Immune response to infections

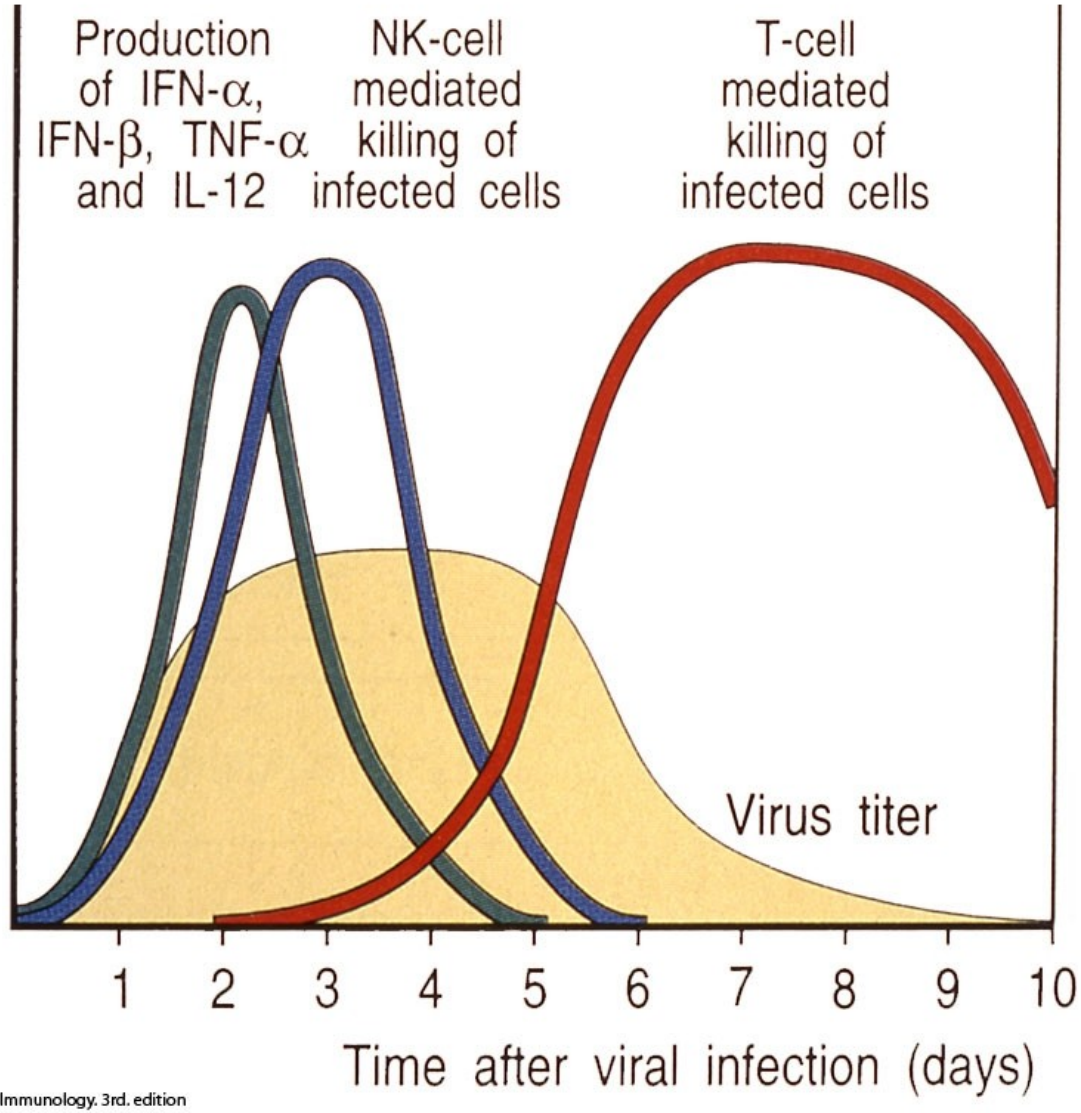
Factors influencing the extent and severity of infection

- Pathogen factors
  - Dose
  - Virulence of organism
  - Route of entry
- Host factors
  - Integrity of non-specific defences
  - Competence of the immune system
  - Genetic influences
  - Previous exposure to antigen
  - Existence of co-infection

Immune response to viral infections

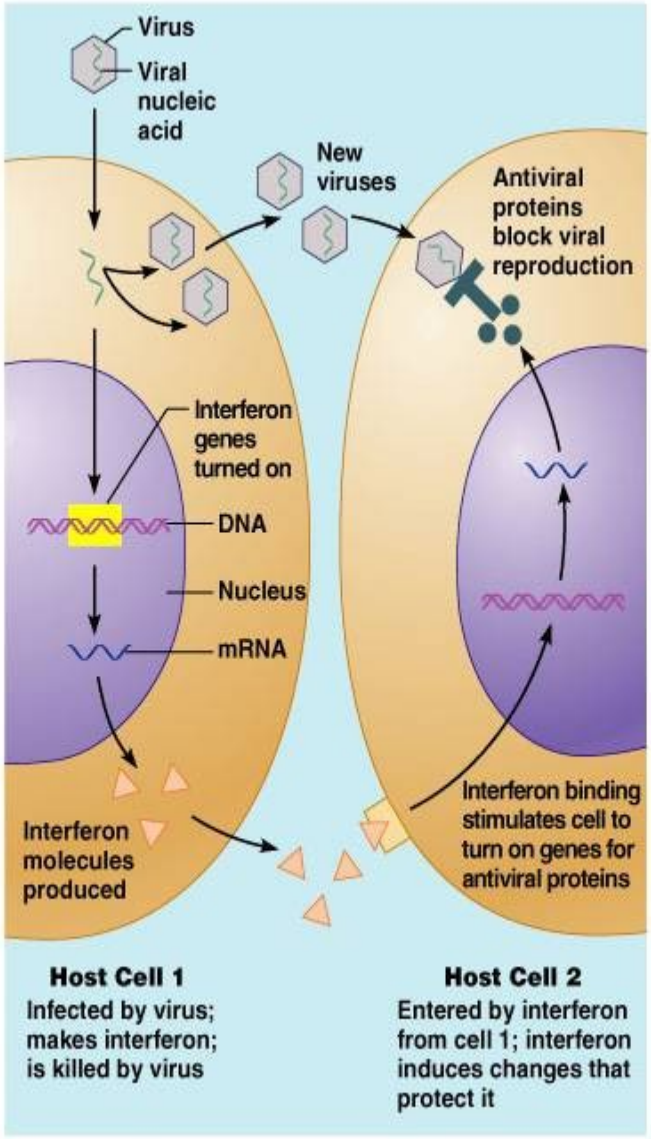
- **Non-speciphic immunity**
  - **Interferons (α and β)**
  - **Natural killer cells (NK buňky)**
  - **Activation of the complement system (EBV)**
  - **Phagocytosis**
  - **Receptor-like molecules in various secretions**
- **Speciphic immunity**
  - **Antibodies – neutralization of extracellular viruses**
  - **Tc lymphocytes – elimination of virus-infected cells**

Mechanisms of antiviral immunity



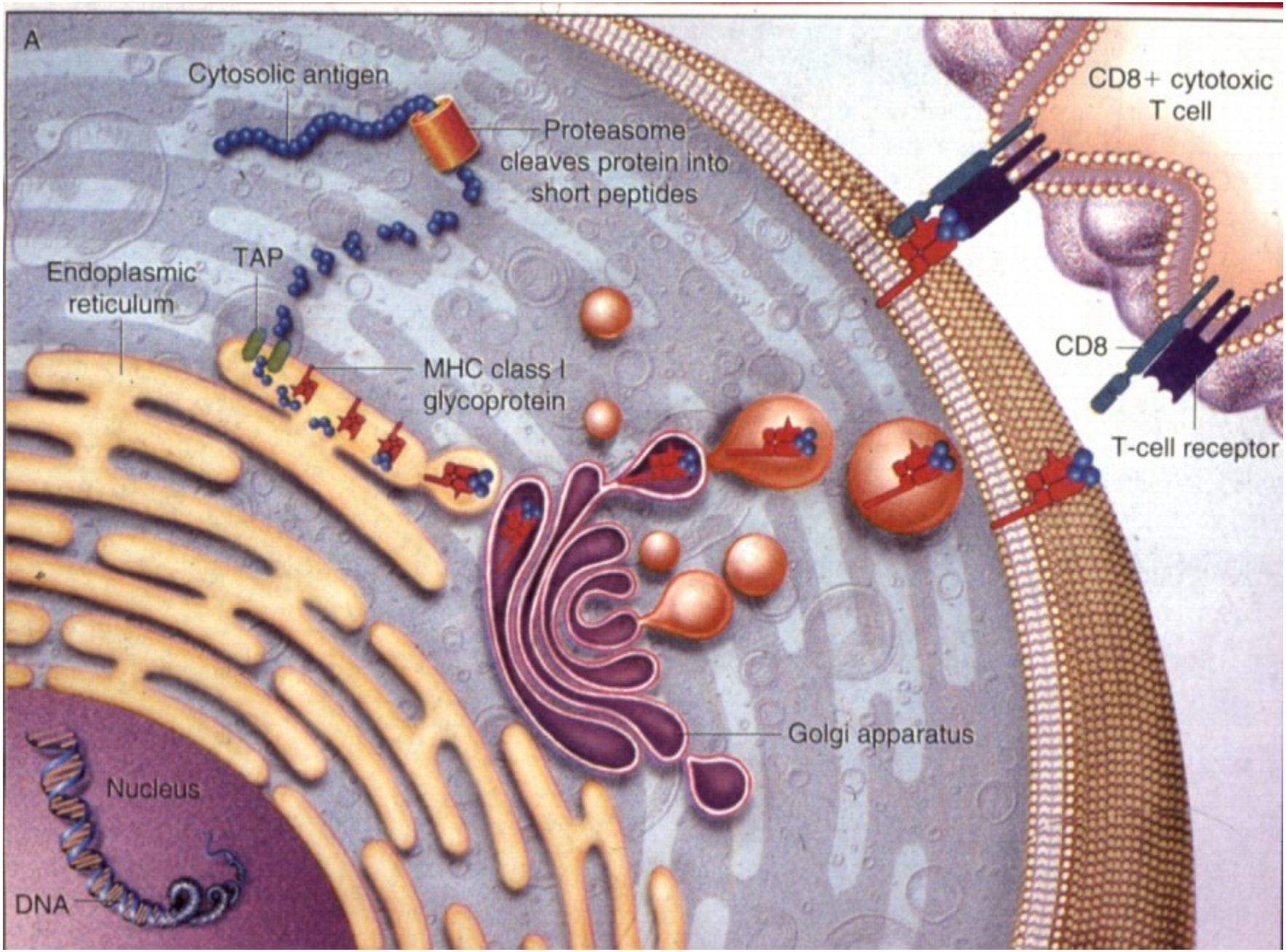
From: I. Roit et al: Slide atlas of Immunology. 3rd. edition

The action of interferon (IFN)



Natural killers (NK cells)

- Originate in non-T non-B lymphocyte lineage.
- Morphologically: large granulated lymphocytes (LGL).
- Recognition of target cells in antigen non-speciphic.
- Virus infected and tumor cells are killed.
- Target cells are characterised namely by decreased HLA-I expression.
- Cytotoxic mechanisms are similar to Tc cells: perforin and induction of apoptosis.


A
Cytosolic antigen
Proteasome cleaves protein into short peptides
TAP
Endoplasmic reticulum
MHC class I glycoprotein
CD8+ cytotoxic T cell
CD8
T-cell receptor
Golgi apparatus
Nucleus
DNA

Viral strategies to evade the immune response

- Antigenic variations
  - antigenic drift - minor changes
  - antigenic shift - major changes
- Long-term survival in a host
  - Viral persistence
  - Viral latency
  - Oncogenic transformation
- Immunosuppressive effect of viruses

Immunosuppressive effects of viruses

- Suppression of T-cells : HIV, morbilli, CMV,
- Inhibition of MHC antigens expression: CVM (binds β-2 microglobulin), Adenoviruses, RSV - decreases expression of HLA antigens
- Production of inhibitory cytokies: EBV (IL-10 - like factor)

Damage of a host caused by anti-viral immune response

- **Autoimmune diseases: hemolytic anemia after EBV infection, autoimmune hepatitis induced by hepatitis-B virus**
- **Immune complex diseases: arthritis in hepatitis B, vasculitis**
- **Tc - meadited diseases: rash in exanthematic viral diseases, myocarditis caused by coxackie virus**

Immune responses to bacterial infections

- **Non-specific immunity**
  - **Mechanical barriers**
  - **Phagocytosis**
  - **Complement system**
- **Specific immunity**
  - **Antibodies - opsonisation, complement-activation, neutralisation of toxins, binding to receptors**
  - **T-lymphocytes - against intracellular parasites**

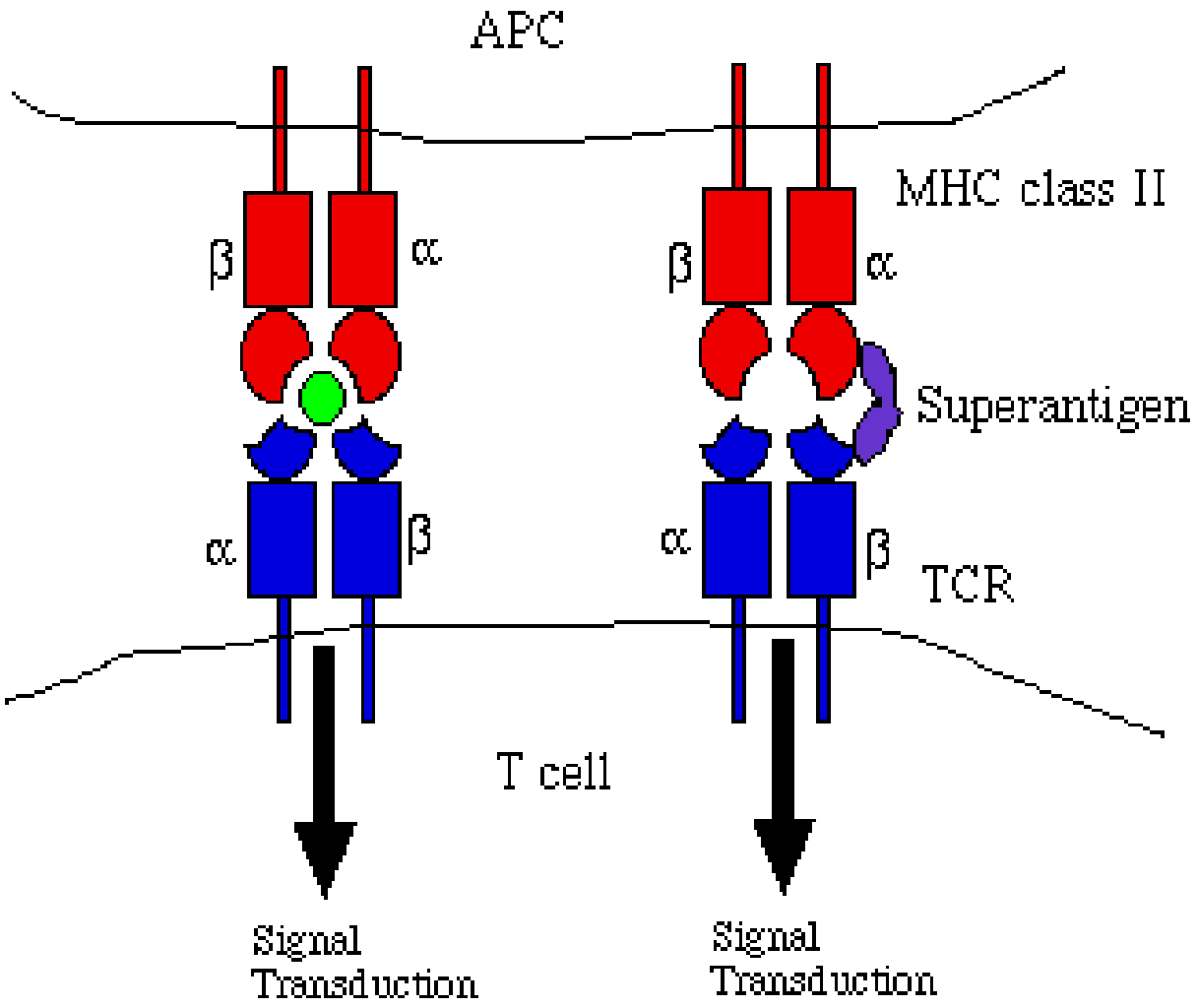
Bacterial evasions of immune defences

- Antiphagocytic machanisms: toxins, capsular polysaccharides
- Inhibition of the complement system: *Str. pyogenes, E. coli, N. meningitidis*
- Antigenic variations: *Borrelia recurrentis*
- Proteases lysing IgA - *Neisseria, Haemophilus*
- Sequestration in avascular regions- *Salmonella typhi* in the gall bladder and urinary tract
- Intracellular parasitism

Bystander damage caused by the immune response to bacterial infection

- Autoimmune diseases
  - Cross-reactivity of bacterial and corporal antigens - rheumatic fever
  - Type-II hypersensitivity - autoimmune hemolytic anemia caused by *Mycoplasma* infection
  - Heat shock proteins
  - Superantigens (streptococcal, staphylococcal)
- Immunocomplex diseases
- Type IV hypersensitivity- cavitatoin in pulmonary tuberculosis

Activation of TCR by antigen and superantigen



Mechanisms of anti-fungal resistance

- Normal bacterial flora
- Phagocytic cells
- T-lymphocytes -probably most important
- Antibodies - usually present, but no protective effect