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)

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

<table>
<thead>
<tr>
<th>Effect on</th>
<th>Physiological effects</th>
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<tbody>
<tr>
<td>IL-1, TNF-α, GM-CSF</td>
<td>Inflammation caused by cytokines</td>
</tr>
<tr>
<td>IL-3, IL-4, IL-5, IL-8</td>
<td></td>
</tr>
<tr>
<td>NOS</td>
<td>NO</td>
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<tr>
<td>Phospholipase A2</td>
<td>Prostaglandins</td>
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<td>Cyclooxygenase type 2</td>
<td>Leukotrienes</td>
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<td>Lipocortin</td>
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<tr>
<td>Adhesion molecules</td>
<td>Reduced emigration of leukocytes from vessels</td>
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<tr>
<td>Endonucleases</td>
<td>Induction of apoptosis in lymphocytes and eosinophils</td>
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</tbody>
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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.