

Querschnitt Immunologie-Infektiologie
7. Semester - Mittwochs 10.15 Uhr
Hörsaal III; Bergmannsheil-Universitätsklinik



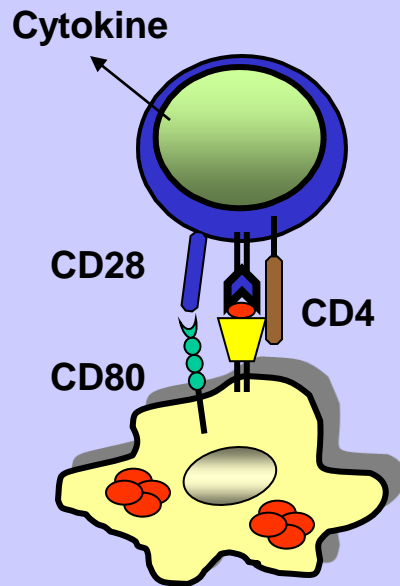
Fin de partie
(Gibt es ein Leben nach der Klausur ?)

Albrecht Bufe

www.ruhr-uni-bochum.de/homeexpneu

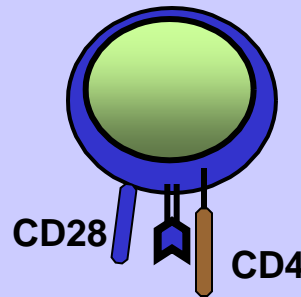
Mechanismen der peripheren Toleranz

Aktivierte T-Zelle

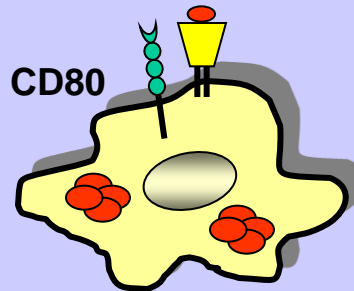


Normal

Nicht aktivierte T-Zelle

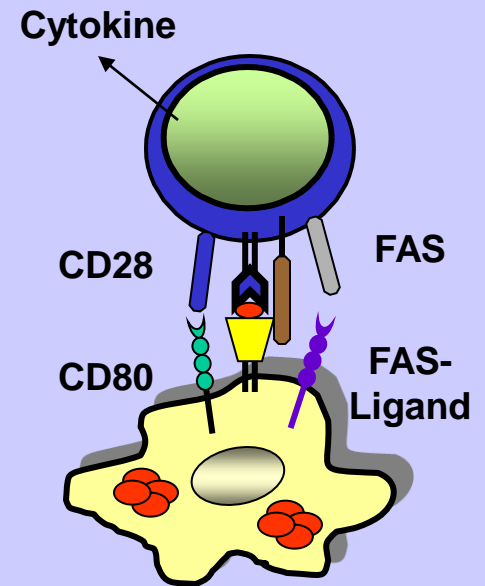


Barriere (anatomisch)



Ignoranz

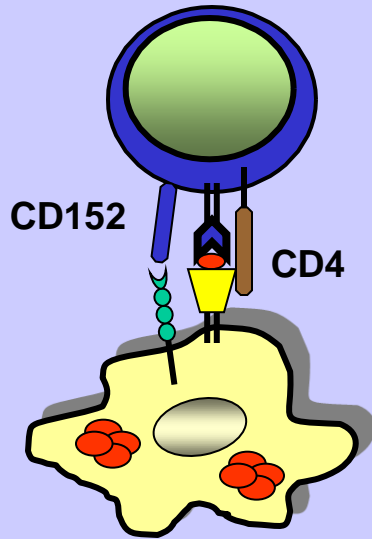
Apoptose



Deletion

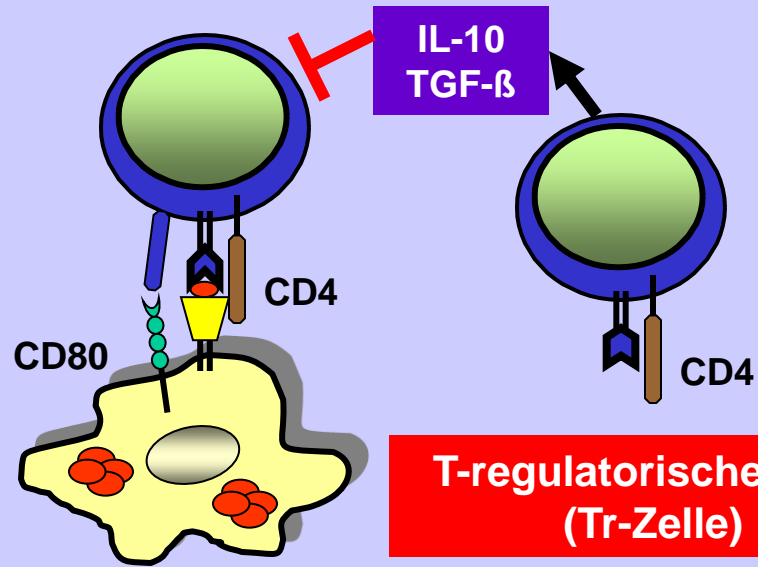
Mechanismen der peripheren Toleranz

Nicht aktivierte T-Zelle



Inhibition

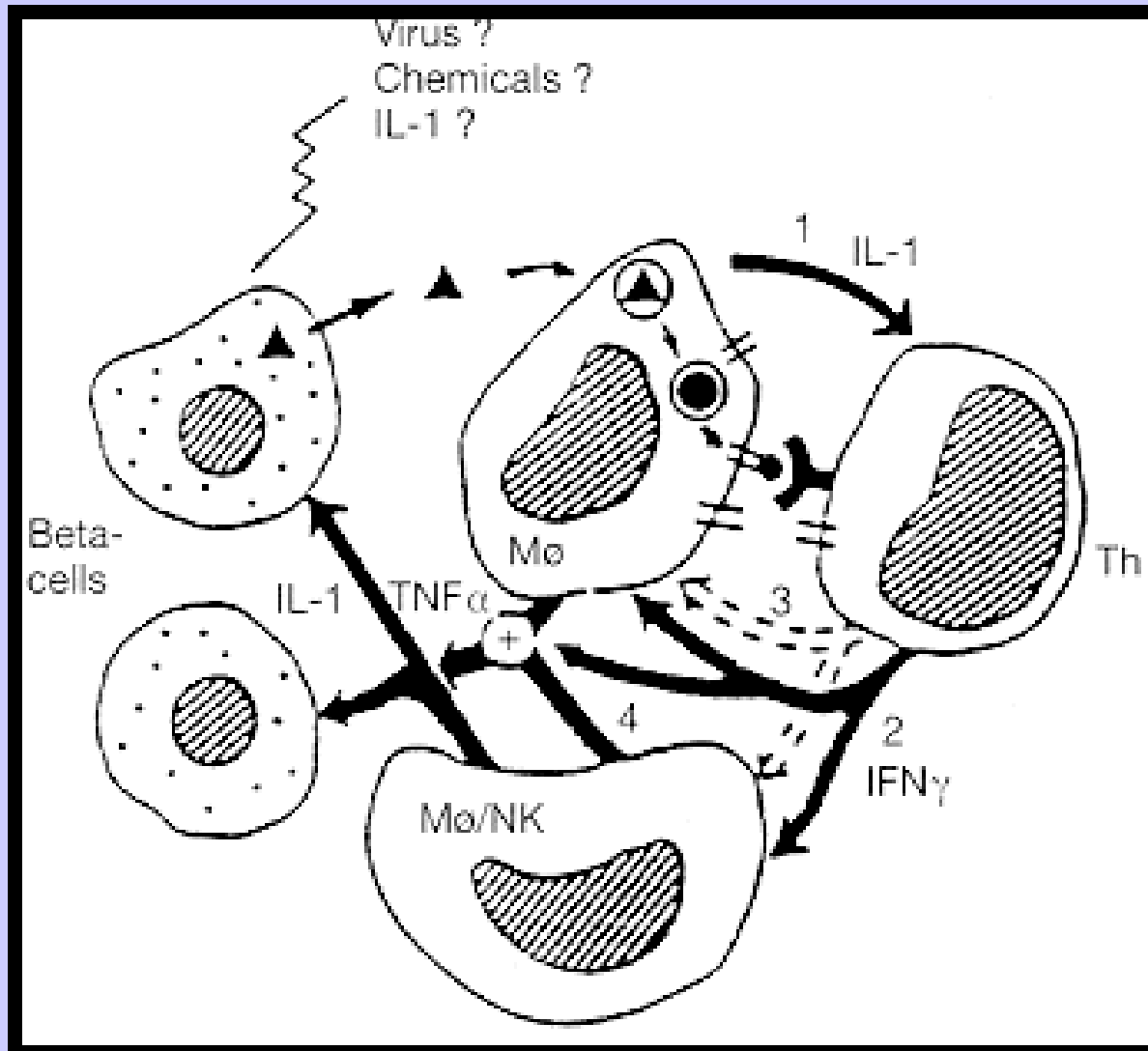
Nicht aktivierte T-Zelle



Suppression

Aufhebung der Toleranz

- Freisetzung von großen Mengen Antigen durch Zellzerstörung (z.B. bei einer Virusinfektion)
- Aktivierung von einer großen Population von Th1 Zellen durch Superantigen
- Freisetzung von proinflammatorischen Zytokinen (IL-1, IL-6, IL-8, TNF- α , durch mikrobielle Produkte



Virus, Toxine oder Chemikalien zerstören β -Zellen, die damit Antigene freisetzen

Antigene werden von APZ aufgenommen, T-Zellen präsentiert;

Th1-Zellen aktivieren Monozyten und NK-Zellen,

die ihrerseits die β -Zellen zerstören (Granzyme, INOS)

TNF- α und IL-1 lösen eine lokale Entzündung aus.

Tc-Zellen zerstören β -Zellen direkt über Zytotoxine oder Aktivierung der Apoptose (über FasL)

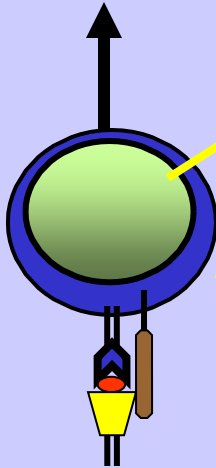
Histologie der Thyreoiditis



Nekrose der Schilddrüsenepithelzellen

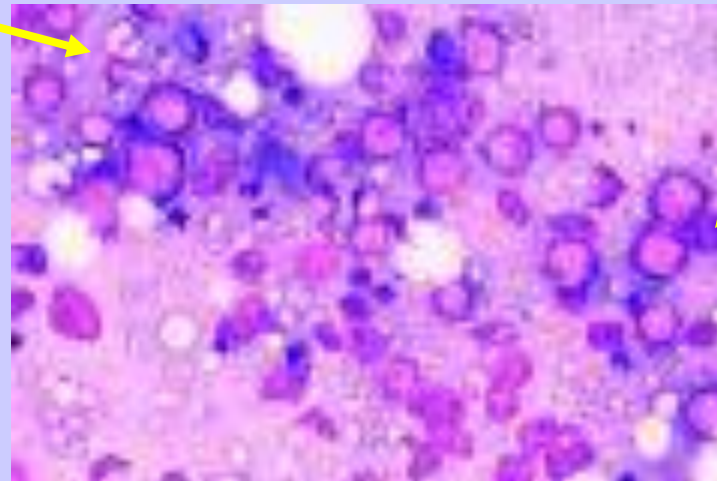
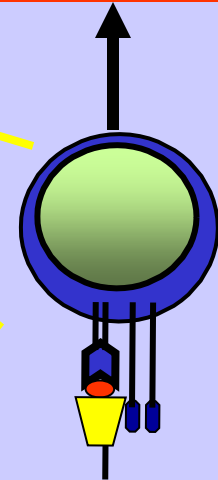
TNF- α
IL-1
IFN- γ

Th1



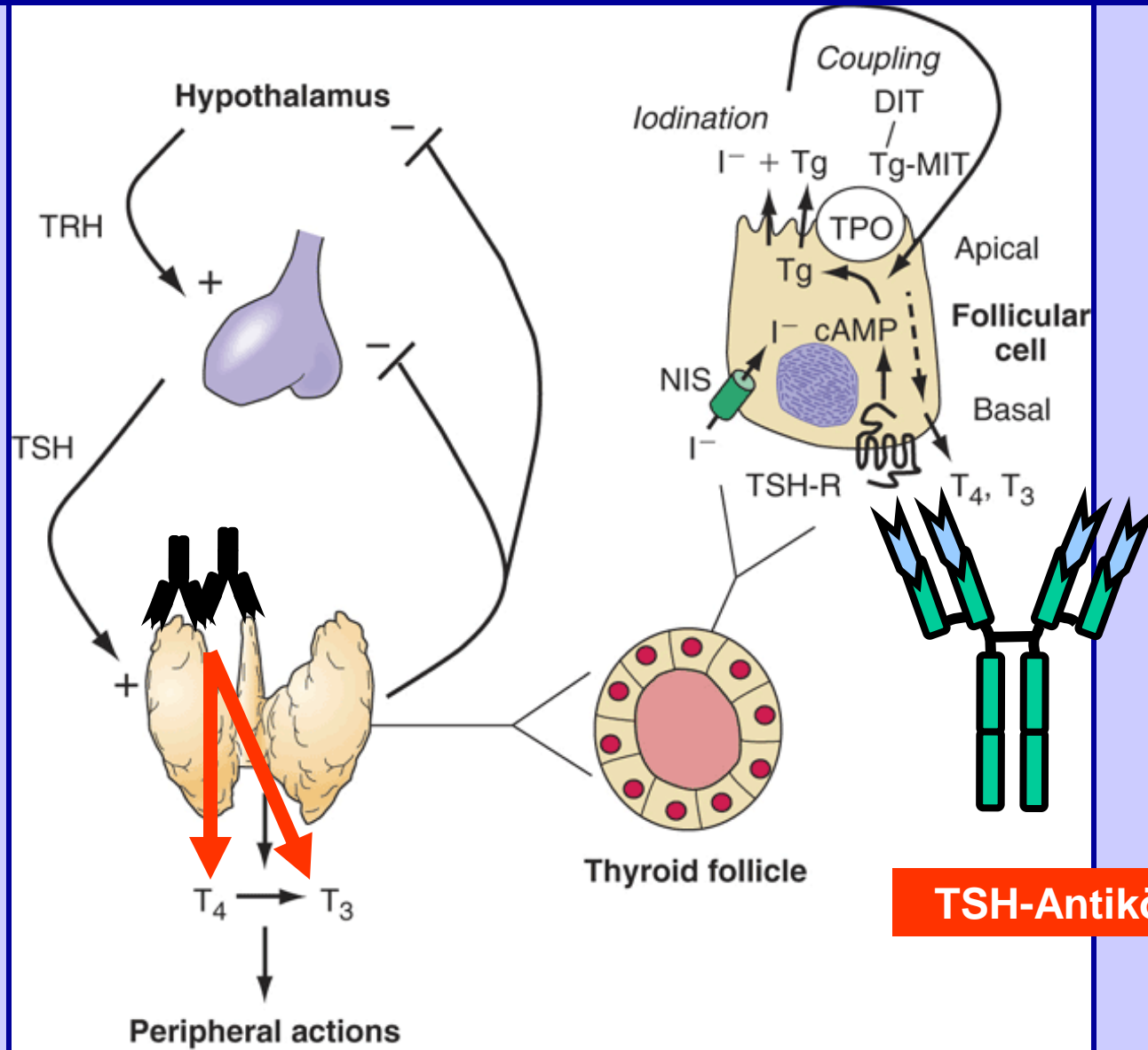
Perforin 1
Granzym
Fas-Ligand

Tc1

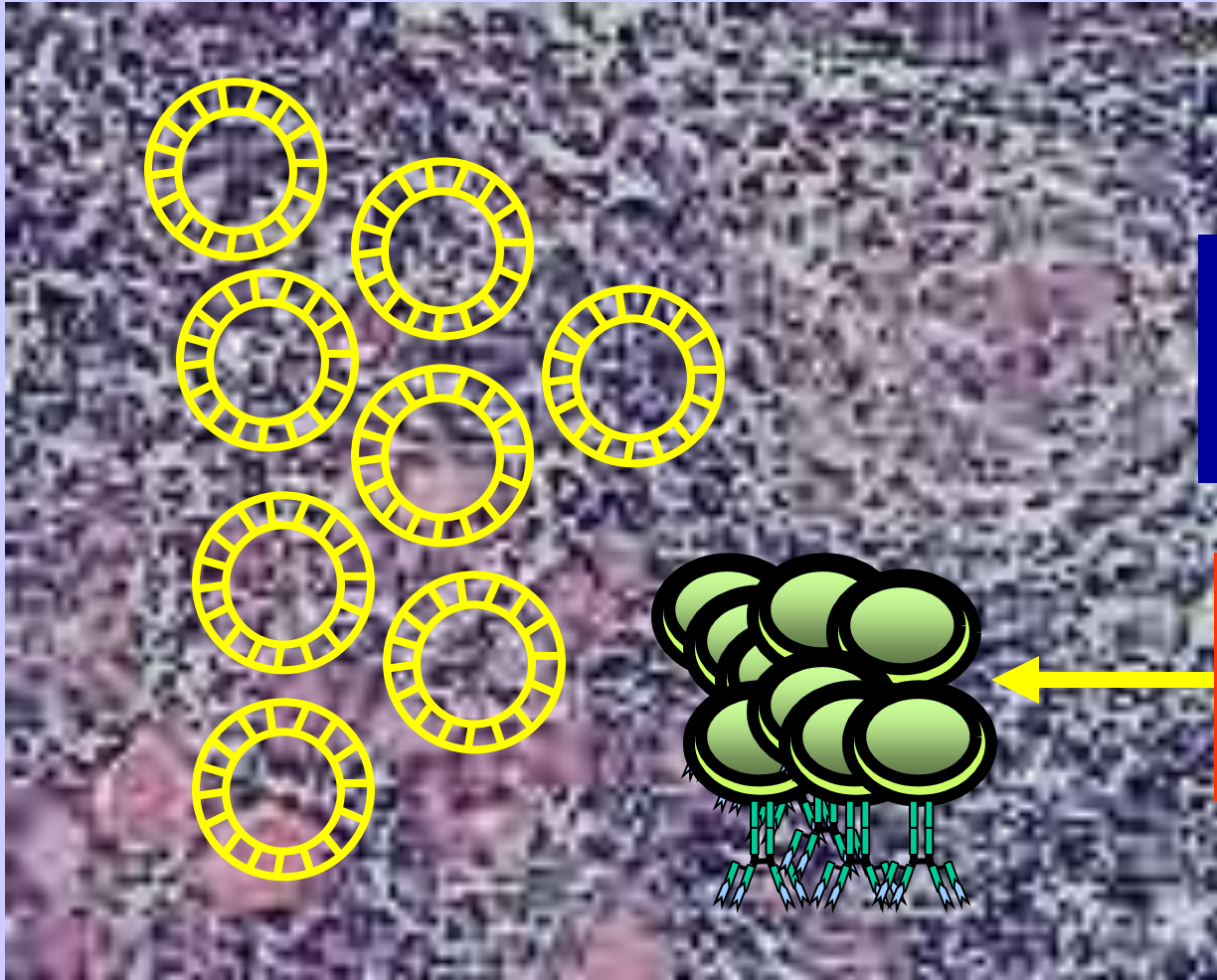


Thyreoiditis im Punktat eines Schilddrüsenknotens

Durch Bindung an den TSH-Rezeptor aktivieren die TSH-AK die vermehrte Freisetzung von T4 und T3

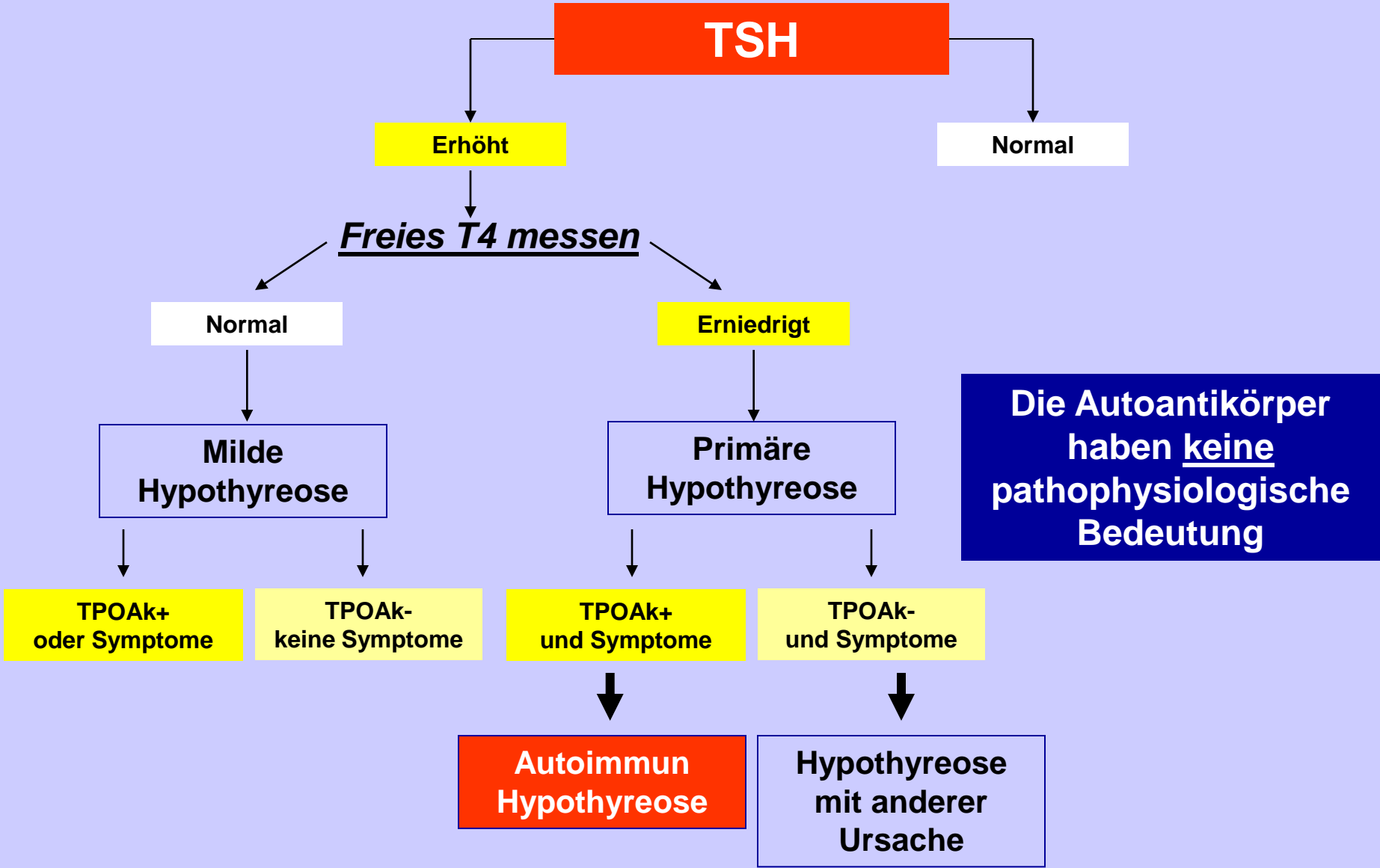


Besonderheiten der Histologie der Autoimmunhyperthyreose.



Neben einem T-Zell-Infiltrat findet man:

Keimzentren in der Schilddrüse



TPO = Thyroidea Peroxidase Antikörper

Mechanismen des Tumorzell-/Tumorantigen-Escape

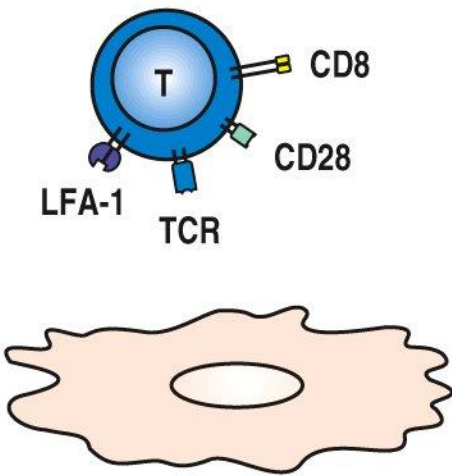
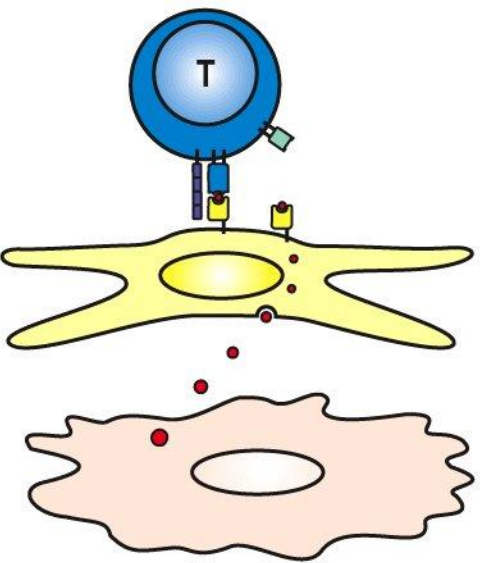
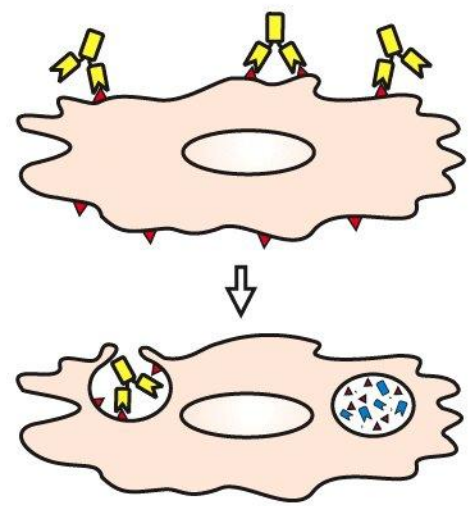
Low immunogenicity	Tumor treated as self antigen	Antigenic modulation
<p>No peptide:MHC ligand No adhesion molecules No co-stimulatory molecules</p>	<p>Tumor antigens taken up and presented by APCs in absence of co-stimulation tolerize T cells</p>	<p>Antibody against tumor cell-surface antigens can induce endocytosis and degradation of the antigen. Immune selection of antigen-loss variants</p>
 <p>A blue circular T cell is shown with four surface receptors: CD8 (yellow), CD28 (green), LFA-1 (purple), and TCR (blue). Below it is a pink, irregularly shaped cell representing a tumor cell.</p>	 <p>A blue circular T cell is interacting with a yellow, star-shaped Antigen Presenting Cell (APC). The APC is presenting tumor antigens (red dots) to the T cell. The T cell's TCR and CD8 co-receptor are bound to the APC's MHC-peptide complex.</p>	 <p>A pink tumor cell is shown with yellow Y-shaped antibodies bound to its surface. An arrow points down to a second tumor cell where the antibodies have induced endocytosis, leading to the degradation of the antigen into smaller fragments.</p>

Figure 14-14 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)

Mechanismen des Tumorzell- /Tumorantigen-Escape

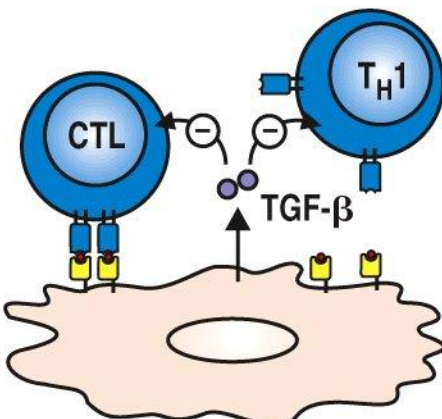
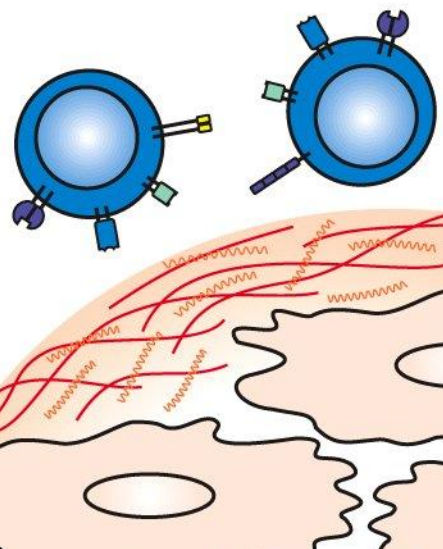
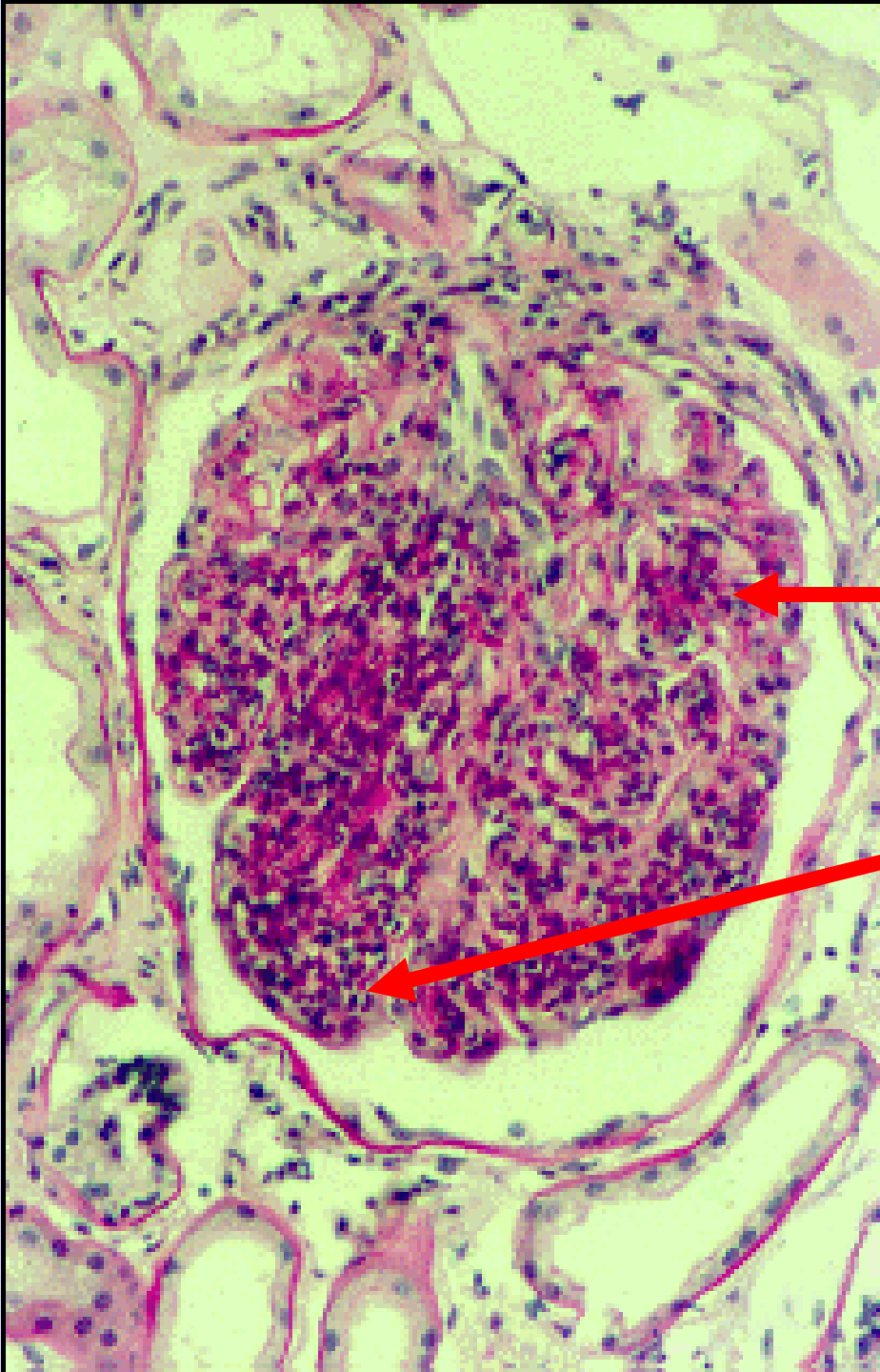
Tumor-induced immune suppression	Tumor-induced privileged site
<p>Factors (eg, TGF-β) secreted by tumor cells inhibit T cells directly</p>	<p>Factors secreted by tumor cells create a physical barrier to the immune system</p>
 <p>The diagram shows a tumor cell (orange) with a CTL (blue) and a TH1 (blue) cell. The tumor cell is secreting TGF-β (purple dots) which is acting on both the CTL and the TH1 cell, indicated by minus signs. The CTL and TH1 cell are both interacting with the tumor cell via their receptors.</p>	 <p>The diagram shows two TH1 cells (blue) interacting with a tumor cell (orange). The tumor cell is secreting factors (red wavy lines) that create a physical barrier to the immune system, preventing the TH1 cells from interacting with the tumor cell.</p>

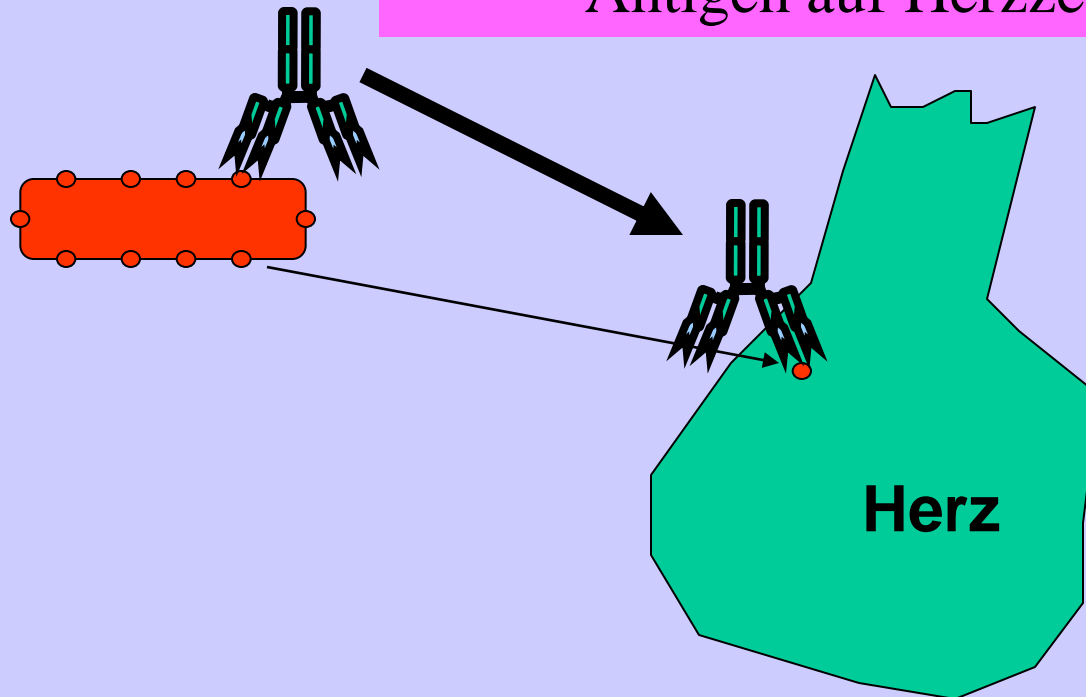
Figure 14-14 part 2 of 2 Immunobiology, 6/e. (© Garland Science 2005)



**Diffuse endokapilläre
Glomerulonephritis mit
Glomerulusvergrößerung
durch Endothelproliferation
und zahlreiche neutrophile
Granulozyten in den
Kapillarschlingen**

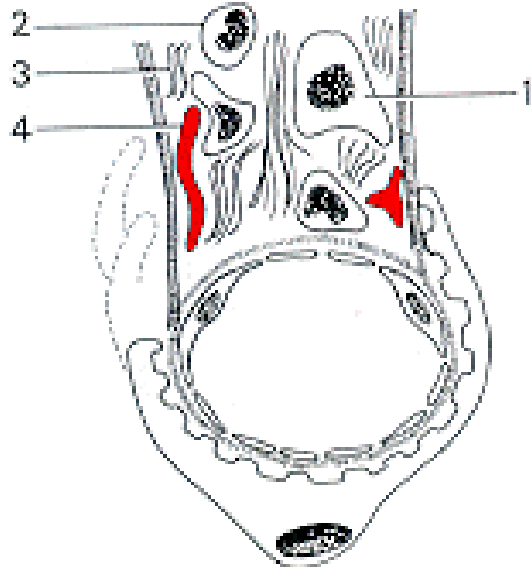
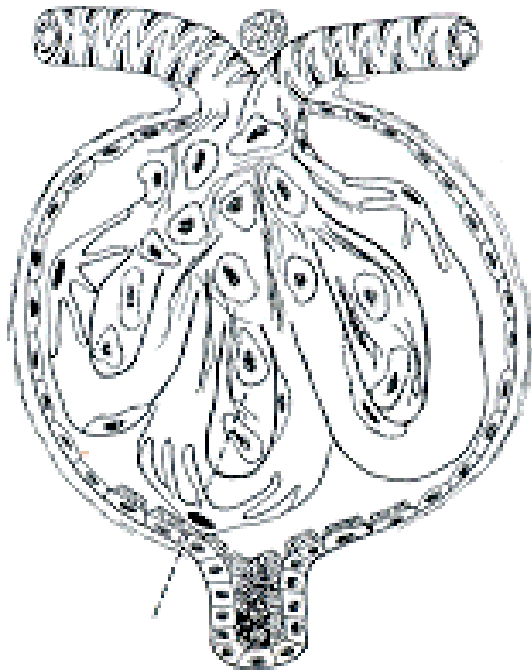
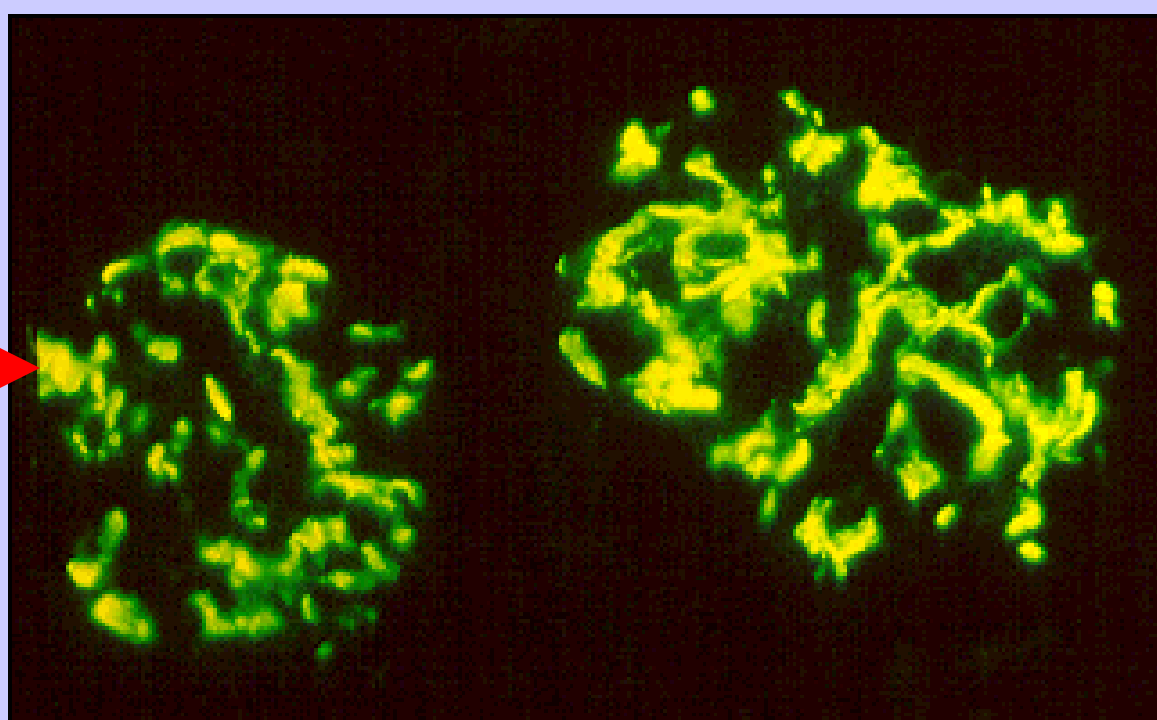
Virus- oder Bakterienantigene als Mimotope

Antikörper gegen β -hämolisierende Streptokokken erkennen auch ein Antigen auf Herzzellen



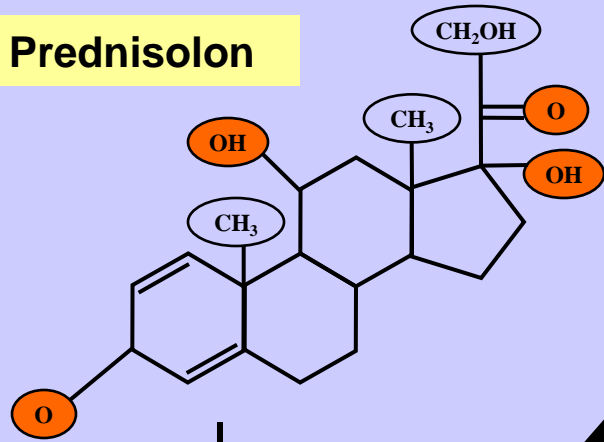
Akutes rheumatische Fieber nach einer Mandelentzündung durch Streptokokken

**Fluoreszenz-
mikroskopischer
Nachweis von
IgA-Ablagerungen
im Mesangium**

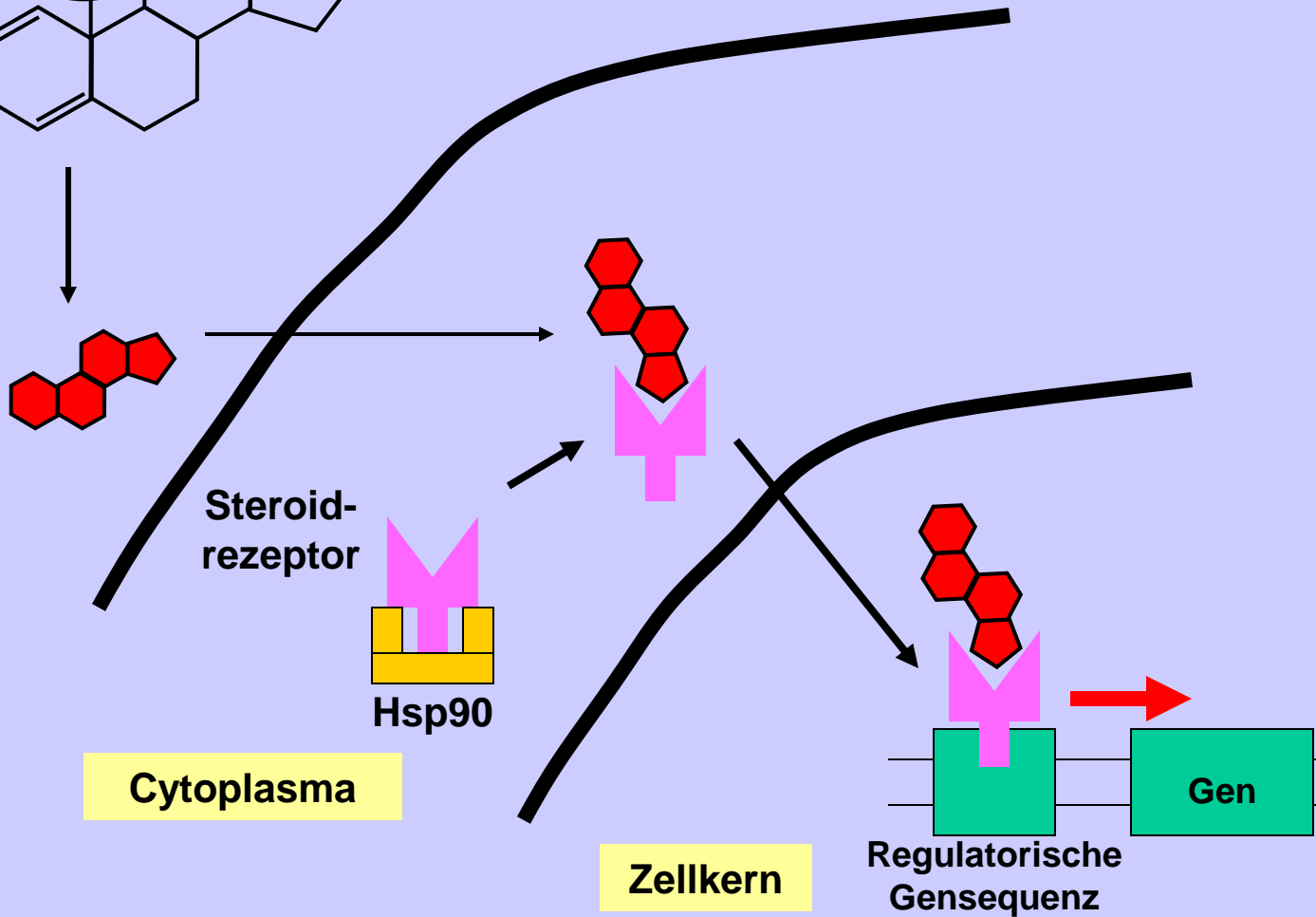


- 1. Mesangium**
- 2. Monozyt**
- 3. Mesangium-
matrix
(verbreitert)**
- 4. IgA-Depot**

Prednisolon



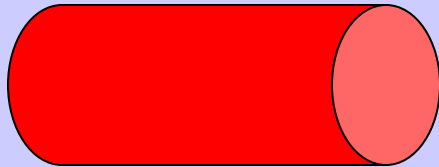
Wirkung der Steroide über den intrazellulären Steroidrezeptor



Kortikosteroidtherapie

Wirkung auf		Physiologische Effekte
IL-1, TNF- α , GM-CSF, IL-3, IL-4, IL-5, IL-8	↓	Entzündung
Stickoxide	↓	Entzündung
Phospholipase A2 Cyclooxygenase Typ 2	↓	Prostaglandine Leukotriene
Adhäsionsmoleküle	↓	Leukozytenwanderung
Endonukleasen	↑	Apoptose bei Lymp./Eos.

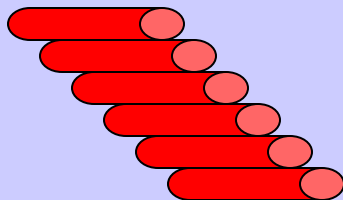
Chapel-Hill Definition der systemischen Vaskulitiden (Inflammation, Lokalisation)



große Gefäße



mittelgroße Gefäße

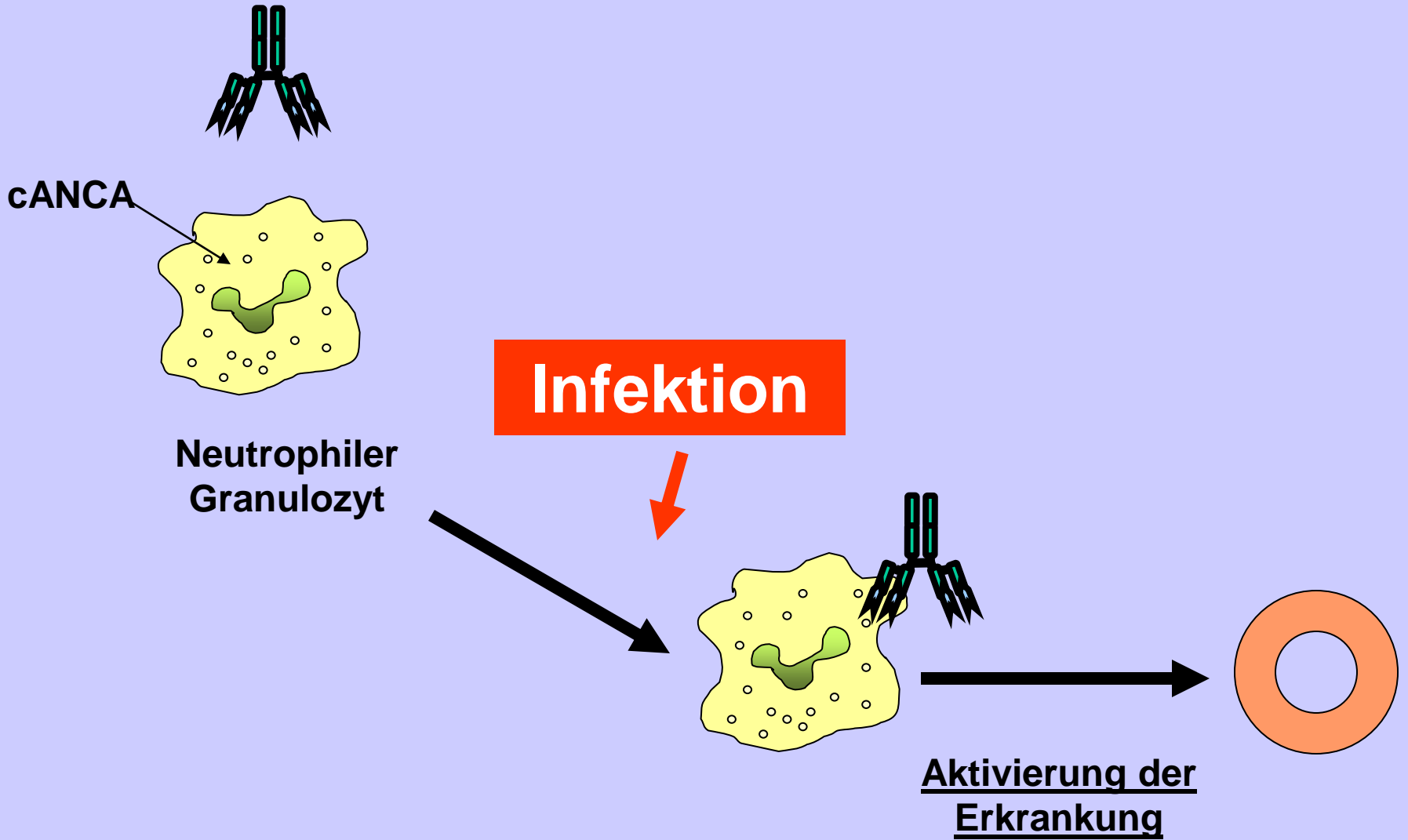


kleine Gefäße

- Riesenzell-(temporal)-arteriitis
- Takayasu-Arteriitis

- Panarteriitis nodosa
- Kawasaki-Syndrom

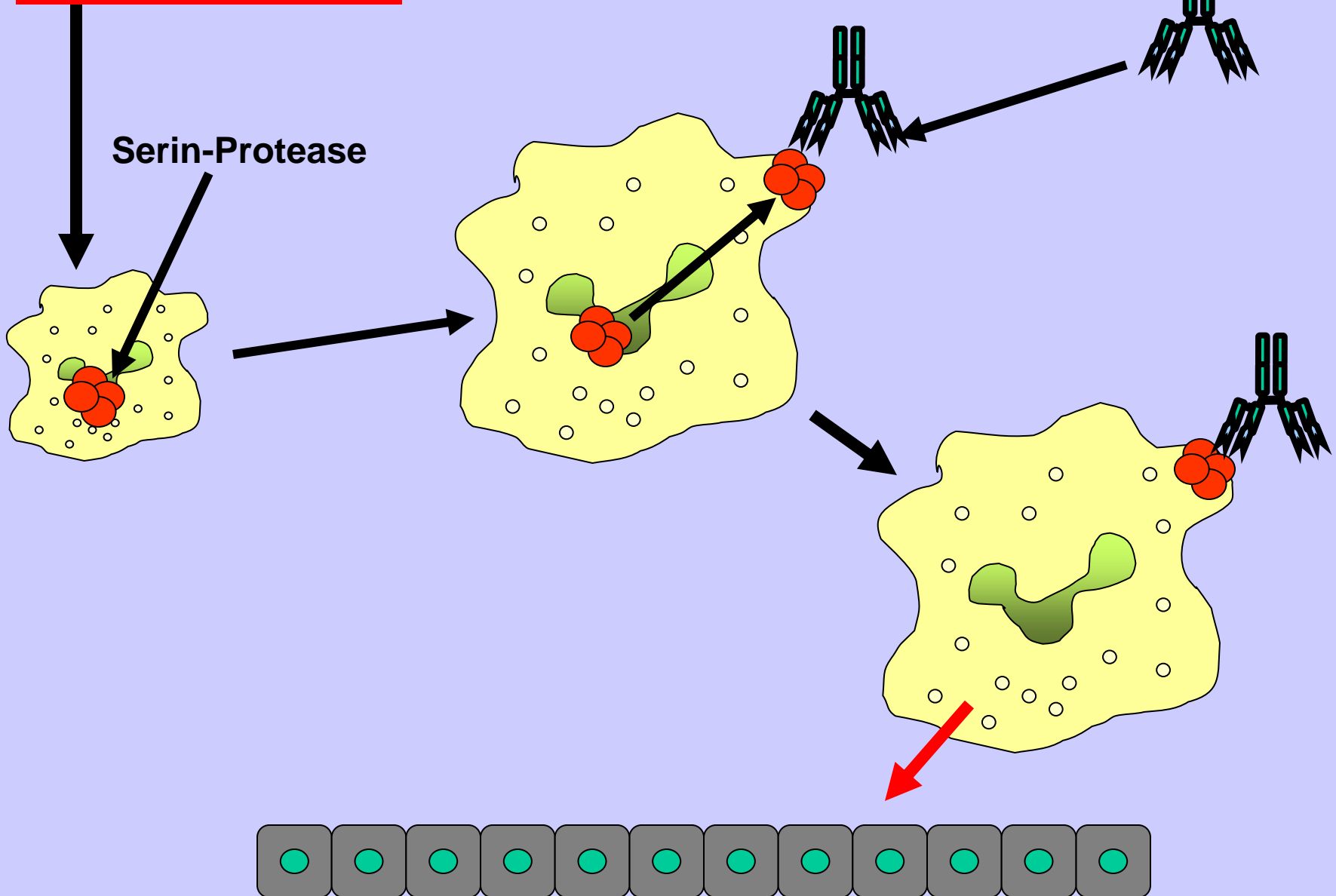
- Wegenersche Granulomatose
- Churg-Strauss-Syndrom
- Mikroskopische Polyangiitis
- Purpura Schönlein-Henoch
- Essentielle Kryoglobulinämische Vaskulitis
- Kutane leukozytoklastische Angiitis

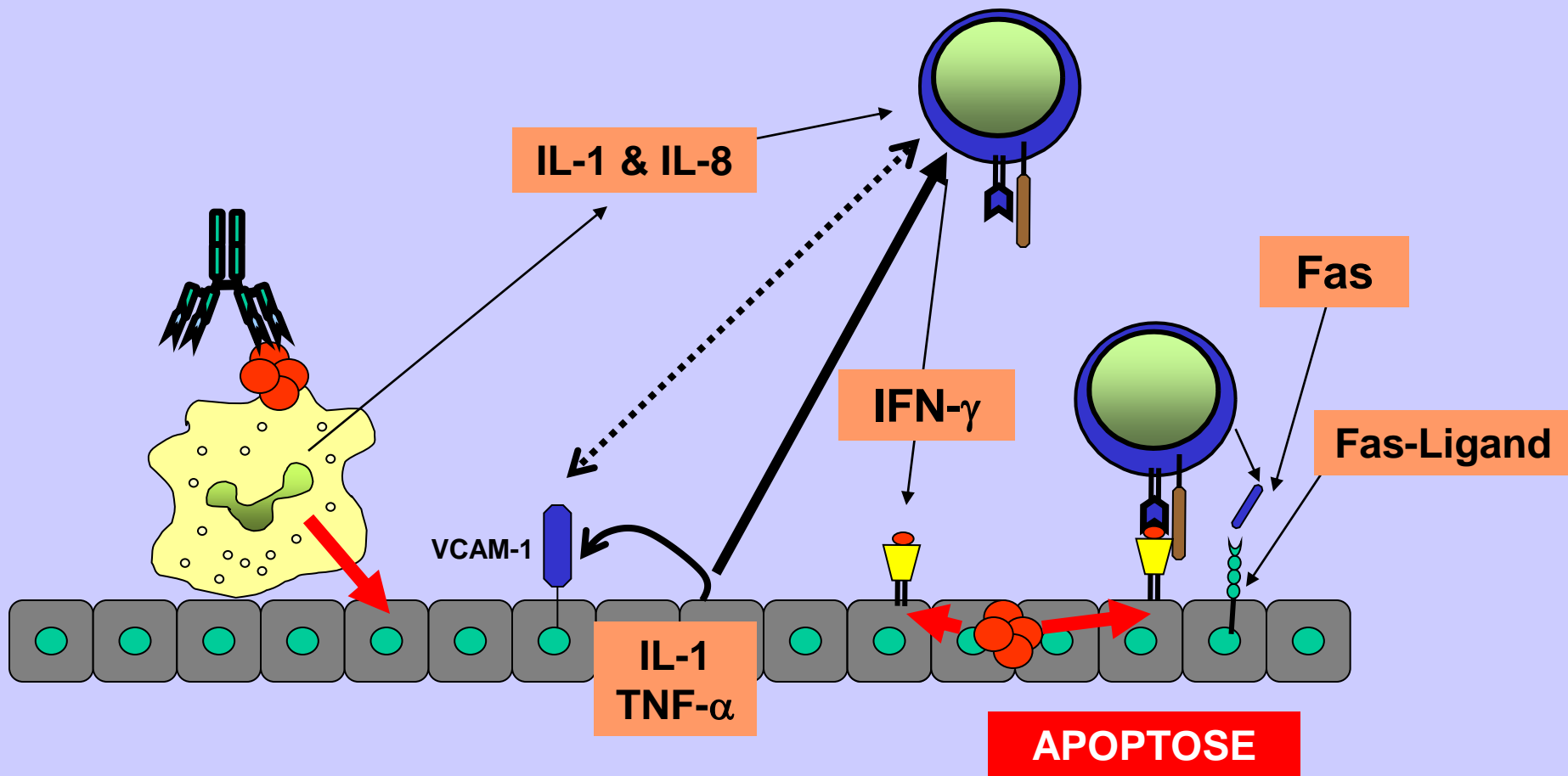


TNF- α und IL-1

Serin-Protease

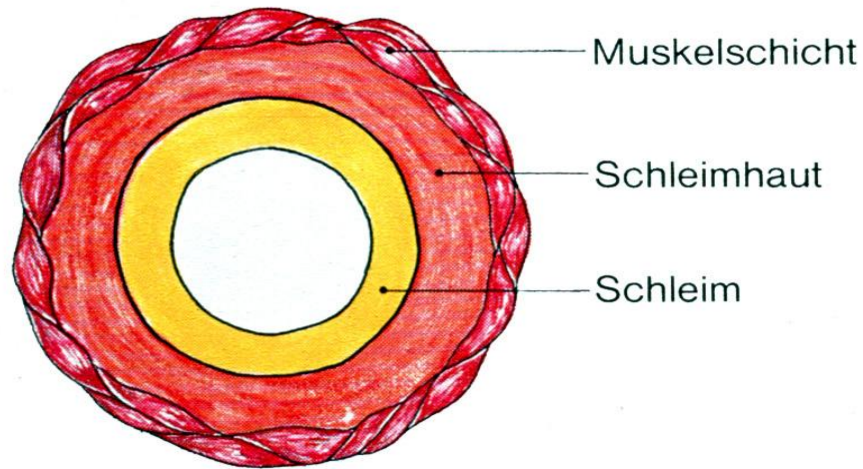
Autoantikörper



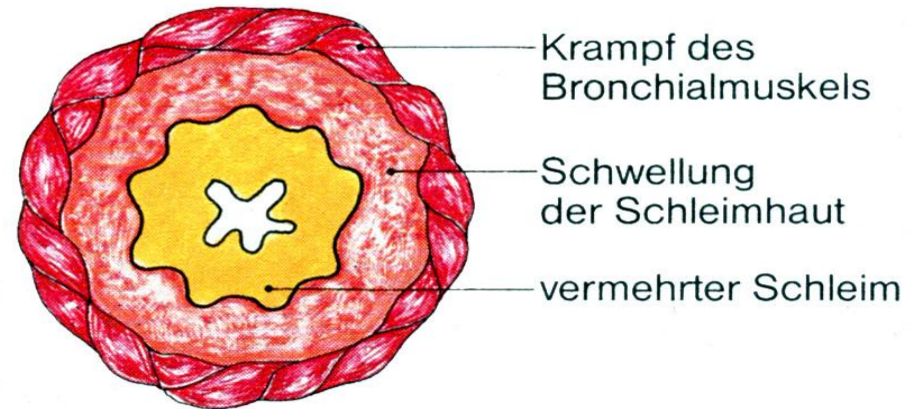


Pathophysiologie des Asthma

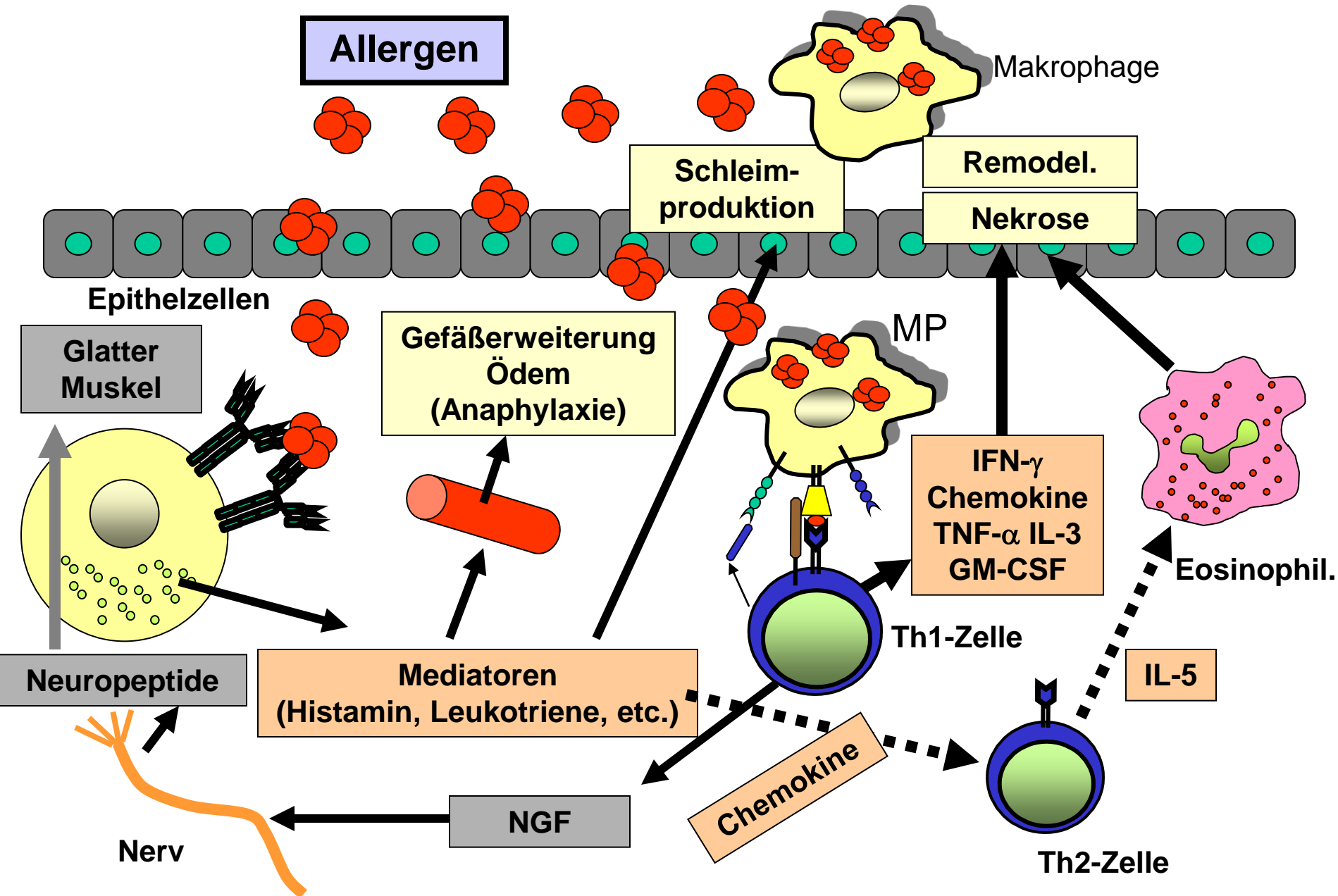
Normalzustand



Einengung der Bronchiallichtung



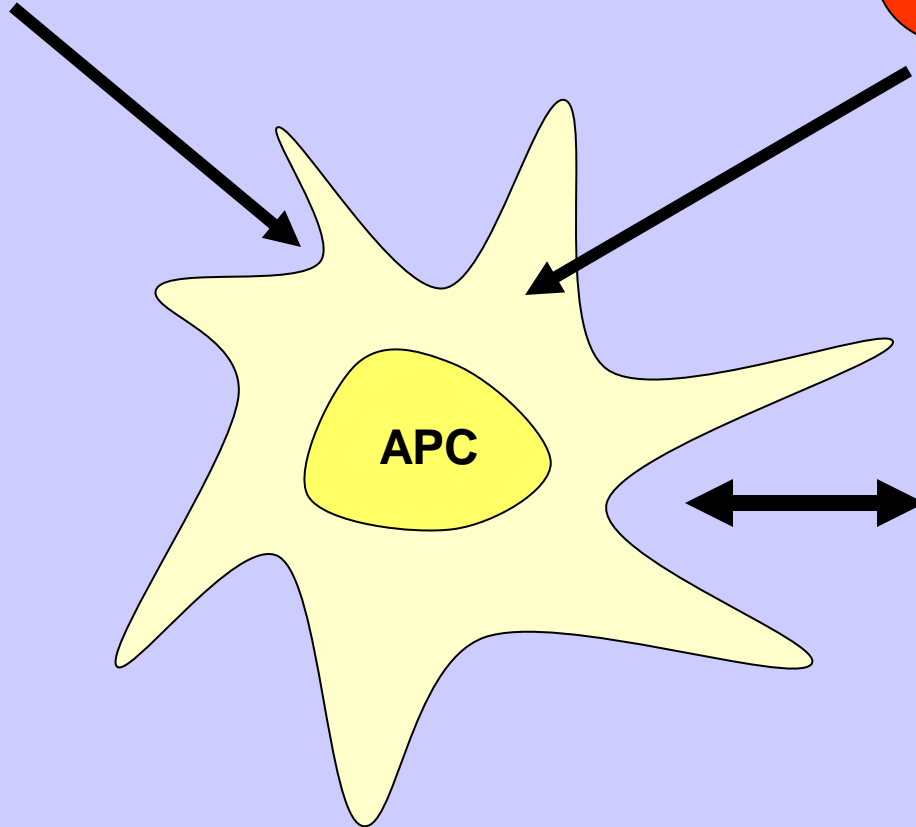
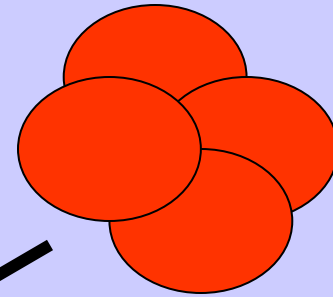
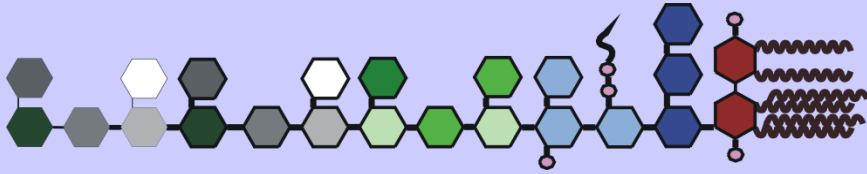
Entzündungsreaktion beim Asthma



Zwei Signalmodell

Gefahrensignal (z.B. LPS)

Antigen



APC

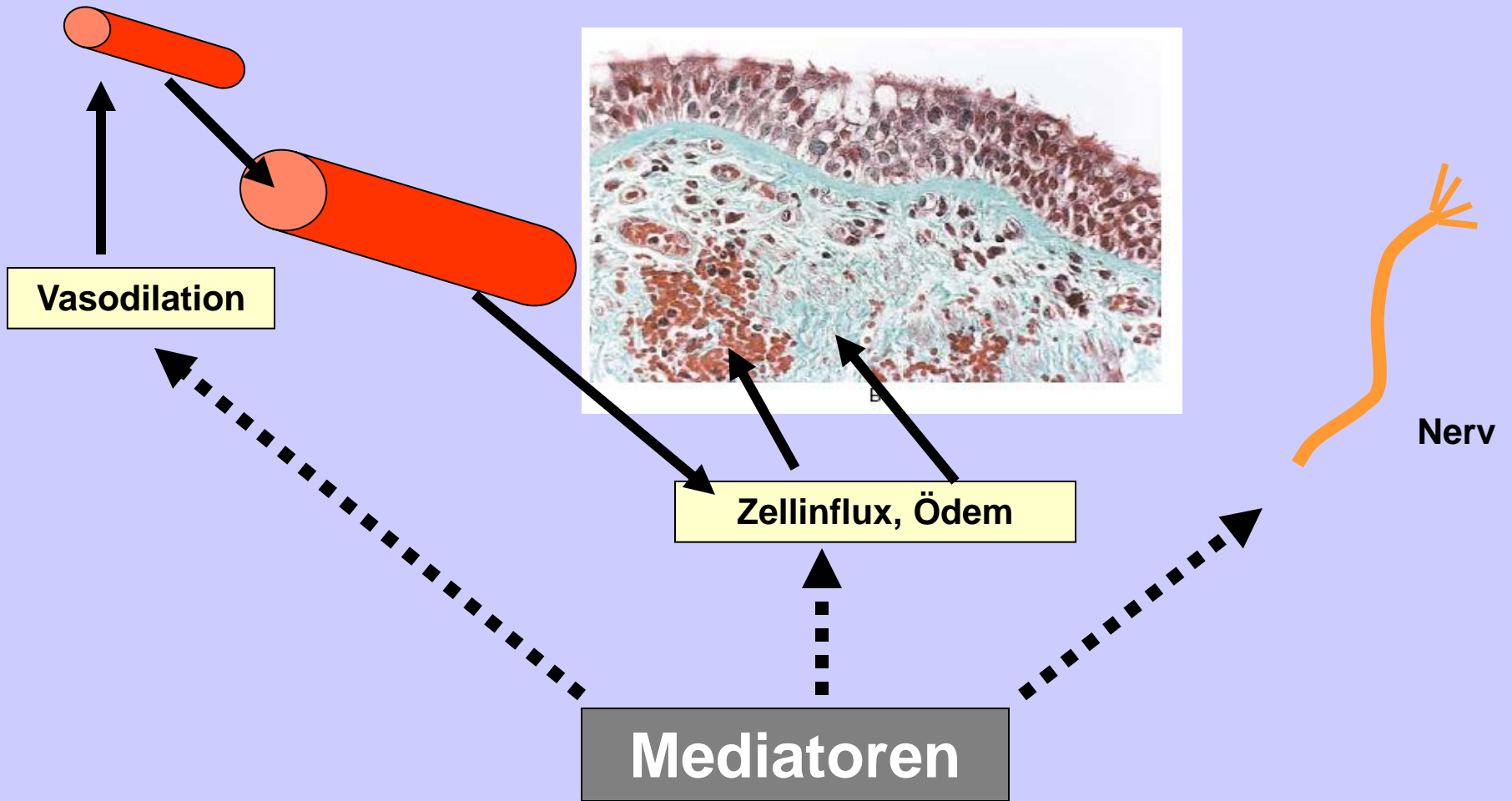
Naive T-Zelle

Rubor

Calor

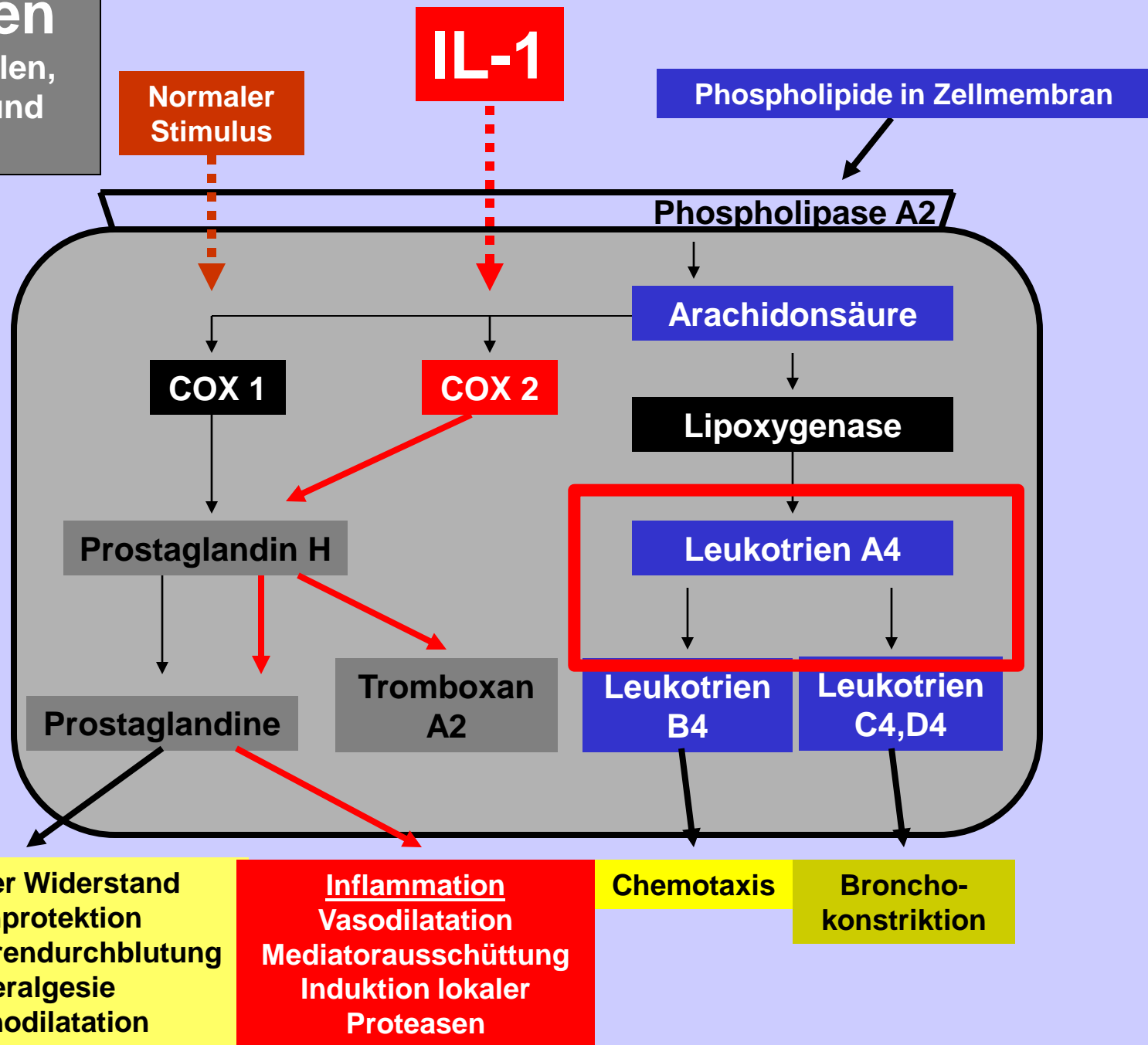
Tumor

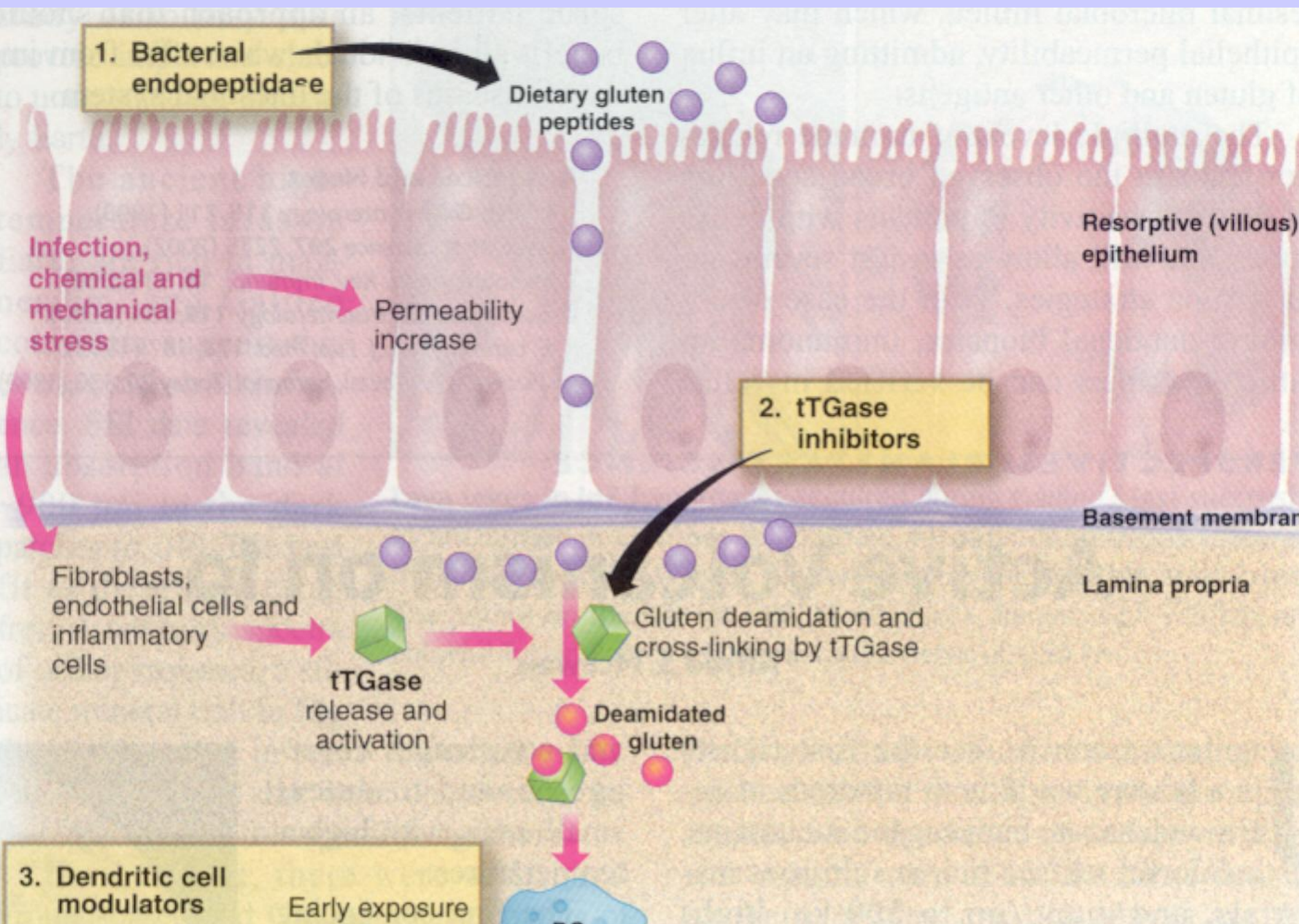
Dolor



Mediatoren

aus Endothelzellen,
Makrophagen und
Mastzellen





1. Bacterial endopeptidase

Dietary gluten peptides

Infection, chemical and mechanical stress

Permeability increase

Resorptive (villous) epithelium

2. tTGase inhibitors

Basement membrane

Lamina propria

Fibroblasts, endothelial cells and inflammatory cells

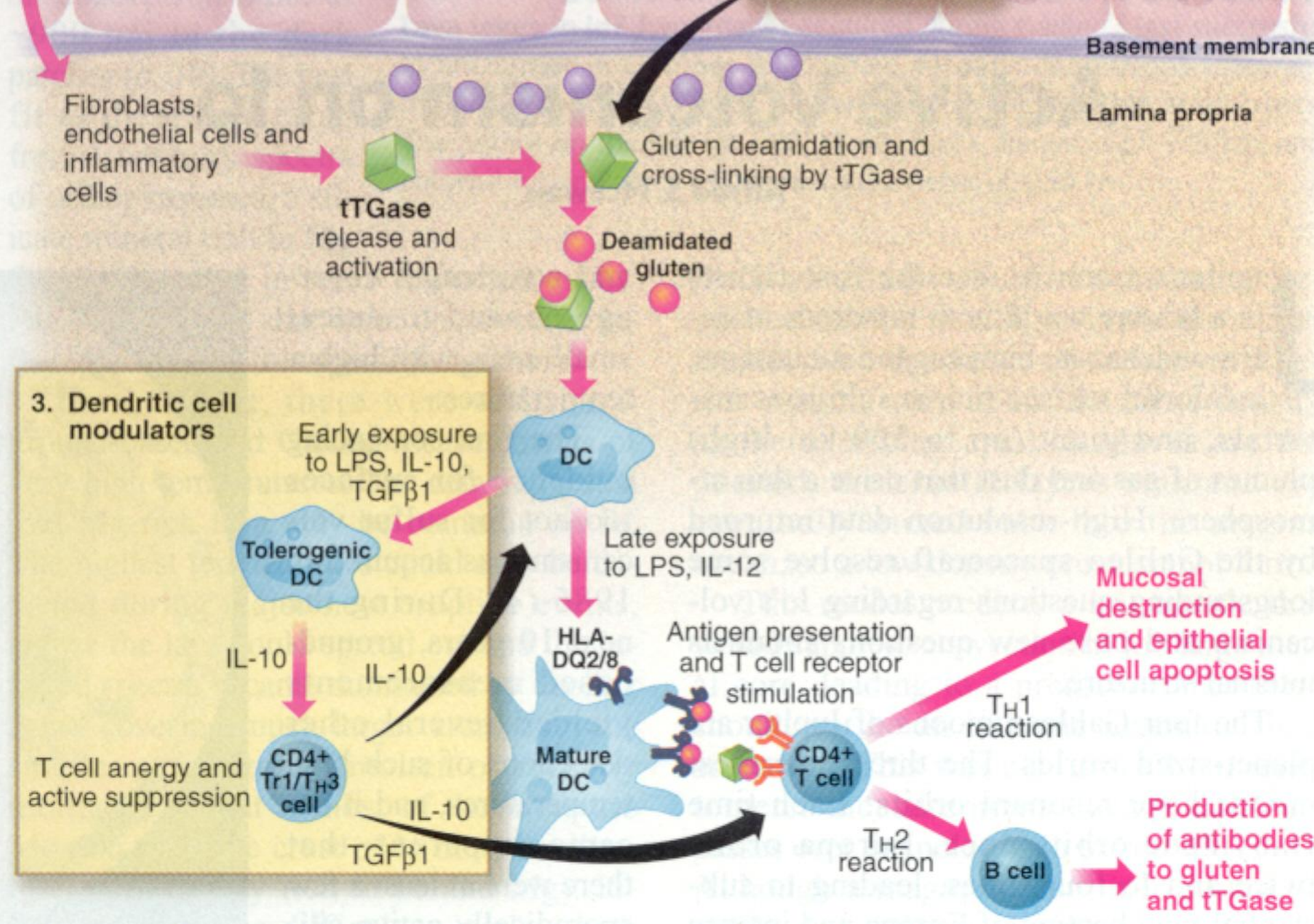
tTGase release and activation

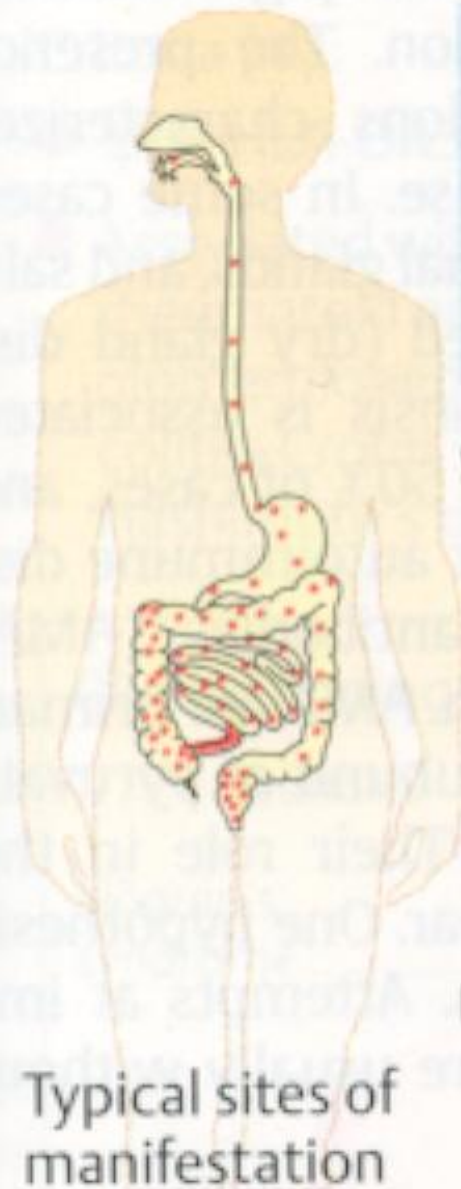
Gluten deamidation and cross-linking by tTGase

Deamidated gluten

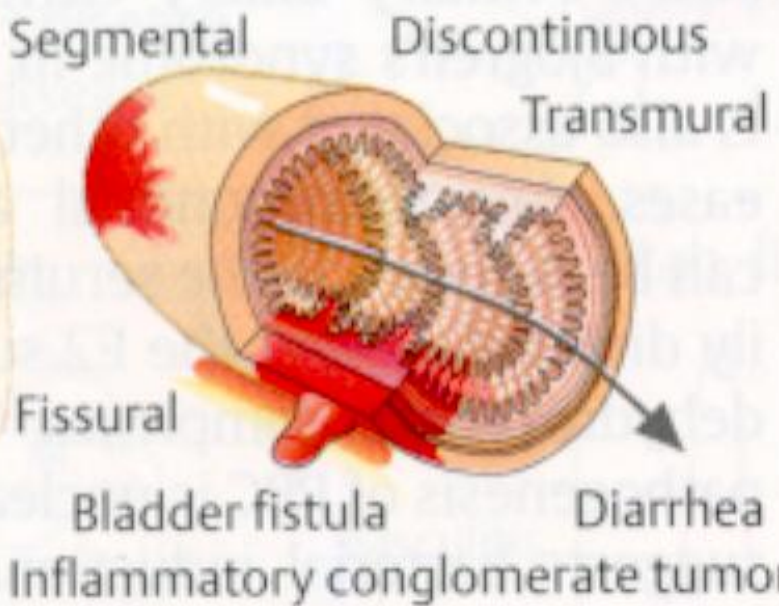
3. Dendritic cell modulators
Early exposure to LPS, IL-10

DC





HLA-DR1	Shorter breast feeding period
-DQw5	
Assoc. with smoking	Refined carbohydrate



Typical sites of manifestation

Typical pattern

A. Crohn's disease

Entzündungsreaktion beim Crohn

