Understanding basic immunology

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Immunology

- Immunology
  - the study of how the body fights disease and infection

- Immunity
  - State of being able to resist a particular infection or toxin
Overview

- Function of defences
- Immune response to infection and vaccines
- Generating specific immunity
- Enhancing the immune defences
Functions of the immune system

- **Protection**
  - Identify and destroy pathogens
  - Cancer

- **Housekeeping**
  - Removal of debris and dead cells
  - Surveillance

- **Communication**
  - Chemical messages
  - Antigen presentation
  - Memory
Hierarchy of defences

Barriers and chemicals
- Effective but crude – Prevention
- First line of defence

Non-specific
- Actively identifies and removes unwanted invaders

Specific
- Highly targeted
- Powerful but slow to develop
- Memory
Self from non-self
First step to immunity

- Recognise molecular shapes
- Our own cells have a unique ‘self’ tags on them
- Learn to ignore ‘self’ in early development
Antigens - molecular shapes

- Drive the immune response
- Include proteins, sugars or nucleic acids
- Vaccines often contain purified antigen
Innate immunity - non-specific

Recognition and response to non-self
Inflammation

Swelling, redness, heat

Damage → danger signal

Inflammatory mediators
  Increased blood flow
  Increased capillary permeability

Attracts cells

Alerts immune system

Clotting
Fight back - second line of defence

Innate response

- Identifies foreign molecular shapes
- Recognises class of microbe
- Direct killing
- Communication with chemical messengers
  - Cytokines, chemokines
- Antibodies and cytokines enhance this response
Non-specific, innate immunity

These cells respond to danger

Neutrophil engulfing thrush fungus

Macrophage

Dendritic cell

Natural killer cells attacking a cancer cell

Pictures Joel Dubin 2010
Adaptive immunity - specific
(includes humoral immunity, cellular immunity)

Antigen specific T cells and B cells
Antigen presentation

Dendritic cell entering the lymph to travel to local lymph node
Antigen-specific T and B cells are activated in lymph nodes

T cells require three signals from antigen-presenting cells:
1. Antigen recognition
2. Co-stimulation
3. Cytokine exposure
T cells

- Cytotoxic T cells
  - Kill infected cells, cancer cells
- Helper T cells
  - drive specific B-cell responses and antibody class
- Memory T-cells remain to fight the same infection another day
Specific – B cells and antibody

• Plasma cells
  – activated B-cells
  – secrete antigen-specific antibodies

• T cell dependent or independent responses

• Memory B-cells and antibody
Antibody – humoral immunity

- Immunoglobulins
- Secreted by plasma cells
- Bind to specific antigen
  - Neutralise
  - Block attachment
  - Label
  - Activate complement
  - Trigger cytokine release
  - Present antigen to T cells
Key classes of antibody

IgM – low affinity, in primary immune responses; complement activation; largest Ab, does not cross placenta

IgG – high affinity, most important class of Ab in secondary immune responses, crosses the placenta

IgA - found primarily in secretions such as breast milk, tears, saliva and mucosal membranes

IgE - Evolved to provide protection for parasitic infections; associated with allergic diseases e.g. asthma & hay fever; histamine release
What happens to the injected vaccine?

- Antigen carried to lymph node where specific response takes place
- Other ingredients excreted via blood, kidneys, urine.
Development of specific immunity

Primary immune response
- Activation of T and B cells
- Antibody produced by short-lived plasma cells
- Low affinity antibody appears in serum - IgM
- Takes 2 weeks, peaks around 30 days

Immune memory
- Immune memory is slow - at least four months
- T cell dependent
- High affinity IgG
- Only immune memory can be ‘boosted’

Secondary response
- rapid (4 days)
### Lymph node

- **Cortex** – containing dividing B cells and T cells
- **Medulla** – macrophages and antibody producing plasma cells
- **Sinuses** – net of reticular fibres spanning lymphatic capillaries
Specific immunity – generation of high affinity antibodies

Affinity maturation – in germinal centres

1. Activated B cells proliferate
2. Mutations in DNA coding for antigen binding site
3. Presented antigen by DC and T cells
4. Positive – high affinity => clones proliferate
5. Negative – low affinity => death †

- Differentiation and class switching - IgM to IgG – long lived memory
Summary

From microbial recognition to adaptive response and memory
Innate works with adaptive immunity

**Barriers**
- Innate (non-specific)
  - Complement
  - Granulocytes
    - NK cells
  - Antigen-presenting cells
  - Lymph nodes
    - B cells
    - T cells

**Adaptive (specific)**
- Antibodies
Immune memory

- Specific, adaptive immunity
- Long lived protection from reinfection
Communication enhances immunity

**Innate**
- Specific antibodies label targets
- Instruct B cells
- Enhance innate response
- New cell production

**Adaptive**
- Antigen-specific T and B cells activated

**Antigen presented by DC**
- IL-1
- IL-6
- IL-12

**IL-5**
**IL-4**
**IL-2**
**IFN-γ**

**IL-1**
**IL-6**
**IL-12**