Topics

• Immune regulation
  – γδ T cells
  – Fc receptor binding in B cells
  – Early response mechanisms
  – Antigen concentration
• Immunological memory

Immune regulation

Idiotypic network

– Variable regions of Ab are able to serve as antigens that elicit the production of anti-idiotopic Ab by the same individual

– i.e. Modulation of the immune response in Schistosomiasis
Regulatory T cells

- The immune system has to:
  - Protect the host from pathogens
  - Distinguish between self and non-self structures
  - Distinguish harmful from innocuous Ag to prevent non-essential responses
- Induction of Ag-specific self tolerance

Tregs = CD4+ regulatory T cells
- CD4+ CD25+ (IL-2 Rα chain)
  - Naturally occurring
  - Cell-cell contact (molecules not yet defined)
  - Depletion leads to autoimmune diseases
  - 5 – 10 % of all peripheral CD4+ T cells
  - Anergic (hyporesponsive)
  - Suppress activation of CD25- T cells
  - Inhibit IL-2 transcription
- TH3 and Type 1 T regulatory (Tr1)
  - Contact independent
  - IL-10, TGF-β
  - Altered state of development (not an independent cell lineage)

γδ T cells
- TCR composed of γ δ chains
- 2 sets
  - Found in lymphoid tissues of all vertebrates
  - Display some diversity of TCR
  - Intra-epithelial in some vertebrates
  - Limited diversity of TCR
  - Limited recirculation
  - Recognize ligands expressed by infected cells
  - Heat shock proteins, MHC IB molecules
  - Direct and rapid response to the presence of infected cells
γδ T cell as regulators of IR

- Mice deficient on γδ T cells mount exaggerated responses to foreign and to self Ag.

Fc receptor binding in B cells

- Engagement of Fc receptors in B cells reduces the B activation and reduces production of antibodies

Early response mechanisms

- Th0 differentiate into Th1 and Th2 and determines if the response is cellular or humoral
- Cytokines present at the site of proliferation
**Th1 induction**

- IL-12, IFN-γ
- Produced by dendritic cells, macrophages, NK cells in response to viral infection and invasion by some intracellular bacteria

**Th2 induction**

- IL-4 and IL-6
- Produced by NK1.1 CD4 T cell
  - Invariant TCR
  - Do not require TCR:MHC interaction of recognition
  - Recognize some MHC IB molecules
**Immunoregulation**

- **Th0**
  - IL-2
  - IFN-γ

- **Th1**
  - IL-2
  - IFN-γ

- **Th2**
  - IL-4
  - IL-5
  - IL-10

**Antigen concentration**
- High amounts of Ag → Th1
- Low amounts of antigen → Th2
- Strong MHC-peptide to TCR interaction → Th1
- Weak MHC-Peptide to TCR interaction → Th2
- High affinity of peptide to MHC → Th1
- Low affinity of peptide to MHC → Th2
Immunological memory

- Effective responses eliminate pathogen or Ag from the system
  - Removal of most effector cells as part of the restoration of tissue integrity
    - Cells die via apoptosis and are cleared by macrophages
    - Cells that survive become memory cells.
    - T cells survive almost indefinitely.

- B cells develop primary focus of proliferation 5 days after inoculation of Ag
  - Initial Ab production
    - Early response
      - Trapping of Ag
    - FDC presentation (iccosomes)
– Differentiation, germinal center formation
– Somatic hypermutation, selection
– Exponential proliferation for 2 or 3 days (6 or 7 cell division cycles)
– 90% Differentiation into plasma cells (2 – 3 day life span, then apoptosis)
– 10% life longer, fate is unknown

• Germinal centers last for 3 – 4 weeks
• Some B cells continue to proliferate for months
  – Migrate to the mucosas
  – Differentiate into plasma cells
  – Last for years