

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

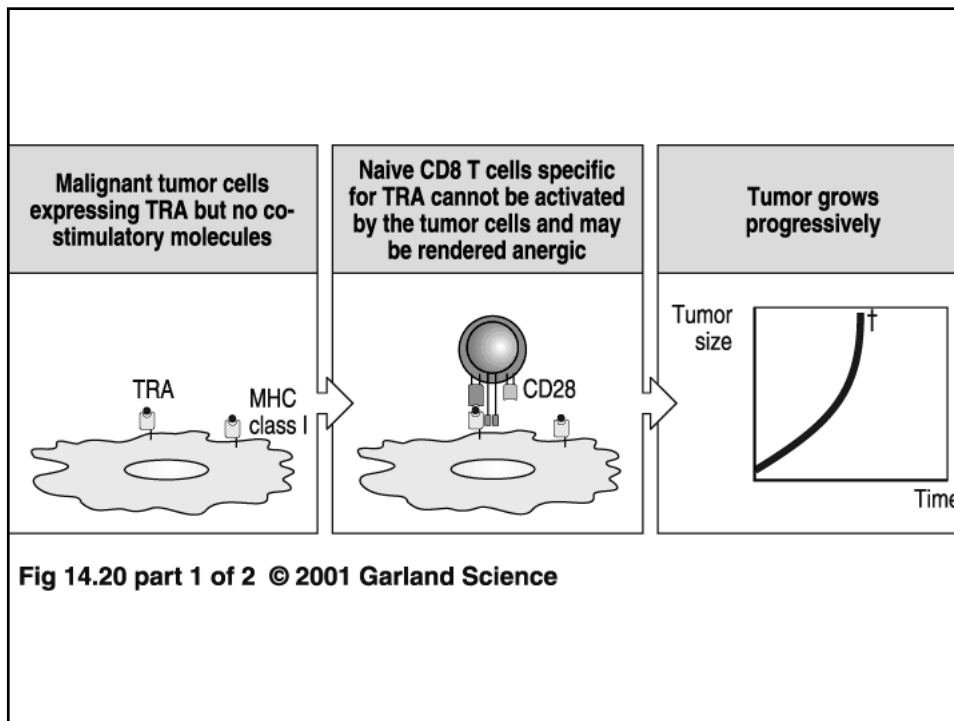
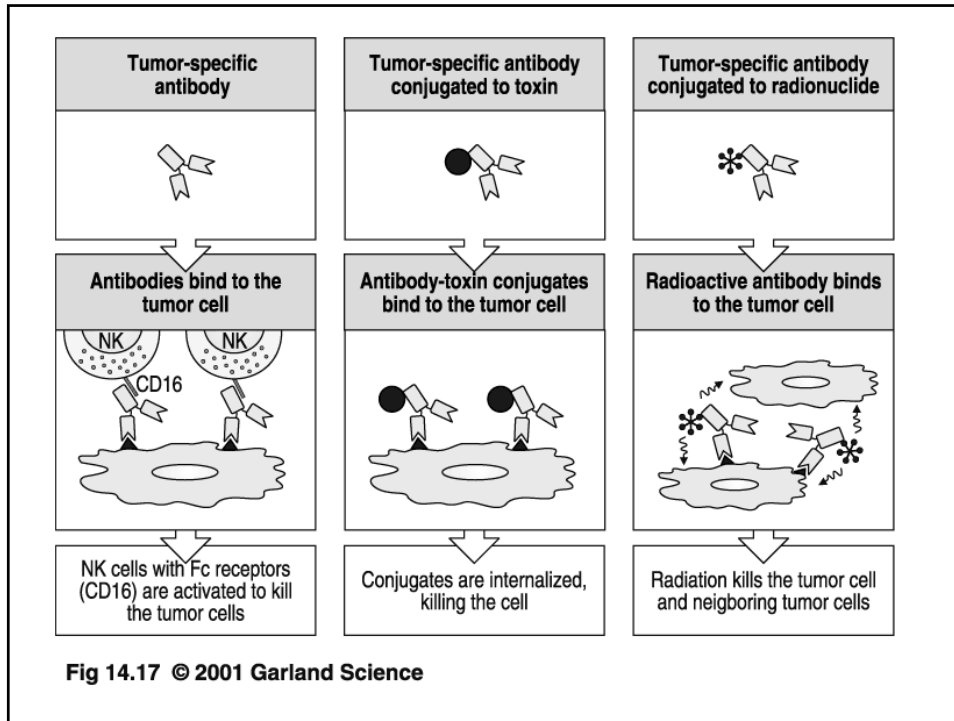
- **Anti-TNF-alpha: inflammatory bowel disease and rheumatoid arthritis: inhibits inflammatory actions of TNF-alpha**
- **Anti-CD20: non-Hodgkin's lymphoma: ADCC destruction of B cells**
- **Anti-lymphocyte globulin: treatment of acute graft rejection: depletes T cells via ADCC or inhibits of cell function**

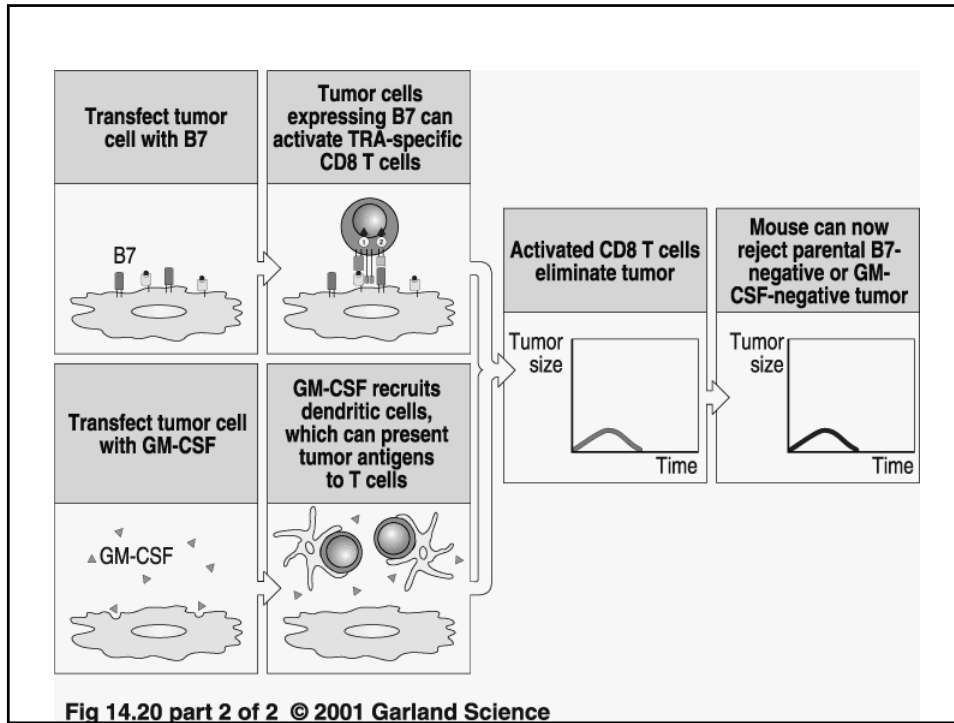
**Immunotherapeutic agents :
applications: mechanisms of action**

- **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										
<i>Haemophilus B</i> 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.**