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-idiotipic 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 R \(\alpha\) 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-\(\beta\)
  - Altered state of development (not an independent cell lineage)

\(\gamma\delta\) T cells
- TCR composed of \(\gamma\ \delta\) 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
\( \gamma \delta \) T cell as regulators of IR

- Mice deficient on \( \gamma \delta \) 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-\(\gamma\)
- 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
- 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.
Immunological memory

- B cells develop primary foy 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