A brief introduction

CYTOKINES
- Small proteins that are secreted by specific cells of the immune system which carry signals locally between cells
- They are proteins, peptides, or glycoproteins that act like hormones
- Examples: interleukins (IL), interferons, etc.

IMMUNOGLOBULINS = ANTIBODIES

LYMPHOCYTES: T cells, B cells, and NK cells
- NK cells
  - Innate immune system
  - Defend against tumors and virally infected cells
  - Distinguish between infected cells from normal using MHC class I
  - Activated by interferons
  - Release cytotoxic granules that destroy
- T cells
  - Adaptive immune system
  - Cell-mediated immunity
  - Goal: antigen presenting: recognize non-self
  - Helper T cells (CD4): produce cytokines that direct the immune response
  - Cytotoxic T cells (CD8): produce toxic granules that induce pathogen cell death
  - Also produce memory cells for future attacks
- B cells
  - Adaptive immune system
  - Humoral immunity (think antibodies)
  - Goal: antigen presenting: recognize non-self
  - Produce lots of antibodies that neutralize bacteria and viruses
  - Also produce memory cells for future attacks

INNATE IMMUNITY
- Physical/chemical barriers, extracellular killing via phagocytes, extracellular killing via cells
- NK cells: produce toxic metabolites to break apart DNA, secrete proteins that form transmembrane pores to destroy voltage difference, or get rid of infected cells by apoptosis
- PMN leukocytes (aka granulocytes): “BENM”: basophils, eosinophils, neutrophils, mast cells
- Macrophages & dendritic cells (APCs): phagocytose pathogens & foreign substances

Antibodies
- Made from B cells in response to an immunogen and binds antigens
- 2 heavy + 2 light chains, each with a V and C region
- F_{ab}=arms, F_{c}=base
- NH_{3}-terminals bind antigens
- Hinge region: β-pleated sheet absent, flexible, allows stronger/specific binding, cross-linking
- CDR: “Complementarity Determining Region”: binding site for epitope/hapten via non-covalent interactions (H-bonding, ionic, Van der Waals, hydrophobic effect)
- 5 classes of Ig based on the type of heavy chains: IgG, IgA, IgM, IgD, and IgE (Think “GAMED”)
- F_{a} and C domains: for biological responses (e.g. complement cascade), interaction with B cells and T cells, and stimulation of phagocytosis and antibody secretion
### IgG vs. IgM vs. IgA vs. IgD & IgE

<table>
<thead>
<tr>
<th>IgG</th>
<th>IgM</th>
<th>IgA</th>
<th>IgD &amp; IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predominant</td>
<td>Pentameric with 5 subunits</td>
<td>In external secretions</td>
<td>IgD: unknown functions</td>
</tr>
<tr>
<td>Long t_{1/2}=23 days</td>
<td>J chain &amp; extra C_{H} domain</td>
<td>J chain for dimeric form with 4 binding sites</td>
<td>IgE: parasitic infections &amp; hypersensitivity</td>
</tr>
<tr>
<td>Good for passive immunity by transfer of antibodies</td>
<td>Can bind up to 5 epitopes, cross-linking possibilities</td>
<td>Monomeric not important, dimeric important form</td>
<td>F_{C} binds to mast cells and basophils to release histamine</td>
</tr>
<tr>
<td>Agglutinate insoluble antigens, precipitates</td>
<td>Agglutination for phagocytosis</td>
<td>Good for defense against bacteria coming in through secretory membrane</td>
<td>Crosslinking (via dimeric structure) stimulates cells to degranulate, e.g. in allergic reactions</td>
</tr>
<tr>
<td>Opsonization leading to phagocytosis</td>
<td>Isohemagglutinins: Ab against RBC antigens (ABO blood types)</td>
<td>Main defense against local infections</td>
<td></td>
</tr>
<tr>
<td>F_{C} stimulates NK and activates complement system</td>
<td>Activates complement for extracellular killing of pathogens w/o engulfing</td>
<td>No receptor for complement</td>
<td></td>
</tr>
<tr>
<td>Neutralizes toxins by keeping Es from operating</td>
<td></td>
<td>Agglutination good for defense against viruses</td>
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**MEMORY:** Immune system’s antibody synthesis

1. First makes IgM then IgG (IgG>IgM) → 10 days
2. Body massively responds to 2nd exposure because of memory; makes a lot more IgG the 2nd round → 3 days

**ANTIGENS**

A non-self, complex molecule that is susceptible to being broken down into immunogenic pieces
What makes a good antigen? Proteins and carbohydrates
What makes a bad antigen? Nucleic acids (not enough difference in chemical features), lipids (not enough variety/complexity in nonpolar alkyl chains, but works when conjugated to proteins → lipoproteins)

**EPITOPES/HAPTENS**

Part of antigen that acts as an identifier to be picked up by antibodies and T cell receptors
The more the merrier! → The more epitopes on an antigen, the more variety of antibodies produced

**AGGLUTINATION vs. PRECIPITATION**

Precipitation: soluble → crosslinking=alternating lattice of Ag-Ab-Ag-Ab...etc.
Agglutination: insoluble → crosslinking=clumping of particles
Differs from each other in terms of size of particles

**OPSONIZATION**

The process by which a pathogen is marked for ingestion and destruction by a phagocyte. Opsonization involves the binding of an antibody to a receptor on the pathogen’s cell membrane, and then phagocytes are attracted to the pathogen. The Fab portion of the antibody binds to the antigen, whereas the Fc portion of the antibody binds to an Fc receptor on the phagocyte, facilitating phagocytosis.
B Lymphocytes

B cells are a type of APC
Main role: make antibodies
Other roles: memory, non-self discrimination

DEVELOPMENT & DIFFERENTIATION
B cells start out in fetal liver → migrate to bone marrow to differentiate and develop
Get expression of different proteins and chromosome rearrangement
D+J → DJ + V → VDJ
VDJ unit gives antigen specificity
Igμ + Igα + Igβ → pre-B cell receptor on cell surface
Igα + Igβ: soluble immunoglobulins (unlike IgM, which is a membrane Ig), therefore are only involved in signal transduction, not antigen binding

INACTIVATION: what happens when the B cell binds to self 😓
Anergy: long term inactivation, turning off the light switch
Deletion: apoptosis, controlled cell death
Receptor editing: VDJ recombination, changing the amino acid sequences for a different specificity, like a second chance

MATURING B CELLS
Started out with just IgM, now have both IgM and IgD
If they passed the test, they migrate out of the bone marrow to secondary lymphoid tissues (lymph nodes, spleen)
When they interact with antigens and become activated → B-cell blasts
Some become antibody factories called plasma cells (make soluble antibodies that aren’t expressed on membrane surface, i.e. they lost IgM and IgD)

B CELLS AT WORK
1. B cell binds antigen and breaks it down into smaller pieces
2. MHC Class II takes an antigenic piece and displays it on the membrane surface to present to T cells
3. B and T cell chat for a bit, T cell flirts and secretes cytokines
4. B cell takes the hint and switches to produce different types of antibodies (e.g. IgG, IgA, IgE) but which have the same antigen specificity as the original IgM and IgD

FINE TUNING
- In the meantime, some other activated B cells decide to get into a clique and aggregate in secondary lymphoid organs, forming germinal centers and undergoing clonal expansion
- Here they do some rearranging (genetic recombination) and end up producing different kinds of antibodies with different specificities. The genetic recombination consists of mutations in the V regions; the whole thing is called somatic hypermutation, which allows for improved affinity for the antigen, like survival of the fittest
- Some B cells get stimulated to become plasma cells that are like antibody factories pumping out soluble Ab
- A few get stimulated to become memory cells for future protection, and display IgA, IgG, and IgE on their surface (think “AGE,” as in when the body ages and needs protection later)
- IgA plasma cells → mucosal tissue
- IgG plasma cells → bone marrow to make more IgG