, such that the appropriate cell pairings can occur between antigen presenting cells and T<sub>H</sub>-cells. This is facilitated by circulation of B and T cells through the lymphatic system.

3A. Spleen:
- Traps foreign particles from the blood via dendritic cells & macrophages. T-cells activated by dendritic cells and macrophages. B-cells activated in a manner similar to lymph nodes.
- RBCs bring opsonized pathogens to the spleen.

3B. Mucosal-Associated Lymphoid Tissue (MALT/GALT):
- Lymphoid follicles adjacent to mucosal membranes (e.g. tonsils, Peyer's patches).
- Specialized M-cell in wall of mucus membrane entraps foreign particle, delivering it to lymphocytes on the other side of the mucosa. This leads to activation of B-cells which migrate to the mucosa and deliver antibodies of a specific class (IgA class) across the mucosal membrane.
- T<sub>C</sub> cells can also be activated, providing mucosal immunity to viruses.
- Activated immune cells circulate and provide protective immunity to the entire mucosal system.
3C. Lymphatic system:
- Traps local foreign bodies near the source of infections. Drains fluid from cells to lymph nodes and follicles, eventually returning fluid to the blood. Nodes and follicles contain B-cells, T-cells, macrophages, and dendritic cells.
- Lymphocytes can enter either from the lymph fluid or cross the endothelial wall of a blood vessel in a manner similar to neutrophils (diapedesis).
- Dendritic cells in tissue engulf foreign particles, migrate to the lymph node, activating T_H cells (and potentially T_C cells.)
- Antigen trapped in lymph node activates both B- and T-cells.
- B-cells activated by T_H cells, form a germinal center
- Plasma cells release antibody into circulation.
- Plasma cells may migrate to bone marrow.
- Activated T-cells also migrate to site of infection. They secrete INF-γ, which recruits macrophages.