

Immunotherapy

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Immunotherapies

- **Vaccines** (toxoid, attenuated live, killed cell vaccines, subcellular, DNA, peptide)
- **Adjuvants** (nonspecific immune stimulant)
- **Passive Antibody** (IVIg, humanized monoclonal antibodies or immunotoxins)
- **Cytokines** (IFN, IL-10, IL-12) or **cytokine antagonists** (anti-TNF, soluble cytokine receptors)

Immunotherapies

- **Co-stimulator or suppressor signaling molecules** (CTLA-4)
- **Adoptive transfer of immune cells**
 - Immune Tc cells
 - Lymphokine activated NK cells
- **Antagonist peptides** (inhibit specific T cells by blocking TcR)
- **Oral tolerance** (ingestion of antigen induces suppressive factors [TGF- β])

Immunosuppressive agents

- **Corticosteroids** (block cellular infiltration, cytokine release, T cell maturation, etc.)
- **Azathioprine** (inhibit lymphocyte proliferation)
- **Cyclosporine** (inhibit IL-2 gene expression)
- **Anti-lymphocyte serum** (causes lymphocyte destruction and removal)

Immunosuppressive agents

- **Anti-CD3** (causes T cell destruction)
- **Anti-CD4** (causes T cell destruction)
- **Cytotoxic drugs and ionizing radiation** (block cell proliferation, lymphopoiesis)

Immunotherapeutic agents : applications: mechanisms of action

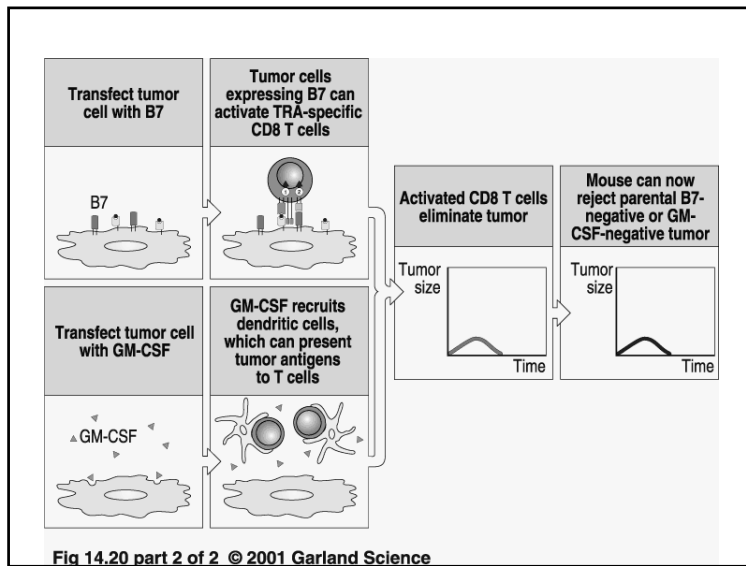
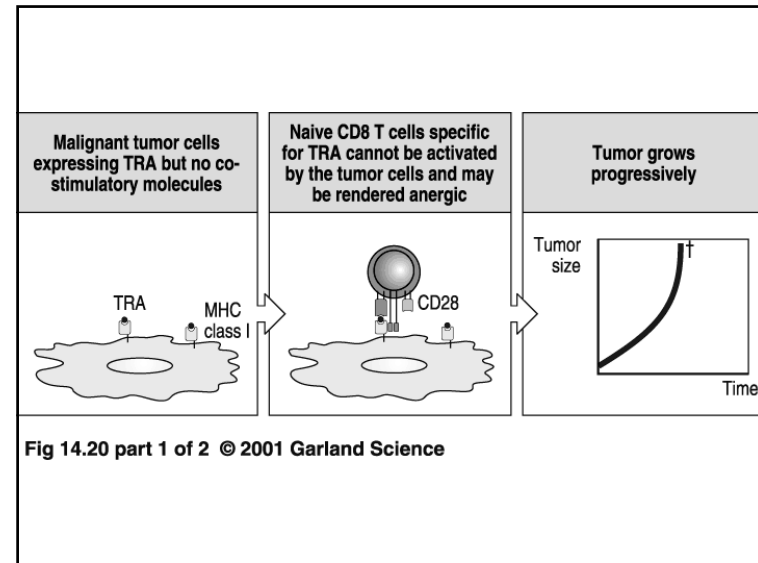
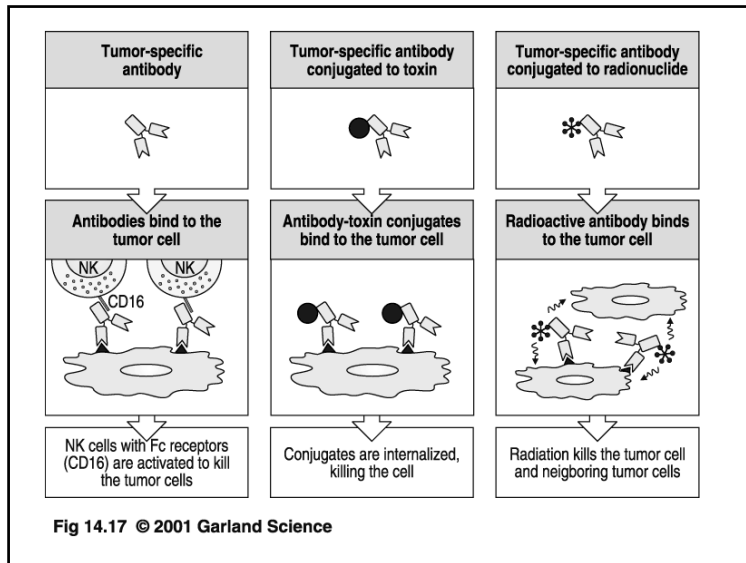
- **Anti-TNF-alpha**: inflammatory bowel disease and rheumatoid arthritis: inhibits inflammatory actions of TNF-alpha
- **Anti-CD20**: non-Hodgkin's lymphoma: ADCC destruction of B cells
- **Anti-lymphocyte globulin**: treatment of acute graft rejection: depletes T cells via ADCC or inhibits of cell function

Immunotherapeutic agents : applications: mechanisms of action

- **Interferon-alpha**:
 - viral hepatitis: anti-viral
 - Hairy cell leukemia: anti-proliferative
- **Interferon-beta**:
 - Gliomas: anti-proliferative?
 - Multiple sclerosis: anti-viral, antagonism of interferon-gamma

Corticosteroid therapy	
Effect on	Physiological effects
↓ IL-1, TNF- α , GM-CSF ↓ IL-3, IL-4, IL-5, IL-8	↓ Inflammation ↓ caused by cytokines
↓ NOS	↓ NO
↓ Phospholipase A ₂ ↓ Cyclooxygenase type 2 ↑ Lipocortin-1	↓ Prostaglandins ↓ Leukotrienes
↓ Adhesion molecules	Reduced emigration of leukocytes from vessels
↑ Endonucleases	Induction of apoptosis in lymphocytes and eosinophils

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Current immunization schedule for children (USA)

Vaccine given	months						years			
	1	2	4	6	12	15	18	4-6	11-12	14-16
Diphtheria-tetanus-pertussis (DTP/DTaP)	█	█	█	█	█	█	█	█	█	*
Inactivated polio vaccine	█	█	█	█	█	█	█	█	█	█
Measles/mumps/rubella (MMR)	█	█	█	█	█	█	█	█	█	█
Pneumococcal conjugate	█	█	█	█	█	█	█	█	█	█
Haemophilus B conjugate (HiBC)	█	█	█	█	█	█	█	█	█	█
Hepatitis B	█	█	█	█	█	█	█	█	█	█
Varicella	█	█	█	█	█	█	█	█	█	█

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Humanized monoclonal antibodies

- **Use of mouse monoclonal antibodies for immunotherapy in humans is limited by immune responses in humans against the foreign mouse antibody proteins.**
- **Complementarity determining regions (CDR) of mouse monoclonal antibodies can be grafted onto the framework of a human immunoglobulin. Recombinant antibodies are less immunogenic and induce less allergic reactions.**