

# **Immunotherapy**

Ivo Minárik, 2007

# Immunotherapy 2

- Suppress immune response
- Encourage immune response

# Suppressing immune response

- immunosuppressive drugs – e.g. Cyclosporin, tacrolimus, corticosteroids, etc.
- Antibodies
- Dendritic cells
- Regulatory T cells

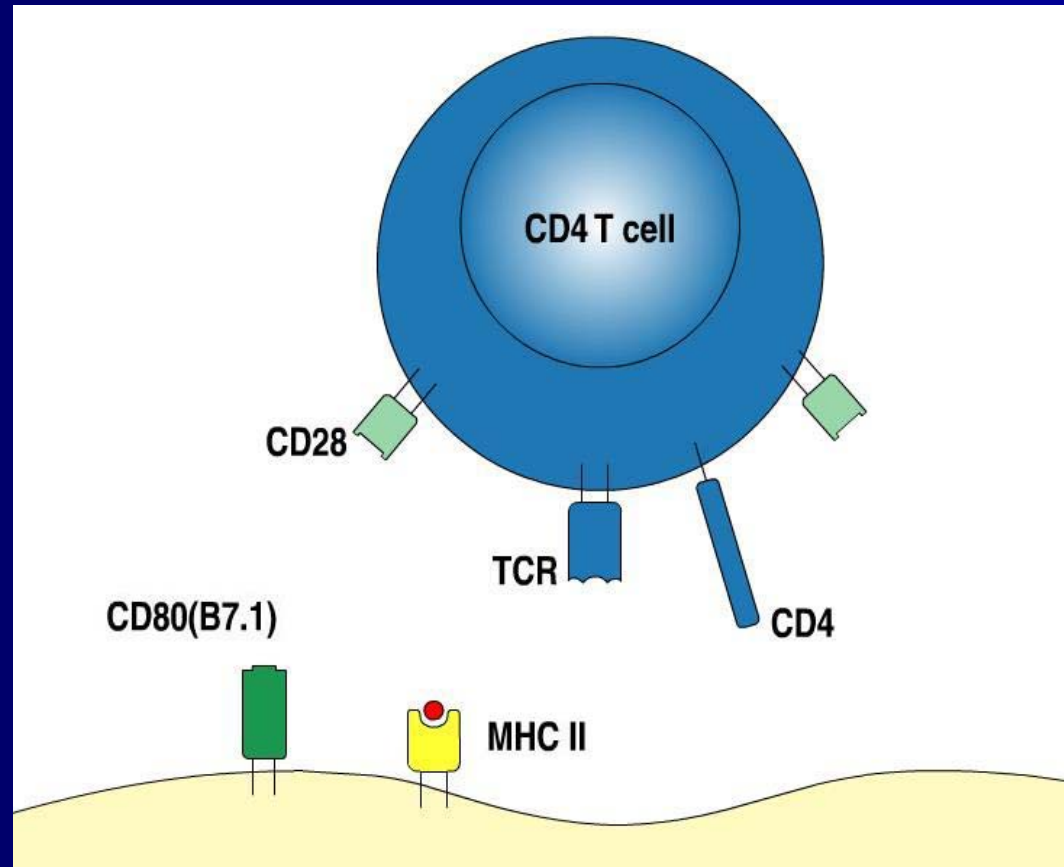
# Antibodies

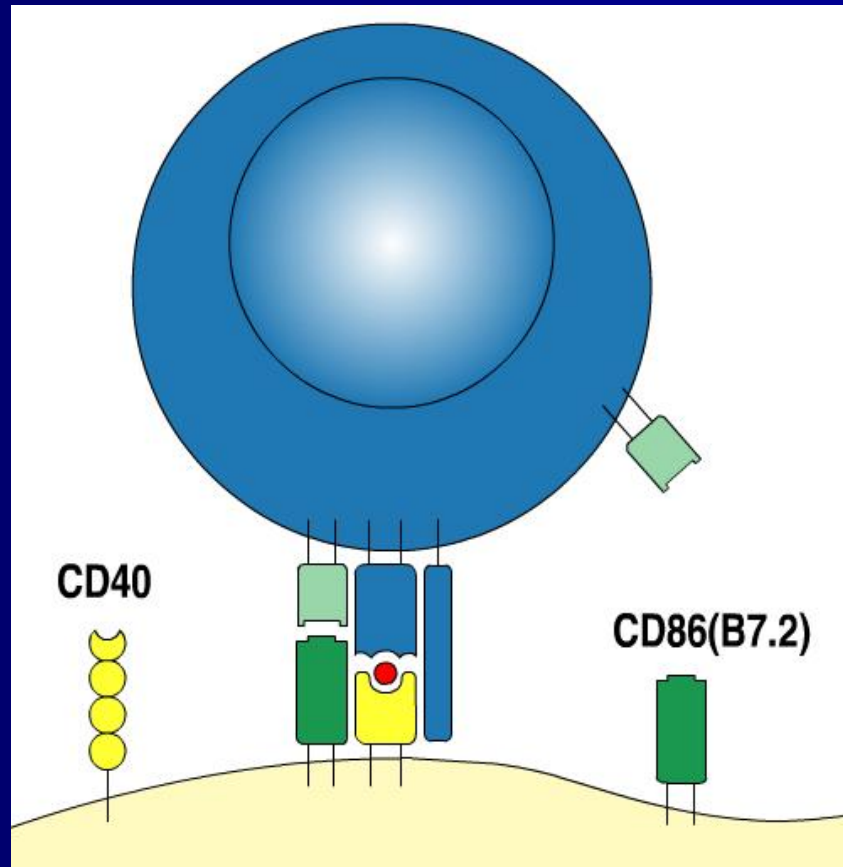
- Anti-lymphocyte globulin – depletion of allogenic lymphocytes before organ transplatation
- Anti-CD3 – promising in DM1
- Anti-CD4 - disappointing

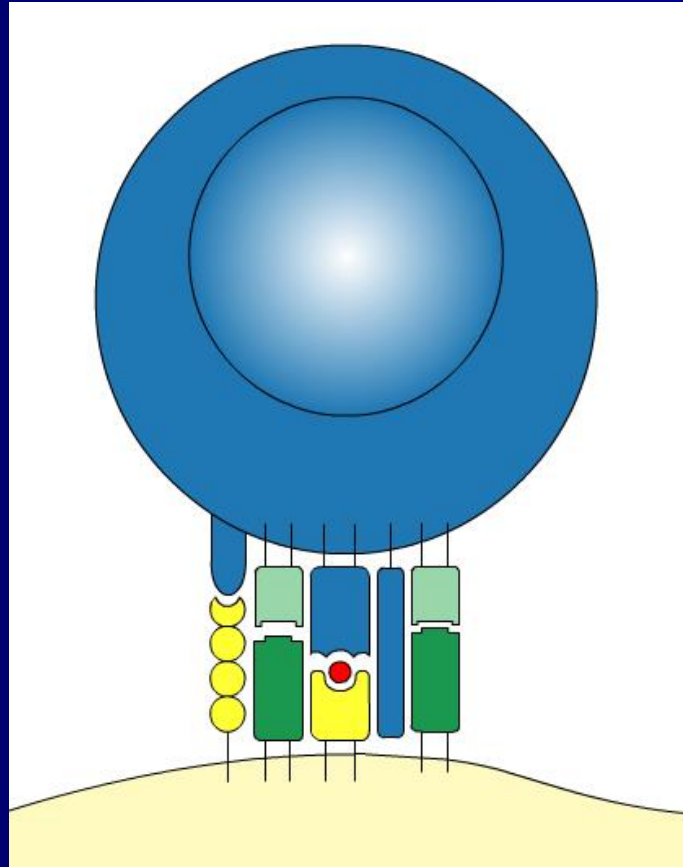
# Antibodies 2

- Anti-TNF $\alpha$  therapy (infliximab) – rheumatoid arthritis
- Receptor for TNF $\alpha$
- Receptor for IL-1
- Antibodies against adhesion molecules (natalizumab) – block migration of lymphocytes to the site of inflammation – Crohn's disease, multiple sclerosis

# Role of costimulatory molecules



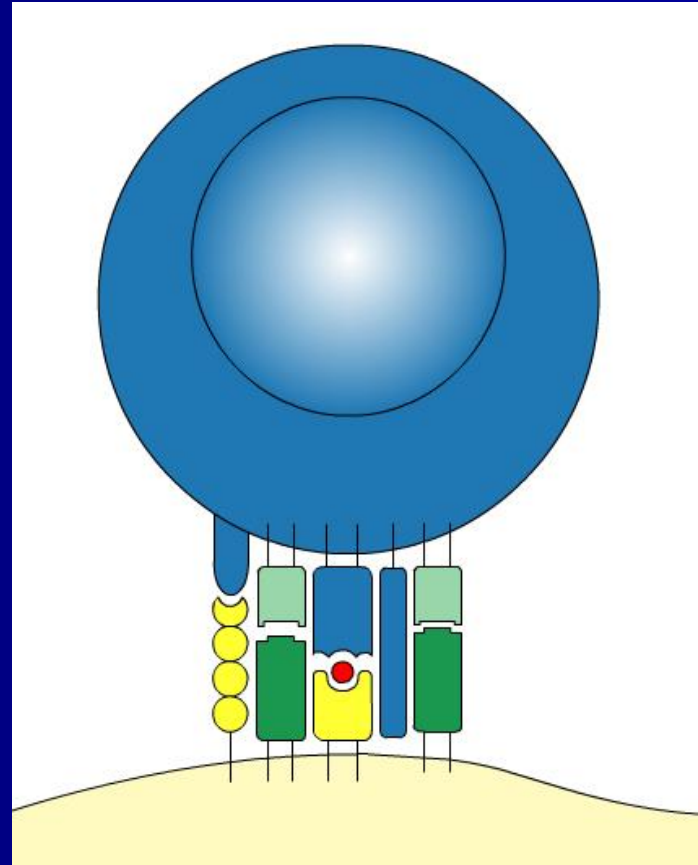






# Interference with costimulatory pathways

- CTLA4Ig – binds to CD80 and CD86
- Psoriasis
- Anti-CD40L – on surface of T cells



# Immune modulation

- Manipulating T regulatory cells (IL-10, TGF $\beta$ ), immature dendritic cells

# Dendritic cells

- TLR receptors (Toll-like) – essential for the initiation of immune response
- If no TLR costimulation – Tcell anergy, expansion of regulatory T cells

# Allergy

- Hyposensitization – repeated application of gradually growing doses of allergen
- Lasts for 3-5 years
- Isotype switch, degranulation of mast cells
- Subcutaneous, inhalation, ingestion

# Encouraging immune response

- Cancer therapy – nonspecific (IL-2, IFN $\alpha$ ) × specific
- Tumor cells – lower expression of MHC I, production of IL-10, TGF $\beta$ , VEGF, frequent mutations

# Antibodies

- Ab+cytotoxic drug/radioisotope/toxin  
– difficult to assign appropriate antigen for targeting
- Disappointing – antigen instability, inefficient killing, inefficient penetration
- Especially used for lymphomas and leukemias

# Antibodies 2

- Targeting growth factors + other molecules
- Bevacizumab (VEGF) – colon cancer, renal cancer
- rituximab (anti CD20) – non-Hodgking lymphoma

# Strategy to enhance Tcell immunity

- Antigens + adjuvant (GM-CSF, extract from *Corynebacterium parvum*, CpG)
- Dendritic cells – antigens in the form of peptide (HLA restriction), cDNA, RNA, necrotic or apoptotic cells
- TILs (tumor infiltrating lymphocytes)
- Adoptive cell transfer