Topics

- Humoral Immune Response Part II
  - Accessory cells
  - Fc Receptors
  - Opsonization and killing mechanisms of phagocytes
  - NK, mast, eosinophils
- Immune regulation
  - Idiotype network

Distribution of IgS
- IgG, IgM:
  - Plasma
- IgG, IgA (monomeric):
  - Extracellular fluid
- IgG
  - Fetus
  - IgA (dimeric):
    - Secretions, cross epithelia
- IgE
  - Mast cells beneath epithelia
Viral neutralization

Neutralization of bacterial adhesion to host cells

– Adhesins

Complement fixation

This involves two types of molecules:
1. IgG molecules bind to antigens on the bacterial surface
2. Complement molecules bind to antigens on the bacterial surface
Accessory cells

- Removal of pathogens after neutralization
- Destruction of pathogens that can not be neutralized
- Phagocytic cells
  - Macrophages, neutrophils
- NK, eosinophils, basophils, mast cells
  - Secrete stored mediators

Fc receptors

- Bind the Fc portion of immunoglobulins
- Signaling receptors – molecular complexes
- γ chain transduce the signal
- Crosslinking is necessary for effector function activation
- α Chain provides specificity
  - Different cells express different Fc receptors
  - Different Fc receptors bind to different isotypes
  - Then isotype produced determines cells that will be activated
FC receptors bind to FC portion of Ab

<table>
<thead>
<tr>
<th>Receptor</th>
<th>FcγRII (CD89)</th>
<th>FcγRIIA (CD16a)</th>
<th>FcγRIIB (CD32)</th>
<th>FcγRIII (CD16b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structure</td>
<td>Phagocytes (1)</td>
<td>Phagocytes (1)</td>
<td>Phagocytes (1)</td>
<td>Phagocytes (1)</td>
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<tr>
<td>Binding</td>
<td>1 + TrkA</td>
<td>5 + 4-1D6</td>
<td>12 + 4-1D6</td>
<td>18 + 4-1D6</td>
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<tr>
<td>Effect of aggregation</td>
<td>1 + TrkA</td>
<td>5 + 4-1D6</td>
<td>12 + 4-1D6</td>
<td>18 + 4-1D6</td>
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<tr>
<td>Distinguish</td>
<td>Free Ab and Ab bound to pathogen due to aggregation or multimerization of Ab.</td>
<td></td>
<td></td>
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<tr>
<td>Avidity</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Identification of the pathogen coated by Ab.</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>B cells</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Macrophages</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Dendritic Cells</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Langerhans cells (Skin)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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</tbody>
</table>

Other Fc-Accessory cell function
- Same receptor can stimulate different functions in different cells
  - FcγRII-B
    - Negative regulation of B cells
    - Activation of macrophages, mast cells and neutrophils by immune complexes
  - Langerhans cells (Skin)
    - Ingestion of Ag-Ab complexes, ingestion of pathogens
    - Ag presentation
  - Follicular Dendritic Cells
    - Immobilization of antigens
    - Maturation of humoral response

Fc-Ab aggregation
- Fc receptors in phagocytes bind mainly IgG.
- Distinguish between free Ab and Ab bound to pathogen due to the aggregation or multimerization of Ab.
- > avidity
- Identification of the pathogen coated by Ab.
• FC receptors enable accessory cells to detect pathogens through bound Ab molecules
  • Accessory cells lack intrinsic specificity
  • Ab + Fc receptors give specificity

Opsonization

• Many bacteria are recognized directly by phagocytes, they are non-pathogenic
• Polysaccharides prevent direct recognition
• Opsonization allows engulfment of these bacteria
• Polysaccharides are T independent antigens EARLY RESPONSE
• IgM is produced leading to Complement activation
• Opsonization with Complement leads to phagocytosis via binding to complement receptors present in phagocytes.
Response to larger pathogens

- Parasitic worms
- Ab coat surface of parasite
- Phagocyte attaches through Fc receptor
- Lysosomes fuse with plasma membrane, releasing lysosome content into the extracellular space.
- Damage to the parasite

NK cells

- Virally infected cells express viral proteins in their surface
- Ab bind to viral antigens
- Fc in NK cells binds to IgG1 and IgG3
- NK cells:
  - Large, intracellular granules, no specific receptors, cytotoxic
  - Antibody dependent cell mediated cytotoxicity (ADCC)
  - Mechanism similar to T cells

Mast cells

- Large
- Contain granules with chemical mediators (histamine)
- Beneath epithelial and submucosal surfaces
- Fc binds to free IgE and IgG
- IgE + Fcε bind with high affinity
- Activated by cross-linking of IgE
- Release granules immediately
- Synthesize Prostaglandins, Leukotrienes, TNF-α (local inflammation)
IgE mediated response:

- mast cells, basophils, eosinophils

• Histamine:
  - Increases blood flow to the area
  - Increases vascular permeability and fluid accumulation
  - Inflammation
  - Facilitates influx of Ab and Cells, recruitment of specific and non-specific elements of immune response
  - Increases lymph flow from site to lymph nodes
  - Causes muscular contraction, expulsion of pathogens

- Phagocytic cells
  - Macrophages
  - Neutrophils

- Granulocytes
  - Eosinophils
  - Basophils
  - Mast cells
    - Secrete stored mediators
• Secrete stored mediators
• ADCC