defenses against disease 11-19-01 (part 3 of 3)

• effector activities; memory

• lymphocyte development (& failures/defects)
  – generating diversity in antibodies and T cell receptors
    • defects: SCID and agammaglobulinemia
  – tolerating self
antibody effector activities

**HUMORAL RESPONSE**

Activation phase

- Class II MHC protein
- Helper T cell
- T cell receptor
- Antibodies

Macrophage

Antigen

Effector phase

- B cell
- Plasma cell
- Endoplasmic reticulum

Memory cells
CELLULAR RESPONSE

 Activation phase

 Antigen → Infected cell → Class I MHC protein → T cell receptor → Cytotoxic T cell precursor

 Effector phase

 Infected cell → Tc

 CTL killing mechanisms:

 GRANULE EXOCYTOSIS PATHWAY

 Granule → Perforin → Granzyme → Extracellular space → Fas ligand

 Target cell → Perforin pore → Ca²⁺ → Fas death domains

 FAS PATHWAY

 Fas ligand → FADD → Initiator caspase → Caspase cascades → Apoptosis
demonstrating antibody specificity
Ab and TCR diversity generated in “primary” lymphoid organs

Thymus

Bone marrow

Lymphocyte DNA
(B cell antibody genes, and T cell TCR genes)

Somatic recombination
(a) DNA rearrangement

Embryonic DNA

VDJ joining

Embryonic μ gene for heavy chain of IgM

(b) RNA splicing

1. After V, D, J, and C DNA segments have been joined, the resulting functional gene for a heavy chain is transcribed.

2. Splicing of the primary RNA transcript removes the transcripts of any introns, along with transcripts of any extra J segments.

Translation of immunoglobulin heavy chains
Ab class switching: changing *function*, not specificity

David, the Bubble-boy
immune developmental defects:
x-linked agammaglobulinemia

"primary" lymphoid organs

thymus

bone marrow
CELLULAR RESPONSE

**Activation phase**

Antigen → Infected cell → Class I MHC protein → T cell receptor → Cytotoxic T cell precursor

**Effector phase**

Infected cell → Tc