Topics

- Immune regulation
  - $\gamma\delta$ 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 α 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 precence 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

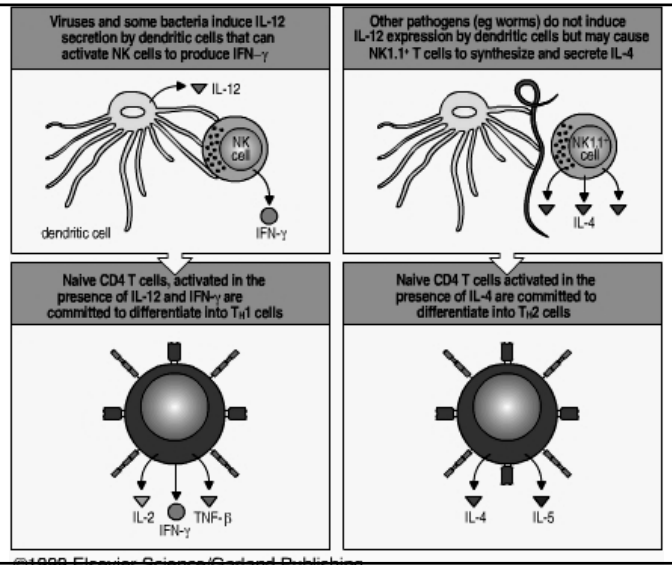
- Th0 differentiate into Th1 and Th2 and determines if the response is cellular or humoral
- Cytokines present at the site of proliferation

Th1 induction

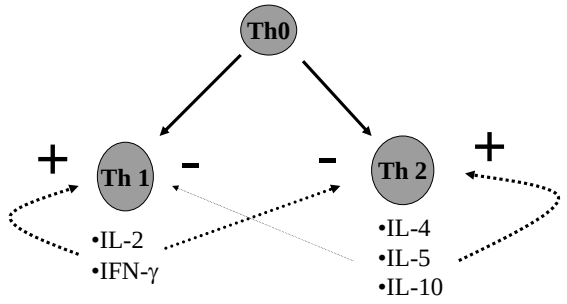
- IL-12, IFN-γ
- Produced by dendritic cells, macrophages, NK cells in response to viral infection and invasion by some intracellular bacteria

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



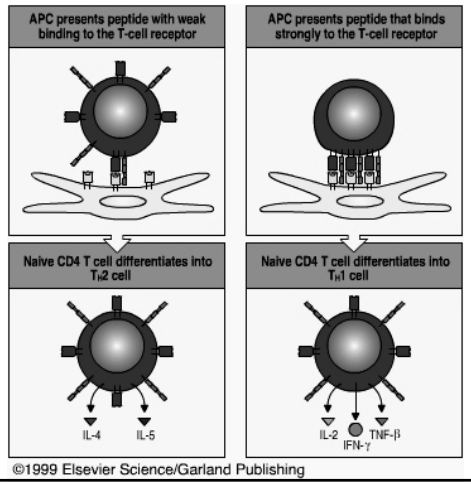
Antigen concentration

- High amounts of Ag -> Th1
- Low amounts of antigen -> Th2

- Strong MHC-peptide to TCR interaction ->Th1
- Weak MHC-Peptide to TCR interaction -> Th2

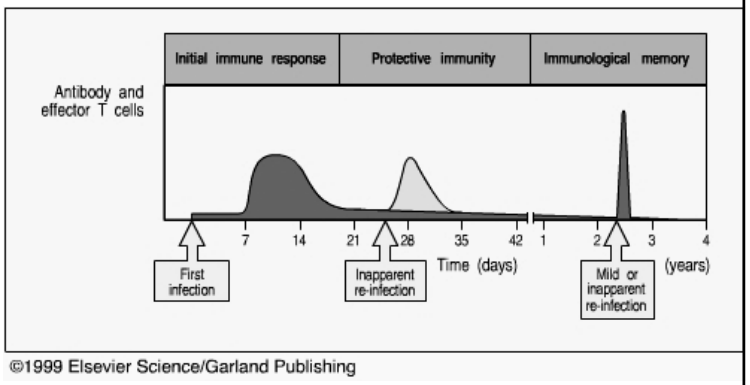
- High affinity of peptide to MHC ->Th1
- Low affinity of peptide to MHC ->Th2

Antigen concentration



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 focy 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