Amphibian Immunology

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March 4, 2014

Vertebrate Immunology

Lymphoid Organs

![Organs of the Immune System](image)
Innate Immunity: Terminology

- **Antigen**: something foreign or toxic to the cell or body
- **Macrophages**: “Big-eater”
  - role is to phagocytose
  - stimulate lymphocytes
  - attach foreign substances, infectious microbes, and cancer cells
- **Dendritic Cells**: Process antigen and present it to cell surface of T cells of the immune system
  - Messengers between innate and adaptive
- **Natural Killer Cells**: Cytotoxic lymphocyte
  - rapid response
  - release cytokines (signals and chemicals)

**Innate Immunity: Terminology**

- **Pattern Recognition Receptors**
  - primitive part of the immune system
  - found on host cell surface
  - recognize pathogen-associated molecular patterns
- **Pathogen-associated Molecular Patterns (PAMPs)**
  - molecules associated with groups of pathogens
  - activate immune responses
- **Antimicrobial and serum proteins**
  - potent, broad spectrum antibiotics
  - enhance immunity

Figure 5. Innate immunity and inflammation.
**Innate Immunity Summary**

- **Non-specific** defense mechanisms
- Immediately or within hours of antigen appearance
- Physical barriers, chemicals in the blood, immune system cells
- Activated by chemical properties of the antigen (PAMPs)

**Adaptive Immunity**
Adaptive Immunity: Terminology

- T cells (mature in Thymus)
  - T<sub>C</sub>
  - T<sub>H1</sub>
  - T<sub>H2</sub>
- Major Histocompatibility Complex Proteins (Found on Host Cells)
- Antigen presenting cell
- B cells (produced in the bone marrow)
- Antibody

T cells

- Type of lymphocyte
- Matures in the thymus
- CD4 T cells-Helper T cells
  - T<sub>H1</sub>: promote macrophage activation and cytotoxic T cell proliferation
  - T<sub>H2</sub>: Evoke strong antibody response
- CD8 T cells-Cytotoxic T cells
  - kills infected/dysfunctional cells
Major Histocompatibility Complex

• Series of genes that code for cell surface proteins controlling the adaptive immune response.
• Class I MHC contains three genes; proteins from these genes are expressed on almost all cells.
• Class II MHC genes contain 3 genes whose proteins are expressed on antigen-presenting macrophages, dendritic cells and B cells.
Antigen Presenting Cell (APCs)

- Cell that displays foreign antigens complexed with MHCs on their surfaces (called antigen presentation)
- T cells recognize using their T-cell receptors (TCRs).
- Most cells in the body can present antigen to CD8⁺ (cytotoxic) T cells via MHC class I molecules and act as APCs.
- Term is often limited to specialized cells (macrophages, dendritic cells and B cells) that generally express MHC class I and II and stimulate CD4⁺ (Helper) and CD8⁺ (cytotoxic) T cells.

Immune system

- Acquired
  - T-cell immunity
  - B-cell immunity
- Innate
  - Natural killer cells
  - Phagocytes
  - Complement system

Bloodstream

- Plasma cells
- Lymphocytes
- Natural killer cells
- Eosinophils
- Neutrophils

Physiologic barriers

1. Skin
2. Mucous membranes
3. Saliva
4. Stomach acid
5. Stool and bile
6. Airways

- Cell walls of the body's cells
- Mucous membranes
- Skin

Pathology

- Inflammation
- Immune response
- Pathogen burden
- Infection
- Injury
- Autoimmune disease

- Directing of defense
B cells

- Formed in the bone marrow
- Has B cell receptor protein that allows B cell binding to specific antigen
- Makes antibodies
- Develops into memory cells
Active Immune Response Summary

- **Antigen specific** immune response
- More complex than innate
- Antigen must first be processed and recognized
- Once recognized, specific cells attack specific antigen
- Also includes memory

Tolerance

- Ability to discriminate self versus non-self
  - Prevents over reactivity to environmental stimuli (allergens, normal microbes, etc)
  - Important for fetus, organ transplants, skin grafts

Amphibian Immunity
**Xenopus**

- Connecting taxon that links ancient vertebrates and mammals
- Comparative model of choice for immunological studies
- Little is known of other amphibians

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**Great Model**

Southern Leopard Frog Eggs

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**Differences between developmental stages**
Juvenile Immunity

Summary of the Main Developmental Stages of the European Texton System

<table>
<thead>
<tr>
<th>Blood stage (day)</th>
<th>Liver</th>
<th>Thymus</th>
<th>Spleen</th>
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<td>48-54 hours</td>
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<td>(Lymphocytes in lymph node)</td>
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<td>72-96 hours</td>
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<td>(Lymphocyte development)</td>
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<td>179-216 days</td>
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<td>adulthood</td>
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<td>(Lymphocyte development)</td>
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Fig. 1: Diagram summarizing the major developmental stages of the European Texton system. For abbreviations, see text.
Larval Immunology

- Competent Innate Immune System
- Weak Adaptive Immune System
  - Small amount of T cells and B cells in larvae
  - NK cells only right before metamorphosis

Immune Remodeling During Metamorphosis

What is going on during Metamorphosis?

- Tadpoles are free-living so must be protected against potential pathogens
- During metamorphosis, they acquire adult specific molecules
- Must show tolerance to new self molecules
- T cell function becomes impaired
- Express different antibody repertoire
- Lessening of skin graft tolerance
- The appearance of MHC class I antigens
- Persistence of immunological memory
Adult Immunology

- Immune system becomes complete 2-3 weeks after metamorphosis
- Strong innate and adaptive immune responses
  - Antimicrobial peptides
  - NK cells
  - Complement
- Adaptive immune system similar to other mammals
  - Except B cells differentiate mostly in the liver and spleen (instead of bone marrow)
Temperature and Immune Status

- Helminth clearance is slower at 15°C than 25°C
- Skin grafts are rejected faster at 27°C than at 21°C
- These and other data suggest selective inhibitory effect of low temperature on T-cell function

Other modulators of immune response

- Temperature
- UV
- pH
- Predators
- Man-made modulators
- Psychosocial factors
- Xenobiotics

Susceptibility of amphibians to infectious diseases
Review of what you just learned

• First defenses of pathogens through the skin and digestive tract are anti-microbial peptides
• Pathogens are killed by chemical cascades (complement) and/or macrophages
• Adaptive immune response requires time to activate in the presence of antigen
  - highly specific
  - generation of memory cells

Increases in Susceptibility not simply due to poor immunity

• Exposure to new, highly virulent pathogens
• New pathogens are immunosuppressive
• Pathogen "bloom"
• Stress response
• Environmental contaminants