



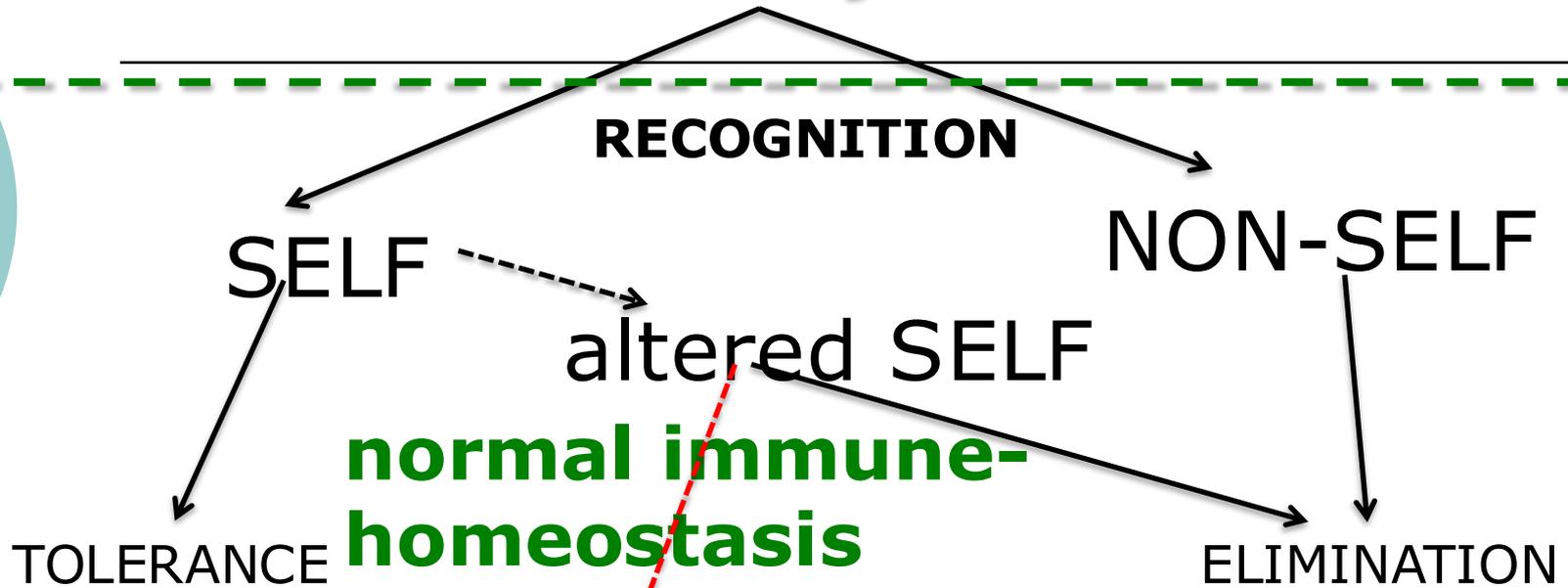
# Applied Immunology

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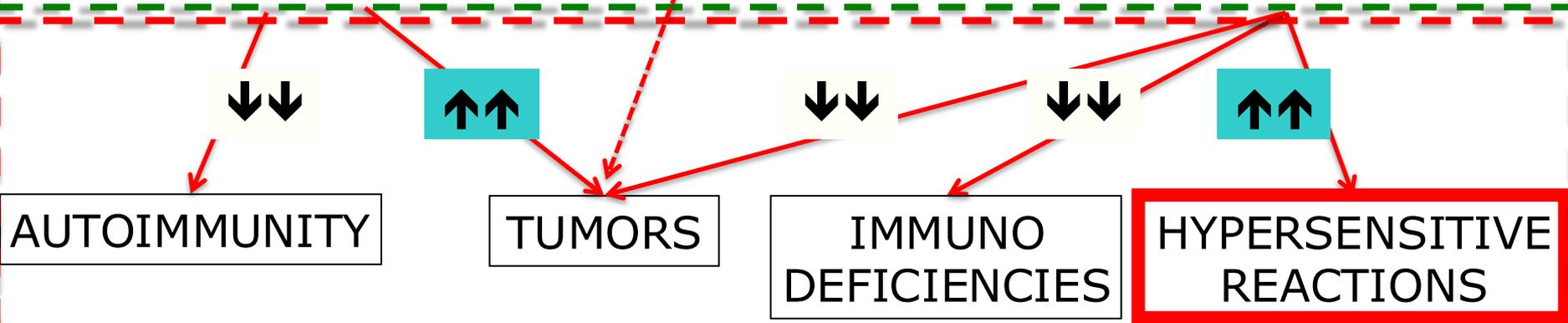
**Hypersensitive reactions,  
allergies**

**Timea Berki**

# Immune system



**normal immune-homeostasis**



**ALTERED immune-homeostasis = IMMUNOPATHOLOGY**



Altered immune homeostasis

# **HYPERSENSITIVE REACTIONS**

# Hypersensitive reactions

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- Pathological overreactions of the immune response with **severe tissue damage** (necrosis) in the effector phase.
- The immune system itself initiates these diseases.
- Different background mechanisms.
- Gell and Coombs distinguished 4 types of reactions originally (1963). More recently these were further subdivided.
- **Significance:**
  1. Allergic diseases
  2. Autoimmune diseases

# Based on the immunological mechanisms we distinguish 4 types of hypersensitive reactions

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## Immunoglobulin-mediated

- Type I.** Atopy or Allergy  
(IgE-mediated immediate form)
- Type II.** Humoral cytotoxic immune reactions  
(IgG against cellular antigens)
- Type III.** Immunocomplex-diseases  
(soluble self or non-self antigens)

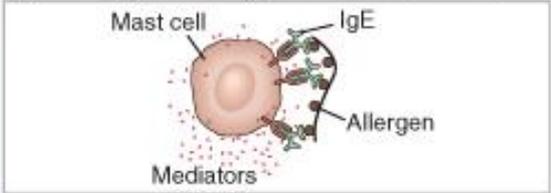
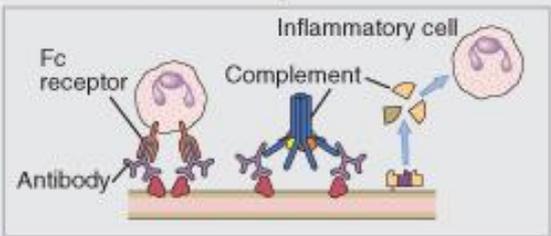
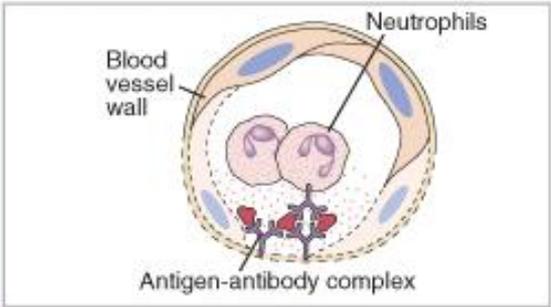
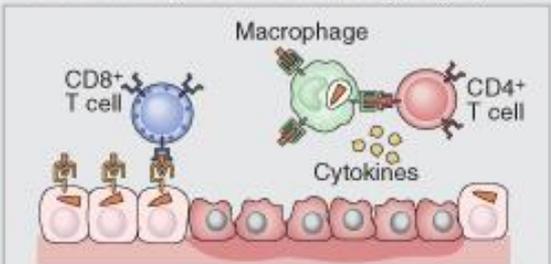
## Cell-mediated

- Type IV.** T cell-mediated → Th1- and Tc-cytokines  
(DTH=Delayed Type Hypersensitivity)

# Hypersensitivity - intolerance

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- is a set of undesirable reactions produced by the normal immune system, including allergies and autoimmunity.
- They are usually referred to as an over- reaction of the immune system and these reactions may be damaging, uncomfortable, or occasionally fatal.
- Hypersensitivity reactions require a pre-sensitized (immune) state of the host.
- They are classified in four groups after the proposal of P. G. H. Gell and Robin Coombs in 1963

Type of hypersensitivity	Pathologic immune mechanisms	Mechanisms of tissue injury and disease
Immediate hypersensitivity (Type I)	<p>T<sub>H</sub>2 cells, IgE antibody, mast cells, eosinophils</p> 	<p>Mast cell-derived mediators (vasoactive amines, lipid mediators, cytokines)</p> <p>Cytokine-mediated inflammation (eosinophils, neutrophils)</p>
Antibody-mediated diseases (Type II)	<p>IgM, IgG antibodies against cell surface or extracellular matrix antigens</p> 	<p>Complement- and Fc receptor-mediated recruitment and activation of leukocytes (neutrophils, macrophages)</p> <p>Opsonization and phagocytosis of cells</p> <p>Abnormalities in cellular function, e.g., hormone receptor signaling</p>
Immune complex-mediated diseases (Type III)	<p>Immune complexes of circulating antigens and IgM or IgG antibodies deposited in vascular basement membrane</p> 	<p>Complement and Fc receptor-mediated recruitment and activation of leukocytes</p>
T cell-mediated diseases (Type IV)	<p>1. CD4<sup>+</sup> T cells (delayed-type hypersensitivity) 2. CD8<sup>+</sup> CTLs (T cell-mediated cytotoxicity)</p> 	<p>1. Macrophage activation, cytokine-mediated inflammation</p> <p>2. Direct target cell lysis, cytokine-mediated inflammation</p>

## IgE:

Atopy  
Anaphylaxis  
Urticaria  
Asthma

## IgG:

AIHA  
Erythroblastosis  
Organ specific autoimmune diseases

## IgG:

Serum sickness  
SLE, RA,  
Post-Streptococcal glomerulonephritis

## T cell-Macrophage-Cytokine

Contact dermatitis  
Multiple sclerosis  
Coeliac disease

# Nomenclature of allergic diseases and hypersensitivity reactions: Adapted to modern needs: An EAACI position paper 2023

Allergy, Volume: 78, Issue: 11, Pages: 2851-2874, First published: 10 October 2023, DOI: (10.1111/all.15889)

HYPERSENSITIVITY REACTIONS ▶ AUTOIMMUNITY

## ALLERGY

### INFLAMMATION / IMMUNE SYSTEM-DRIVEN

#### ANTIBODY-MEDIATED

#### CELL-MEDIATED

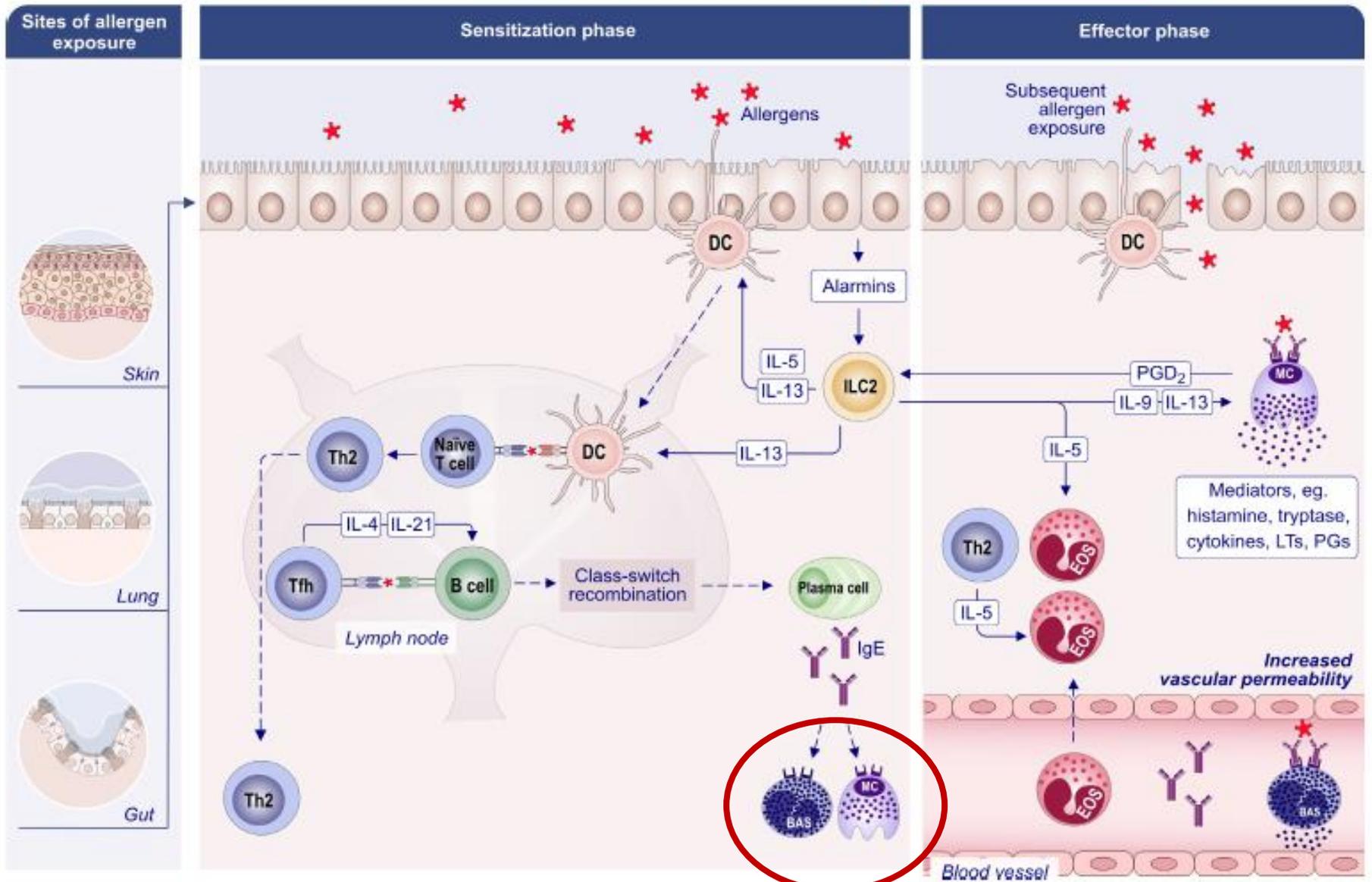
#### TISSUE-DRIVEN MECHANISMS

#### DIRECT RESPONSE TO CHEMICALS

ANTIBODY-MEDIATED			CELL-MEDIATED			TISSUE-DRIVEN MECHANISMS		DIRECT RESPONSE TO CHEMICALS
Type I Immediate	Type II Cytotoxic	Type III Immune complexes	Type IVa T1	Type IVb T2	Type IVc T3	Type V Epithelial	Type VI Metabolic	Type VII
B cells: IgE Th2, ILC2  (IL-4, IL-5, IL-9, IL-13)  Mast cells/BAS	B cells: IgM, IgG  Phagocytes: NEU, MΦ  C-dependent cytotoxicity, NK (ADCC)	B cells: IgM, IgG  Immune complexes  Complement, BAS, Mast cells, Platelets  Phagocytes: NEU, MO, MΦ	Th1, ILC1, Tc1, NK  (IFN-γ, TNF-α, granzyme B, perforines)  MΦ (granulomas)	Th2, ILC2, Tc2, NK-T  (IL-4, IL-5, IL-9, IL-13, IL-31)  EOS, B cells, Mast cells/BAS	Th17, ILC3, Tc17  (IL-17, IL-22, IL-23)  NEU	Epithelial barrier defect, leaky junctions  Resident cells changes (smooth muscle cells, mucous glands, neuroimmune interactions)  Immune modulation (alarmins: TSLP, IL-25, IL-33)  Epigenetic impact	Metabolic-induced immune dysregulation, short-chain fatty acids and other microbiome metabolites	Direct cellular and inflammatory response to chemical substances
AR/ARC, asthma, AD, acute urticaria/ angioedema, food allergy, venom allergy, drug allergy	Drug-induced cytopenia	Acute phase of hypersensitivity pneumonitis, drug-induced vasculitis, serum sickness/ Arthus reaction	ACD, acute phase of hypersensitivity pneumonitis, celiac disease, asthma, AR/ARC, CRS, AD, drug allergy (TEN, SJS, erythema	Asthma, AR/CRS AD (T2 endotypes), EoE, food allergy, drug allergy (DRESS)	Neutrophilic asthma, AD, drug allergy (AGEP)	Asthma, AR/ARC, CRS, AD, FPIES, EoE, celiac disease	Obesity & asthma, histamine-driven disorders	AERD, idiosyncratic reactions

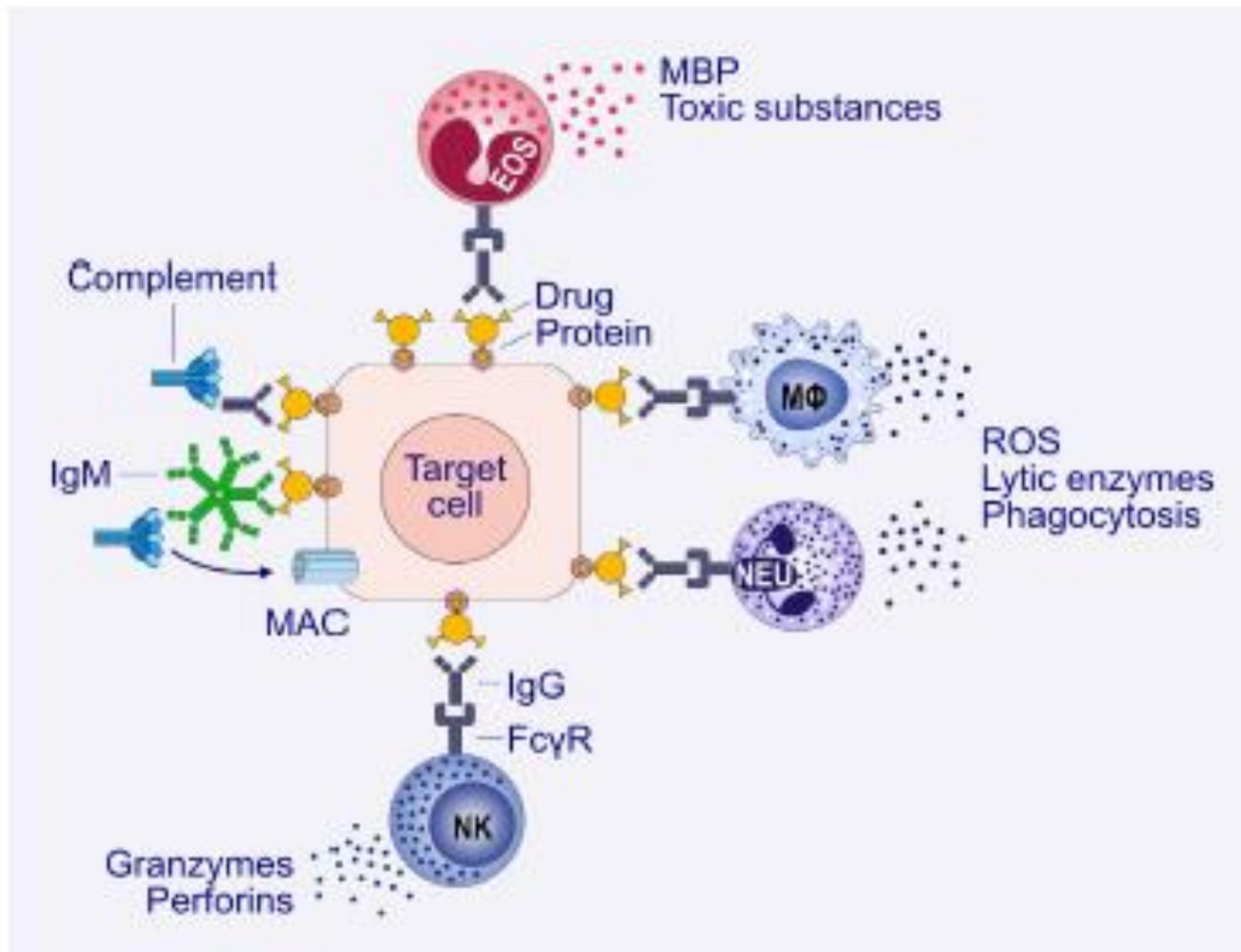
ACD, allergic contact dermatitis; AD, atopic dermatitis; ADCC, antibody-dependent cellular cytotoxicity; AERD, aspirin-exacerbated respiratory diseases; AGEP, acute generalized exanthematous pustulosis; AR, allergic rhinitis; ARC, allergic rhinoconjunctivitis; B, B lymphocytes; BAS, basophil; CRS, chronic rhinosinusitis; DRESS, severe drug reaction with eosinophilia and systemic symptoms; EoE, eosinophilic oesophagitis; EOS, eosinophil; FPIES, food protein-induced enterocolitis syndrome; IFN-γ, interferon-gamma; Ig (E, G, M), immunoglobulin (type E, G, M); IL, interleukin; ILC 1/2/3, innate lymphoid cells type 1/2/3; MO, monocyte; Mφ, macrophage; NEU, neutrophils; NK, natural killer cell; NK-T, natural killer T cell; SJS, Stevens-Johnson syndrome; T1/T2/T3, type 1/2/3 immune response; Tc1/2/17, T cytotoxic lymphocyte type 1/2/17; TEN, toxic epidermal necrolysis; Th, T helper lymphocytes; TSLP, thymic stromal lymphopoietin; TNF-α, tumour necrosis factor-alpha.

# Type I. IgE mediated immediate



Mast cells, basophils

# Type II. Cytotoxicity

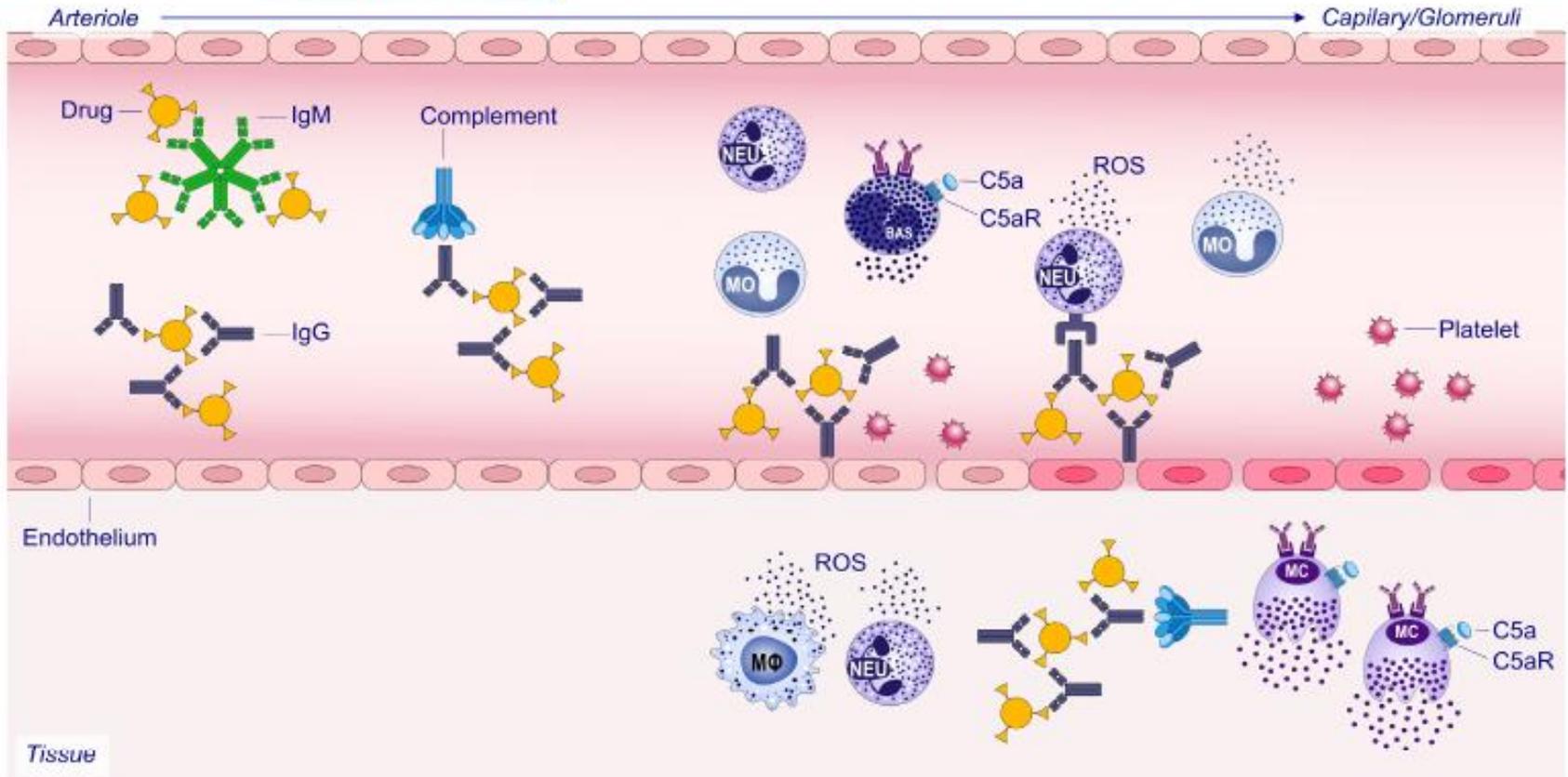


Drug induced cytopenia – ADCC (NK cell)

# Type III. Immunocomplex mediated

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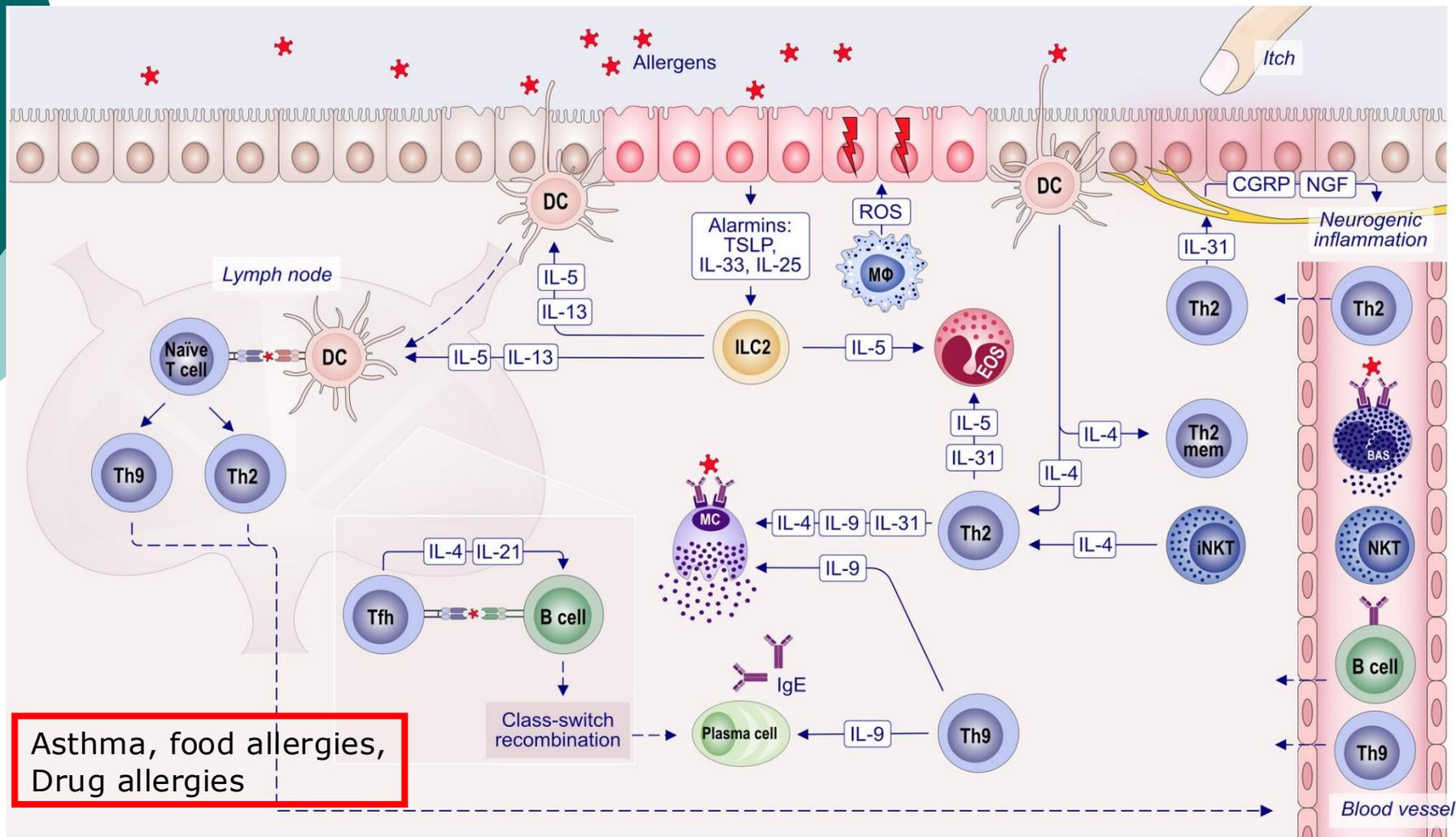
JUTEL ET AL.



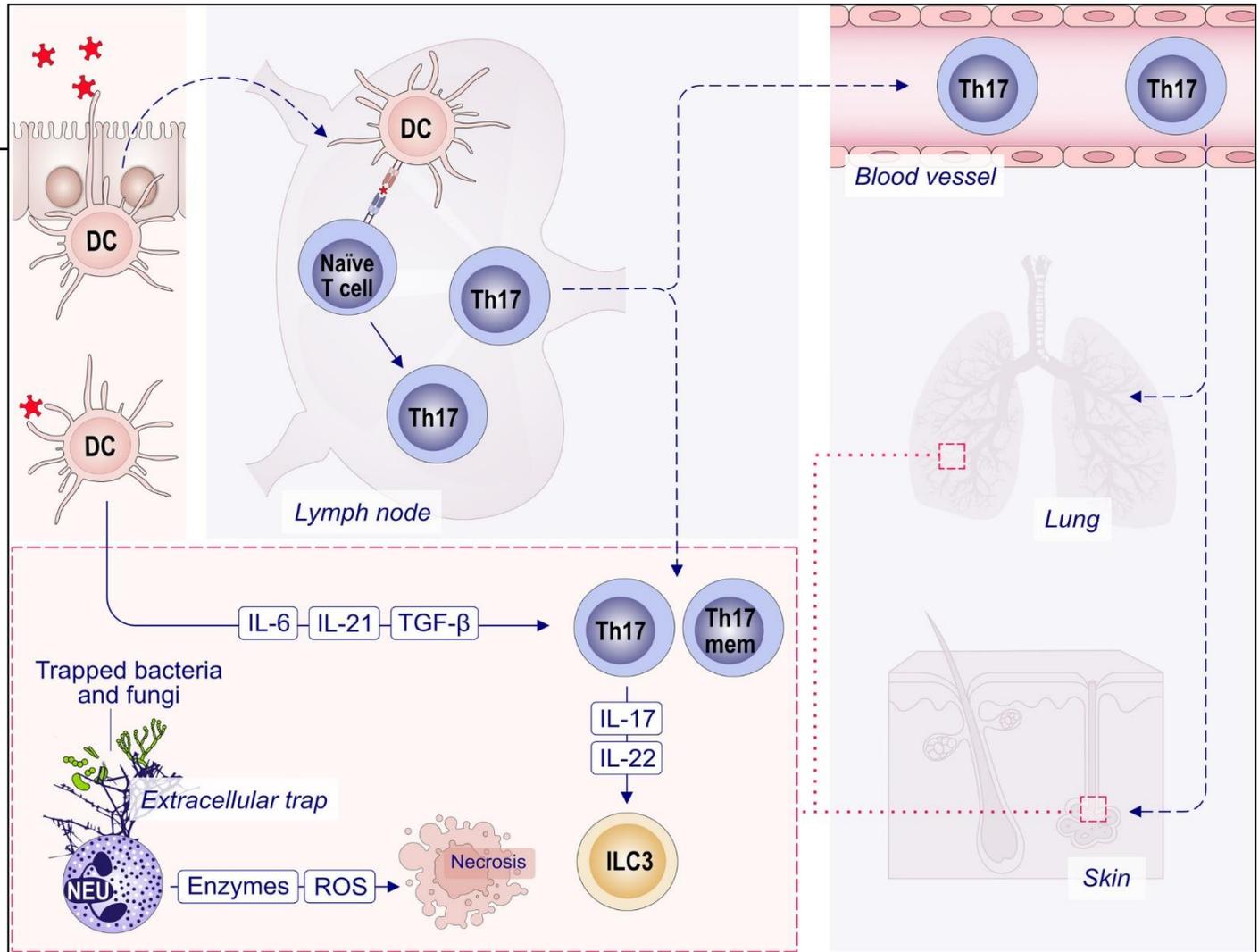
Drug-induced vasculitis: complement, inflammatory cells



# Type IVb cell mediated DTH – TH2, ILC2, Eosinophil mediated

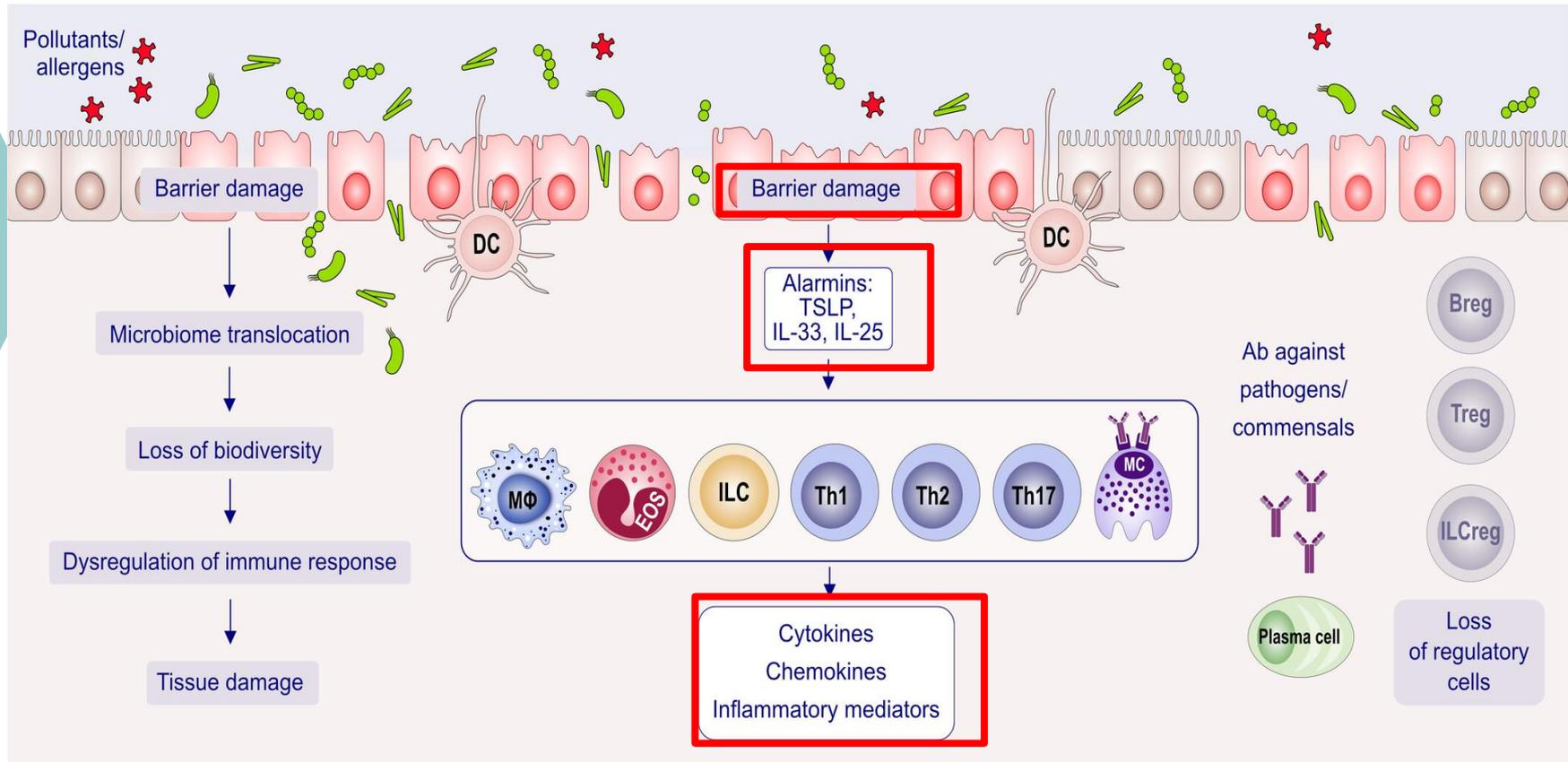


# Type IVc cell mediated allergy TH17, neutrophils

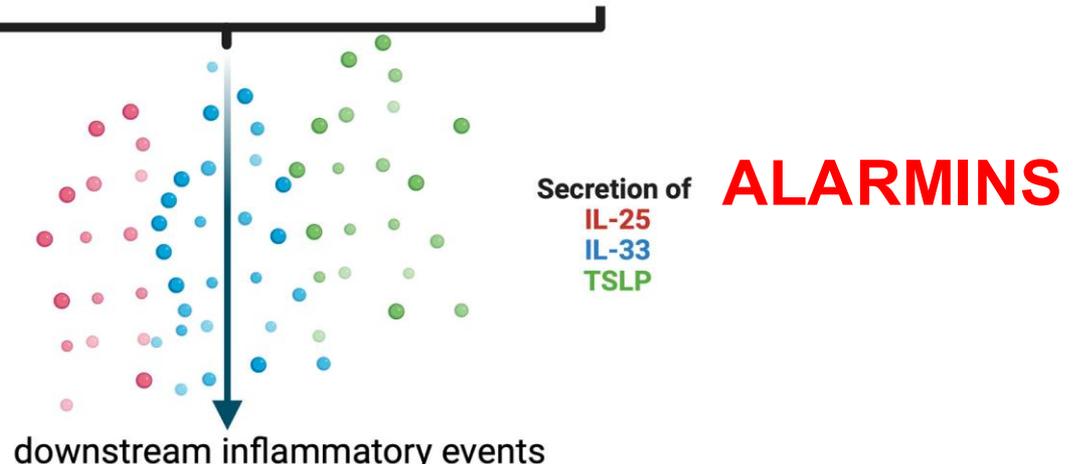
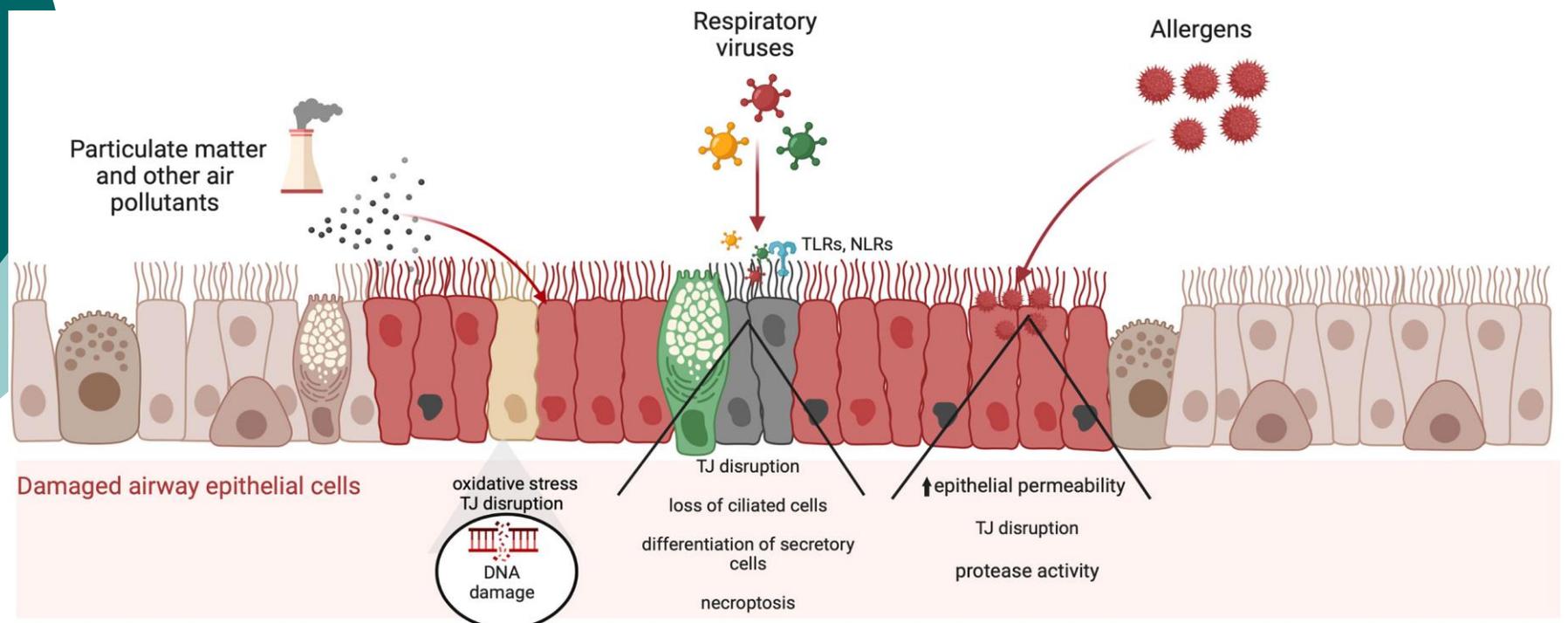


Atopic dermatitis (AD),  
neutrophilic asthma  
Drug allergies

# Type V – epithelial barrier damage, leaky junctions



# Type V – epithelial barrier damage, leaky junctions



# Hypersensitive reactions - Allergies

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- **Type I hypersensitivity** is an allergic reaction provoked by re-exposure to a specific type of antigen referred to as an allergen
- **IgE mediated -Th2 dependent**
- Atopy – hereditary predisposition → Genetic background
- Allergen – abnormal response against common environmental antigens
- Immediate vascular reaction and a late inflammatory response
- Mediated by mucosal and connective tissue **mast cells**
- If the entire body is involved, then anaphylaxis can take place, which is an acute, systemic reaction that can prove fatal
- **Type IV.hypersensitivity** is a late phase cell mediated immune reaction → delayed type
- The reaction takes two to three days to develop
- An inflammatory response driven by T cell recognition of processed soluble or cell-associated antigens leading to cytokine release and leukocyte activation.
- Contact allergy
- Antigen- bacterial, or small Hapten molecule
- Cell mediated: **Th1 cells** and macrophages → cytokine
- Mostly skin reaction



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<https://kahoot.it/challenge/007622552>

A felhasználónév: Immbio  
Jelszó: Immbio2025

# Allergic diseases

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## Type I. Immediate

- Allergic asthma
- Allergic conjunctivitis
- Allergic rhinitis ("hay fever")
- Anaphylaxis
- Angioedema
- Urticaria (hives)
- Eosinophilia
- Penicillin allergy
- Cephalosporin allergy
- Food allergy
- Sweet itch

## Type IV reactions

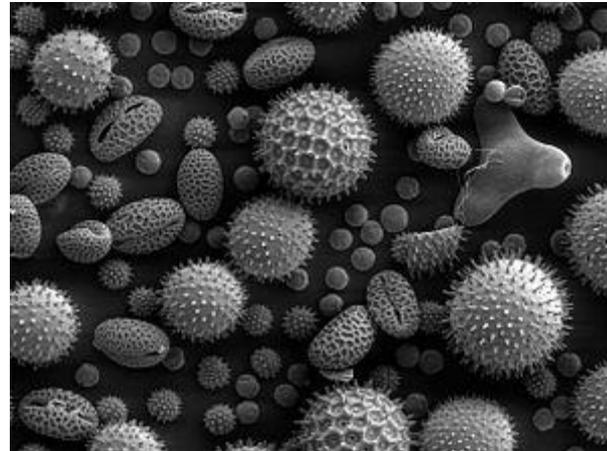
- Allergic contact dermatitis

# Components of type I allergy

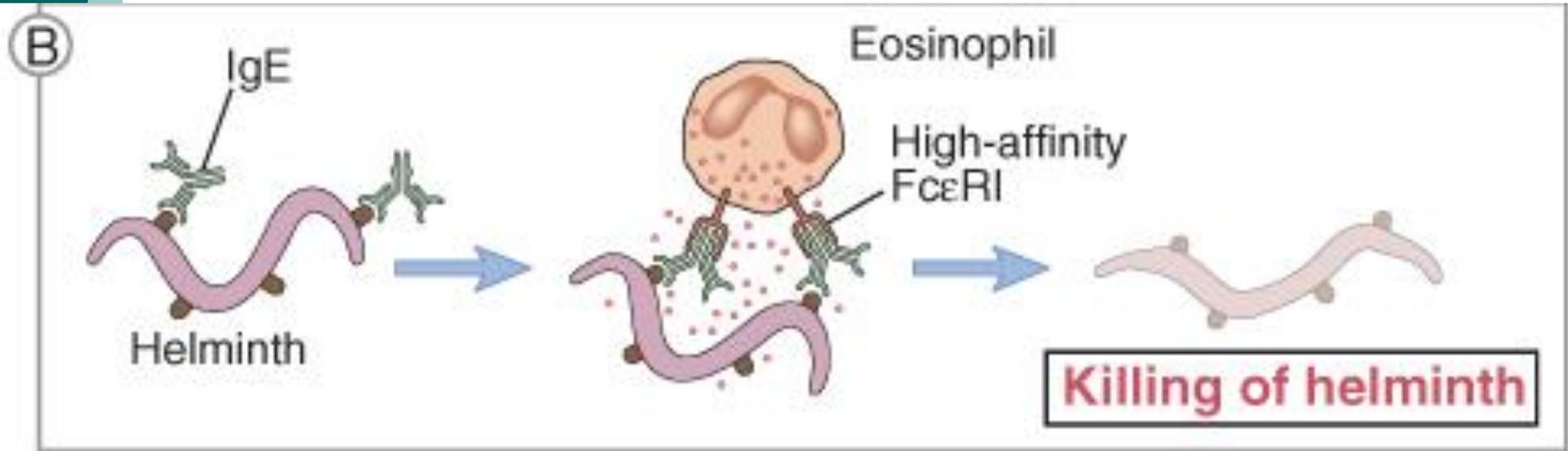
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- IgE-dependent (Th2)
- High-affinity FcεReceptor-dependent
- Mast cells are the primary effector cells
- Allergens

SEM of miscellaneous plant pollens: Pollens are very common allergens.



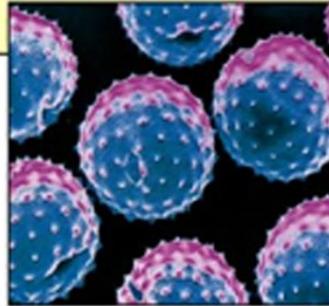
# The antimicrobial effect of IgE mediated immune reaction



## Common sources of allergens

### Inhaled materials

Plant pollens  
Dander of domesticated animals  
Mold spores  
Feces of very small animals  
e.g., house dust mites



pollen



house dust mite

### Injected materials

Insect venoms  
Vaccines  
Drugs  
Therapeutic proteins



wasp



drugs

### Ingested materials

Food  
Orally administered drugs



peanuts



shellfish

Figure 12.1 The Immune System, 3ed. (© Garland Science 2009)

# Allergen sources

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- **Inhalative allergens:** [dust mite](#) excretion, [pollen](#), pet [dander](#) or even [royal jelly](#).
- **Food allergens** are not as common as [food sensitivity](#), but some foods such as [peanuts](#) (a [legume](#)), [nuts](#), [seafood](#) and [shellfish](#) are the cause of serious allergies in many people.
- [Food and Drug Administration](#) (FDA in US) listed eight foods as being common for allergic reactions in a large segment of the sensitive population: peanuts, tree nuts, eggs, milk, shellfish, fish, wheat and their derivatives, and soy and their derivatives, as well as sulfites (chemical based, often found in flavors and colors in foods) at 10ppm and over.
- **Contact allergens:** [urushiol](#), a resin produced by [poison ivy](#) and [poison oak](#), which causes the skin rash condition known as [urushiol-induced contact dermatitis](#) by changing a skin cell's configuration so that it is no longer recognized by the immune system as part of the body. Various trees and wood products such as paper, cardboard, MDF etc. can also cause mild to severe allergy symptoms through touch or inhalation of sawdust such as asthma and skin rash.<sup>[5]</sup>

# Contact mechanisms with the allergens

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- An allergic reaction can be caused by any form of **direct contact** with the allergen:
- **Consuming food** or drink one is sensitive to (ingestion),
- **Breathing in** pollen, perfume or pet dander (inhalation),
- **Direct contact:** brushing a body part against an allergy-causing plant or latex.
- **Systemic exposure:** Other common causes of serious allergy are wasp, fire ant and bee stings, penicillin
- An extremely serious form of an allergic reaction is called anaphylaxis. One form of treatment is the administration of sterile epinephrine to the person experiencing anaphylaxis, which suppresses the body's overreaction to the allergen, and allows for the patient to be transported to a medical facility.

# Properties of inhaled allergens

<b>Features of inhaled allergens that promote priming of the T<sub>H</sub>2 cells that drive the IgE response</b>	
<b>Molecular type</b>	<b>Proteins, because only they induce T-cell responses</b>
<b>Function</b>	<b>Many allergens are proteases</b>
<b>Low dose</b>	<b>Favors activation of IL-4-producing CD4 T cells</b>
<b>Low molecular mass</b>	<b>Allergen diffuses out of particle into mucus</b>
<b>High solubility</b>	<b>Allergen is readily eluted from particle</b>
<b>High stability</b>	<b>Allergen survives in desiccated particles</b>
<b>Contains peptides that bind host MHC class II</b>	<b>Necessary for T-cell priming</b>

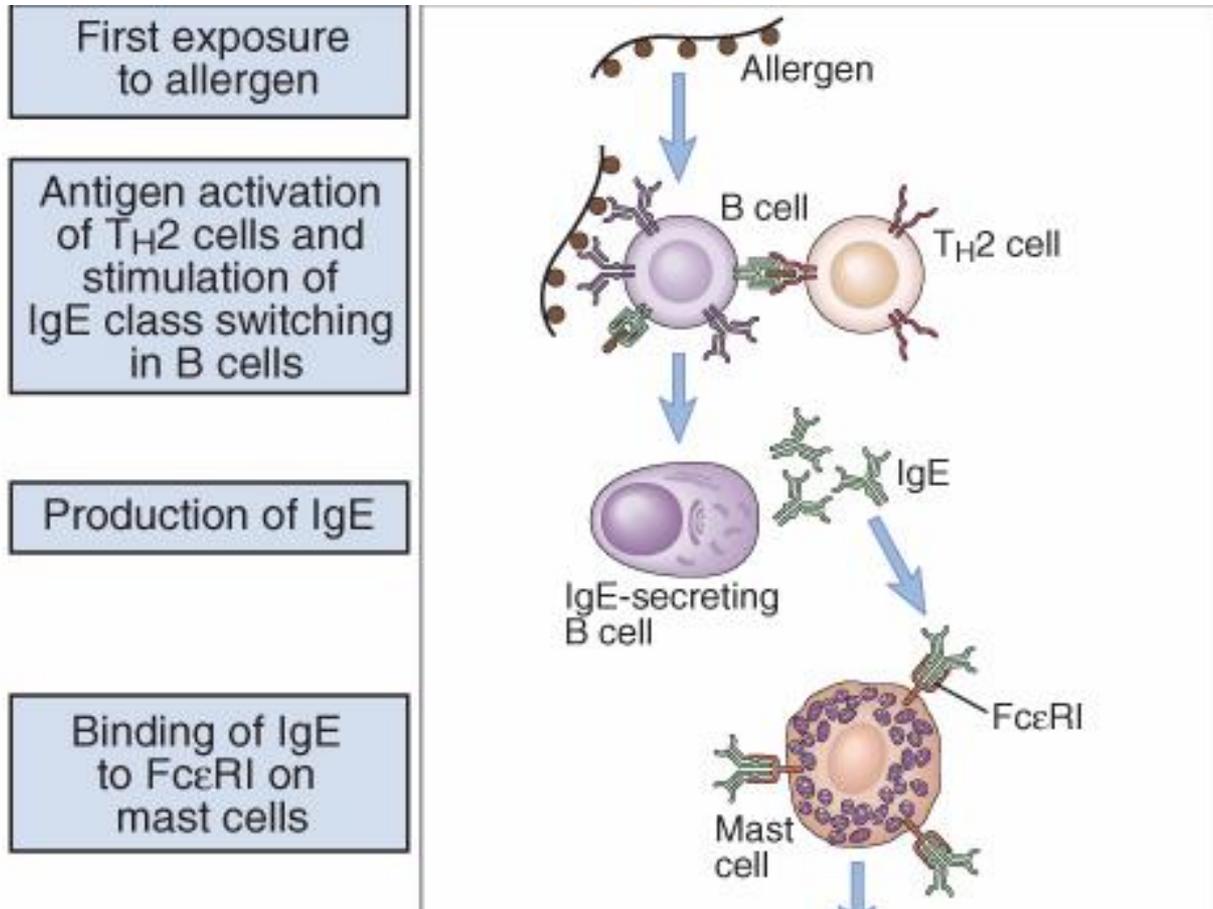
Figure 14.22 The Immune System, 4th ed. (© Garland Science 2015)

# Characteristics of allergens

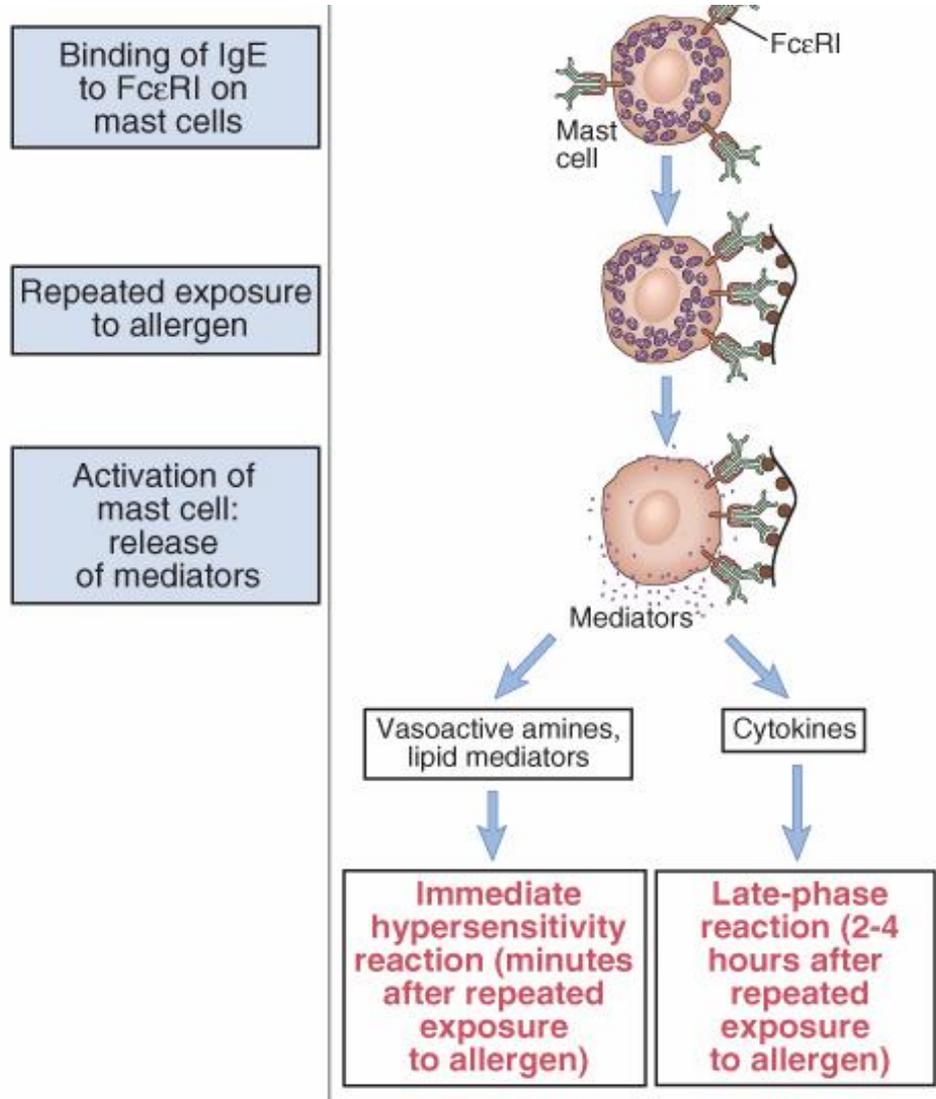
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- Proteins or chemicals (haptens) bound to proteins which we meet regularly or chronically
- They are low molecular weight, glycosylated proteins with good solubility in body fluids
- They might have enzyme activity
- Small hapten molecules (e.g. Penicillin) bound to self-proteins (pl. penicillin)
- They induce T-cell dependent immune response
- These antigens do not stimulate the innate immune response, do not cause macrophage activation → there are no inflammatory reactions → Th2 pathway induction

# Sensitization = primary immune response



# Effector phase



# Events in Immediate Hypersensitivity

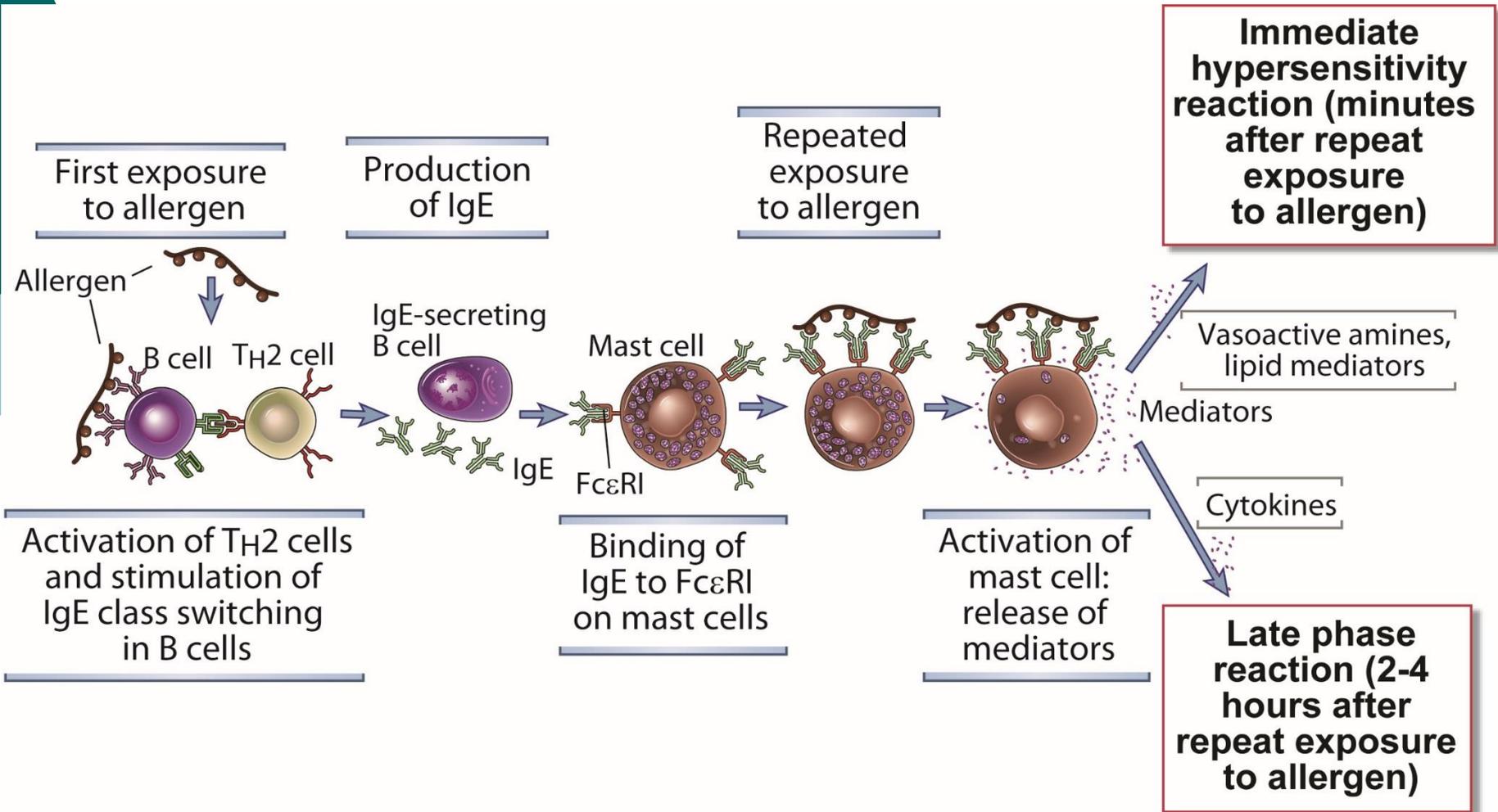


Fig. 19-1

# Differences from the normal immune responses

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- The high affinity  $Fc\epsilon R$  is continuously covered by antigen-specific IgE – is sensitized – even in the absence of antigen.
- This is a long-term binding -  $\sim$  2 weeks
- Multivalent allergen will crosslink a few-hundred  $Fc\epsilon R$  receptors  $\rightarrow$  immediate signal in Mast cells
- Local reaction: Plasma cells produce IgE in the peripheral tissues
- $Fc\epsilon R$ s are expressed on Mast cells, basophils, eosinophils and effector cells and APCs



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# IgE isotype switch

# Switch recombination

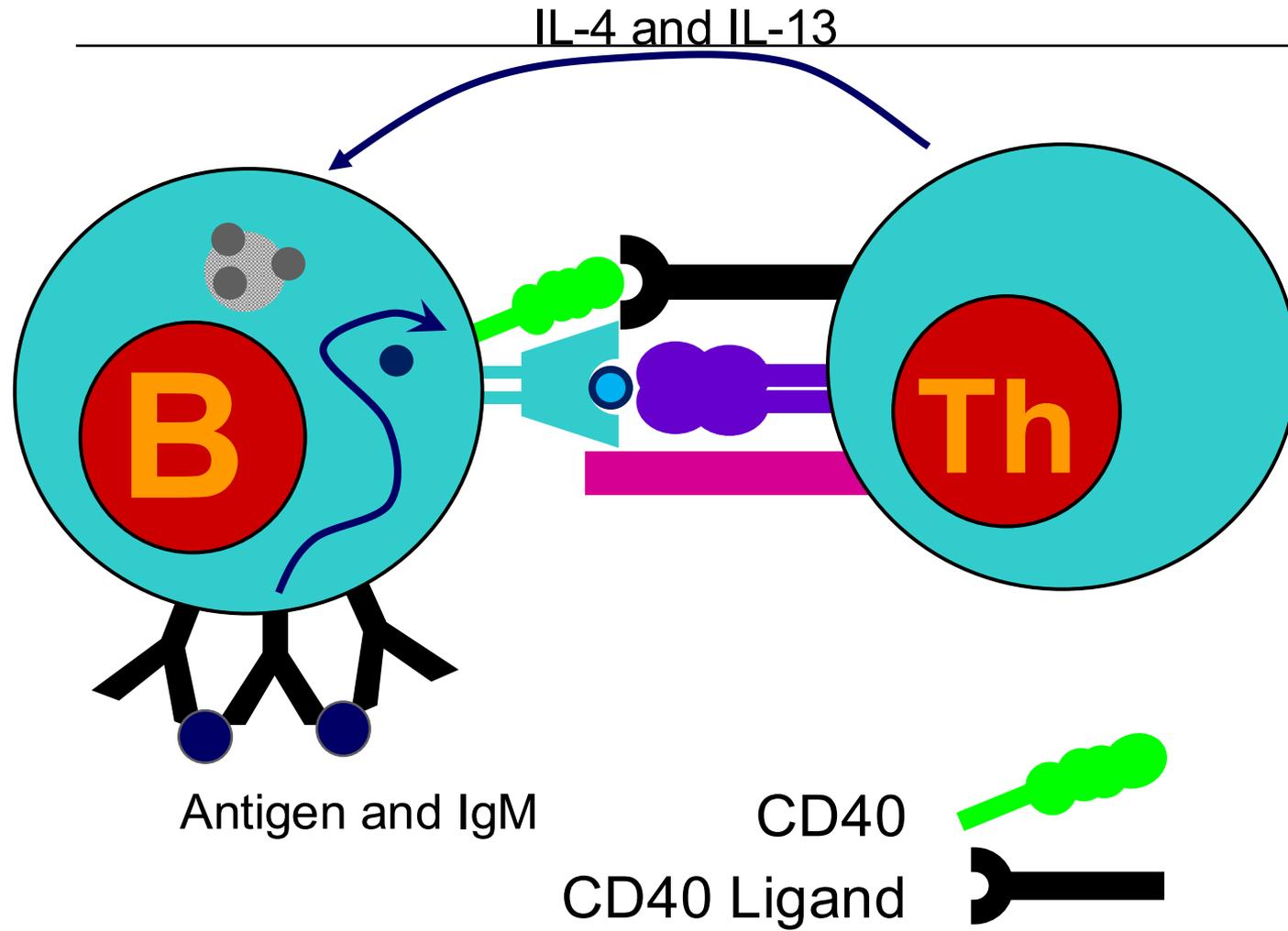
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## 3 signals:

1. Antigen
2. Th2 cytokines: IL-4, IL-13
3. CD40L costimulation by Th2 cells

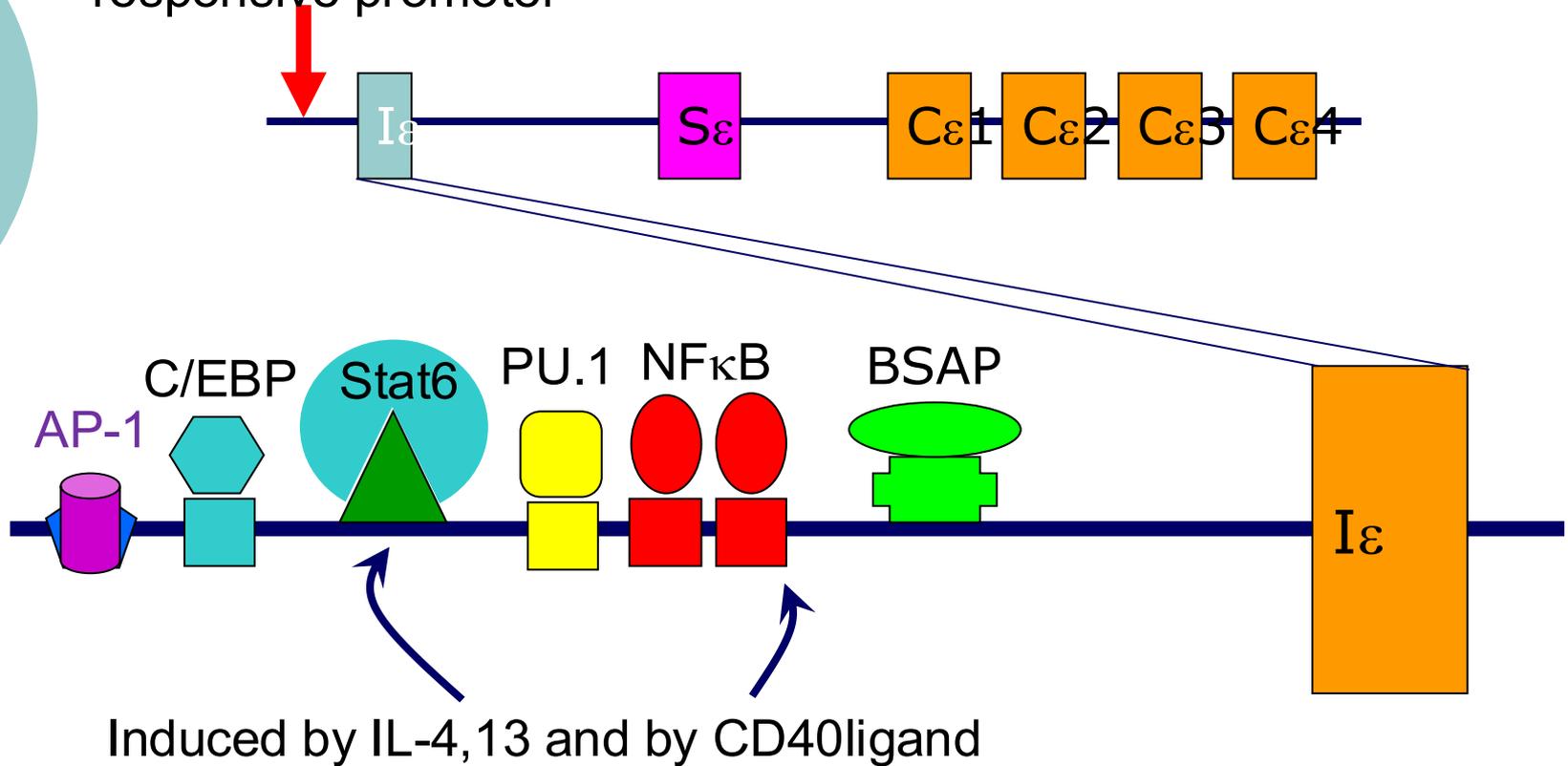
**Convergence by Ig epsilon gene regions (I)**

# 1. Antigen uptake and presentation by B cells

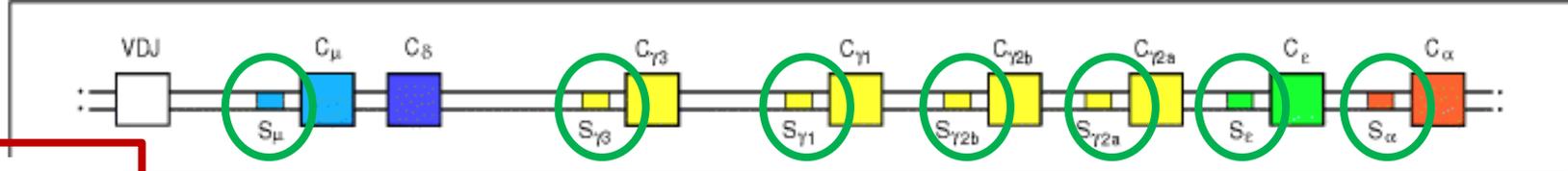


# Place of convergence: I $\epsilon$ promoter

Activation/cytokine responsive promoter

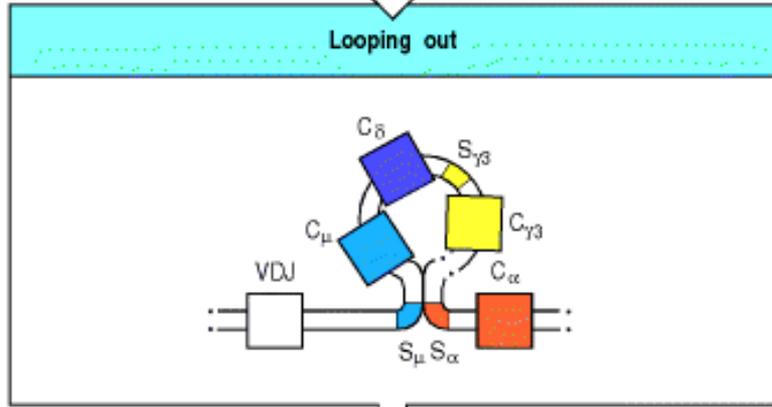
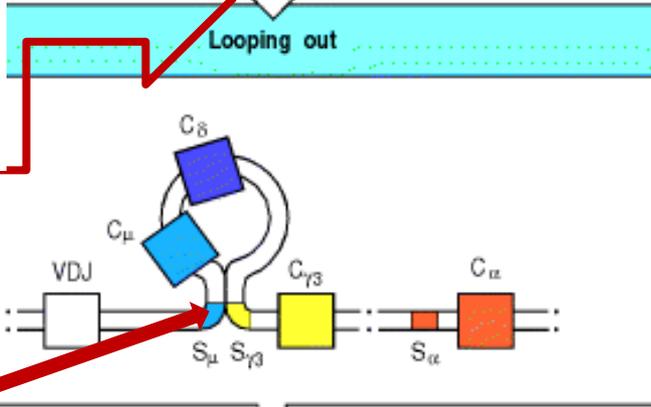


BSAP – B cell specific activator protein. C/EBP CCAAT/enhancer binding protein.  
PU.1 – Spi1 equivalent in humans, ets transcription factor

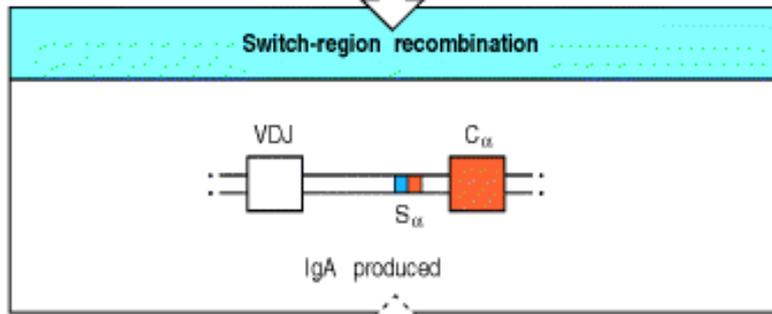
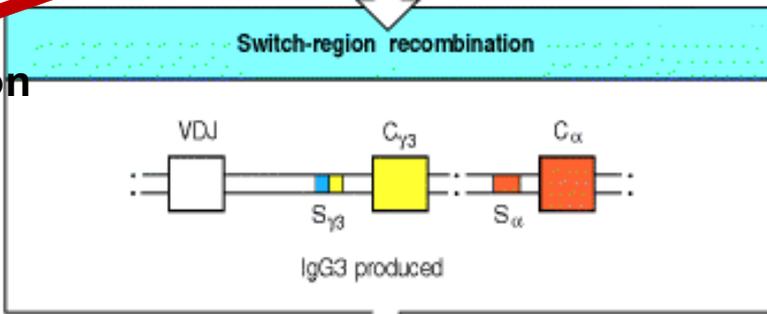


**T helper cytokines → transcriptions factors → binding to DNA regions**

Isotype switching

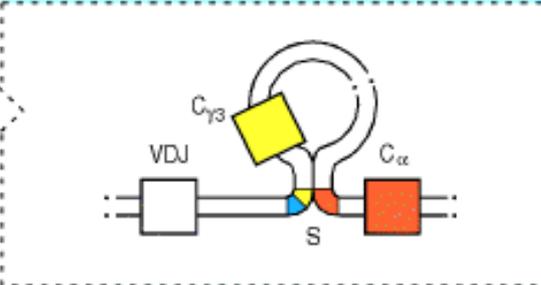


**S-region recombination**



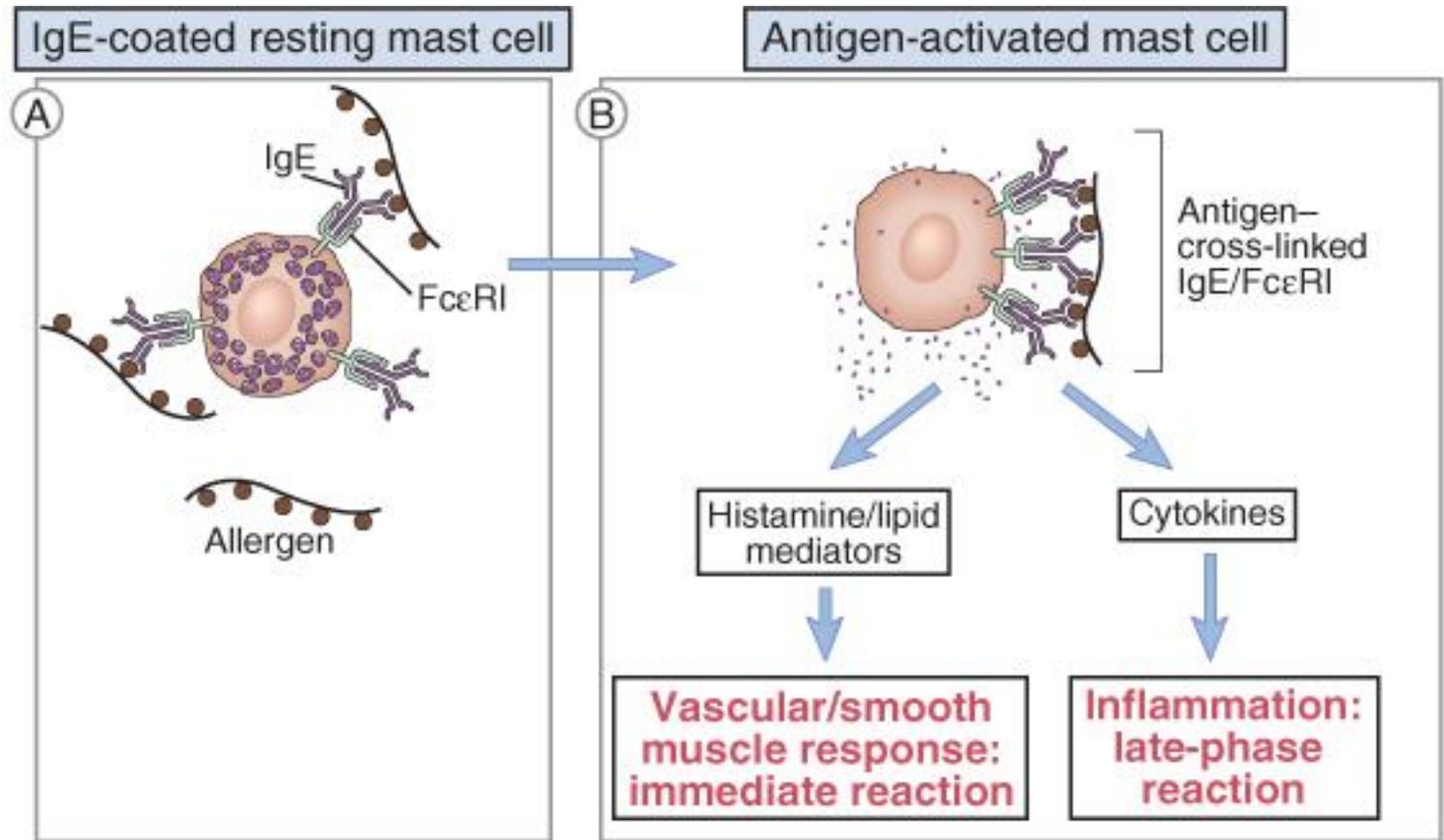
**activation-induced deaminase (AID) !**

Further rearrangement may occur

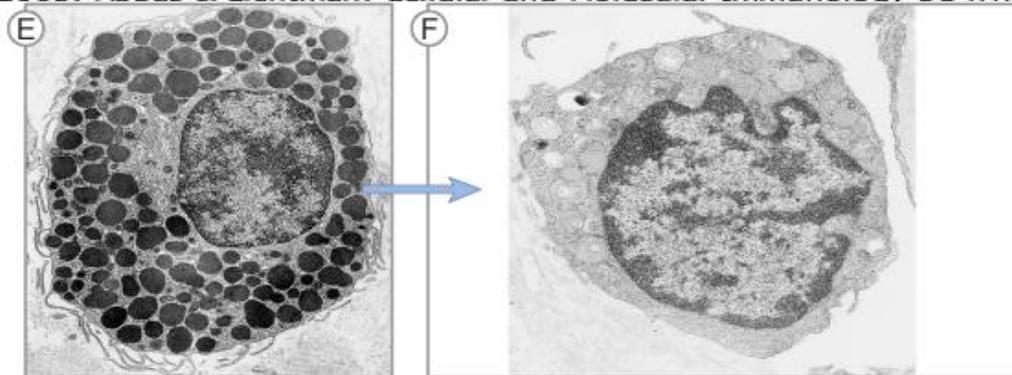


A decorative graphic on the left side of the slide consists of two overlapping teal circles of different shades. A thin, dark horizontal line spans across the upper portion of the slide, starting from the left edge and extending towards the right.

# **ROLE OF MAST CELLS**



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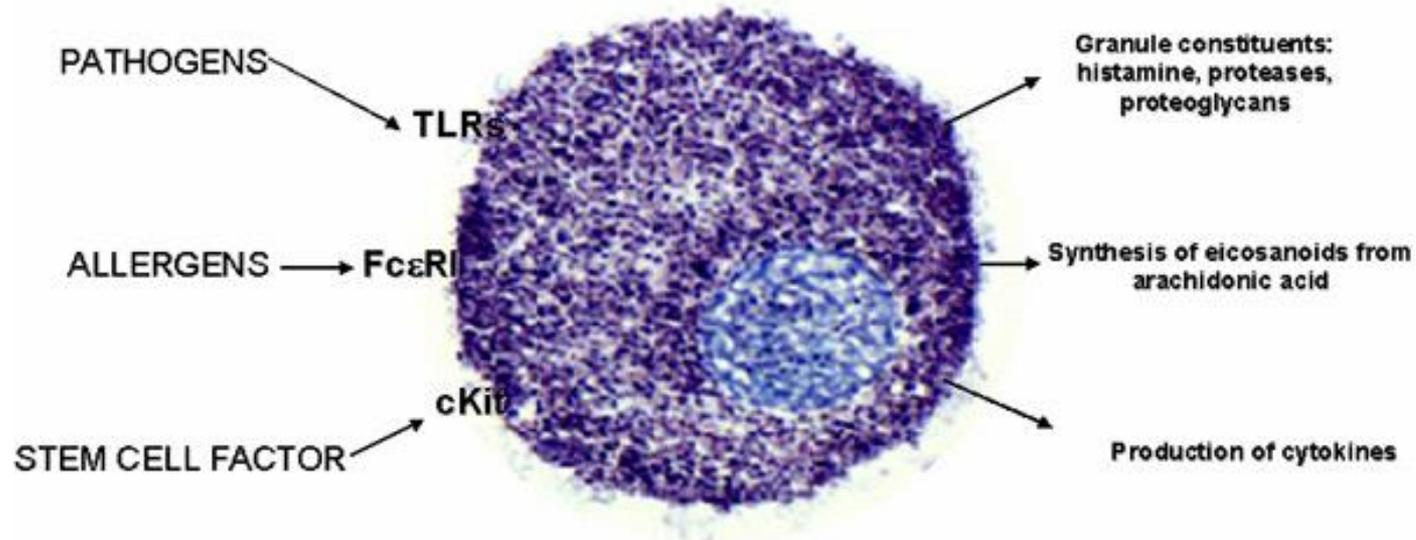
# Mast cell activation mechanisms

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**TLR4** – LPS → IL-1 $\beta$ , TNF- $\alpha$ , IL-6 and IL-13, without mast cell degranulation

**TLR2** – peptidoglycan → mast cell degranulation and production of IL-4 and IL-5, IL-6, IL-13

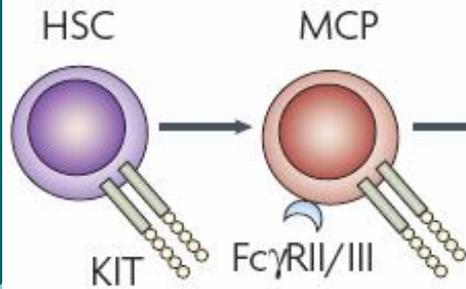
**TLR3,7,9** – Poly (I:C), CpG oligonucleotid → release of pro-inflammatory cytokines and chemokines



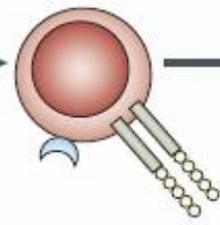
they express several hundred thousand high affinity receptors for IgE (Fc $\epsilon$ R1) and thus respond to IgE-directed antigens

express the pathogen-recognizing Toll-like receptors (TLRs) which probably account for the ability of mast cells to mount an effective innate immune response

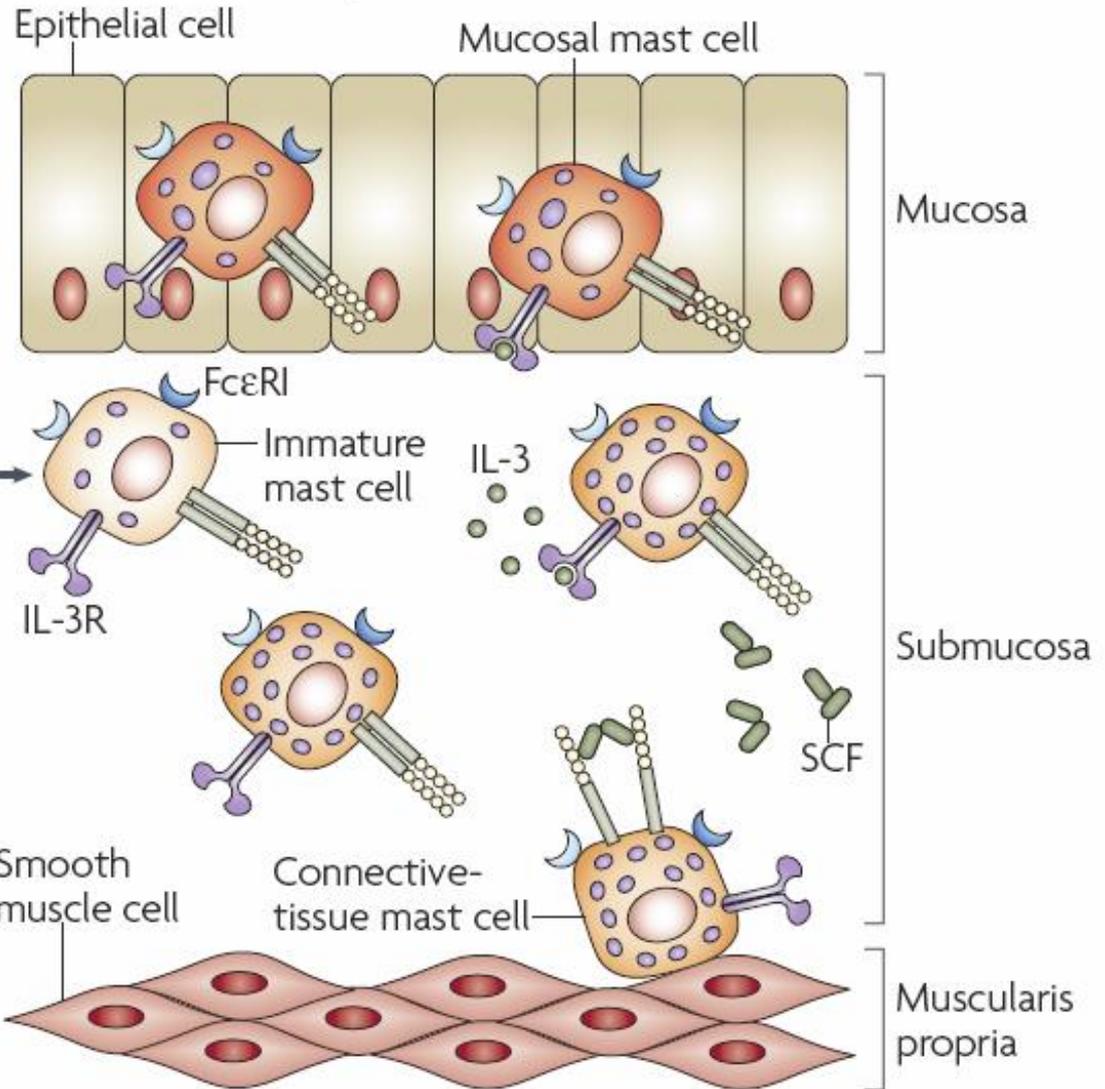
Bone marrow or other haematopoietic tissues



Blood



Peripheral tissue



# Other mast cell activators

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- MIP-1 $\alpha$  – macrophage inflammatory chemokine
- C3a, C5a anaphylatoxin – complement
- Neuropeptides – P-substance, somatostatin, VIP
- Fc $\gamma$ R - IgG

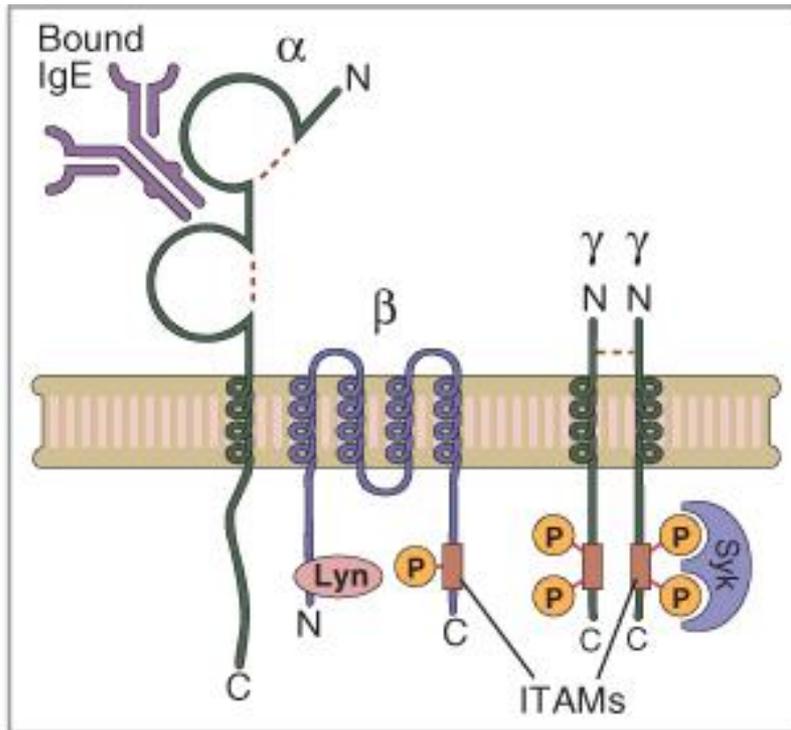
Characteristics	Mas cell	Basophils	Eosinophils
origin	CD34+ hematopoietic precursor	CD34+ hematopoietic precursor	CD34+ hematopoietic precursor
Mediators	Histamin, heparin, chondroitin sulphate, proteases	Histamin, chondroitin sulphate, proteases	Major basic protein, eo. Cationic proteins, peroxidase, hydrolase, lysophospholipase
Prolifaretion capacity	Yes	No	No
Life span	Weeks, month	days	Days-weeks
<b>Growth factor</b>	SCF	IL-3	IL-5
FceRI expression	lot	lot	less



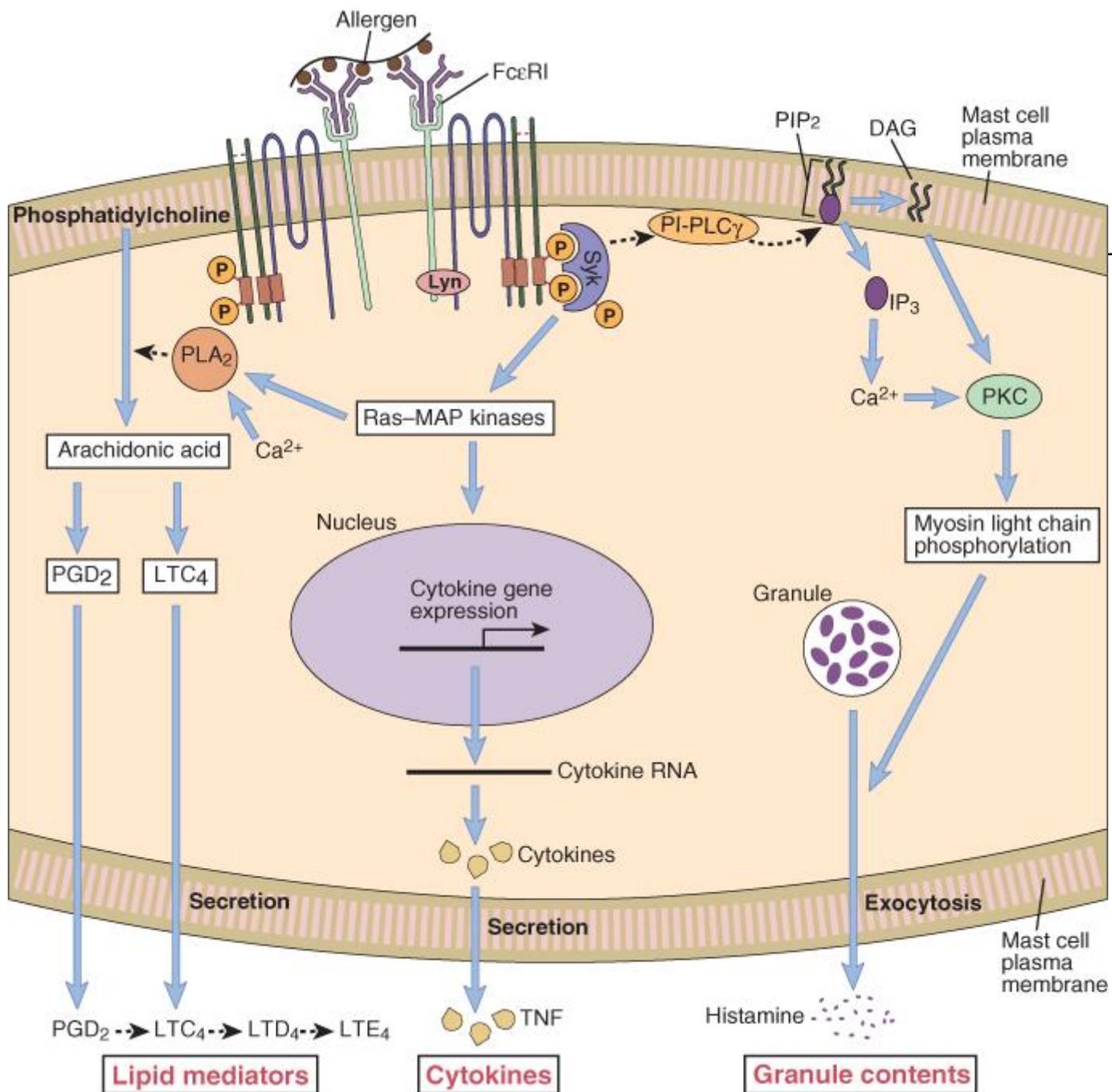
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# ROLE OF Fc&RECEPTOR

# Structure of the high-affinity Fc $\epsilon$ R (IgE) receptor



Mast cells, basophils, eo.,  
Langerhans cells, macrophages



**Lipid mediators**

**Cytokines**

**Granule contents**

# Biochemical Events of Mast Cell Activation (1)

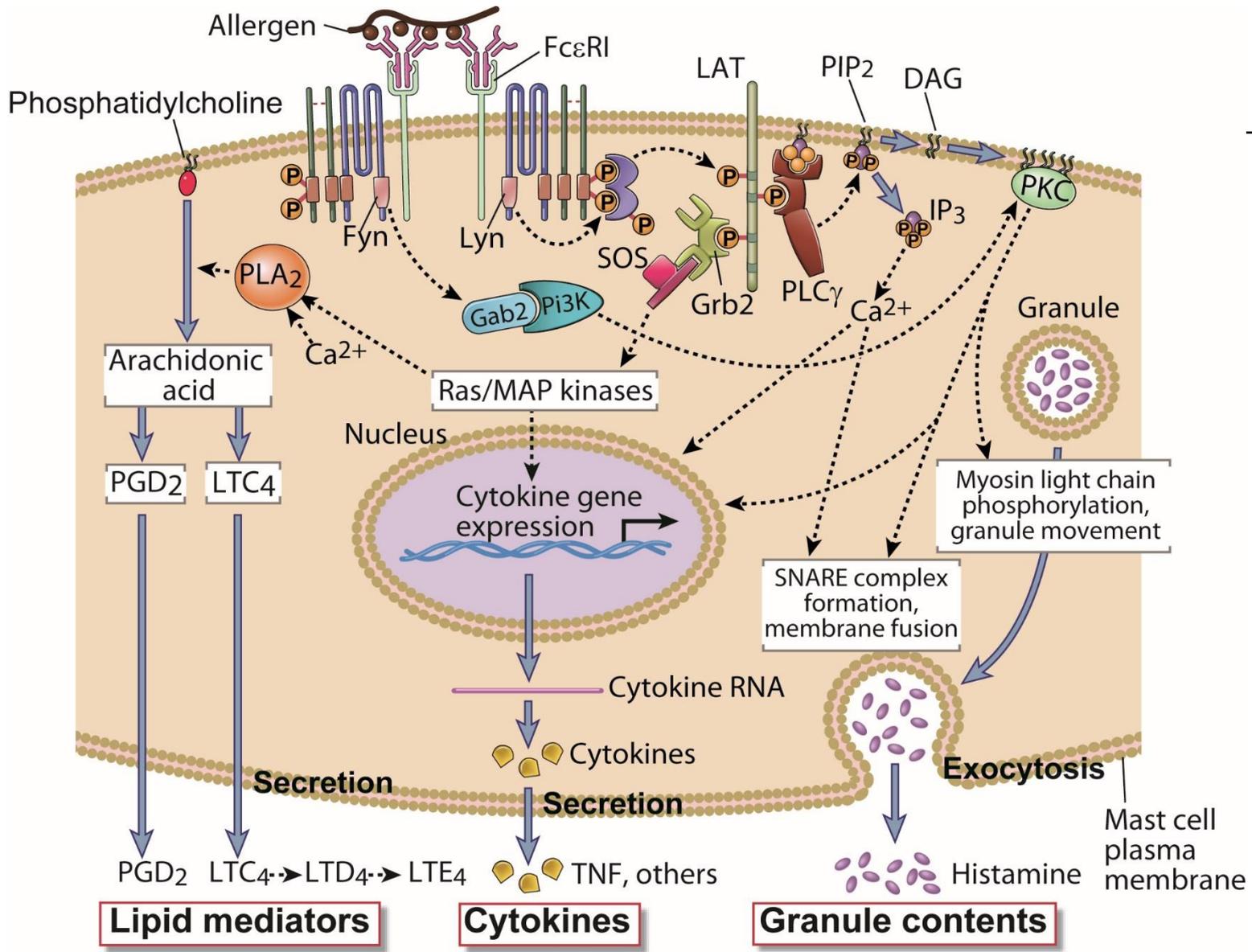


Fig. 17-5

# FcεRI and FcεRII (CD23)

**FcεRI:** - high affinity  
 - Ig-superfamily  
 α, β 2γ chains

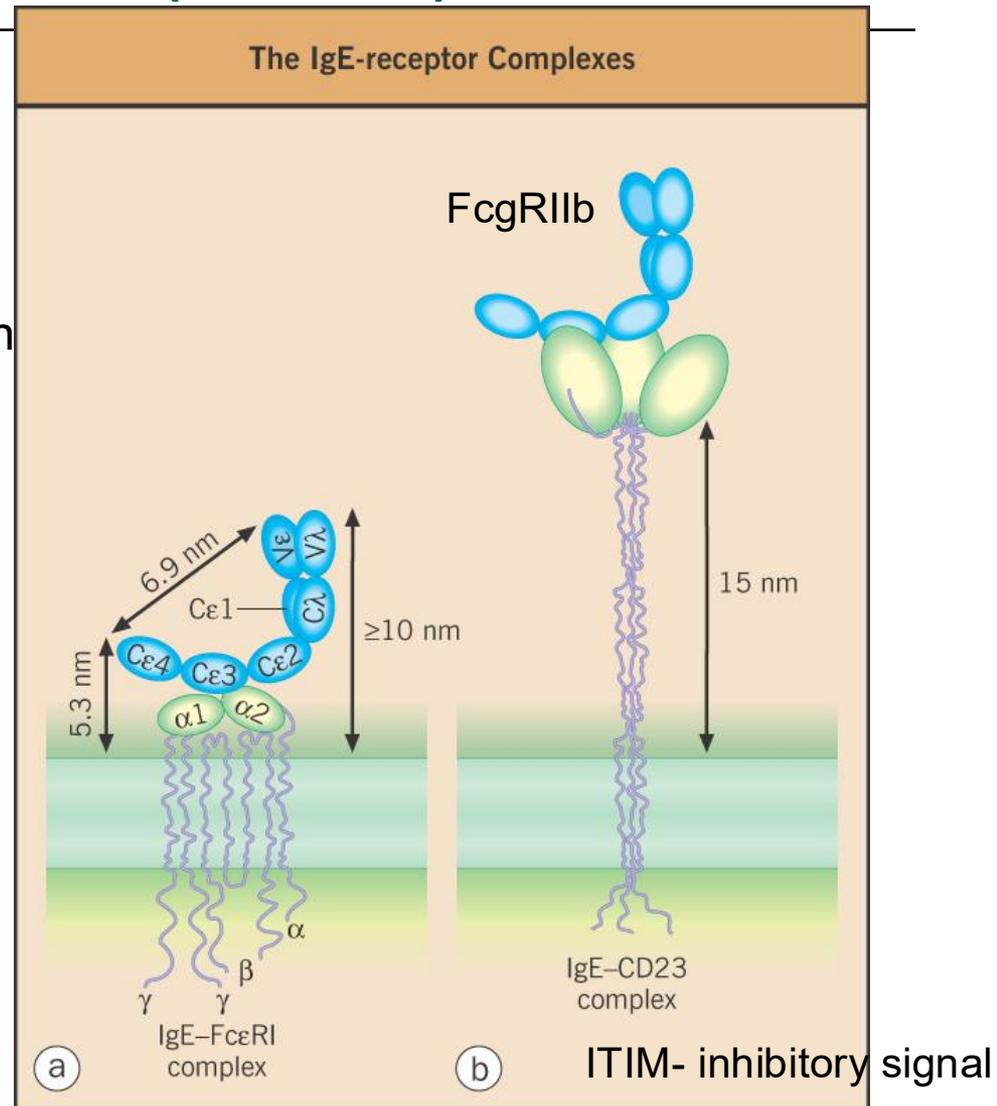
α1 és α2 domain ~80aa.Ig-domain

IgE upregulates its expression

**FcεRII:** - medium affinity  
**(CD23)** - lectin-family  
 - homotrimer

B cells, monocytes, eosinophils  
 IL-4 induces

Ligand: soluble and mIgE  
 - complement receptor 2,3,4

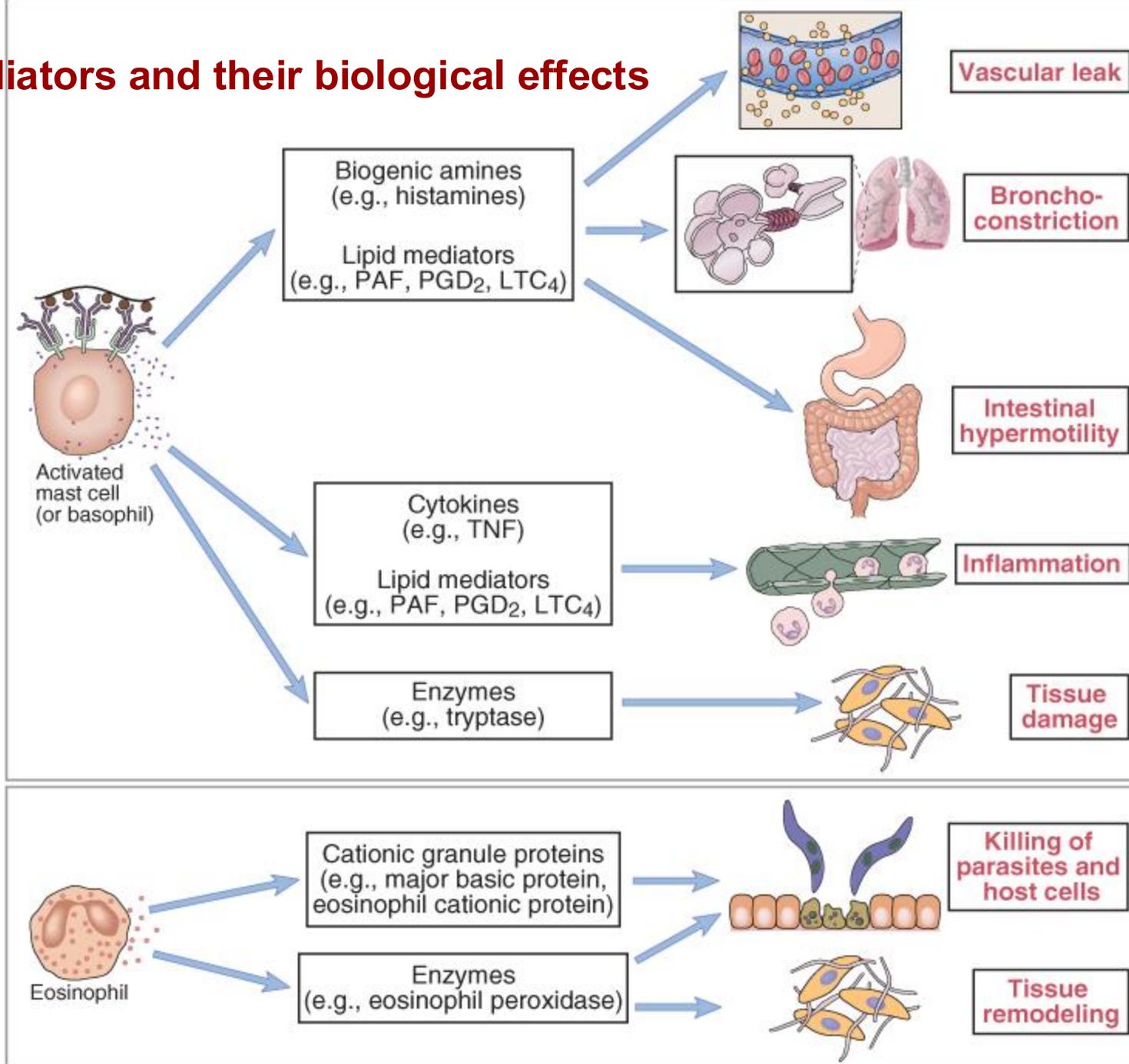


# Overview of mediators released by mast cells in type I hypersensitivity, and their actions:

---

<u>Vasodilation</u> and increased permeability	<ul style="list-style-type: none"><li>•<u>Histamine</u></li><li>•<u>PAF</u></li><li>•<u>Leukotriene C4, D4, and E4</u></li><li>•<u>Prostaglandin D2</u></li><li>•<u>Neutral proteases</u></li></ul>	
Smooth muscle spasm	<ul style="list-style-type: none"><li>•Histamine</li><li>•PAF</li><li>•Leukotriene C4, D4, and E4</li><li>•Prostaglandin</li></ul>	
<u>Leukocyte extravasation</u>	<ul style="list-style-type: none"><li>•<u>Cytokines</u> (e.g. <u>chemokines</u> and <u>TNF</u>)</li><li>•<u>Leukotriene B4</u></li><li>•Chemotactic factors for neutrophils and eosinophils</li></ul>	
Unless otherwise specified, the reference for this table is: <a href="#">[4]</a>		

# Mediators and their biological effects



A decorative graphic on the left side of the slide consists of two overlapping teal circles of different shades. A thin horizontal line extends from the right edge of the circles across the top of the slide.

# DIAGNOSIS

# The Wheal and Flare Reaction in the Skin

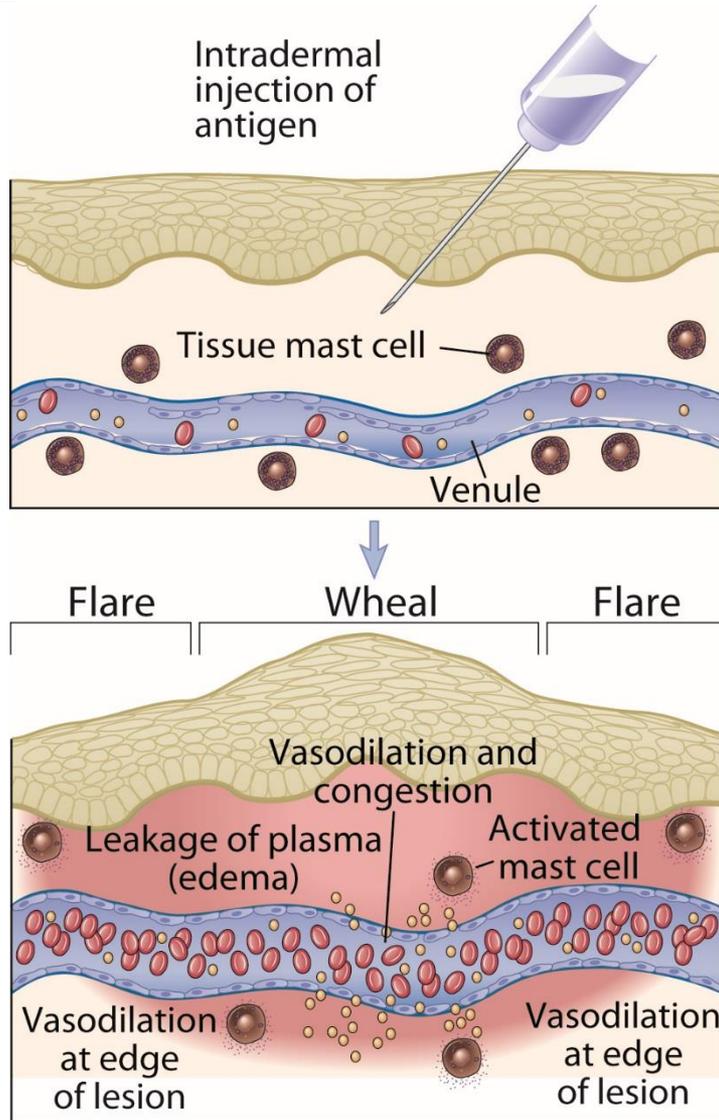
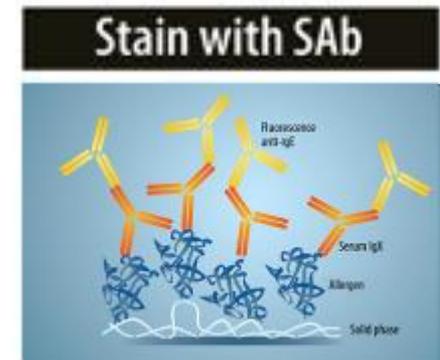
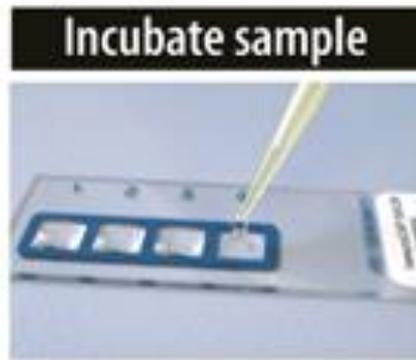


Fig. 19-8



# ImmunoCAP Specific IgE Blood Test



Anti-IgE  
Serum IgE  
Allergen  
Solid phase

Duration: 3 hours



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# **THERAPEUTIC TARGETS**

# Possible approaches to decrease allergic reactions

Enhancement of T reg activity

Inhibition of IgE production

Hyposensitization – IgE vs. IgG4

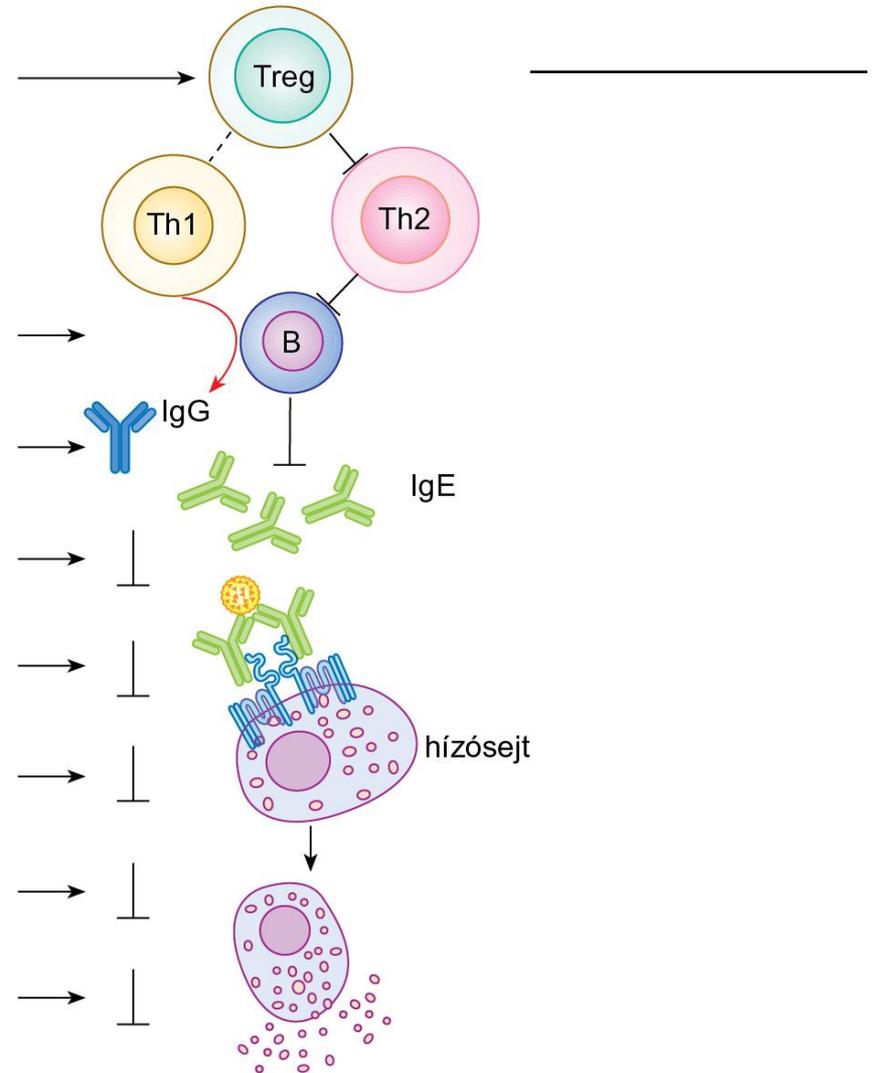
Inhibition of IgE binding

Inhibition of allergen binding

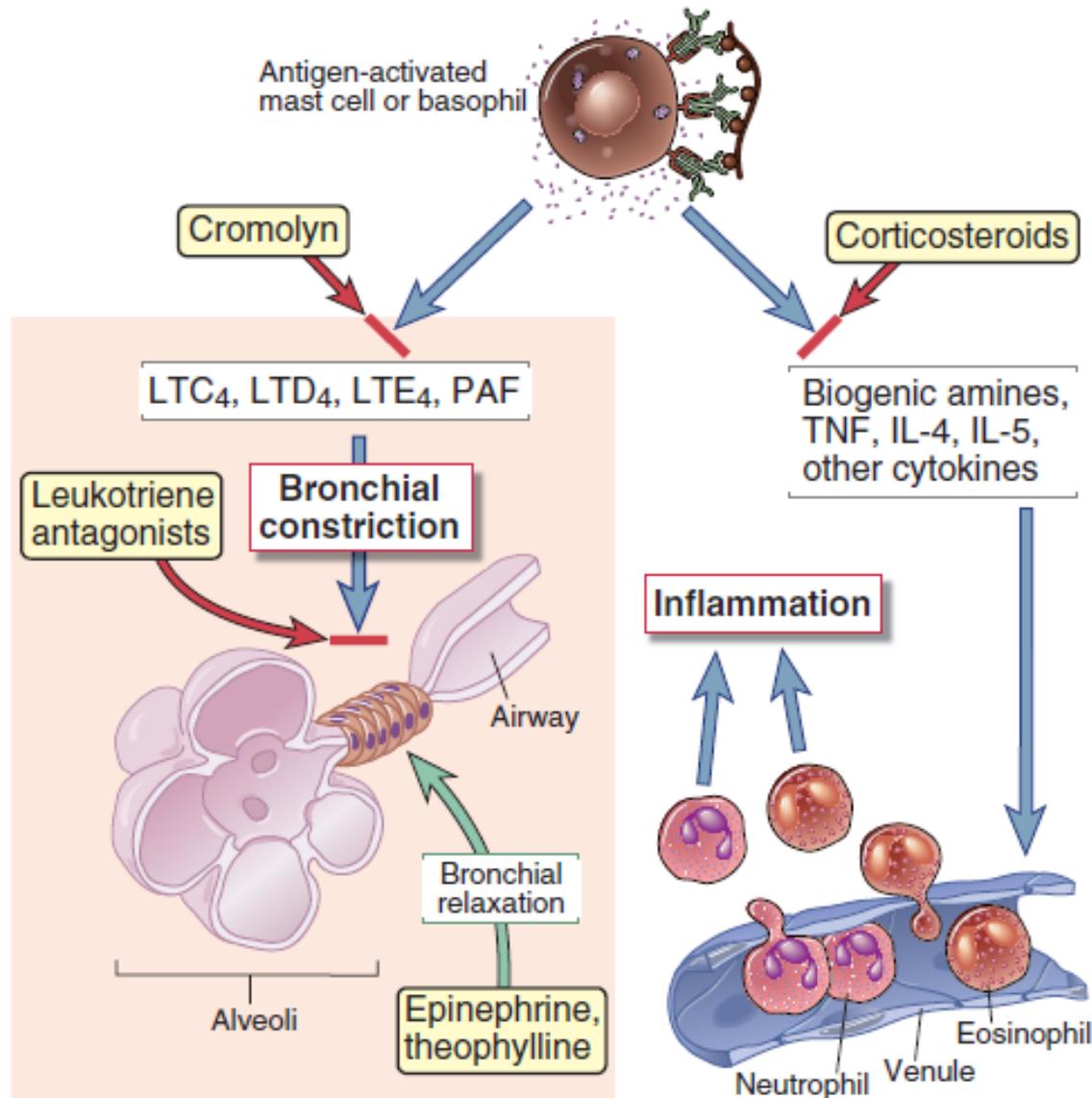
Inhibition of signal transduction

Inhibition of degranulation

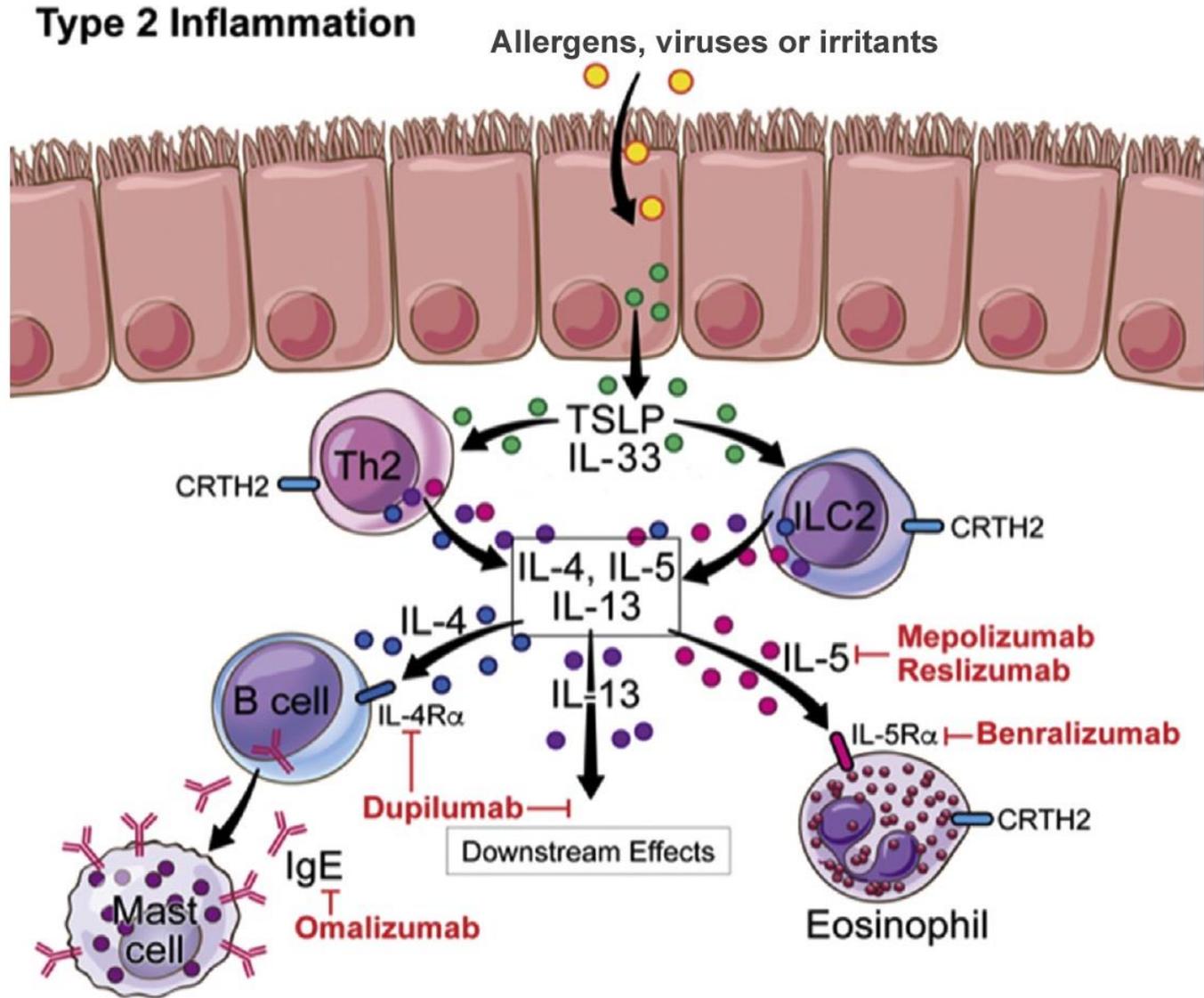
Blocking of mediators' effects



# Mediators and treatment of asthma



# Available biological therapies for allergic diseases



# ANAPHYLAXIS treatment

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- <https://epinephrineautoinject.com/epinephrine-side-effects/how-to-use/>

Epinephrine injection, USP auto-injector contains epinephrine, a medicine used to treat allergic emergencies (anaphylaxis). Anaphylaxis can be life-threatening, can happen within minutes, and can be caused by stinging and biting insects, allergy injections, foods, medicines, exercise or other unknown causes. Symptoms of anaphylaxis may include:

- trouble breathing
- wheezing
- hoarseness (changes in the way your voice sounds)
- hives (raised reddened rash that may itch)
- severe itching
- swelling of your face, lips, mouth, or tongue
- skin rash, redness, or swelling
- fast heartbeat
- weak pulse
- feeling very anxious
- confusion
- stomach pain
- losing control of urine or bowel movements (incontinence)
- diarrhea or stomach cramps
- dizziness, fainting, or “passing out” (unconsciousness).



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# Type IV. Cell-mediated allergies

**Type IV hypersensitivity reactions are mediated by antigen-specific effector T cells**

Syndrome	Antigen	Consequence
Delayed-type hypersensitivity	<p>Proteins:                      Insect venom                      Mycobacterial proteins                      (tuberculin, lepromin)</p>	<p>Local skin swelling:                      Erythema                      Induration                      Cellular infiltrate                      Dermatitis</p>
Contact hypersensitivity	<p>Haptens:                      Pentadecacatechol (poison ivy)                      DNFB                      Small metal ions:                      Nickel                      Chromate</p>	<p>Local epidermal reaction:                      Erythema                      Cellular infiltrate                      Vesicles                      Intraepidermal abscesses</p>
Gluten-sensitive enteropathy (celiac disease)	Gliadin	<p>Villous atrophy in small bowel                      Malabsorption</p>

Figure 12-24 Immunobiology, 6/e. (© Garland Science 2005)

# Type IV. reactions

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<u>allergic contact dermatitis</u> <sup>[1]</sup>	environmental chemicals (e.g., <u>urushiol</u> from <u>poison ivy oak</u> , <u>nickel</u> )	<u>epidermal necrosis</u> , inflammation, skin rash and blisters
<u>autoimmune myocarditis</u> <sup>[1]</sup>	<u>myosin heavy chain</u> protein	<u>cardiomyopathy</u>
<u>diabetes mellitus type 1</u> <sup>[1]</sup>	pancreatic <u>beta cell</u> proteins (possibly <u>insulin</u> , <u>glutamate decarboxylase</u> )	<u>Insulinitis</u> , <u>beta cell</u> destruction
<u>granulomas</u> <sup>[2]</sup>	various, depending on underlying disease	walled off lesion containing <u>macrophages</u> and other cells
some <u>peripheral neuropathies</u>	<u>Schwann cell</u> antigen	<u>neuritis</u> , <u>paralysis</u>
<u>Hashimoto's thyroiditis</u> <sup>[1]</sup>	<u>thyroglobulin</u> antigen	<u>hypothyroidism</u> , <u>hard goiter</u> , follicular <u>thymitis</u>
<u>inflammatory bowel disease</u> <sup>[1]</sup>	<u>enteric microbiota</u> and/or self antigens	hyperactivation of T-cells, cytokine release, recruitment of macrophages and other immune cells, inflammation
<u>multiple sclerosis</u> <sup>[1]</sup>	<u>myelin</u> antigens (e.g., myelin basic protein)	myelin destruction, inflammation
<u>rheumatoid arthritis</u> <sup>[1]</sup>	possibly <u>collagen</u> and/or <u>citruillinated</u> self proteins	chronic arthritis, inflammation, destruction of <u>articular cartilage</u> and bone
<u>tuberculin</u> reaction ( <u>Mantoux test</u> ) <sup>[3]</sup>		

## TABLE 14-3 INTRACELLULAR PATHOGENS AND CONTACT ANTIGENS THAT INDUCE DELAYED-TYPE HYPERSENSITIVITY

### Intracellular bacteria

*Mycobacterium tuberculosis*

*Mycobacterium leprae*

*Listeria monocytogenes*

*Brucella abortus*

### Intracellular fungi

*Pneumocystis carinii*

*Candida albicans*

*Histoplasma capsulatum*

*Cryptococcus neoformans*

### Intracellular parasites

*Leishmania* sp.

### Intracellular viruses

Herpes simplex virus

Variola (smallpox)

Measles virus

### Contact antigens

Picrylchloride

Hair dyes

Nickel salts

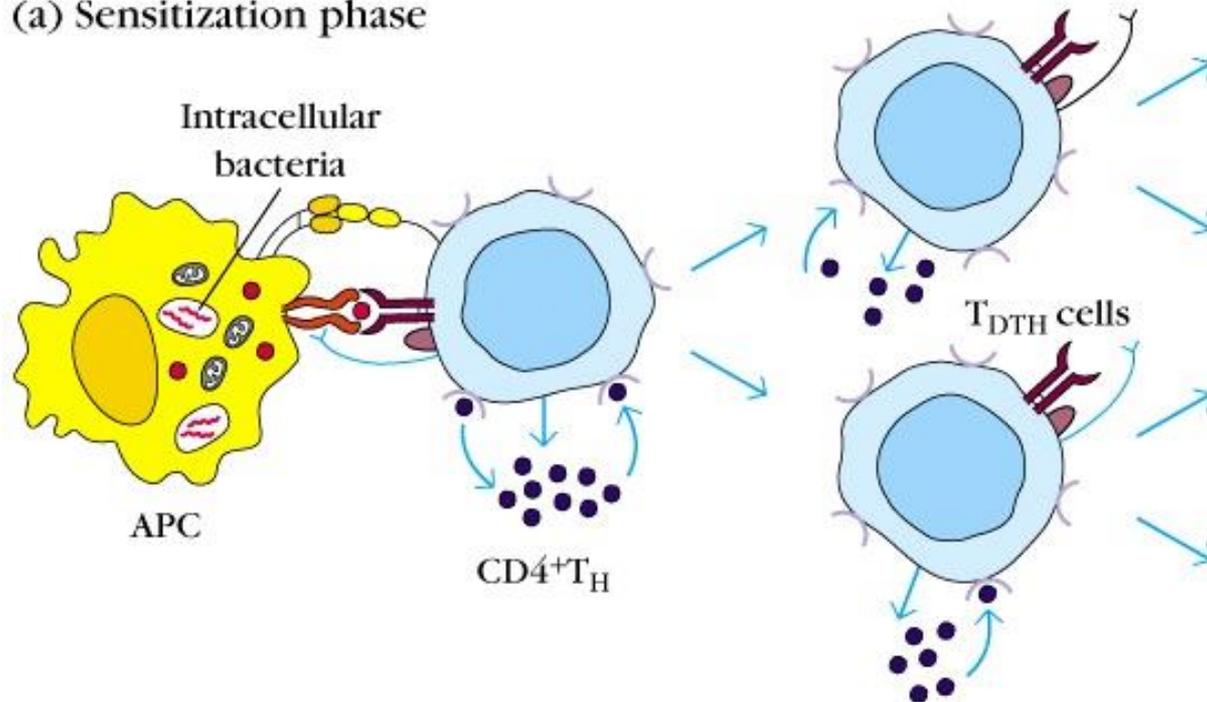
Poison ivy

Poison oak

# Delayed type IV hypersensitivity (DTH)

## I. Sensitization

(a) Sensitization phase

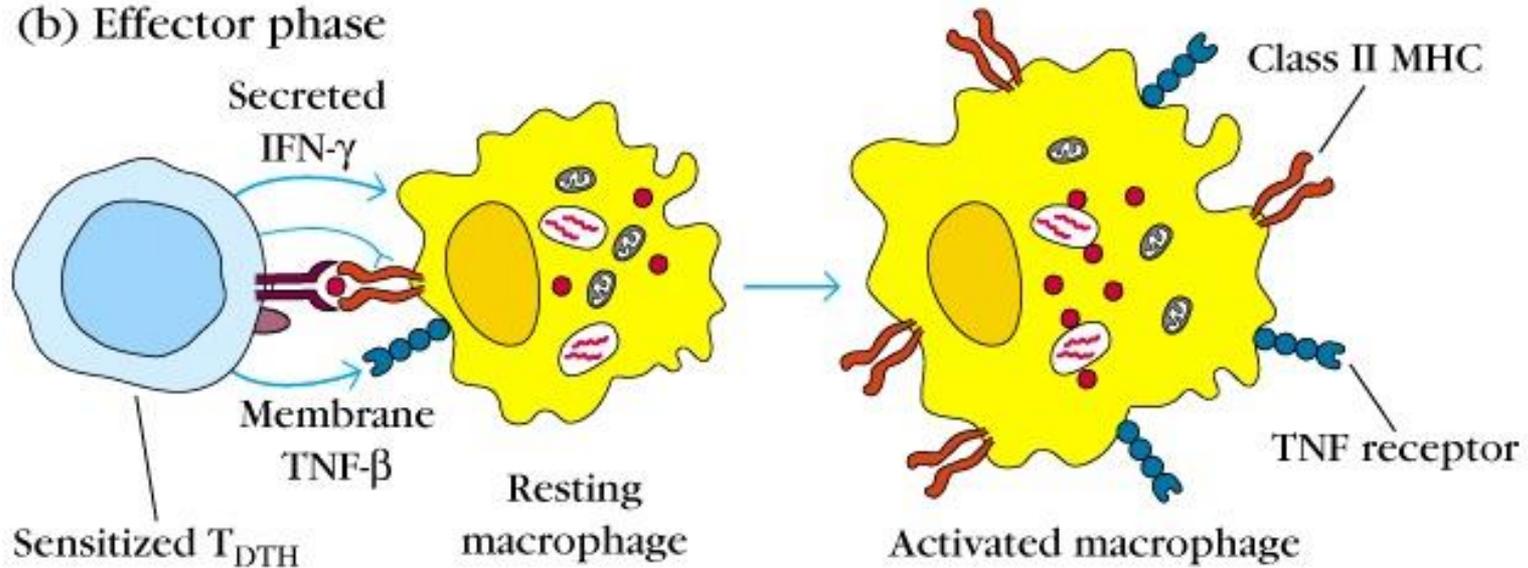


Antigen-presenting cells:  
Macrophages  
Langerhans cells

T<sub>DTH</sub> cells:  
T<sub>H</sub>1 cells (generally)  
CD8<sup>+</sup> cells (occasionally)

## II. Effector phase

(b) Effector phase



T<sub>DTH</sub> secretions:

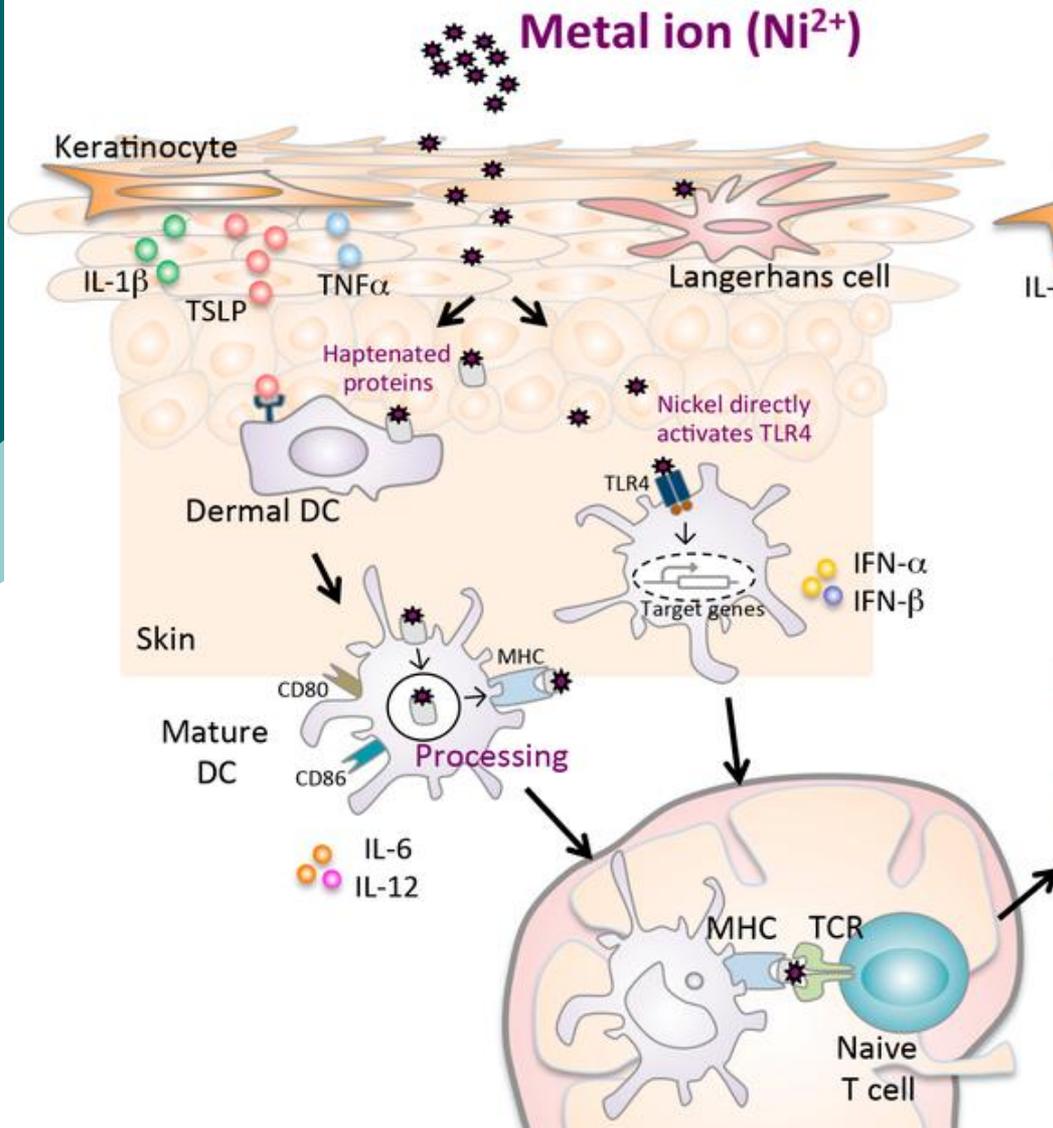
Cytokines: IFN- $\gamma$ , TNF- $\beta$ , IL-2,  
IL-3, GM-CSF

Chemokines: IL-8, MCAF, MIF

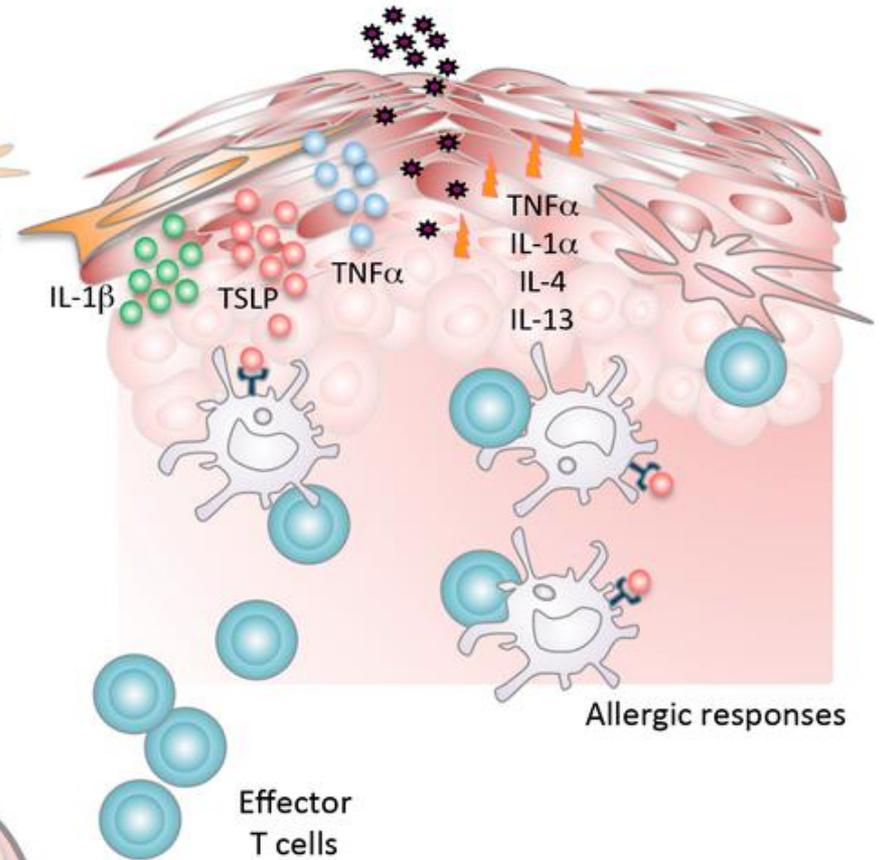
Effects of macrophage activation:

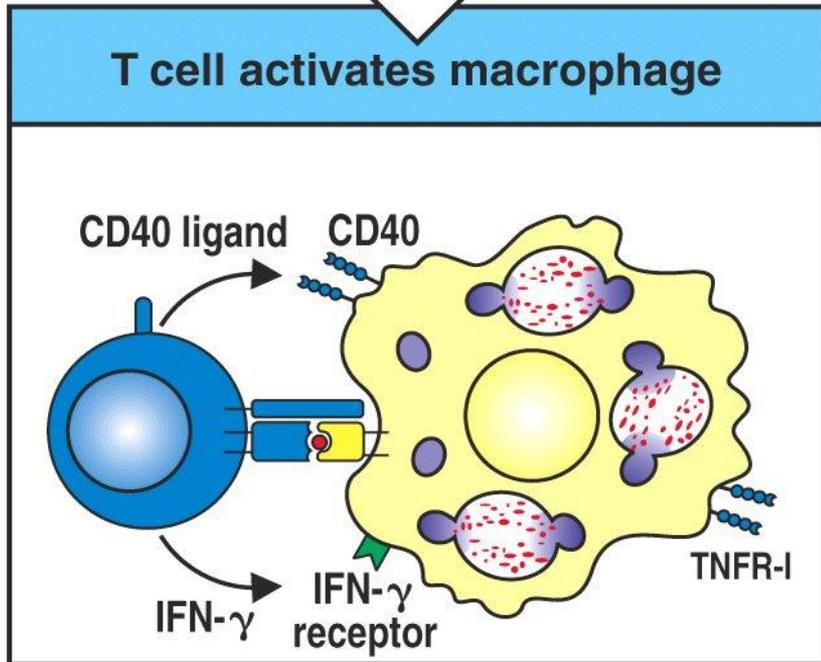
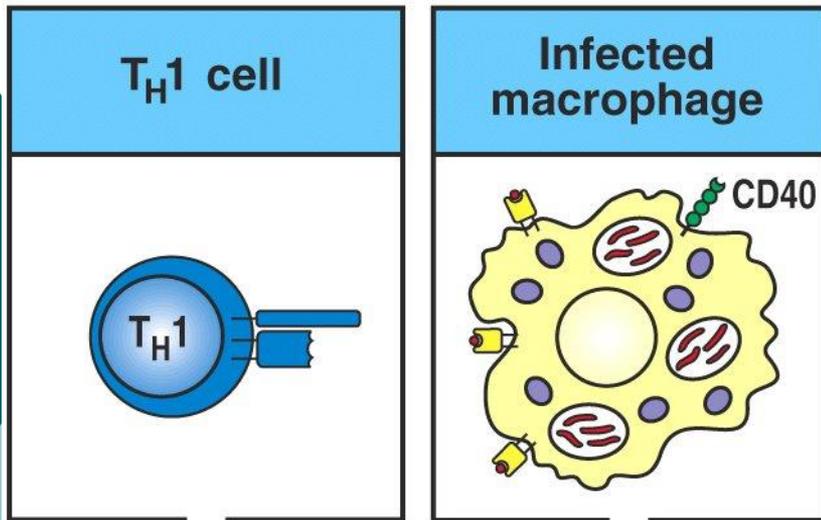
- ↑ Class II MHC molecules
- ↑ TNF receptors
- ↑ Oxygen radicals
- ↑ Nitric oxide

## Sensitization phase



## Elicitation phase





Reactive oxygen species

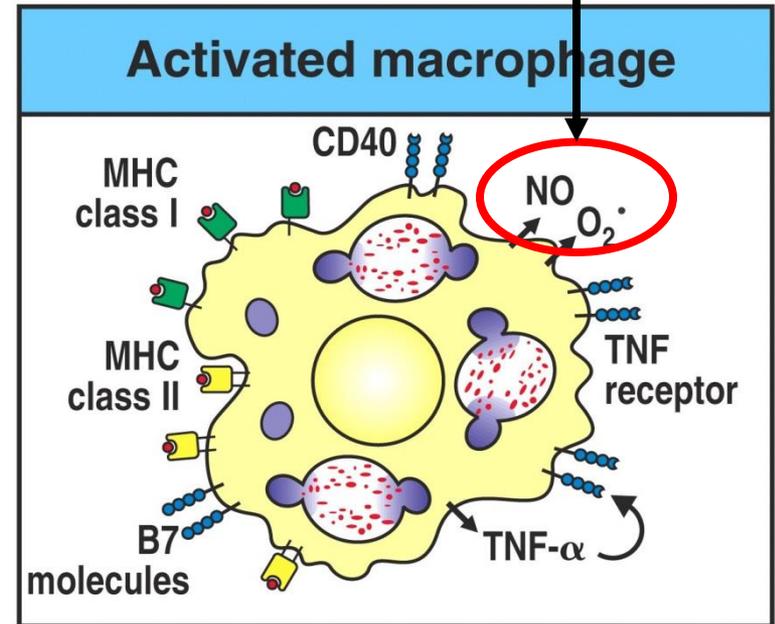
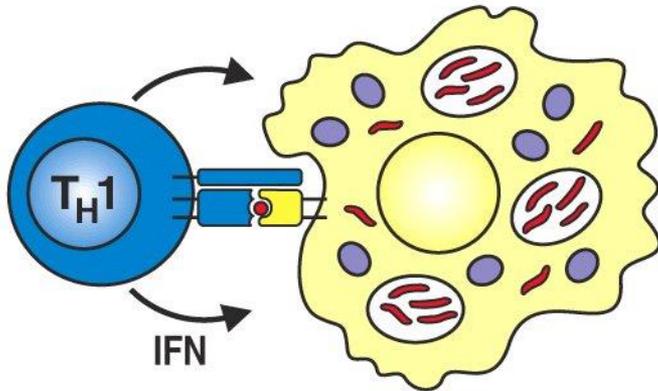


Figure 8-40 Immunobiology, 6/e. (© Garland Science 2005)

Figure 8-39 Immunobiology, 6/e. (© Garland Science 2005)

Partial removal of live *M. tuberculosis*



Granuloma

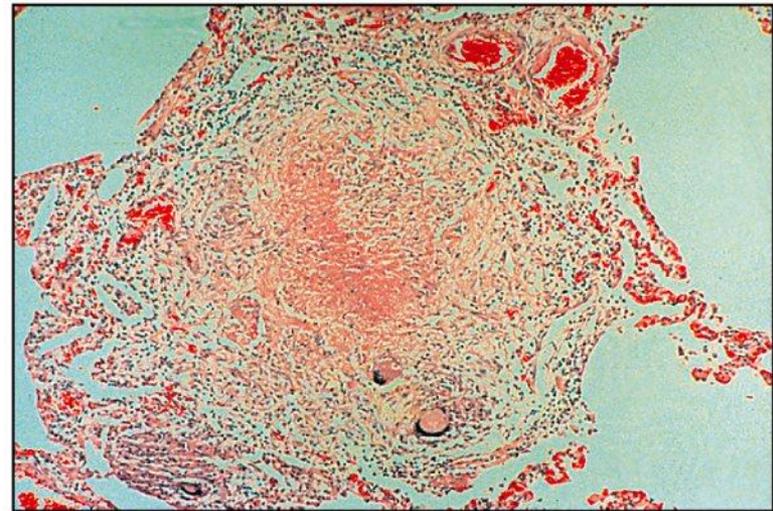
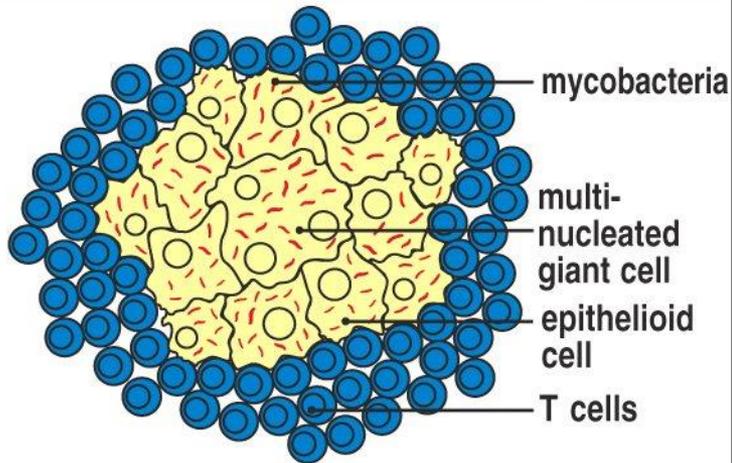
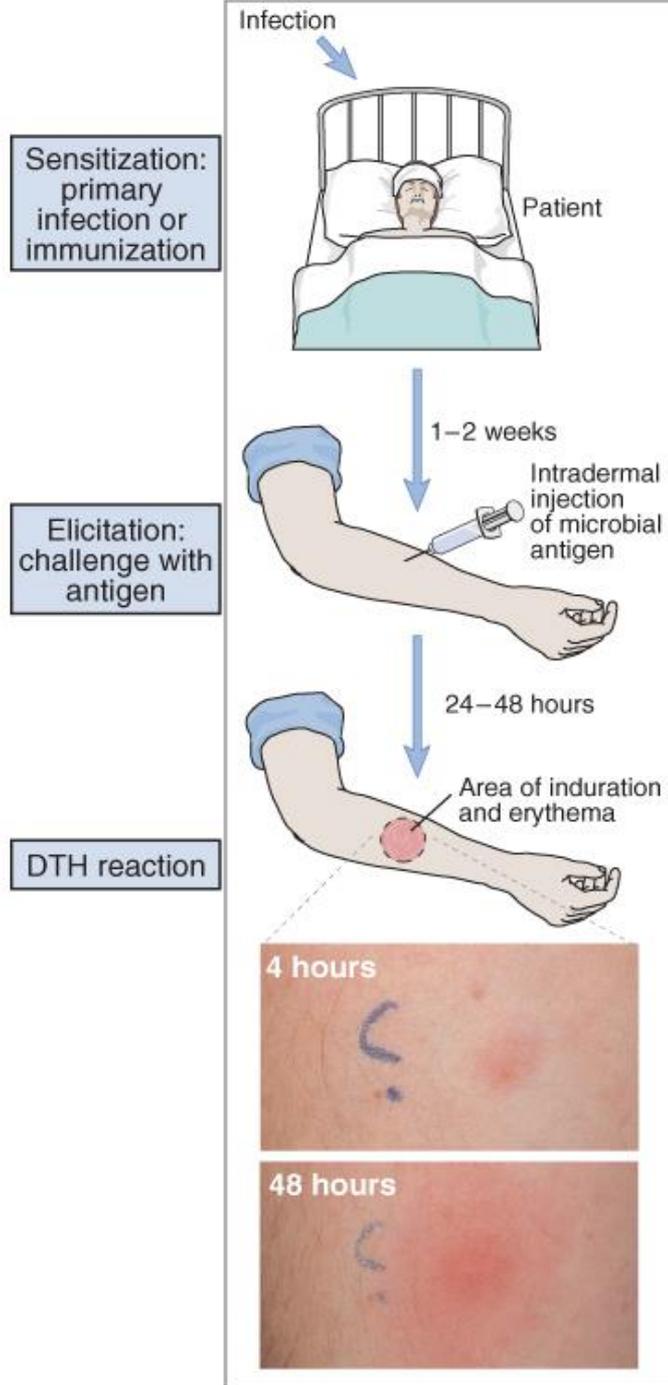


Figure 8-42 Immunobiology, 6/e. (© Garland Science 2005)

# DTH in clinic

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# Patch Testing 101: The Process of Determining Skin Allergy Causes



First appointment: To a sterilized back, the nurse will apply small quantities of anywhere from 25 to 100+ chemicals in individual small plastic or aluminum chambers taped in place by paper hypoallergenic tape. These patches stay in place for 48 hours and cannot be disturbed or washed.

Second appointment: Occurs 48-hours from first procedure. Patches are removed and a preliminary read is done.

Third appointment: Occurs at least 48-hours after the second appointment. Back must be kept dry and free from perspiration to generate a valid result.

- **To determine DTH allergy to something that touches your skin (i.e. skincare products, clothes, chemicals or jewelry)**
- **Patch tests** — not to be confused with skin prick tests.
- Contact allergy resulting reaction is called **Allergic Contact Dermatitis**, which consists of redness, itching, burning, scaling and occasionally blisters. The irritation also lasts for weeks, not just hours or days.
- Patch testing involves a **minimum of three appointments**, typically over the course of a week and follows the below procedure:
-