Innate Immune System Overview

First line of defense: Neutrophils, Macrophages, and Dendritic cells all of these cells can phagocytose things

Analogy: Innate immune cells are low-skilled and untrained but can be effective

Innate receptors: These receptors allow simple Self:Non-self recognition these receptors are responsive to PAMPS, DAMPS, MAMPS

These receptors can be on the plasma membrane or the endosome
TLR4-LPS (Gram neg. bacteria)
TLR2-Lipoteichoic acids (Gram pos. bacteria)
TLR5 – Flagellin

How it works:
Ligand binds to a receptor on the innate immune cell > Stuff happens > inflammatory response begins and cytokines/chemokines are released

Consequences of the innate immune system:

1. Pathogen is destroyed by tissue macrophages
2. Local cytokine and chemokine production
3. Tissue dendritic cells capture antigen and go to lymph nodes

Dendritic cell activation:
Dendritic cell's receptor binds its ligand and becomes activated
Antigen is taken up and processed by the dendritic cell and then loaded onto an MHC
MHC expression is increased in activated dendritic cells
High CCR7 expression
They have decreased phagocytic capability
Increased co-stimulatory molecules (CD80/CD86 also known as B7.1/7.2)
The degraded protein from the ingested pathogen is now presented on MHC molecules displayed on the DC surface

Stepping it up a notch and now we need adaptive immunity

We sometimes need a more trained immune response and that is when the adaptive immune system come into play

Conal selection theory is the basis of adaptive immunity

Thymus

1. Single progenitor cell gives rise to many lymphocytes, each with a different specificity
2. Removal of potentially self-reactive immature lymphocytes by clonal deletion
    a. Now we are in the lymph node
3. Pool of mature naïve lymphocytes

4. Proliferation and differentiation of activated specific lymphocytes to form a clone of effector cells

This process of forming a lymphocyte army takes time (7-10 days)

Naive T cells express CCR7 which pulls them into the lymph node paracortex, the activated dendritic cells also express CCR7 which helps it find T cells

T cell Activation
Signal 1: T cell receptor plus CD4 or 8 binding MHC and peptide on DC (antigen)
Signal 2: CD28 binding B7 molecules on DC (co-stimulation)

B cell Activation
Signal 1: B cell receptor antigen
Signal 2: CD40/40L

Antigen binds to B cell receptor, B cell internalizes this antigen, and presents it on its MHC
CD4+ helper T cells that have already been activated by dendritic cells and primed to recognize the same antigen encounter the B cell with its TCR
TCR and MHC interaction occurs ☺
Interaction between CD40 on B cell and CD40L on TFH cell provides a signal for B cell activation which is necessary for the formation of germinal centers

How do B cells find their antigen?
-Macrophages near the afferent lymphatic vessels gather antigen from the lymph
-Antigen is transferred to follicular dendritic cells in the follicle and kept intact on the surface

Signal 2: How do T cells and B cells find eachother?
T cells express CCR7 so they can locate to the T cell zone
B cells express CXCR5 and locate to B cell follicles
Now things switch so they can meet in the middle

Follicular B cells activated by antigen express CCR6 and migrate to the boundary of the follicle and T-cell area
T cells activated by an antigen express CxCR5 and migrate toward the follicles and encounter the activated B cells

What happens in the germinal center?
Somatic hypermutation of the B cell receptor Variable region
Class switching of the B cell receptor Constant region

Germinal center has two zones; dark and light
Dark zone: Lots of proliferation here – BCR mutations are occurring
Light zone: Ag-driven selection of clones