Adaptive Immunity

Lecture 14
Biology 3310/4310
Virology
Spring 2019

Life is simple, but we insist on making it complicated
—CONFUCIUS
Host defenses

- Intrinsic
  - *Always present* in the uninfected cell
  - Apoptosis, autophagy, RNA silencing, antiviral proteins
- Innate immune system: *Induced* by infection
- Adaptive immune system: *Tailored* to pathogen; memory
Leukocytes and Lymphocytes

- Leukocyte: general term for white blood cell (lymphocytes, neutrophils, eosinophils, macrophages)
- Lymphocyte: Subset of leukocytes (T, B, NK cells; have variable antigen-detecting cell surface receptors)
Innate instruction of adaptive immunity

- Virus, virus protein
- Inflammatory cytokines
- Dead and dying cells

Toll-like receptor
Immature dendritic cell
Endosome
Cytokine receptor
MHC class II
IFN

Maturation
Nf-kb activation
Migration to lymph node

MHC class II viral peptides
CD28
Tcr
Naive T cell
Activated T cells
Helper T cells

CD4 Th cell
(also CD8 T cell or B cell)

Mature dendritic cell
Cytokines IL-12, Tnf-α, IL-1β
HCMV interferes with MHCII transcription
Lymphocyte activation triggers massive cell proliferation

- 1/10,000 - 1/100,000 B or T cells recognize antigen
- 1-2 weeks: 1,000 - 50,000 fold amplification
- Lymphadenopathy
Go to:

b.socrative.com/login/student
room number: virus

What is a property of innate instruction of adaptive immunity?

A. Presentation of viral peptides on MHC II to CD4 T cells
B. Endocytosis of viral proteins
C. Activation of DCs by cytokines
D. Sensing by TLRs
E. All of the above
Effectors of the adaptive response
Antibodies
Antibody response

![Graph showing antibody response over days after immunization for IgG, IgM, and IgA](image)
Neutralizing antibodies

- Essential *defense* against many virus infections
- Neutralize virus particles in the blood, prevent virus spread
- IgA at mucosal surfaces (secretory antibody) blocks entry
- Some neutralizing antibodies are important for *recovery* from infection
Neutralizing antibodies
Passive antibody protects against poliovirus infection
Neutralizing antibodies

**Diagram A:**
- Human rhinovirus 14
- Attachment
- Endocytosis
- Acidic pH
- RNA release

**Diagram B:**
1. Blocked attachment
2. Blocked endocytosis
3. Blocked uncoating
4. Neutralization after replication starts?
5. Aggregation

**Legend:**
- Icam-1
Neutralizing antibody

Virus

Neutralization

Complement-mediated lysis and phagocytosis

Cell protected from infection

Infected-cell lysis or clearance

Inhibition of viral replication

Inhibition of virus release

Inhibition of cell-cell transmission

Infection

Fc-mediated effector systems

Cell signaling

Steric obstruction?

Steric obstruction?
Evasion of Ab

Rhinovirus

Influenza HA

Which statement about anti-viral antibodies is incorrect:

A. They are important for protection against viral infections
B. They only neutralize virus infectivity
C. They may block virus attachment to cells
D. They can be found at mucosal surfaces
E. IgM is the first to appear, then IgG
Cell mediated immunity

- Essential for clearing most viral infections
- CTL and target cells form an immunological synapse
- Lysis of target cell
- Countermeasures
Endogenous antigen presentation

TAP = transporter associated with antigen processing

Herpesviruses (HCMV, HSV, EBV)
## Countering MHC I

<table>
<thead>
<tr>
<th>MHC I pathway</th>
<th>Viral protein</th>
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</thead>
<tbody>
<tr>
<td>MHC I synthesis</td>
<td>Lentivirus Vpu</td>
</tr>
<tr>
<td>TAP synthesis</td>
<td>EBV vIL-10, HCMV UL111A</td>
</tr>
<tr>
<td>TAP function</td>
<td>HCMV US6, HSV ICP47</td>
</tr>
<tr>
<td>MHC I transport</td>
<td></td>
</tr>
<tr>
<td>Retain in ER</td>
<td>HCMV US3, Ad E3-19K</td>
</tr>
<tr>
<td>Dislocate to cytoplasm</td>
<td>HCMV US11, US2</td>
</tr>
<tr>
<td>Increase MHC I endocytosis</td>
<td>HIV nef, HHV-7 K3, K4</td>
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</tbody>
</table>
CTL lysis

- Lysis of target cell by two mechanisms
  - Release of cytoplasmic content
  - Apoptosis
Kinetics of CD8 T cell (CTL) production
Antibody vs cellular immunity in protecting against monkeypox virus infection

<table>
<thead>
<tr>
<th>Day of vaccination</th>
<th>Immune manipulation</th>
<th>Neutralizing Ab day 22</th>
<th>Monkeypox infection</th>
<th>Fatality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
<td>800-6400</td>
<td>Day 28</td>
<td>0/4</td>
</tr>
<tr>
<td>0</td>
<td>B cell depletion</td>
<td>42-59</td>
<td>Day 28</td>
<td>3/4</td>
</tr>
<tr>
<td>0</td>
<td>CD8 cell depletion</td>
<td>268-2963</td>
<td>Day 28</td>
<td>0/4</td>
</tr>
</tbody>
</table>
For some infections, CTL response is more important than the antibody response

How is the correct response made?

*Begins in lymph tissues where sentinels tell naive B and T cells nature of invader*
This decision is made in part by special T helper cells (Th cells)

- Th cells make contact in the lymph nodes with sentinel DCs and macrophages
- Information exchanged (peptides, cytokines) causes differentiation to Th1 or Th2
For some infections, CTLs are more important for protection than antibody. How is the CTL-antibody balance determined?

A. By toll-like receptors  
B. By intrinsic defenses  
C. By autophagy of infected cells  
D. By the mix of peptides and cytokines presented by DCs  
E. It depends on whether the capsid is icosahedral or helical
Adaptive responses also provide memory

- If the host is subsequently infected by the same virus, the response will be rapid and specific
  - Innate responses don’t have memory

- Memory: the basis for vaccination
Infection provides immune memory

- 1781: outbreak of measles on Faroe Islands
- Next 65 years, islands free of measles
- 1846: another outbreak of measles; none of those who survived the 1781 epidemic were infected
- Immune memory lasts a long time, maintained without re-exposure to virus
Immunological memory

![Diagram showing the stages of immunological memory](image-url)
Immunological memory

- Memory B cells
  - In spleen, lymph nodes
  - Do not produce antibodies unless stimulated by Ag
- Long lived plasma cells
  - Bone marrow
- Memory T cells
Cutaneous immune system
Mucosal immune system in gut
Inflammation provides integration and synergy
Next time: Mechanisms of pathogenesis