Adaptive Immunity

Lecture 14
Biology 3310/4310
Virology
Spring 2018

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

Virology Lectures 2018 • Prof. Vincent Racaniello • Columbia University
Exogenous antigen presentation

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
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

A diagram illustrating the structure of antibodies, including key regions such as the light chain, heavy chain, and variable regions. It also shows a graph depicting the titer of serum antibodies over weeks, with responses to different antigens labeled as primary and secondary responses.

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Principles of Virology, ASM Press
Antibody response
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

A
- Human rhinovirus 14
- Attachment
- Endocytosis
- Acidic pH
- Uncoating
- RNA release

B
- Human rhinovirus 14 + antibodies
- Aggregation
- Blocked attachment
- Neutralization after replication starts?
- Blocked endocytosis
- Blocked uncoating

Principles of Virology, ASM Press
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>
</tr>
</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>HCMV US3, Ad E3-19K</td>
</tr>
<tr>
<td>Retain in ER</td>
<td>HCMV US11, US2</td>
</tr>
<tr>
<td>Dislocate to cytoplasm</td>
<td>HIV nef, HHV-7 K3, K4</td>
</tr>
<tr>
<td>Increase MHC I endocytosis</td>
<td></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

- Initial immune response
- Protective immunity
- Immunological memory

Antibody prevalence and T cell number

Time (days)

First infection

Mild or inapparent reinfection

Time (years)
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

- Lumen of intestine
- Intraepithelial lymphocyte
- Antigen
- M cells
- Mucosal epithelium
- Plasma cell
- Blood vessel
- Lymphatic vessel
- Antigen-presenting cell
- T cells
- Peyer’s patch
- Lamina propria
- To mesenteric lymph nodes
- To circulation

Principles of Virology, ASM Press
Inflammation provides integration and synergy