

VORLESUNG 14

Vorlesung
Humboldt-Universität zu Berlin
Institut für Physik

Biologische Physik

Die Dynamik biologischer Prozesse im menschlichen Körper

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**Max Planck Institute
of Colloids and Interfaces**



7 Immune System

difficulties in studying immunology:

- a lot of details – here only the „big picture“
- exceptions exist to every rule
- knowledge of the immune system is still evolving
- immune system is a „network“

three lines of defense:

- 1) **physical barriers:** skin, mucous barriers, ...
- 2) the innate immune system
- 3) the adaptive immune system





7.1 The Innate Immune System

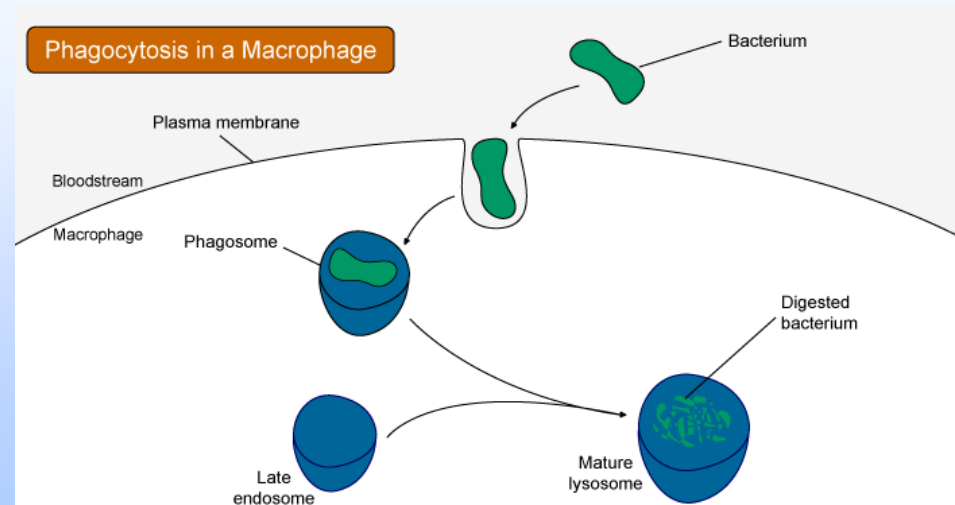
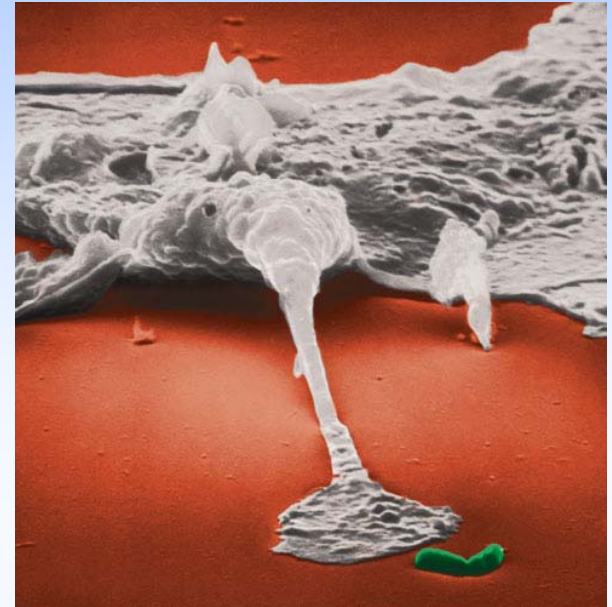
macrophage (as a prominent representative):

- originally monocytes made in the bone marrow
- leave the blood, enter the tissues, and mature into a macrophage
- eat invaders by phagocytosis
- act as garbage collector
- present parts of the meal on its surface (APC)
- give off chemicals (increase in blood flow, swelling, ...)
- act as sentinels to check for invaders send off cytokines to signal that the battle is on

complement system

can punch holes into bacteria

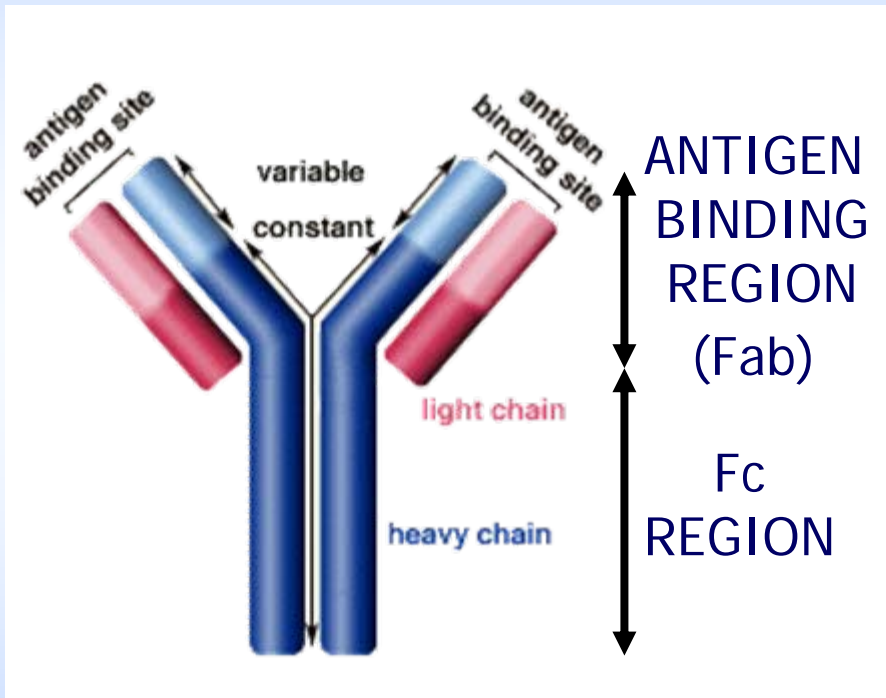
natural killer cells (NKC)





7.1 The Adaptive Immune System

antibodies and B cells:



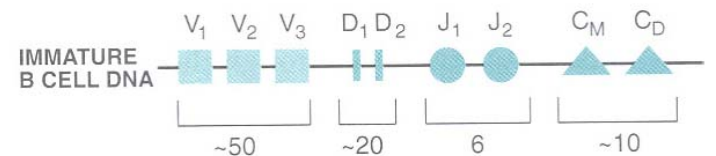
immunoglobulin G (IgG)

generating antibody diversity:

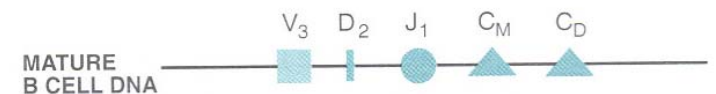
- CLONAL SELECTION

when B cell receptor binds to its cognate antigen, proliferation is started to make a clone of B cells

- MODULAR DESIGN
(+ junctional diversity)



Choice of Gene Segments by Recombination



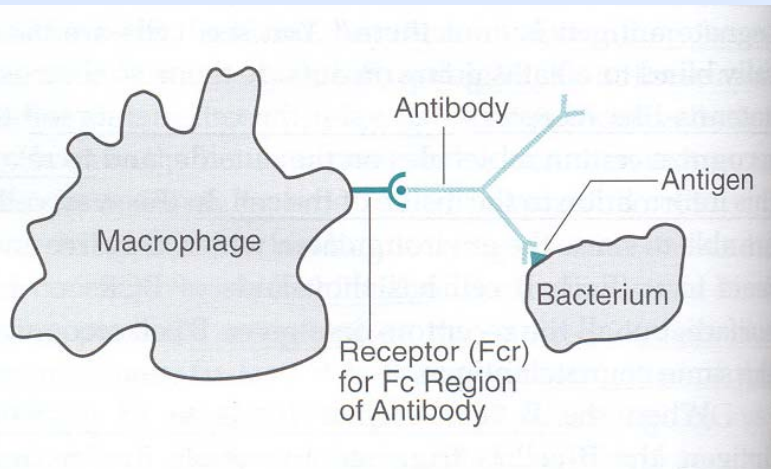
100 million different antibodies





7.1 The Adaptive Immune System

task of antibodies:



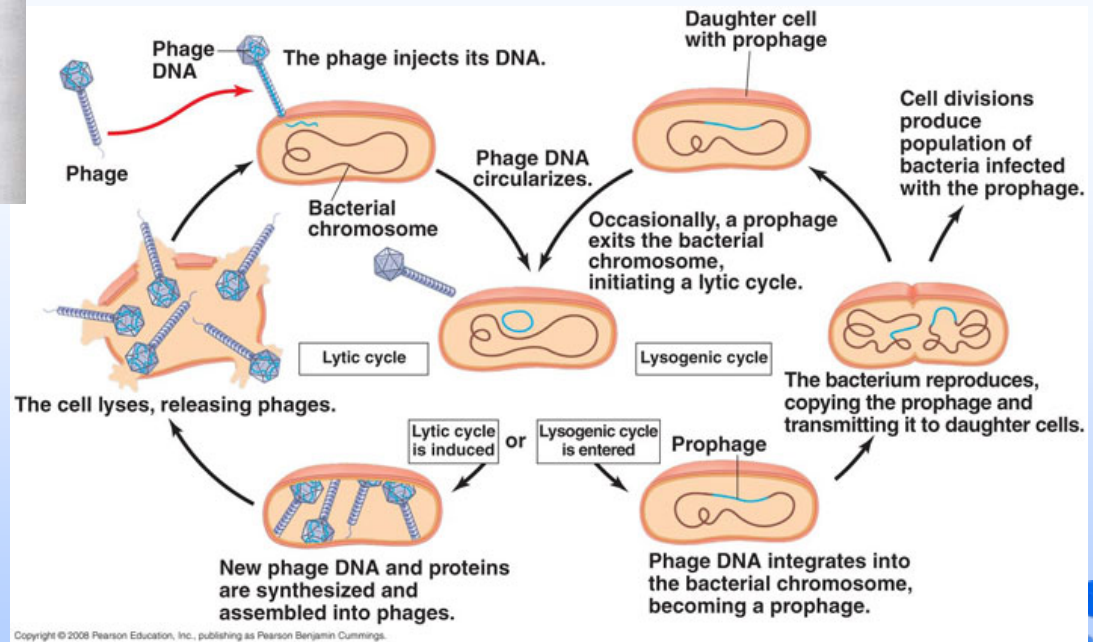
to tag an invader
for destruction – „opsonize“

neutralizing antibodies:

prevent the virus from

- entering into a cell
- replicating once it has entered

LYTIC AND LYSOGENIC CYCLE:





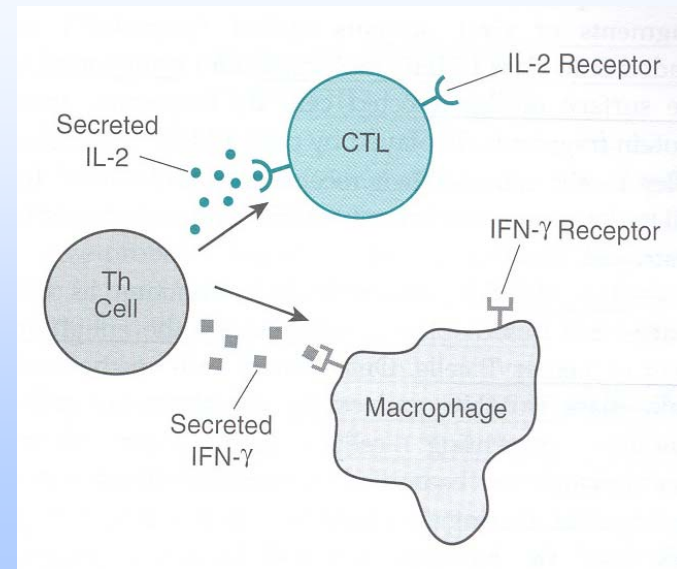
7.1 The Adaptive Immune System

T cells:

10^{12} cells

- **KILLER T CELLS** (cytotoxic lymphocytes – CTLs) – destroys virus-infected cells by „assisted suicide“
- **HELPER T CELLS**
quarterback of the immune system – cytokine factories
directs the action by cytokines like interleukin 2 (IL-2) and interferon gamma (IFN- γ)
- **REGULATORY T CELLS** – keeps other T cells under control (?)

T cell receptors (antibody-like molecules)
(modular design strategy, clonal selection)





7.1 The Adaptive Immune System

antigen presentation (to T cells):

done by

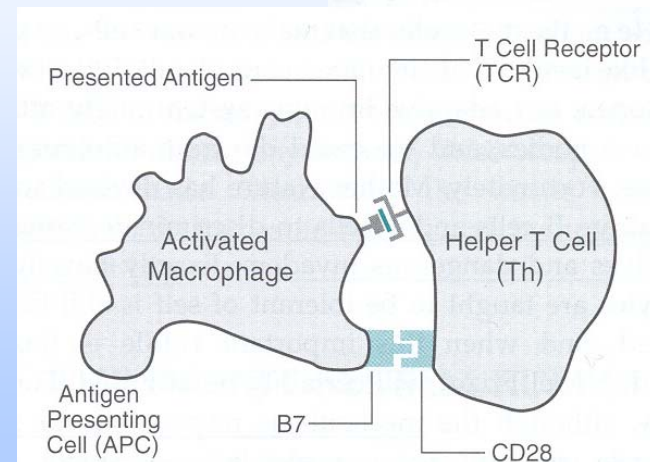
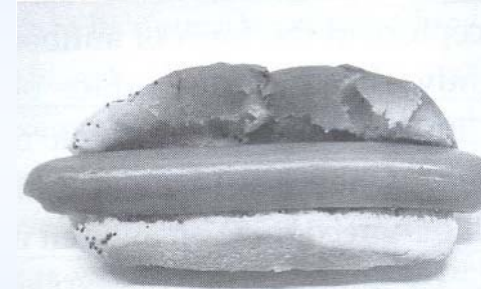
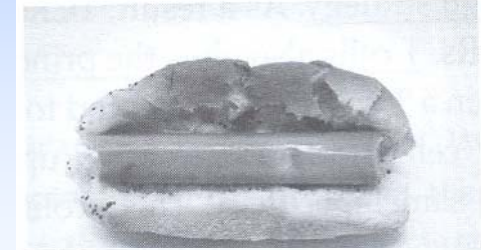
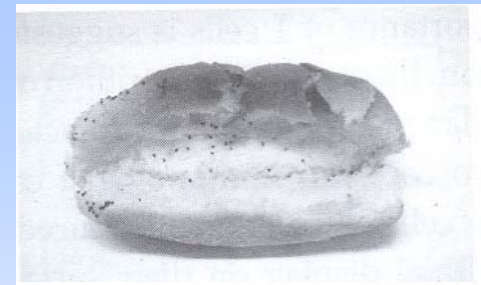
MAJOR HISTOCOMPATIBILITY COMPLEX
proteins (MHC)

- class I MHC molecules: alert killer T cells when something is not right inside the cell
- class II MHC molecules: displayed on antigen presenting cells (APCs, e.g. macrophages) inform helper T cells that problems exist outside of cells

activation of the adaptive immune system:

two-key system (like safe deposit box)

- specific key via antigen presentation
- non-specific key





7.1 The Adaptive Immune System

lymphatic system:

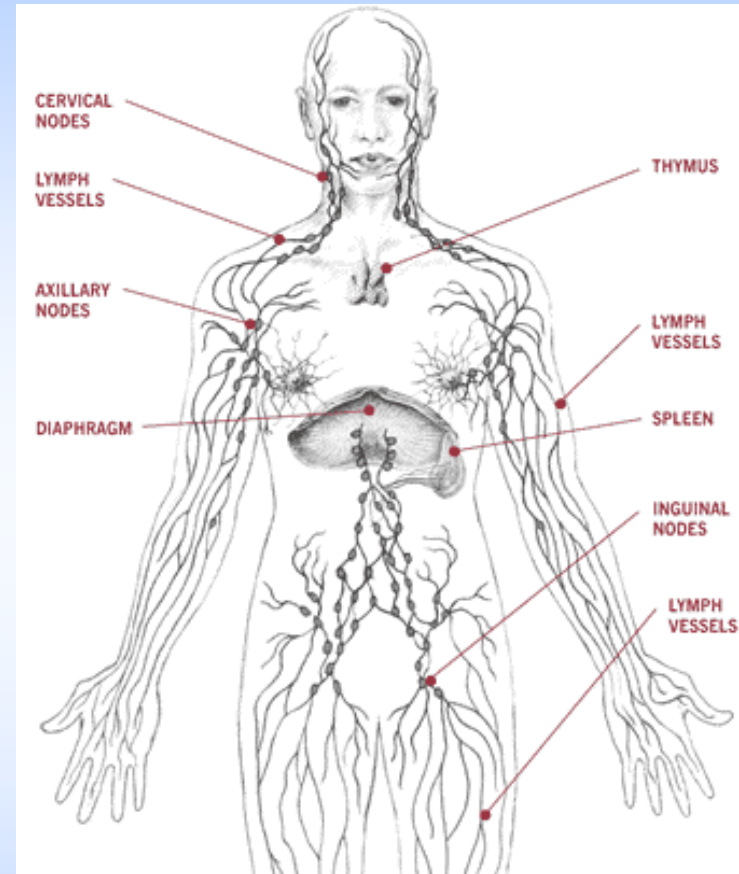
- drains the fluid (lymph) that leaks out of our blood vessels into our tissues
- lymph is collected from our tissues into lymphatic vessels, transported to the upper torso, and recycled back into the blood
- lymph passes through a series of way stations, the lymph nodes
- lymph nodes function as „dating bars“
- T cells and B cells circulate from node to node, looking for antigens for which they are „fated“

IMMUNOLOGICAL MEMORY:

memory cells stick around, just in case ...

TOLERANCE TO SELF:

B cells and T cells are educated to discriminate between ourselves and dangerous invaders





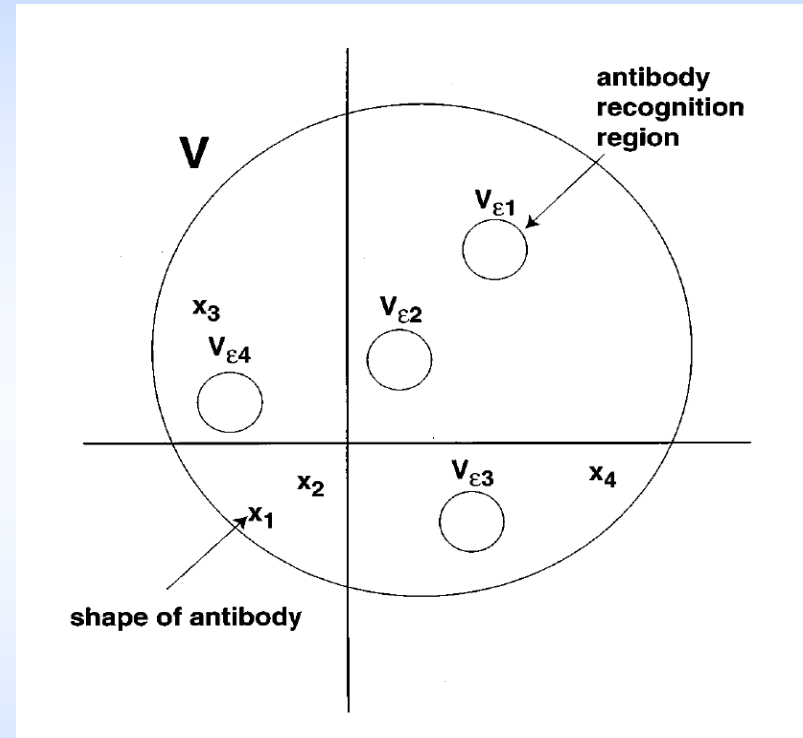
7.1 The Adaptive Immune System

evaluation of the completeness of the repertoire: shape space:

given a set of n distinct, randomly made receptors, what is the probability that a randomly encountered antigen is recognized by at least one receptor?

$$P = (1 - V_{\varepsilon} / V)^n \cong e^{-nV_{\varepsilon}/V}$$

with $p = V_{\varepsilon} / V \cong 10^{-5}$



for this value of p the receptor repertoire is complete if

- each receptor can recognize a set of related epitopes
- the repertoire size is of the order 10^6 or greater
- the receptors in the repertoire have shapes that are randomly distributed throughout shape space





7.1 The Adaptive Immune System

self-nonself discrimination and the probability of recognition:

considering a repertoire size n in an animal with N' self epitopes in an environment with N foreign epitopes, what is the optimal p that all foreign epitopes are recognized but none of the self epitopes?

$$P(N, N'; n) = \left[1 - (1 - p)^n \right]^N (1 - p)^{nN'}$$

$$\text{optimal for } p \cong \frac{1}{n} \ln \left(1 + \frac{N}{N'} \right)$$

predicting the size of epitopes r :

epitopes cannot be **too small** since otherwise it would be expected to be found on both foreign and self proteins

epitopes cannot be **too big** since otherwise the repertoire size would not be reasonable

$$r = -\ln_m p + \ln_m \left[L(m - 1) / m \right]$$

