Classification, pathogenesis and diagnostics of allergic diseases

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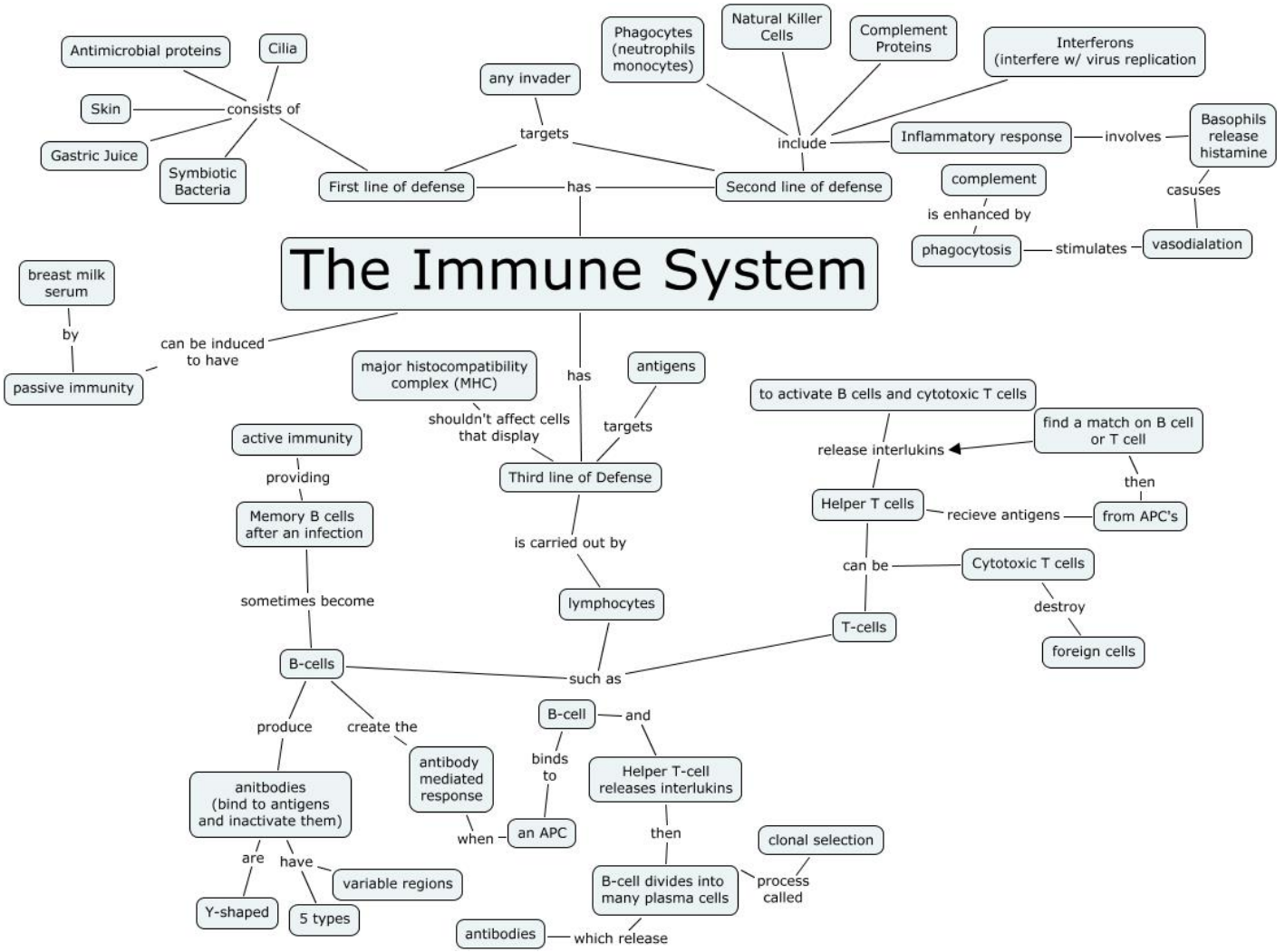
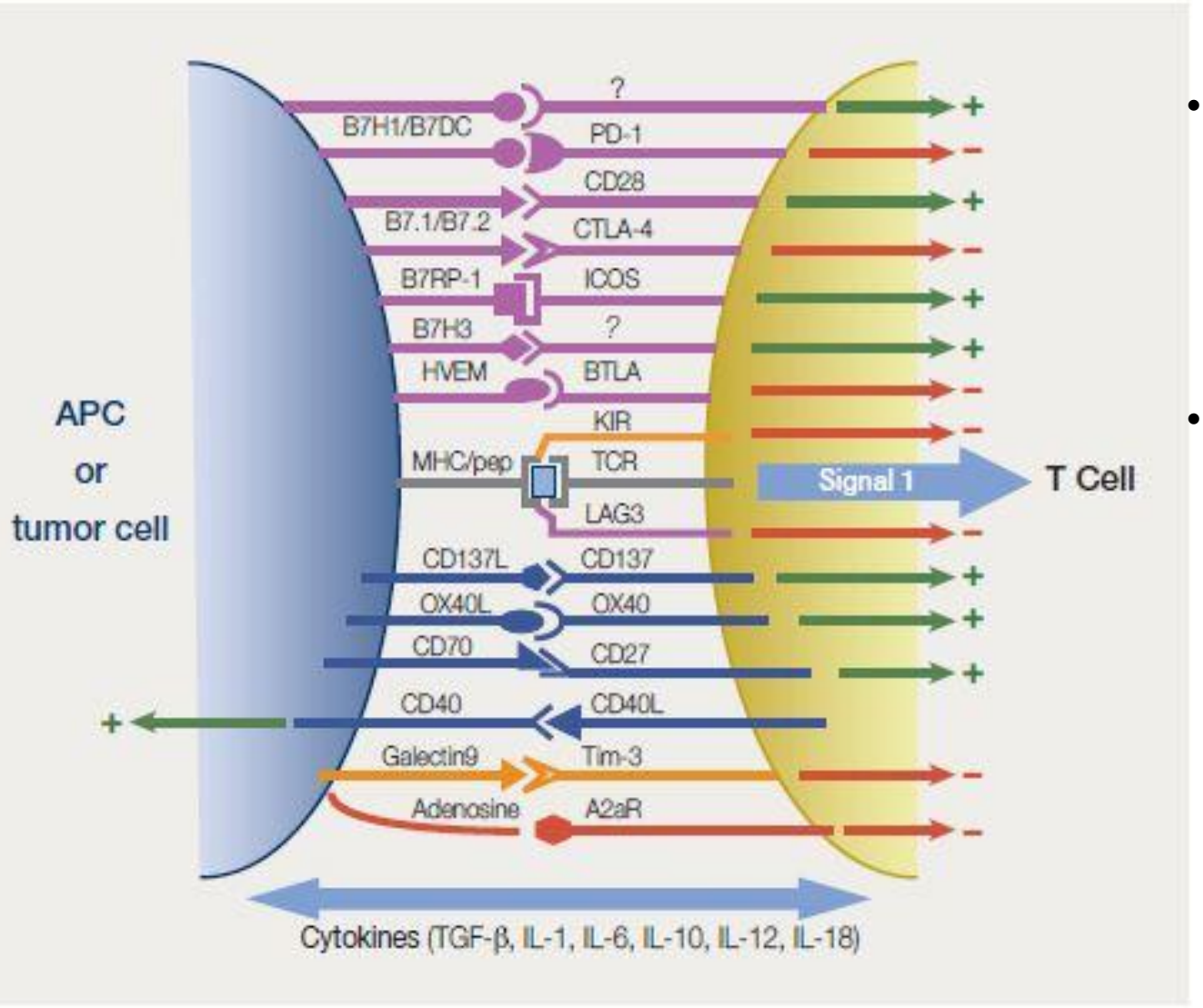
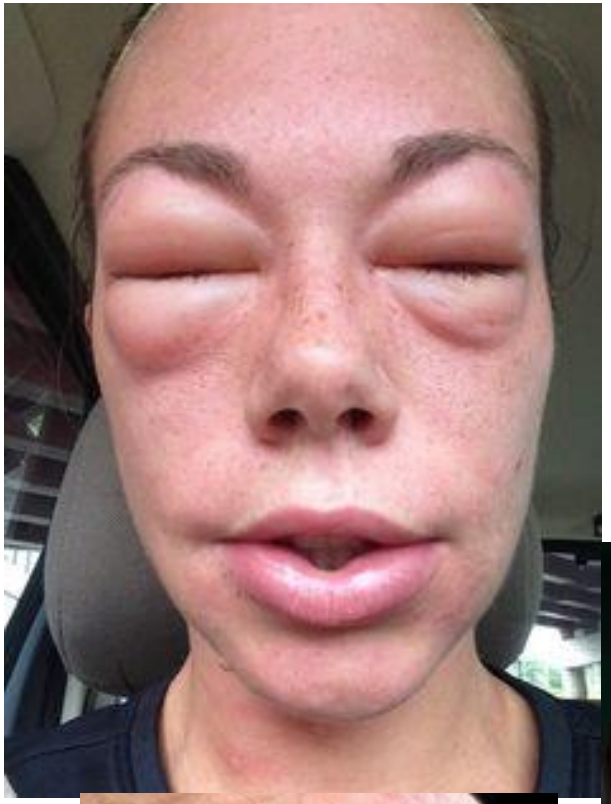
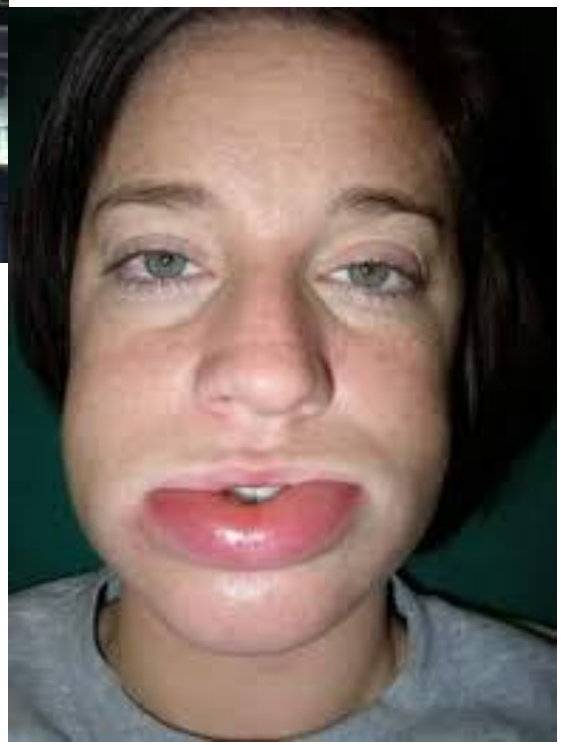
Of all the body's organs, the immune system may be the most challenging to coordinate. The system is collection of individual immune cells, immune cell aggregates, immune tissues, and immune organs.

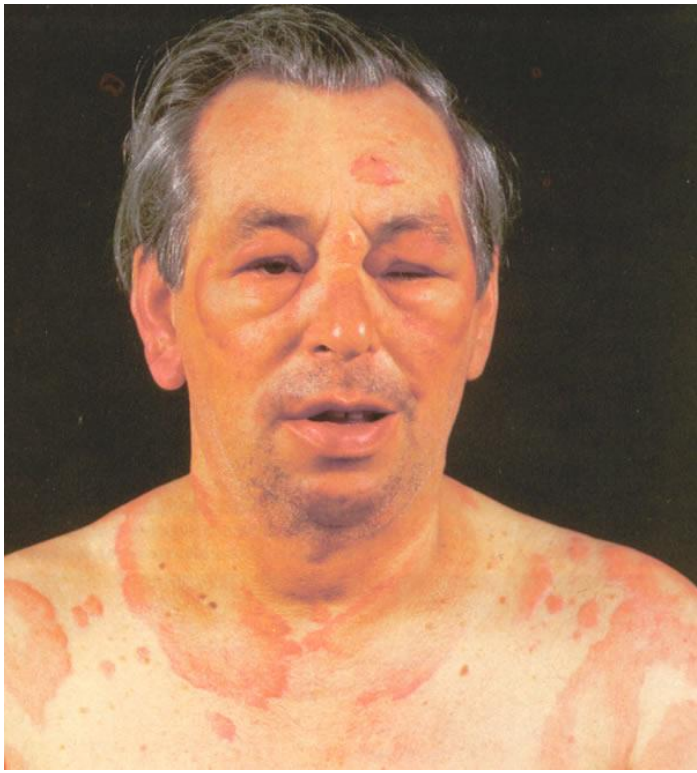


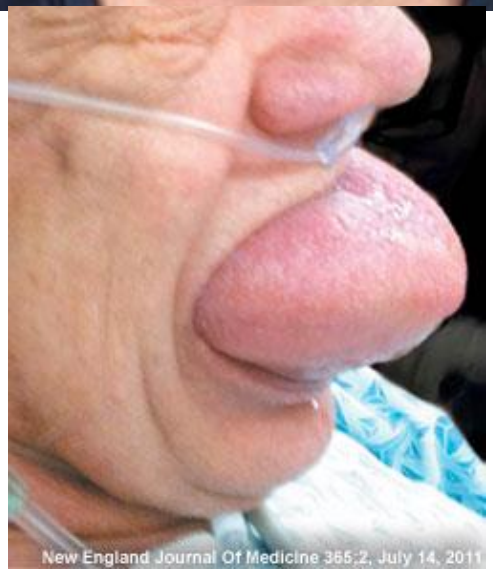


- Billions of immune cells communicate with each other.
- Functional integration of the immune system is accomplished mainly by cell-to- cell communication
- Every immune system cell is equipped with different surffface molecules and is able to synthesize and release a variety of small molecules that travel to other cells and stimulate those cells to become either more active or less active








New England Journal Of Medicine 365;2, July 14, 2011

Allergy: immune reaction to a non replicating (harmles) substance (protein, chemical, drug, metal), which leads to clinical symptoms like.

In contrast to infections: symptoms are caused almost exclusively by the immune reaction, not by the „bug“ (virus, bacteria, etc.)

Allergens

- Non-reproducing foreign substances
- Mostly Proteines/Glykoproteines
  - Of animal or vegetable origin
  - Drugs/Chemicals

Pflanzen: > 3500 Arten Schweiz

Pilze: ~ 10‘000 Arten Schweiz

Tiere: ~ 1,5 Millionen Welt

Hymenopteren: ~ 100‘000 Welt

Berufsstoffe: > 400 beschrieben

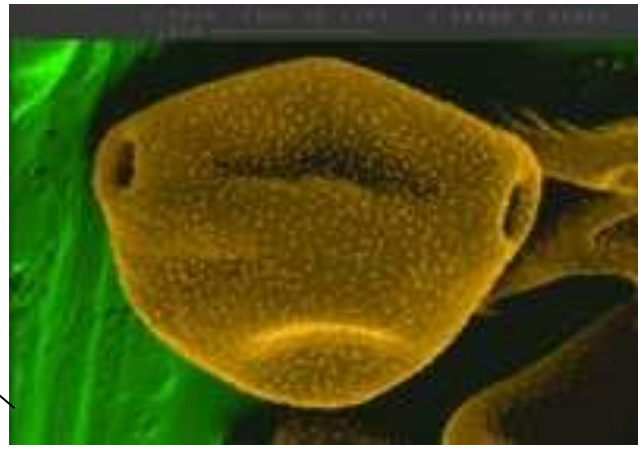
Arzneimittel: ~ 7000 Swissmedic

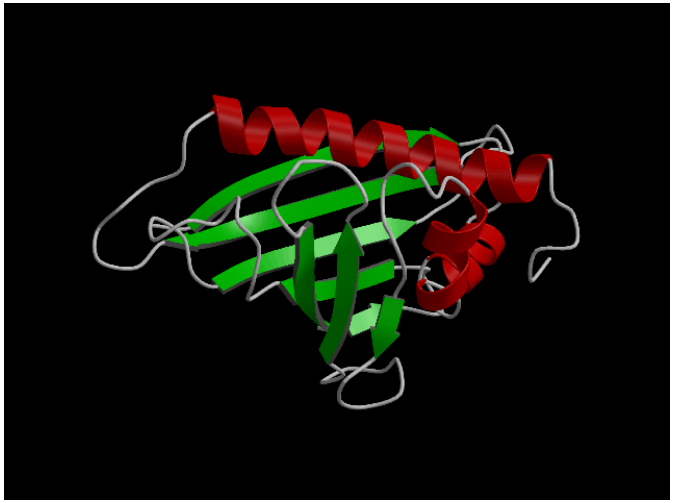
Allergens = 2% of proteins

Radauer et al. J Allergy Clin Immunol 2008

The allergy is **not** directed to pollen, but to proteins within pollen !

Pollen = carrier (grain) + allergen (surface) + lipids





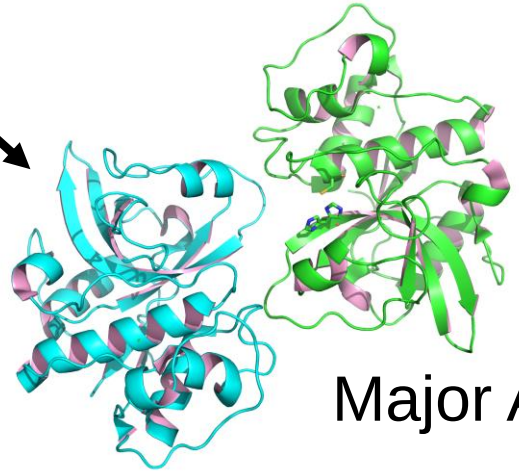
Betula verrucosa 1
Bet v 1

Major Allergen

House dust mites allergens are a common cause of asthma and allergic symptoms worldwide

- *D. pteronyssinus* (european)
- *D. farinae* (american)
- feed on organic detritus, such as flakes of shed human skin

The mite's gut contains potent digestive enzymes (proteases) that persist in their feces



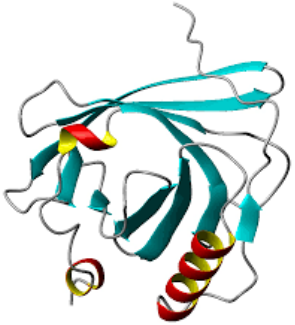
Der p 1

Major Allergen

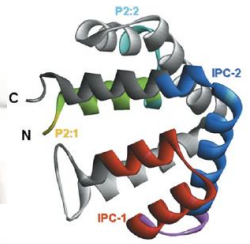
Allergic to your Pet?

Hilger C, Zahradnik E. Allergologie 2015;38:83-90

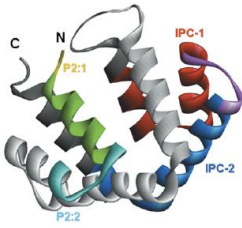
Can f 1
saliva



Fel d 1
saliva and skin



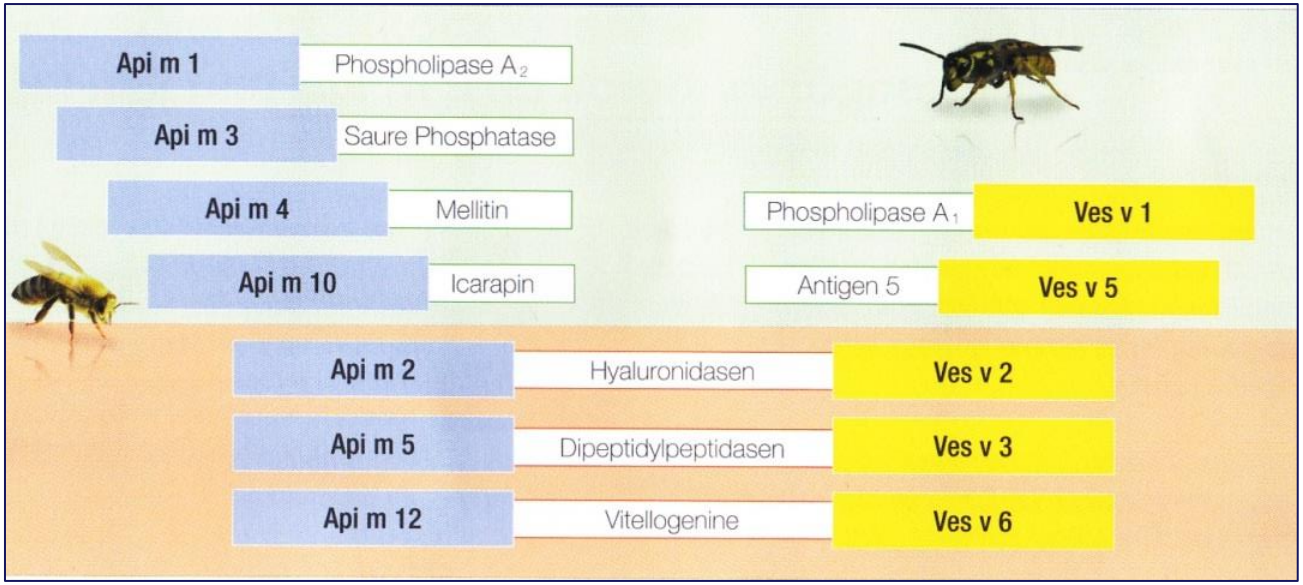
1PUO:A



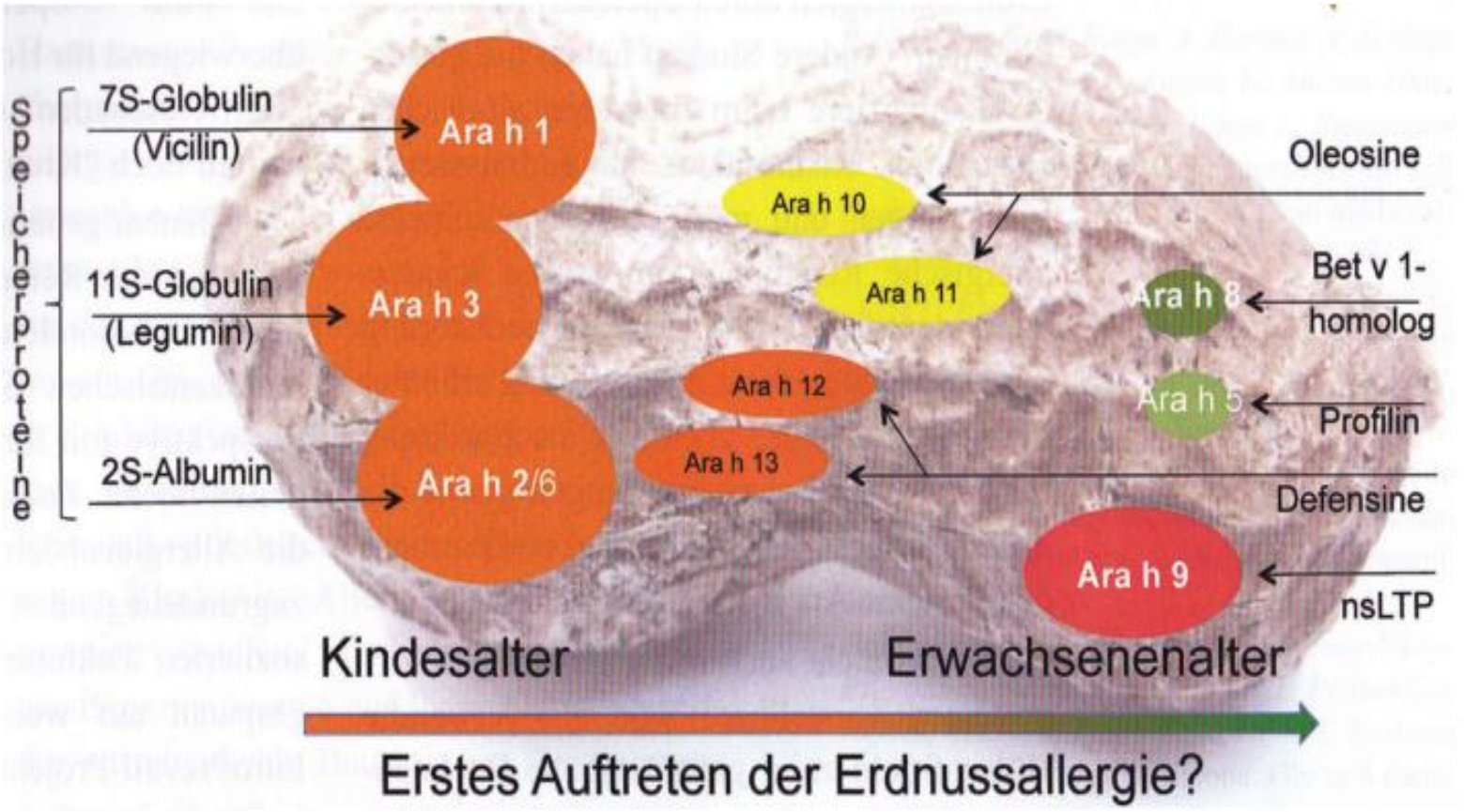
1PUO:B

spezies	Allergen	Proteinfamilie	UniProtKB accession No	Apparentes MG in kDa	Allergenquelle	Sensibilisierungsrate in %[1]	In-vitro-Diagnostik verfügbar
Katze	Fel d 1	Sekretoglobin	P30438; P30440	18	Speicheldrüse, Haut	60 – 100	ja
	Fel d 2	Serumalbumin	P49064	69	Leber	14 – 23	ja
	Fel d 3	Cystatin	Q8WNR9	11	Haut	10	nein
	Fel d 4	Lipokalin	Q5VFH6	22	Speicheldrüse	63	ja
	Fel d 5	IgA	–	400	Speichel, Serum	38	nein
	Fel d 6	IgM	–	800 – 1000	Serum	–	nein
	Fel d 7	Lipokalin	E5D2Z5	17,5	Zunge	38	nein
	Fel d 8	Latherin	F6K0R4	24	Speicheldrüse	19	nein
Hund	Can f 1	Lipokalin	O18873	23 – 25	Zunge	50 – 75	ja
	Can f 2	Lipokalin	O18874	19	Zunge, Speicheldrüse	22 – 30	ja
	Can f 3	Serumalbumin	P49822	69	Leber	25 – 35	ja
	Can f 4	Lipokalin	D7PBH4	18	Zunge	35	nein
	Can f 5	Kallikrein	P09582	28	Urin	70	ja
	Can f 6	Lipokalin	H2B3G5	27 – 29	Speicheldrüse	61	nein

Bee / Wasp Allergy



Peanut allergy



The immune system is highly specific and needs danger signals to become activated

How can a harmless/innocuous substance like a pollen potentially induce an IgE mediated immune reaction ?

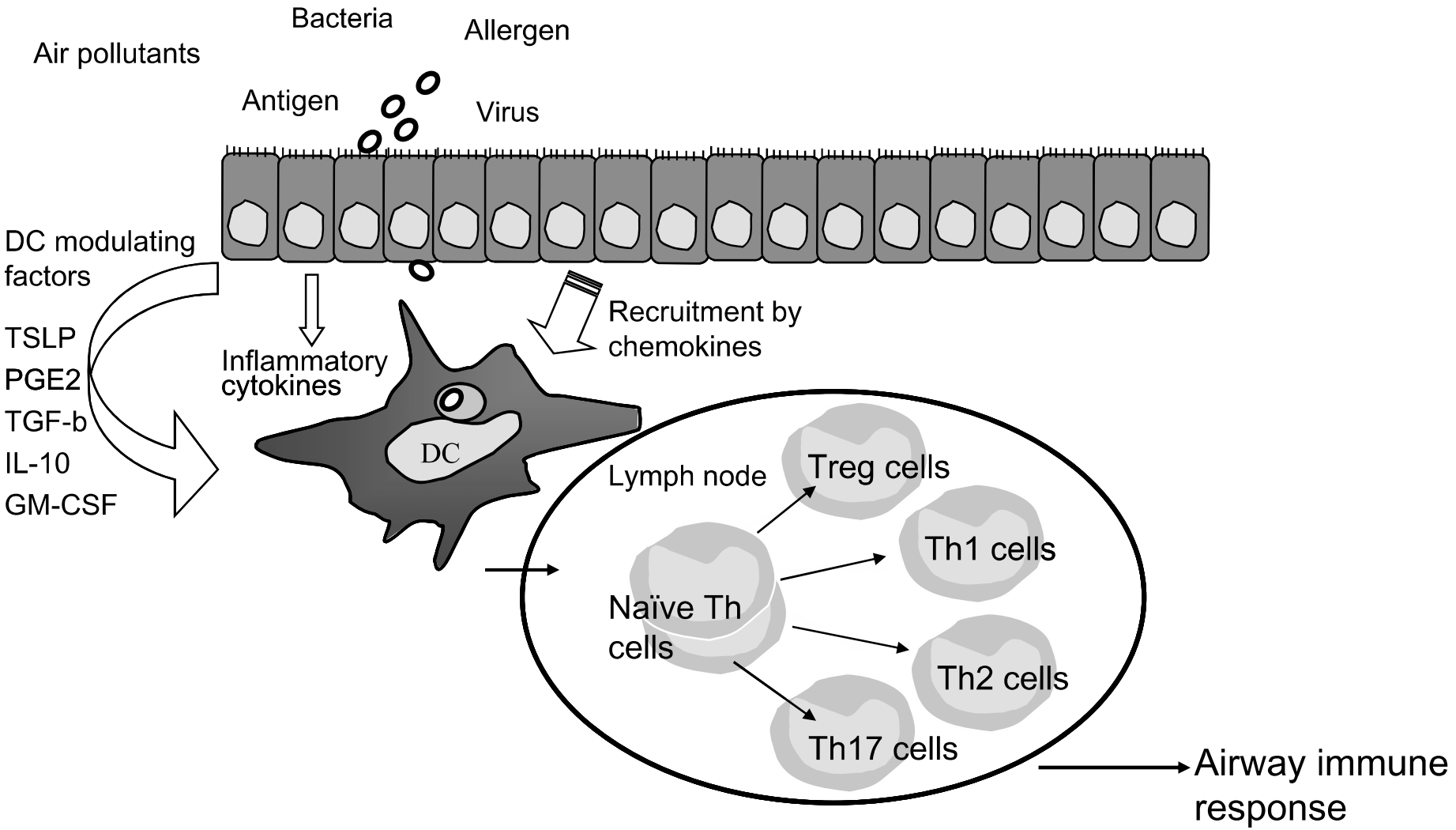
Ability of „innocuous“ proteins to activate immune system

1. House dust mite allergen Der p1: cysteine protease cleaves tight junction protein occludin → Increased epithelial permeability and facilitating its entry into the tissue

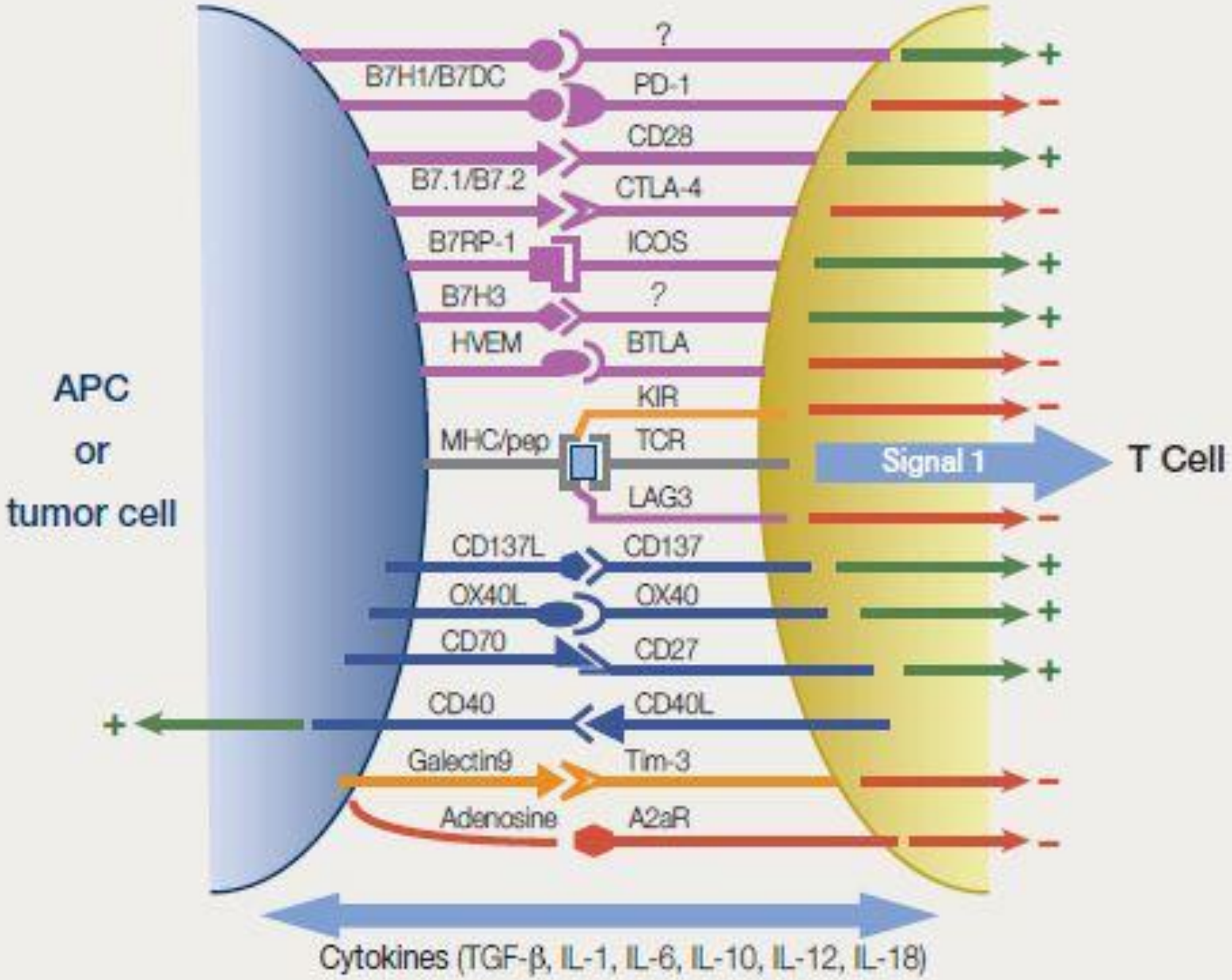
2. House dust mite allergen Der p2: structural and functional homology with MD-2, LPS-binding component of TLR 4 signaling complex → facilitates signaling through direct interactions with the TLR4 complex

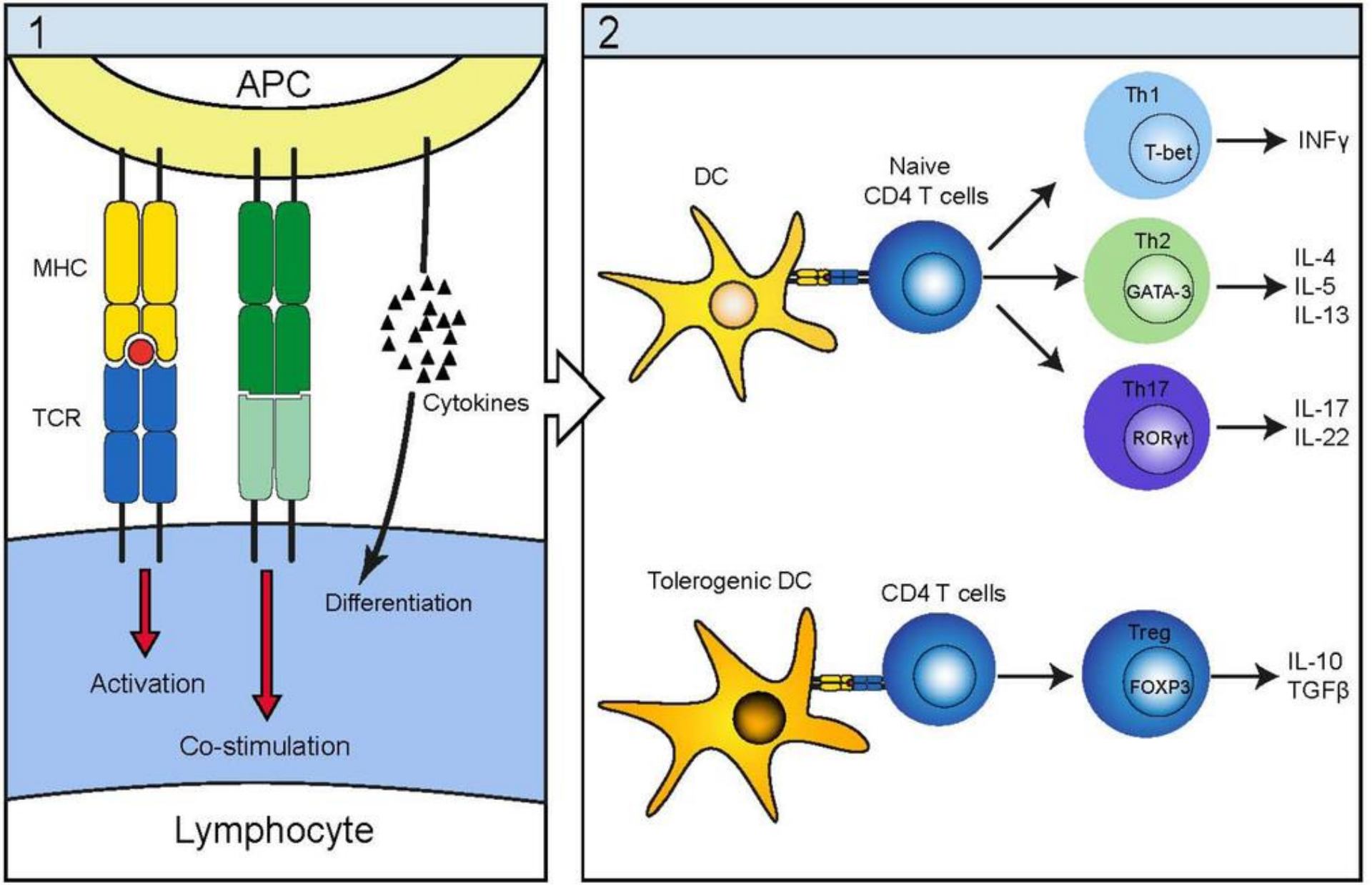
3. Pollen-associated lipid mediators (PALMs): When pollen grains are hydrated on the respiratory epithelia, they release allergens and eicosanoid lipids → so-called pollen-associated lipid mediators (PALMs) → act as stimulators of DC

Airway immune response

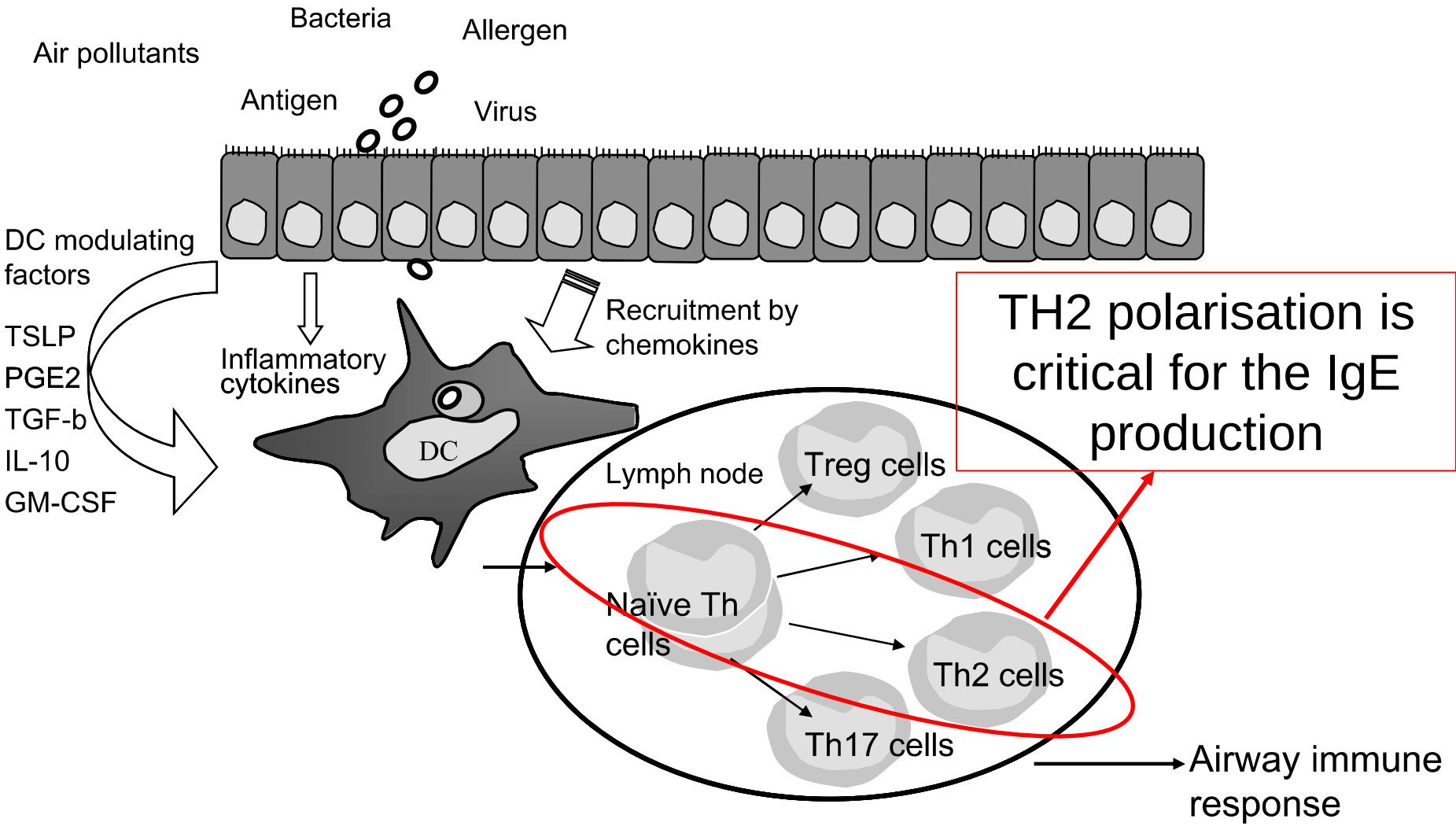


J. van Tongeren et al. Allergy 2008: 63: 1124–1135


APC
or
tumor cell
?
B7H1/B7DC
PD-1
CD28
B7.1/B7.2
CTLA-4
B7RP-1
ICOS
B7H3
?
HVEM
BTLA
KIR
MHC/pep
TCR
LAG3
Signal 1
T Cell
CD137L
CD137
OX40L
OX40
CD70
CD27
CD40
CD40L
Galectin9
Tim-3
Adenosine
A2aR
Cytokines (TGF-β, IL-1, IL-6, IL-10, IL-12, IL-18)

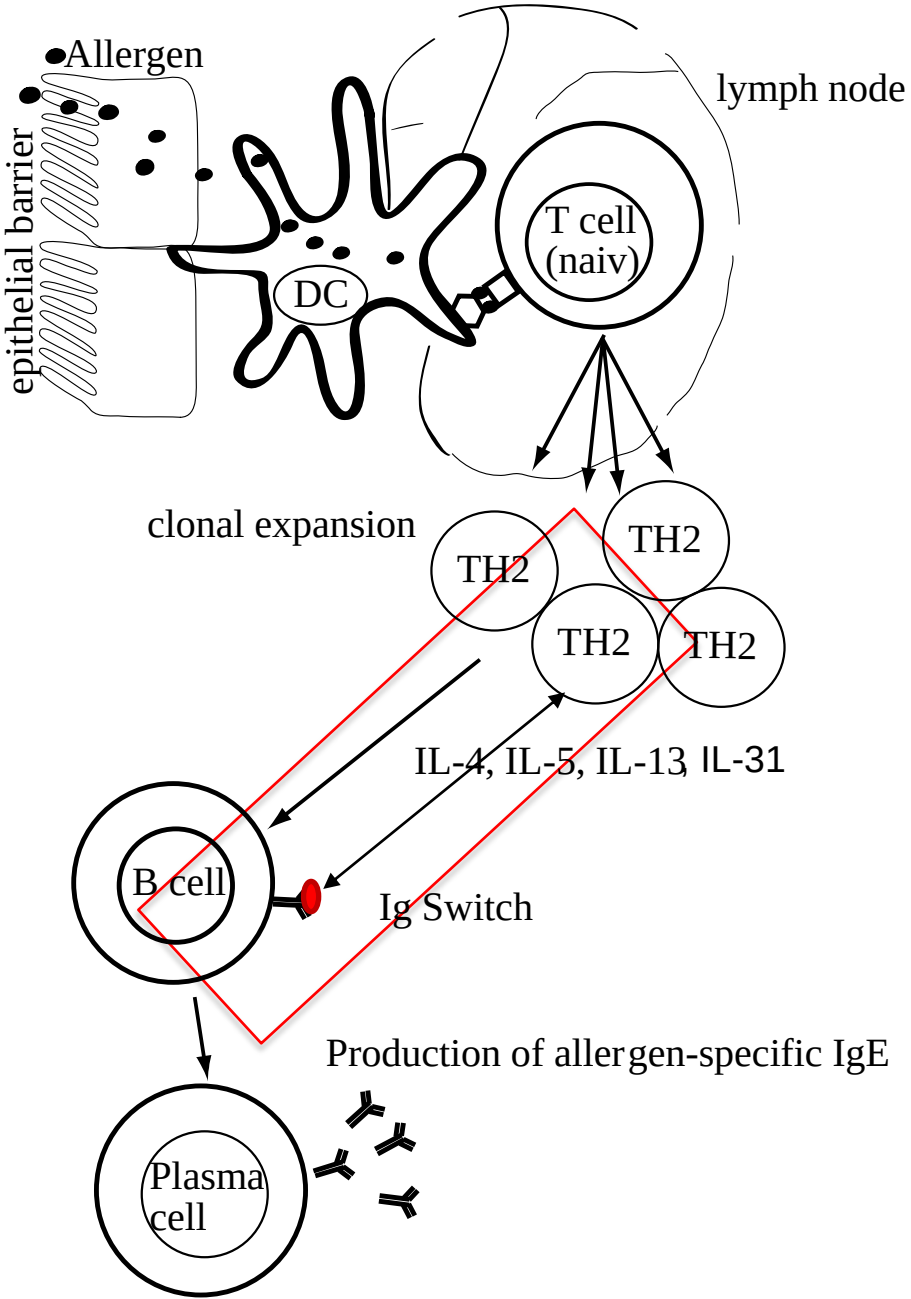

1
APC
MHC
TCR
Cytokines
Differentiation
Activation
Co-stimulation
Lymphocyte
2
DC
Naive
CD4 T cells
Th1
T-bet
INFγ
Th2
GATA-3
IL-4
IL-5
IL-13
Th17
RORγt
IL-17
IL-22
Tolerogenic DC
CD4 T cells
Treg
FOXP3
IL-10
TGFβ

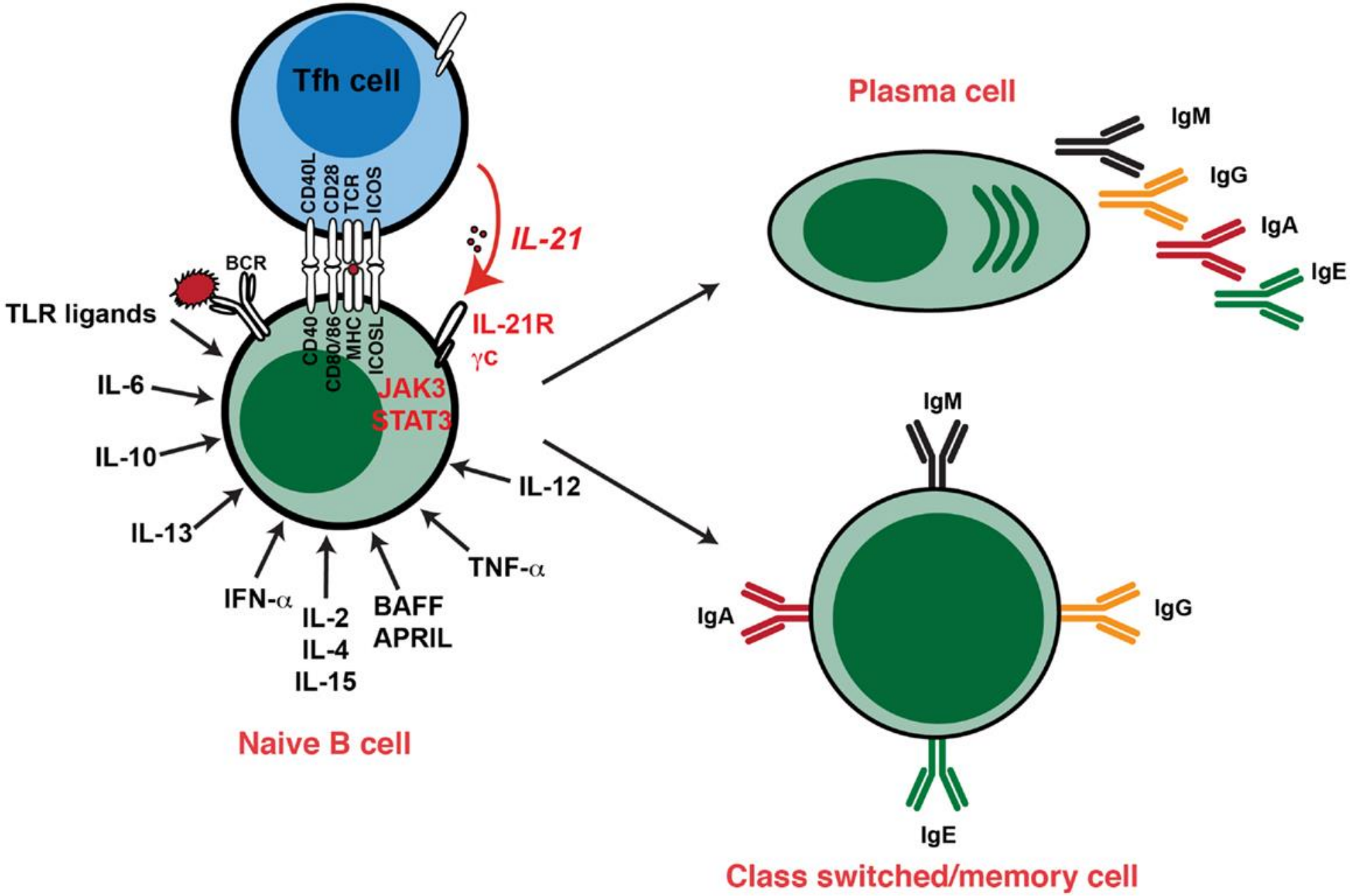
Airway immune response

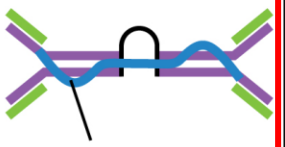


J. van Tongeren et al. Allergy 2008: 63: 1124–1135

Sensitization Phase

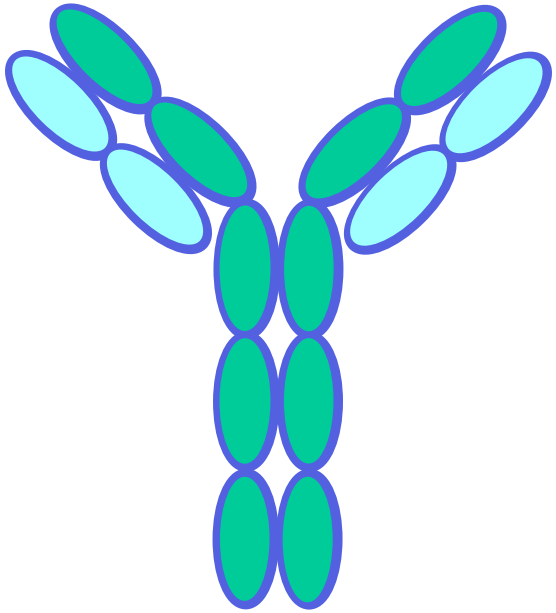



Tfh cell
CD40L
CD28
TCR
ICOS
IL-21
BCR
TLR ligands
IL-21R
γc
CD40
CD80/86
MHC
ICOSL
JAK3
STAT3
IL-6
IL-10
IL-12
IL-13
TNF-α
IFN-α
IL-2
IL-4
IL-15
BAFF
APRIL
Naive B cell
Plasma cell
IgM
IgG
IgA
IgE
IgM
IgA
IgG
IgE
Class switched/memory cell

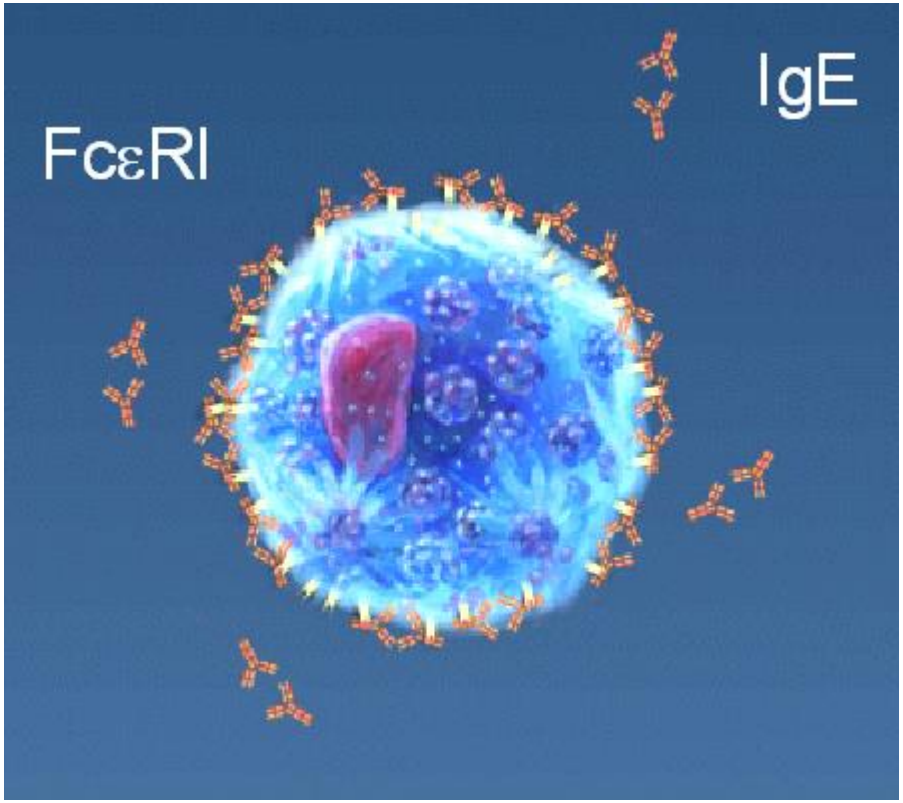
The Five Immunoglobulin (Ig) Classes					
	IgM pentamer	IgG monomer	Secretory IgA dimer	IgE monomer	IgD monomer
					
Heavy chains	μ	γ	α	ε	δ
Number of antigen binding sites	10	2	4	2	2
Molecular weight (Daltons)	900,000	150,000	385,000	200,000	180,000
Percentage of total antibody in serum	6%	80%	13%	0.002%	1%
Crosses placenta	no	yes	no	no	no
Fixes complement	yes	yes	no	no	no
Fc binds to		phagocytes		mast cells and basophils	
Function	Main antibody of primary responses, best at fixing complement; the monomer form of IgM serves as the B cell receptor	Main blood antibody of secondary responses, neutralizes toxins, opsonization	Secreted into mucus, tears, saliva, colostrum	Antibody of allergy and antiparasitic activity	B cell receptor

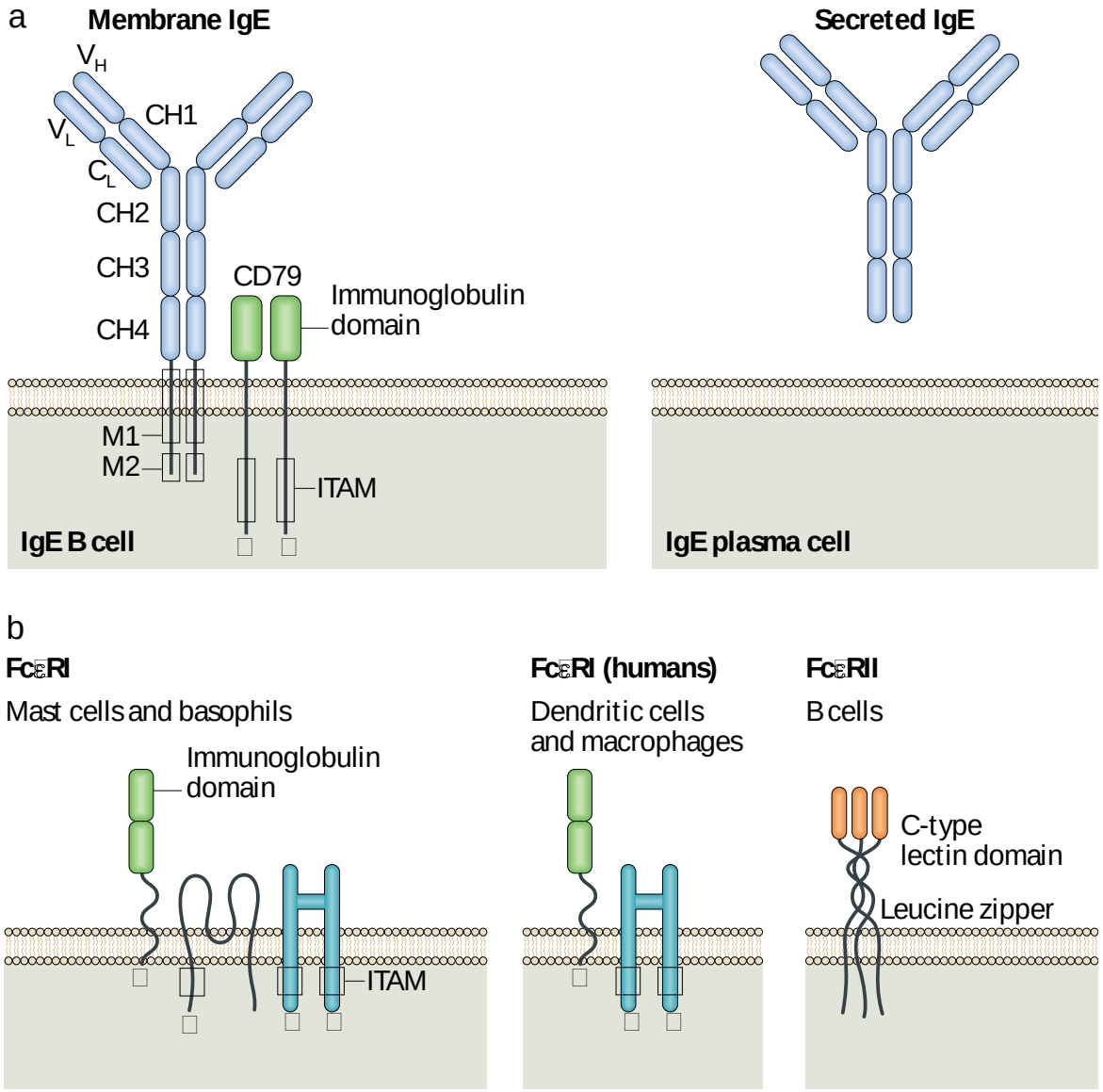
Type-I (immediate hypersensitivity)

IgE Antikörper

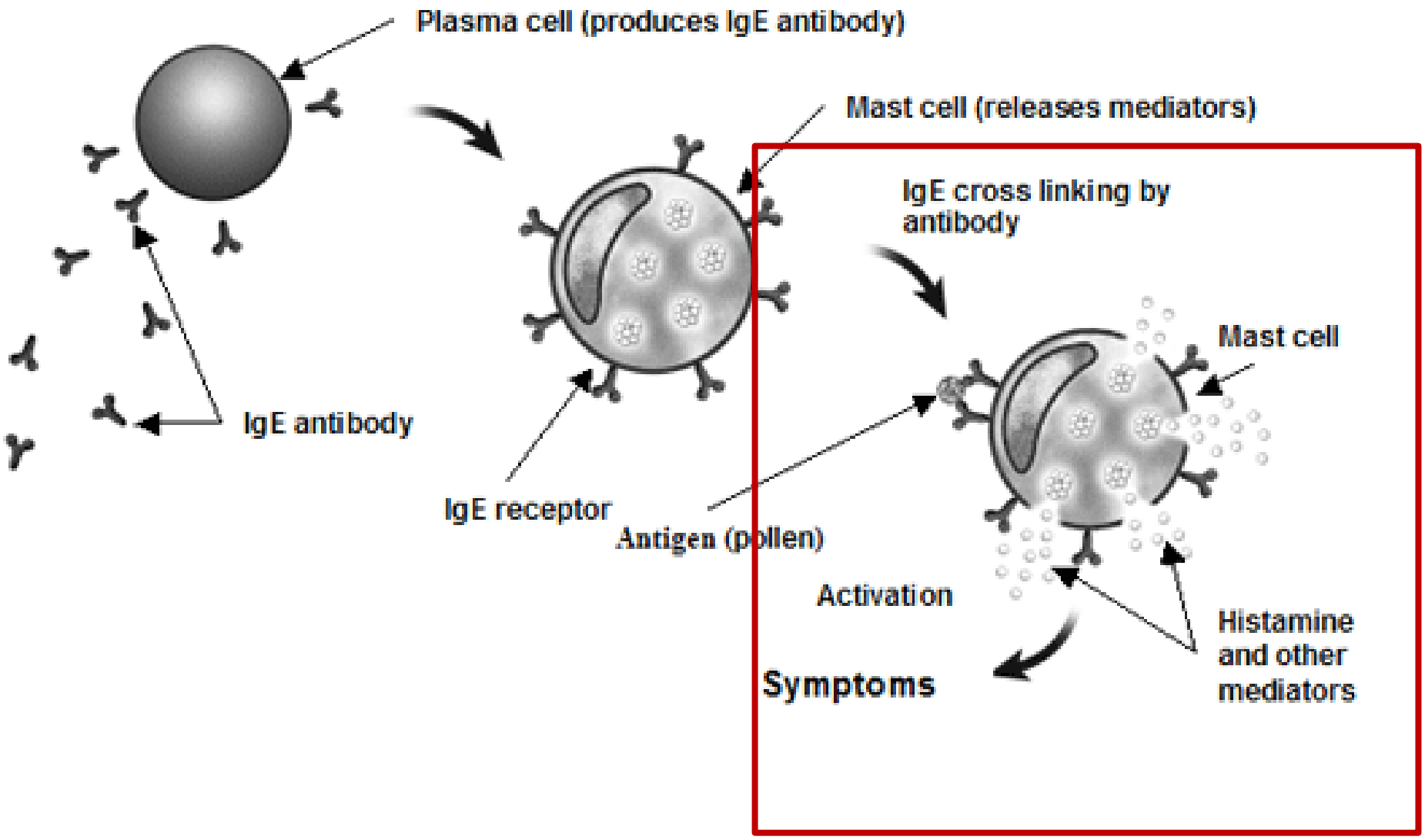


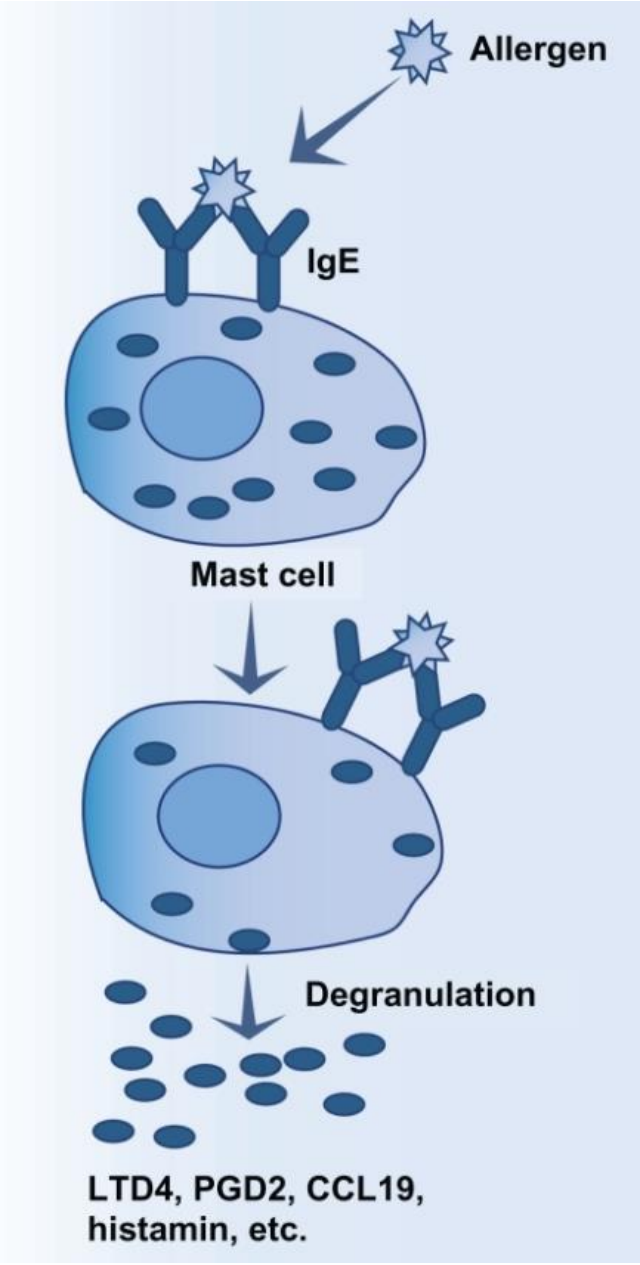
Mastzelle





Lawren C. Wu and Ali A. Zarrin et al. Nature Immunology Review 2014

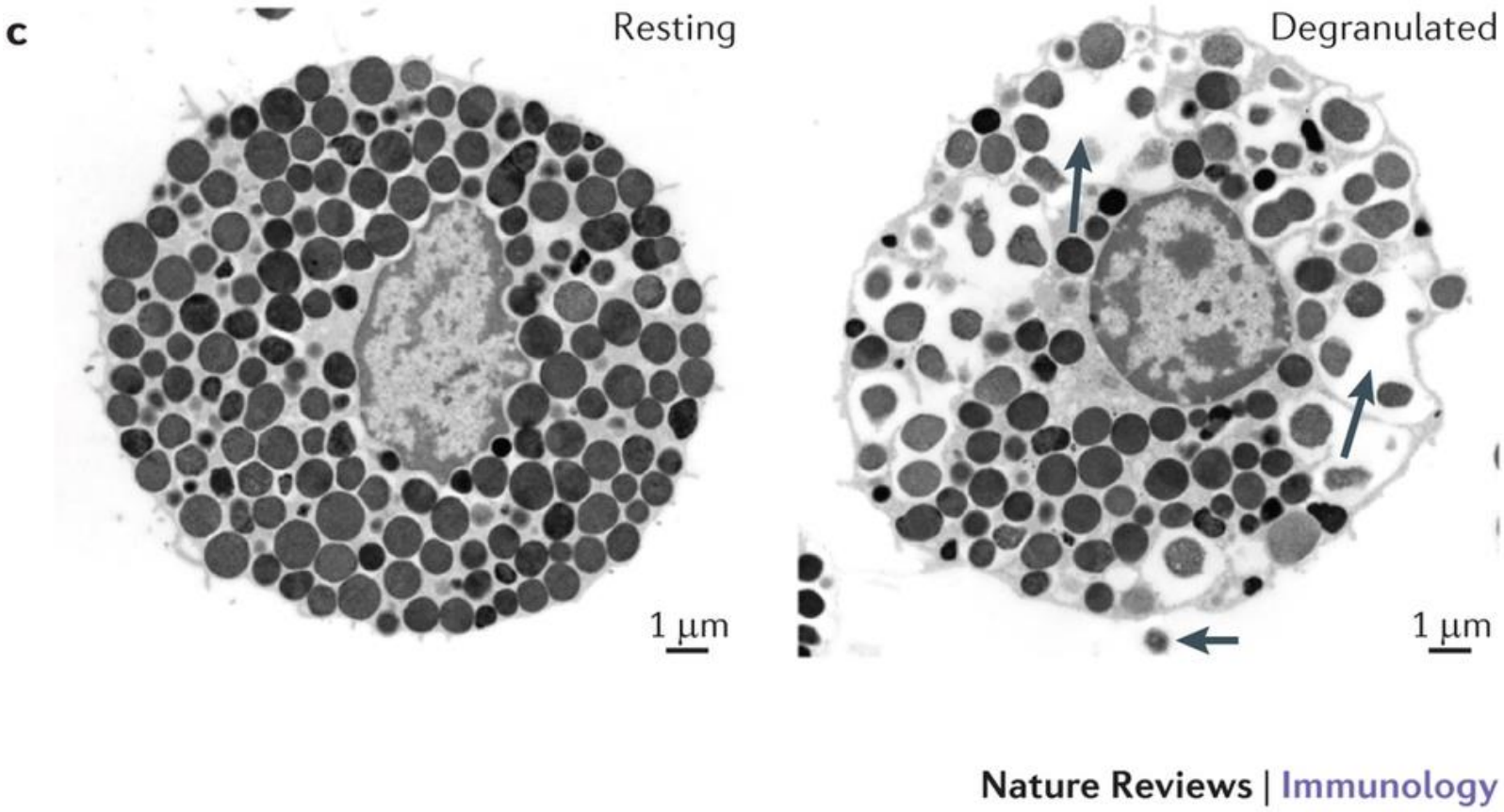

Plasma cell (produces IgE antibody)
Mast cell (releases mediators)
IgE cross linking by antibody
IgE antibody
IgE receptor
Antigen (pollen)
Mast cell
Activation
Histamine and other mediators
Symptoms

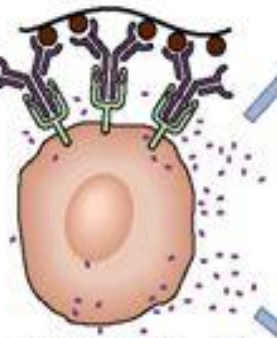


Cross linking of 2 Fc-IgE-RI
Is required for mast cell activation

Mediator release

Mast cell

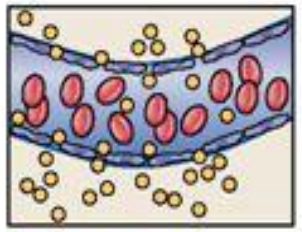




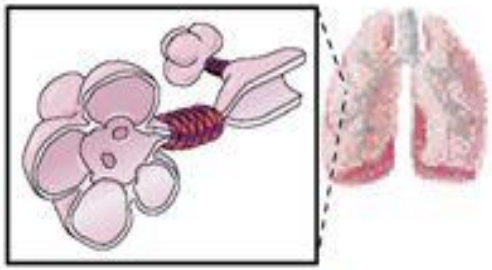
Activated mast cell (or basophil)

Biogenic amines (e.g., histamines)

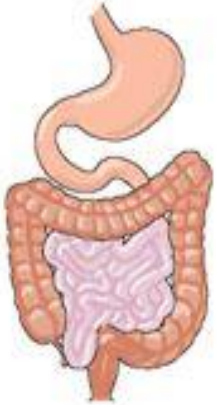
Lipid mediators (e.g., PAF, PGD_2, LTC_4)



Vascular leak



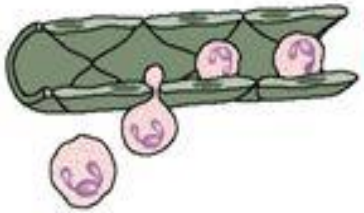
Broncho-constriction



Intestinal hypermotility

Cytokines (e.g., TNF)

Lipid mediators (e.g., PAF, PGD_2, LTC_4)



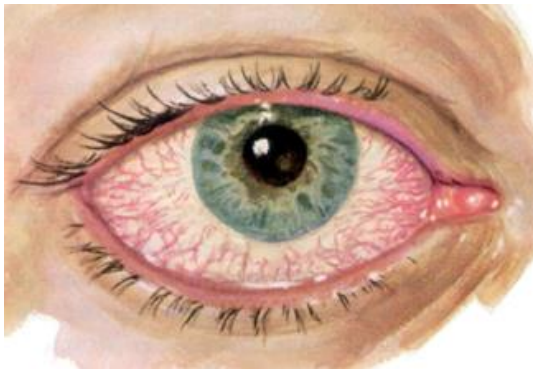
Inflammation

Enzymes (e.g., tryptase)

Tissue damage

Symptoms of IgE mediated (immediatet) reaction

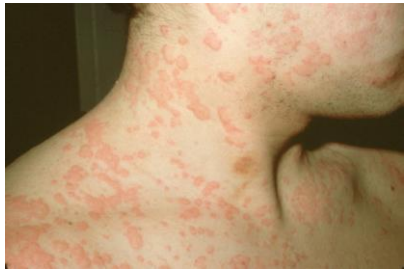
Eyes:
Conjunctivitis

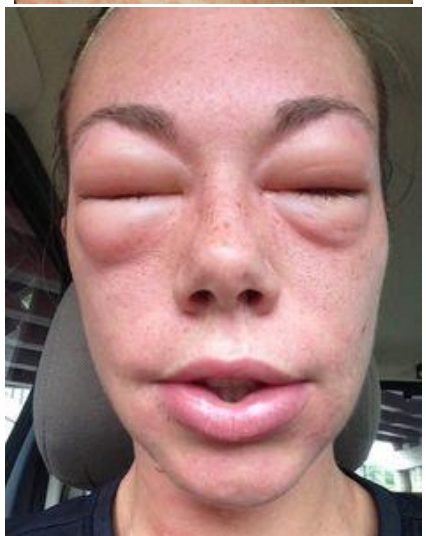


Nose:
Rhinitis

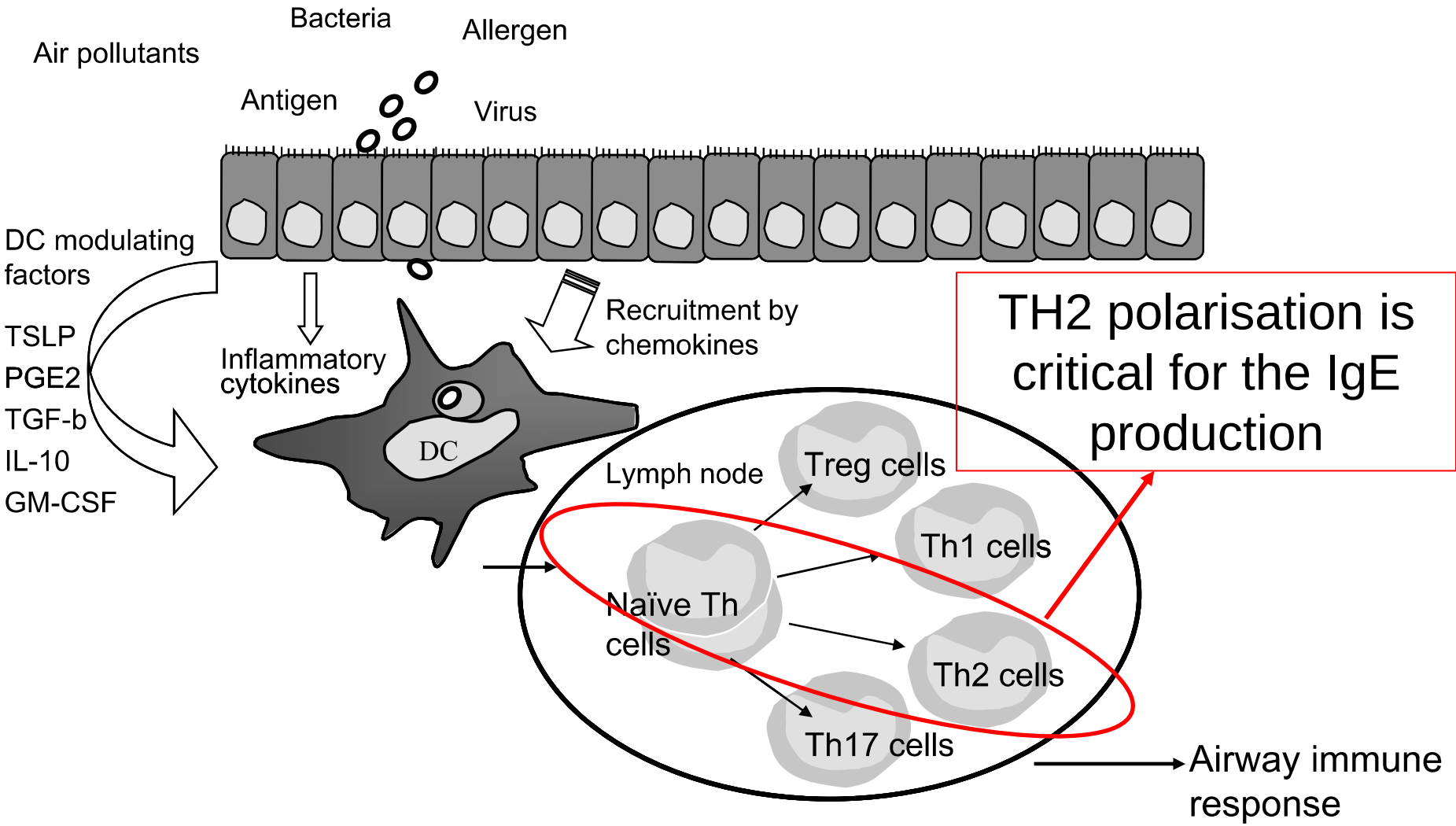
Lungs:
Asthma

Skin:
Urticaria
Angioedema





Airway immune response



J. van Tongeren et al. Allergy 2008: 63: 1124–1135

What drives Th2 polarisation ?

- antigen dose,
- nature of the antigen,
- direct cell-to-cell interaction with APCs
- the cytokine receptors available on the naive cell
- Genetic predisposition
- enviromental factors
- gastrointerstinal Flora

Hygien-Hypothesis

«Western» Lifestyle

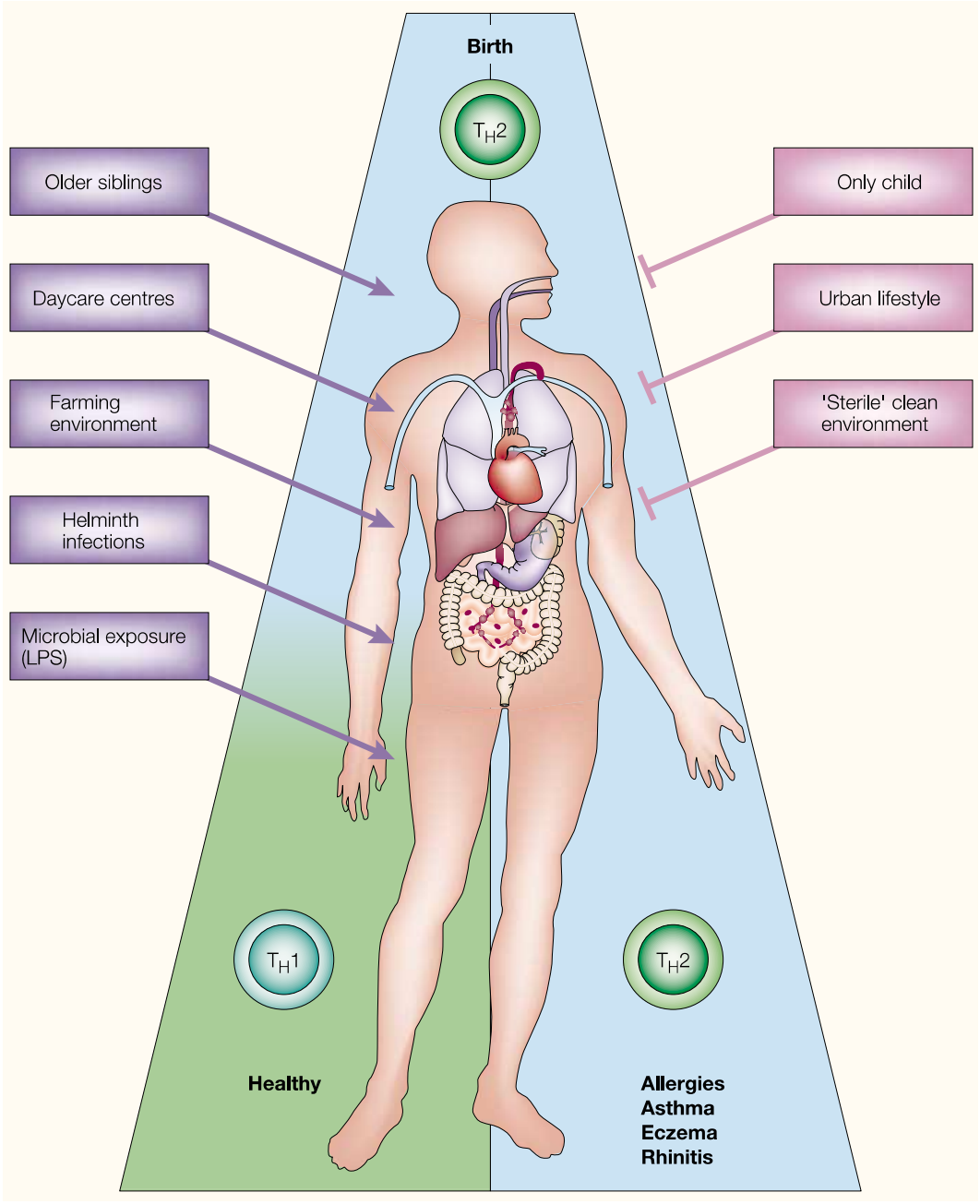
Traditional Lifestyle

Th2

IL-4, IL-5

Allergy-Epidemic

Allergy-Prevention



→ Microbial exposure boosts Th1 response

→ Microbial exposure alters Th2 response

Response starts *in utero*

Protective effect of the farm environment

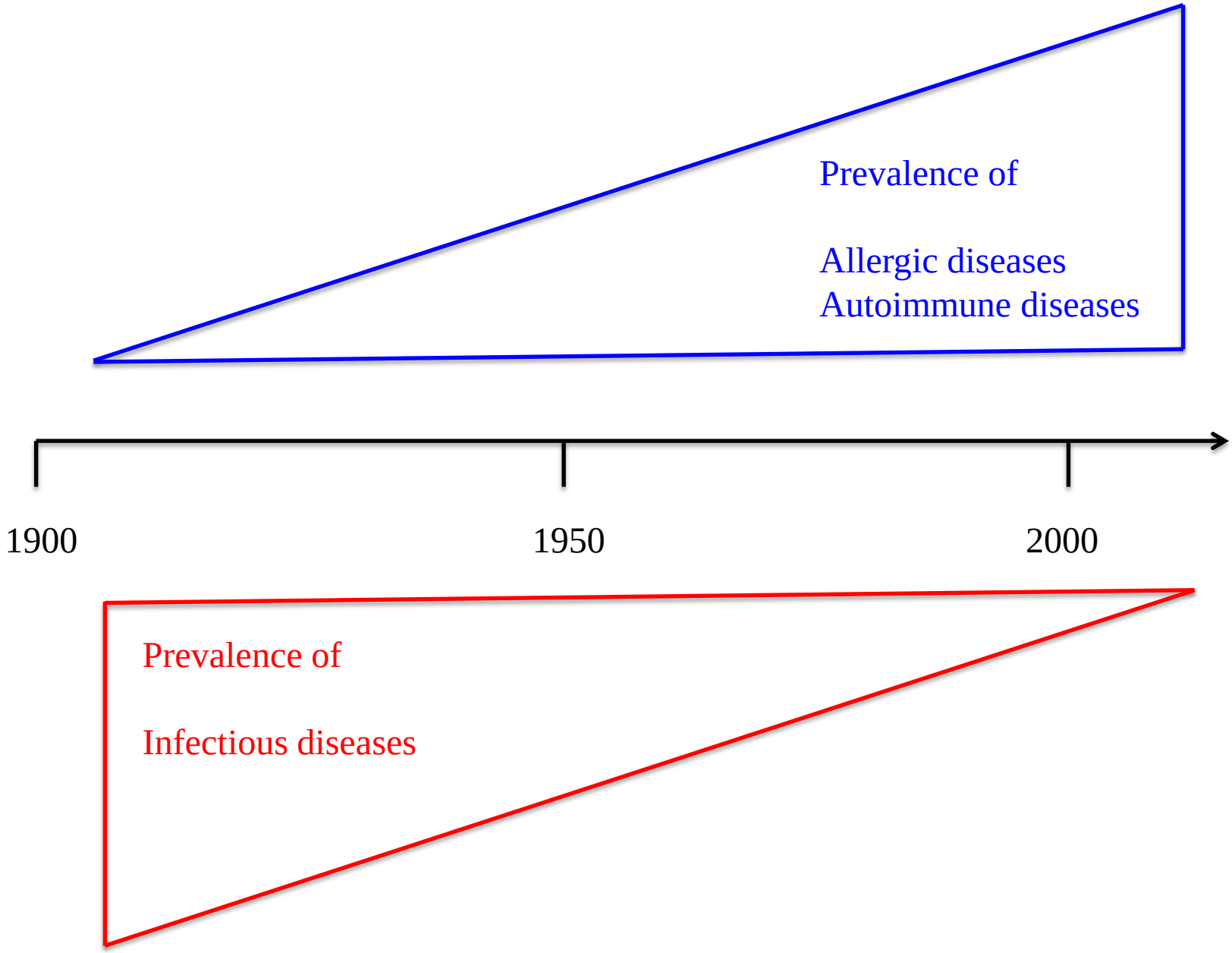
Protective effect by parasite infection

Gern et al. Nature Reviews 2002

Too much hygiene is harmful for horses !!!!

- Clean stables increase allergic diseases in horses.
- - in Switzerland every 10th hors have Asthma to Hay-/stables

Prof. Vinzenz Gerber, Head of Clinics for Horses University of Bern, 2009


Prevalence of
Allergic diseases
Autoimmune diseases
1900
1950
2000
Prevalence of
Infectious diseases

Clinical Manifestations of IgE-mediated (immediate type) allergic reaktions

Immediate type Reaktion

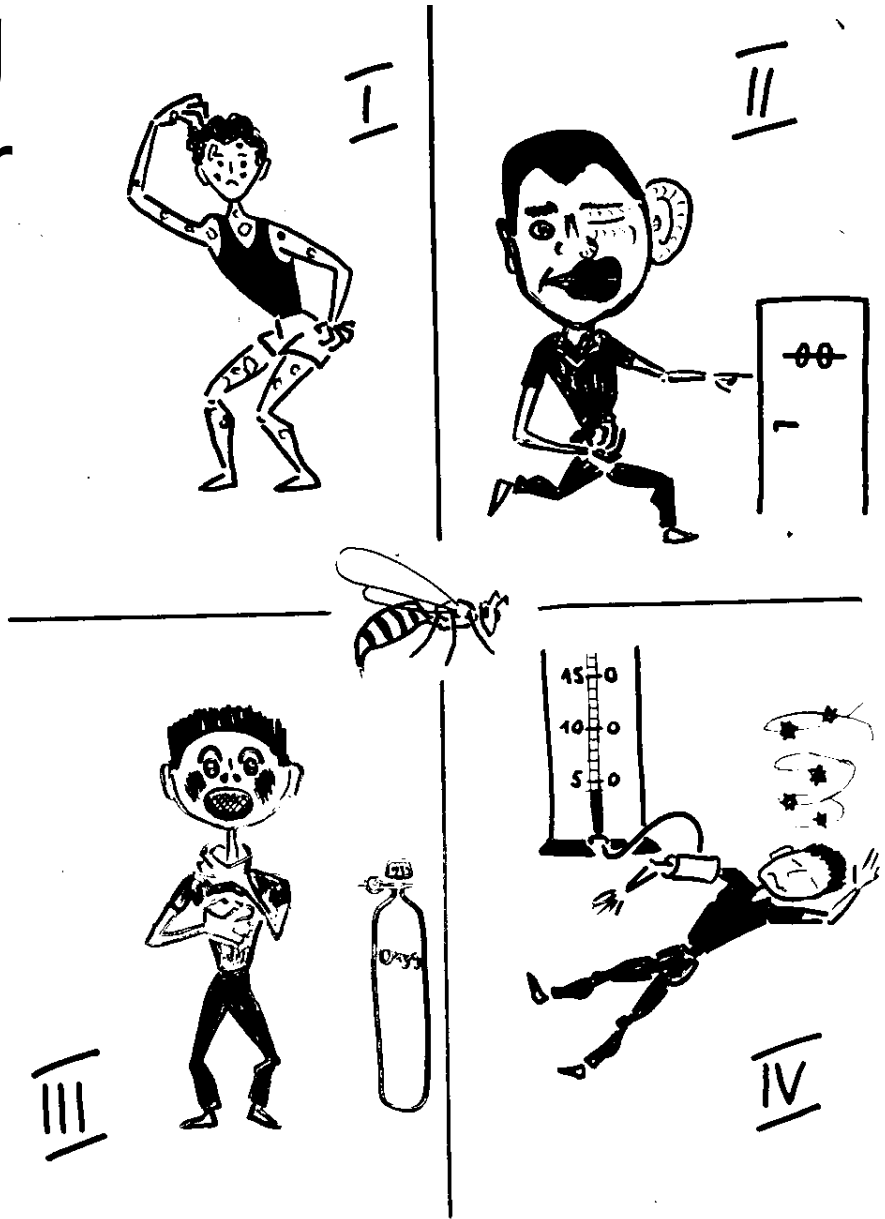
< 1h

Type of Reaction	Time Before Clinical Signs	Characteristics	Examples
Type I (Anaphylactic)	<30 min	IgE binds to mast cells or basophils; causes degranulation of mast cell or basophil and release of reactive substances such as histamine	Anaphylactic shock from drug injections and insect venom; common allergic conditions, such as hay fever, asthma
Type II (Cytotoxic)	5–12 hours	Antigen causes formation of IgM and IgG antibodies that bind to target cell; when combined with action of complement, destroys target cell	Transfusion reactions, Rh incompatibility hemolytic anmenia, thrombocytopenia, granulocytopenia
Type III (Immune Complex)	3–8 hours	Antibodies and antigens form complexes that cause damaging inflammation	Arthus reactions, serum sickness
Type IV (Delayed Cell-Mediated, or Delayed Hypersensitivity)	24–48 hours	Antigens activate T_C that kill target cell	Rejection of transplanted tissues; contact dermatitis, such as poison ivy; certain chronic diseases, such as tuberculosis

delayed type Reaktion

> 24h

Classification of allergic reactions according to Mueller



Anaphylaxis

= potentially life threatening situation; rapid onset

Massive mediator release

different organs are involved (skin, respiratory, cardiovascular system)

most frequent cause in Switzerland: hymenoptera venom allergy, drug allergy, food allergy

Is anaphylaxis always IgE mediated???

No, Anaphylaxis may involve other mechanisms than IgE, e.g.:

- Complement activation
- IgG and IgM immune complexes
- Non-immunologic mechanisms
- Pseudo allergies (radio contrast media)
- Toxic effects of insect venom
- Non-steroidal anti-inflammatory drugs

Food Allergy

Adverse reaction Food

1. Toxic

2. Nontoxic

   A) Immune mediated

      - IgE mediated
      - Non-IgE mediated

   B) Non immune mediated (food intolerance)

      - enzymatic (e.g. lactase deficiency)
      - pharmacological (abnormal reactivity to substances e.g. amines)
      - undefined (e.g. food additive intolerance)

Prevalence

- 6-8% of children have food allergy during the first 3 years of life
- Up to 85% outgrow the food allergy in the first 5-10 years of life
- Adults: USA 4% have food allergy (real allergy?)

Symptoms

- Gastrointestinal tract, skin, airways, anaphylaxis
- Co-factors: alcohol, exercise, medications

2 Groups of food allergy

Food sensitization develops as a consequence of sensitization to airborne allergens

Mostly adults, cross reactivity

Food sensitization occurs by gastrointestinal tract (often stable proteins)

Mostly in children
“real food allergy”

Oral allergy syndrome

Sensitization to heat/pepsine labile plant-derived proteins in patients with pollen allergy

Cross reactivity between homologous plant derived proteins and pollen proteins

Bet v1 → nuts, apple, kiwi

heated normally well tolerated

Allergen cross reactivity seems to be due to IgE antibodies that recognize structurally similar epitopes on different proteins that are phylogenetically closely related or present evolutionarily conserved structures

Birch

Apple Peach Plum Pear Cherry Apricot Almond
Rosaceae

Carrot Celery Parsley Caraway Fennel Coriander Aniseed
Apiaceae

Soybean Peanut
Fabaceae (old Leguminosae)

Hazelnut
Betulaceae

Ragweed

Cantaloupe Honeydew Watermelon Zucchini Cucumber
Cucurbitaceae

Banana
Musaceae

Mugwort

Celery Carrot Parsley Caraway Fennel Coriander Aniseed
Apiaceae

Bell pepper
Solanaceae

Black pepper
Piperaceae

Mustard Cauliflower Cabbage Broccoli
Brassicaceae

Garlic Onion
Liliaceae

Peach
Rosaceae

Orchard

Cantaloupe Honeydew Watermelon
Cucurbitaceae

Peanut
Fabaceae (old Leguminosae)

White potato Tomato
Solanaceae

Swiss chard
Amaranthaceae

Orange
Rutaceae

Food allergy - crossreaktivity

celery-birch-mugwort-**spices** syndrome



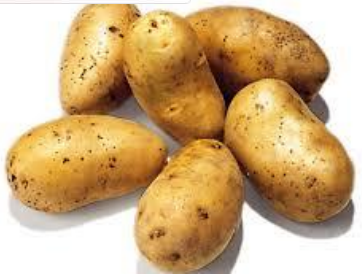

shellfish and dust mite allergy


Food allergy - crossreaktivity

Latex-fruit syndrome



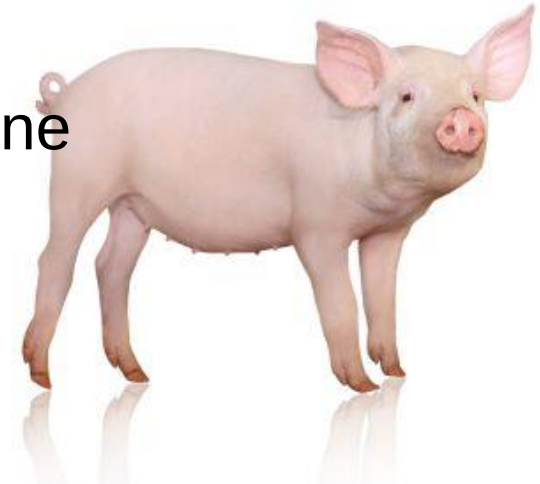


Cat-pork syndrome

Fel d 2

Pig serum albumine



2 Groups of food allergy

Food sensitization develops as a consequence of sensitization to airborne allergens

Mostly adults, cross reactivity

Food sensitization occurs by gastrointestinal tract (often stable proteins)

Mostly in children
“real food allergy”

Lipid transfer proteins

Role in defence against fungi and bacteria

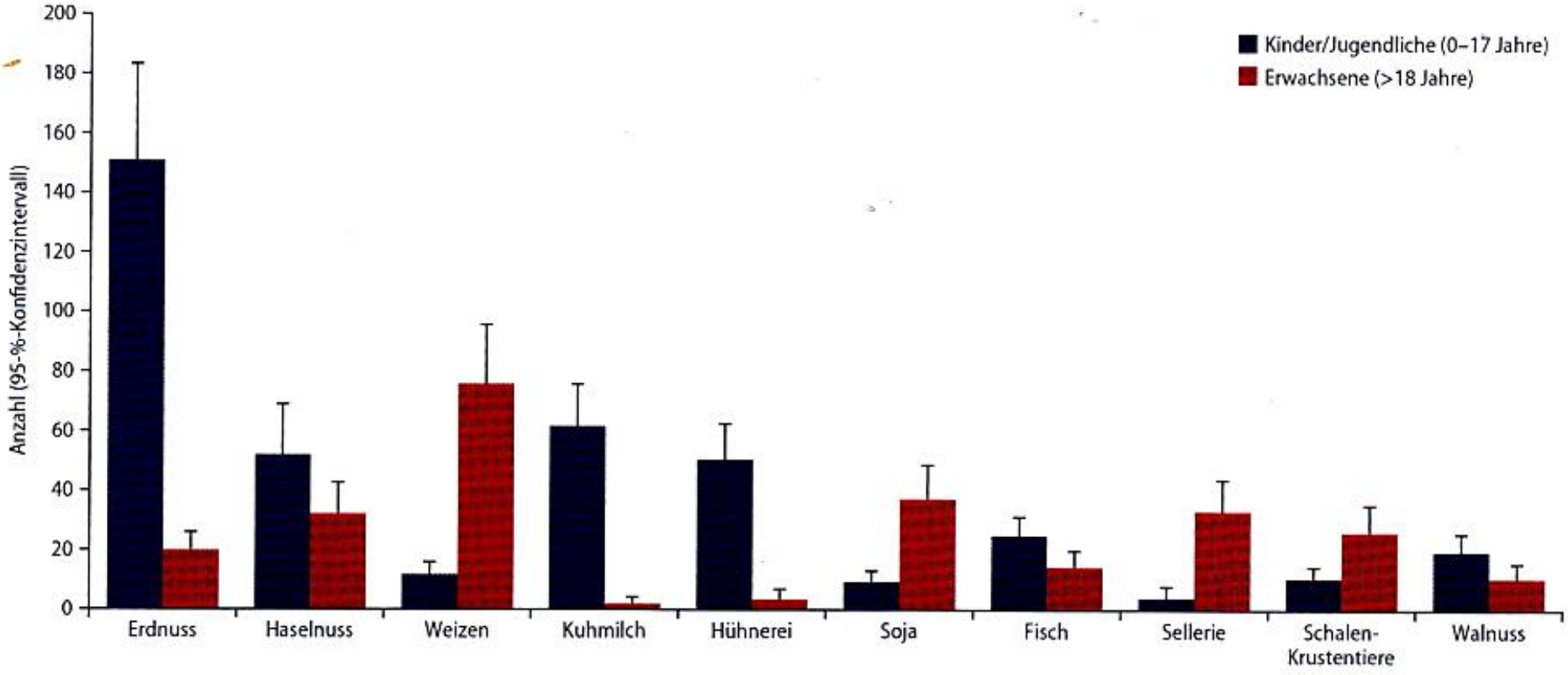
Heat stable, begin to unfold above 95°, protein refold on cooling

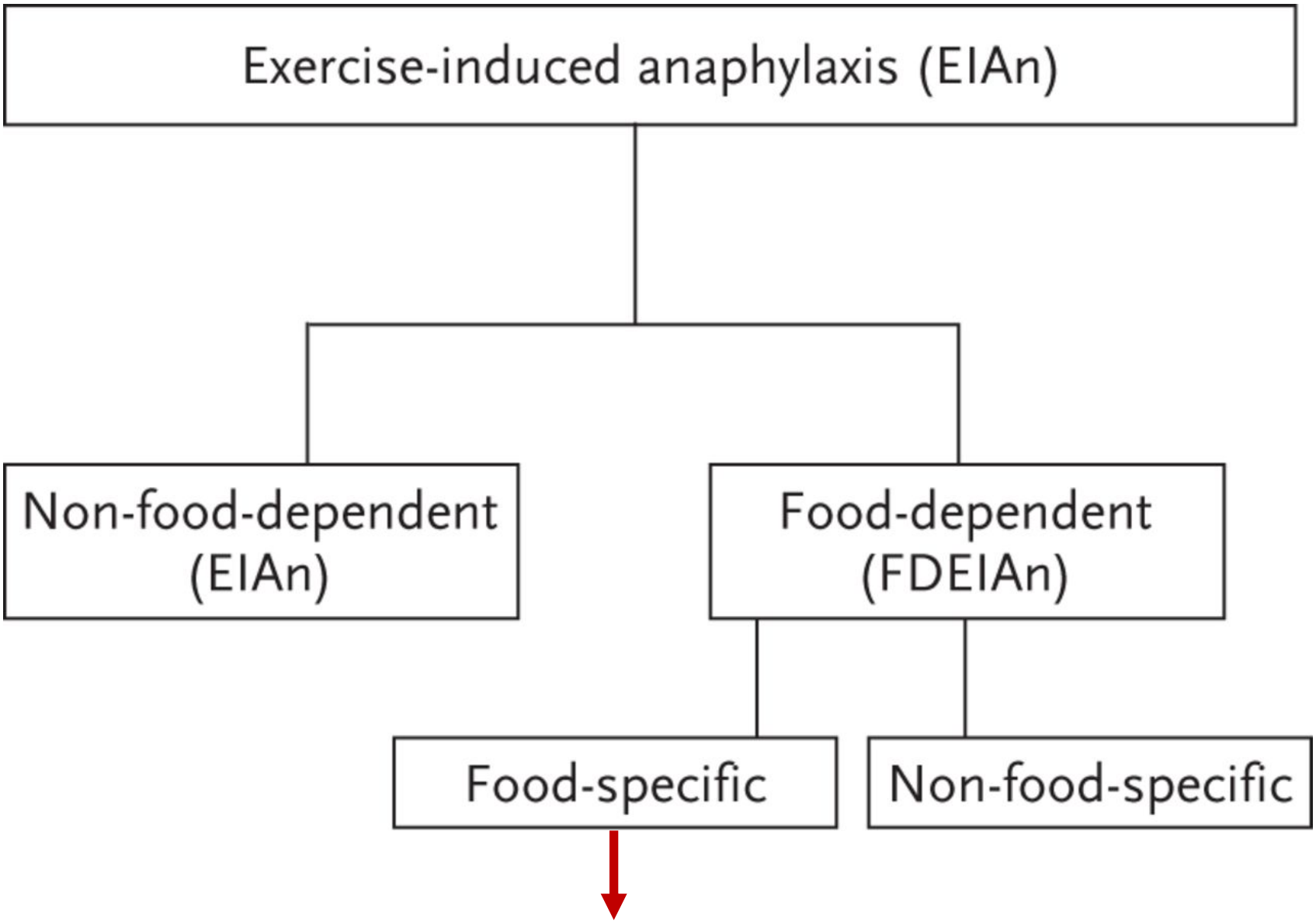
More severe allergic reactions

Triggers of food allergy - age groups

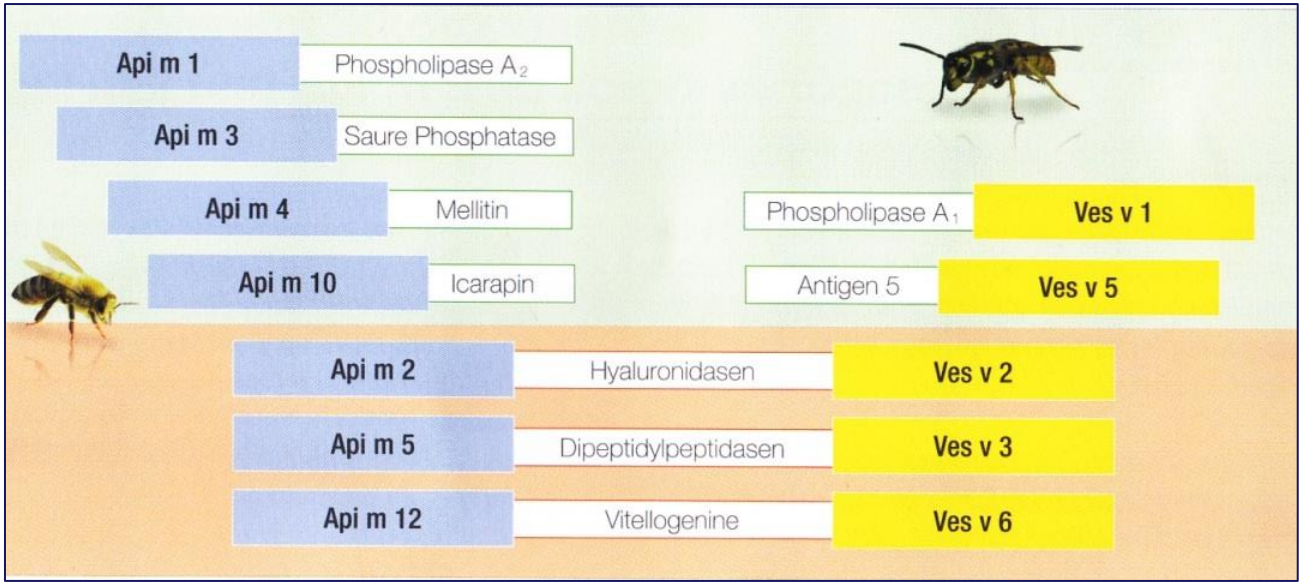
Worm M et al. Dtsch Arzteblatt Int 2014:111: 367-75

Worm M et al. Allergo J Int 2015:24:256-93




Exercise-induced anaphylaxis (EIAn)
Non-food-dependent (EIAn)
Food-dependent (FDEIAn)
Food-specific
Non-food-specific
Tri a 19

Bee / Wasp Allergy



Hymenoptera venom allergy

- the prevalence of an allergy systemic reaction after a Hymenoptera sting is estimated between 1 and 7 % in Europe

- Mortality: 200 cases pro year in Europe

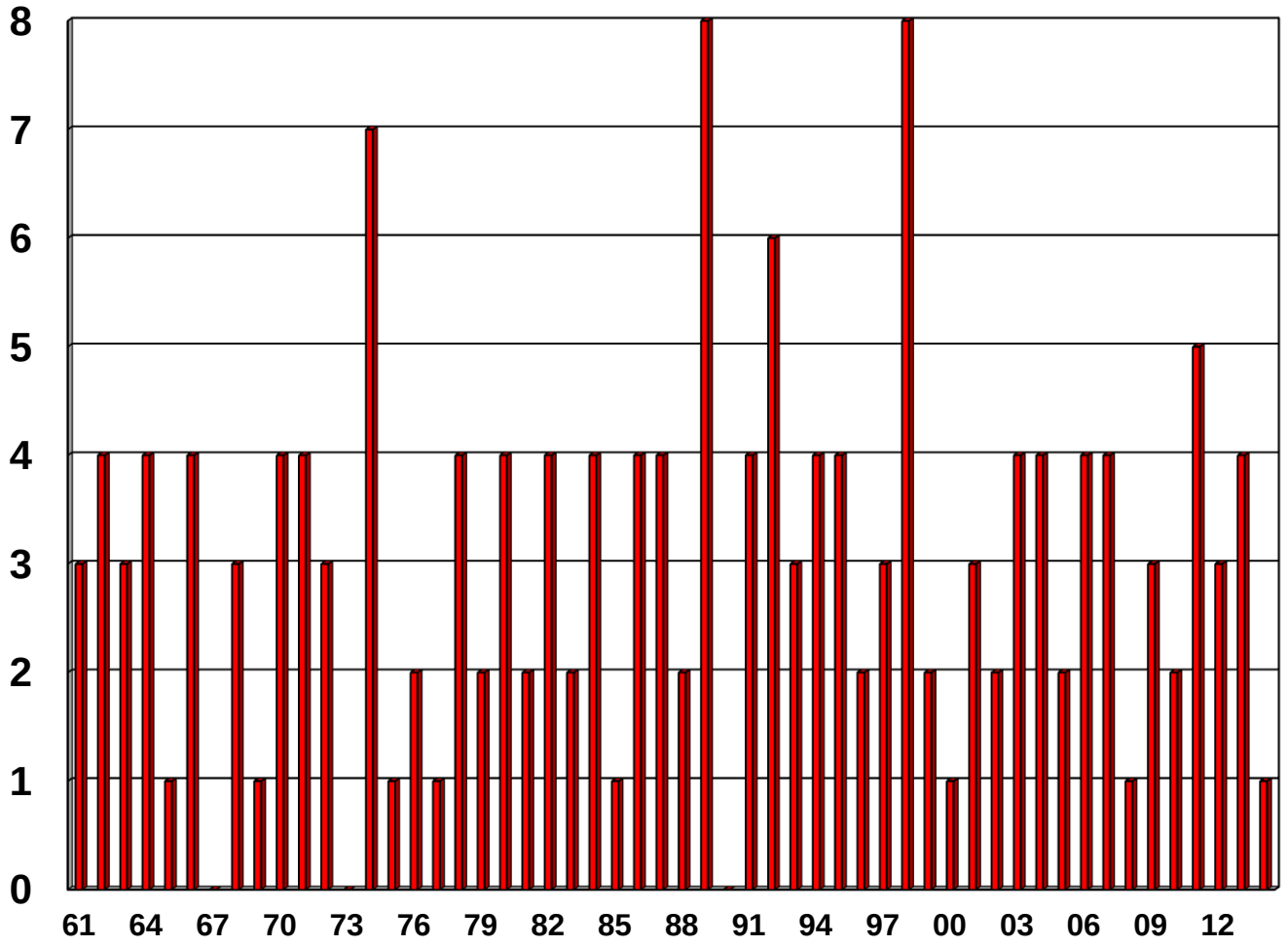
- One of the most frequent cause of Anaphylaxis in adult population

- bee sting 50 µg (30-140 mg) of venom proteins , after a wasp sting 3–5 µg of venom proteins are introduced to the body of the victim

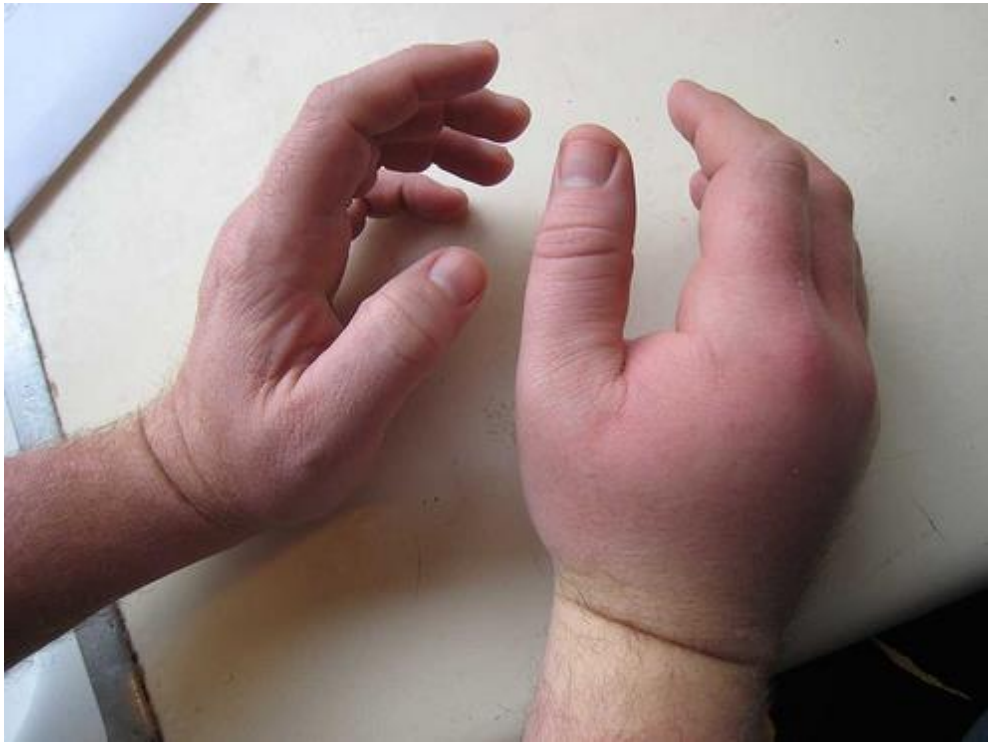
- Toxic reaction > 50-100 stings (in adults); > 10 stings (in children)

Mortality due to bee /wasp sting in Switzerland 1961 – 2012

Erwin K. Wüest, EDI BFS



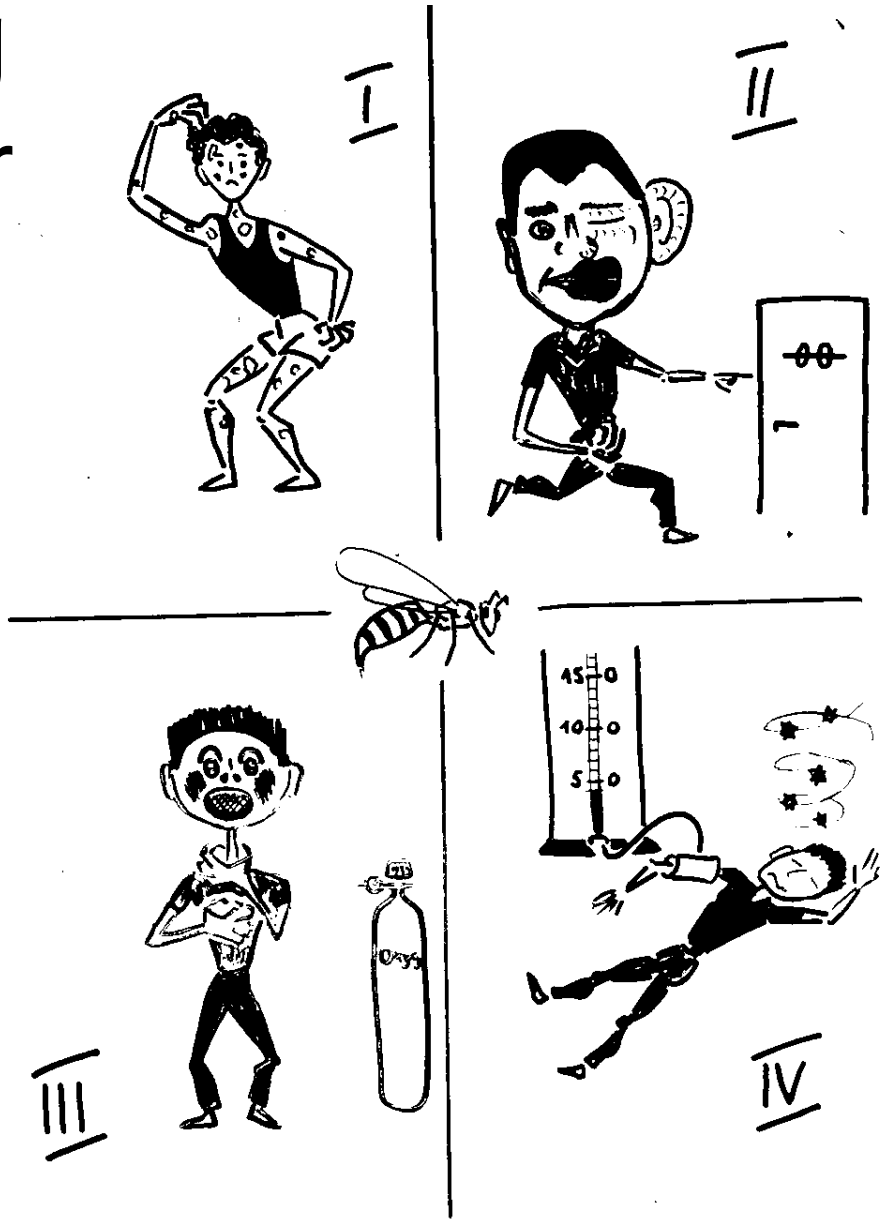
Local reactions after hymenoptera stings



Large local reaction=
Swelling exceeding 10 cm

Not an Allergy !

Classification of allergic reactions according to Mueller



Drug allergy

IgE mediated drug allergies (immediate reactions)

Anaphylactic IgE-mediated reactions Flushing, pruritus, urticaria, angioedema, laryngeal edema, rhinorrhea, conjunctivitis, shortness of breath, wheezing, bronchospasm, nausea, vomiting, diarrhea, hypotension	**Antibiotics** Beta-lactams Penicillins, cephalosporins, amino-penicillins Fluroquinolones Ciprofloxacin, levofloxacin	Sepsis Meningitis Pneumonia Pyelonephritis
	Chemotherapy drugs Platins Carboplatin, cisplatin, oxaliplatin	Primary and recurrent metastatic cancers (breast, ovarian, colon)
	Monoclonal antibodies Rituximab, trastuzumab	Chronic inflammatory diseases, cancers (leukemias, breast, ovarian)

Desensitization often possible!!!

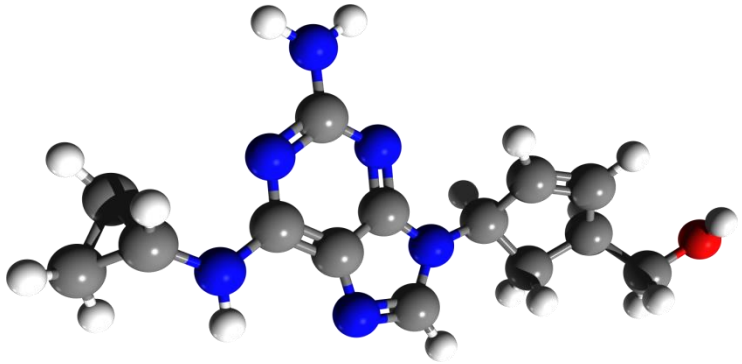
Non-IgE mediated drug allergies (immediate reactions)

Anaphylactoid **Direct mast cell/basophil, complement, and leukotriene metabolism reactions** Flushing, pruritus, urticaria, angioedema, throat tightness, shortness of breath, nausea, vomiting, diarrhea, hypotension, hypertension, back and/or abdominal pain	**Aspirin/NSAIDs**	Cardiac protection, asthma w/ nasal polyposis, chronic inflammatory diseases (RA, Crohn's)
	Vancomycin	MRSA
	Chemotherapy drugs Taxenes Paclitaxel, docetaxel	Primary and recurrent metastatic cancers (breast, ovarian, colon)

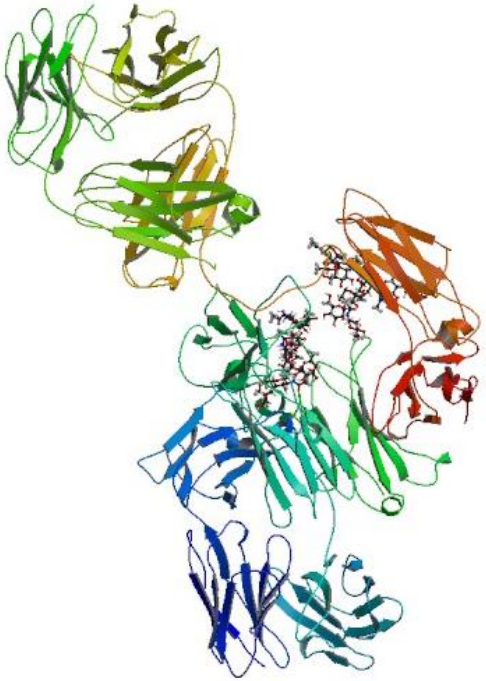
Pseudo-allergic reactions radio contrast media: direct membrane effects related to the osmolarity of contrast media solution

Chemical structure of drug molecule

No protein drugs, small molecules
1-2 kDa, haptens



Protein drugs
Large molecules >20 kDa



Haptens

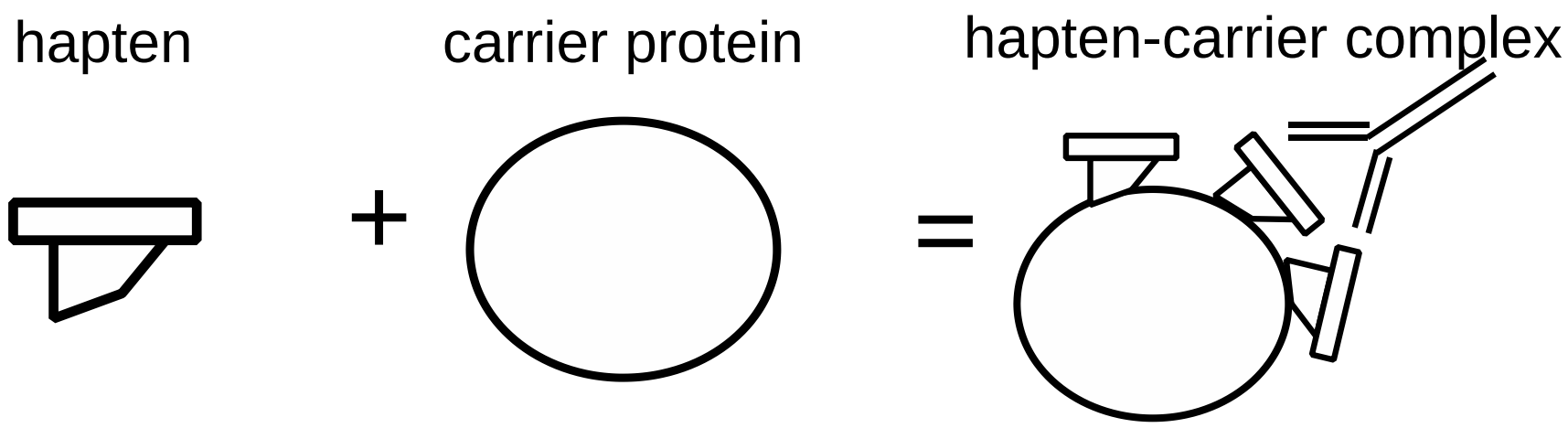
Small molecules alone are not immunogenic!

Haptens = reactive proteins binding to a larger protein → hapten-carrier complex

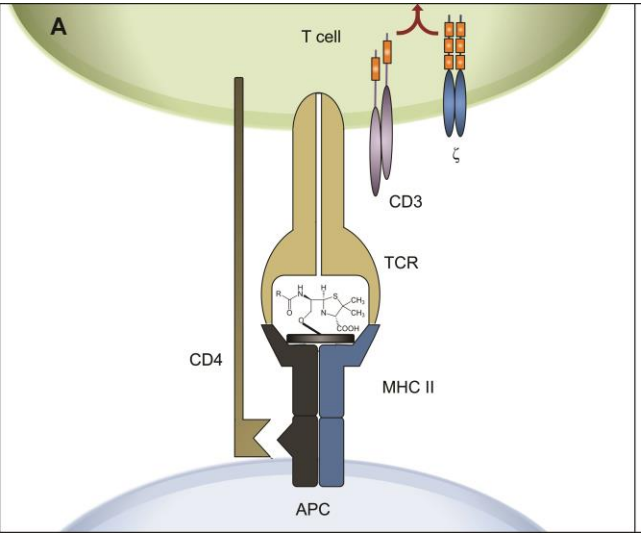
→ resistant to intracellular processing

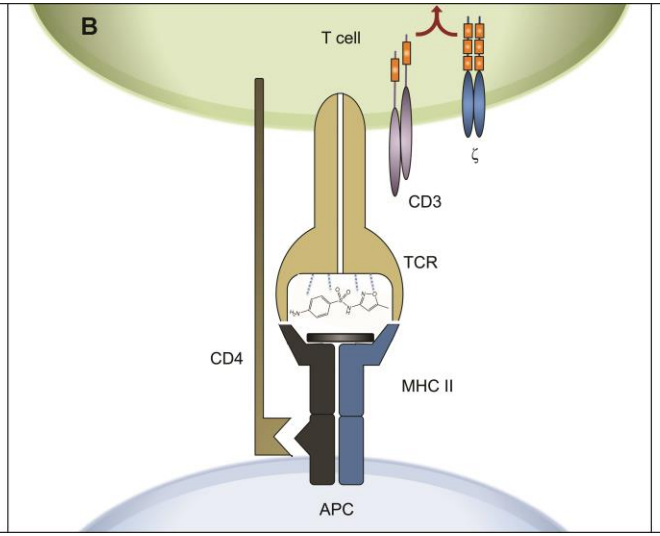
→ danger signal (activation of innate immunity e.g. DC's)

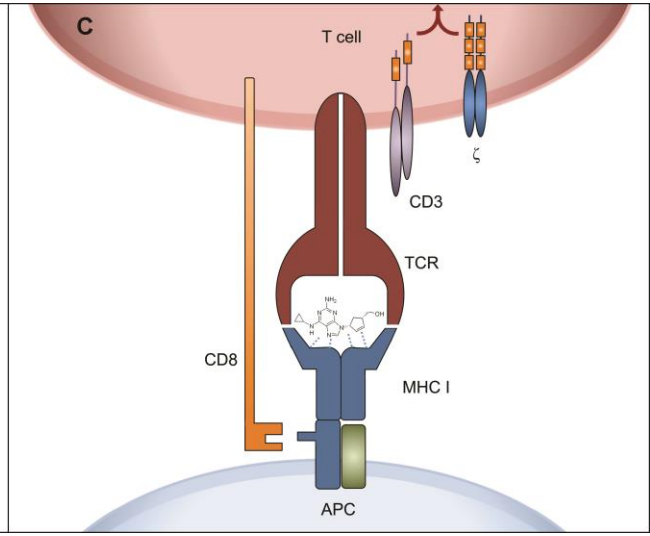
→ forms neo-antigenic determinants able to induce both a T-cell and B-cell immune response.



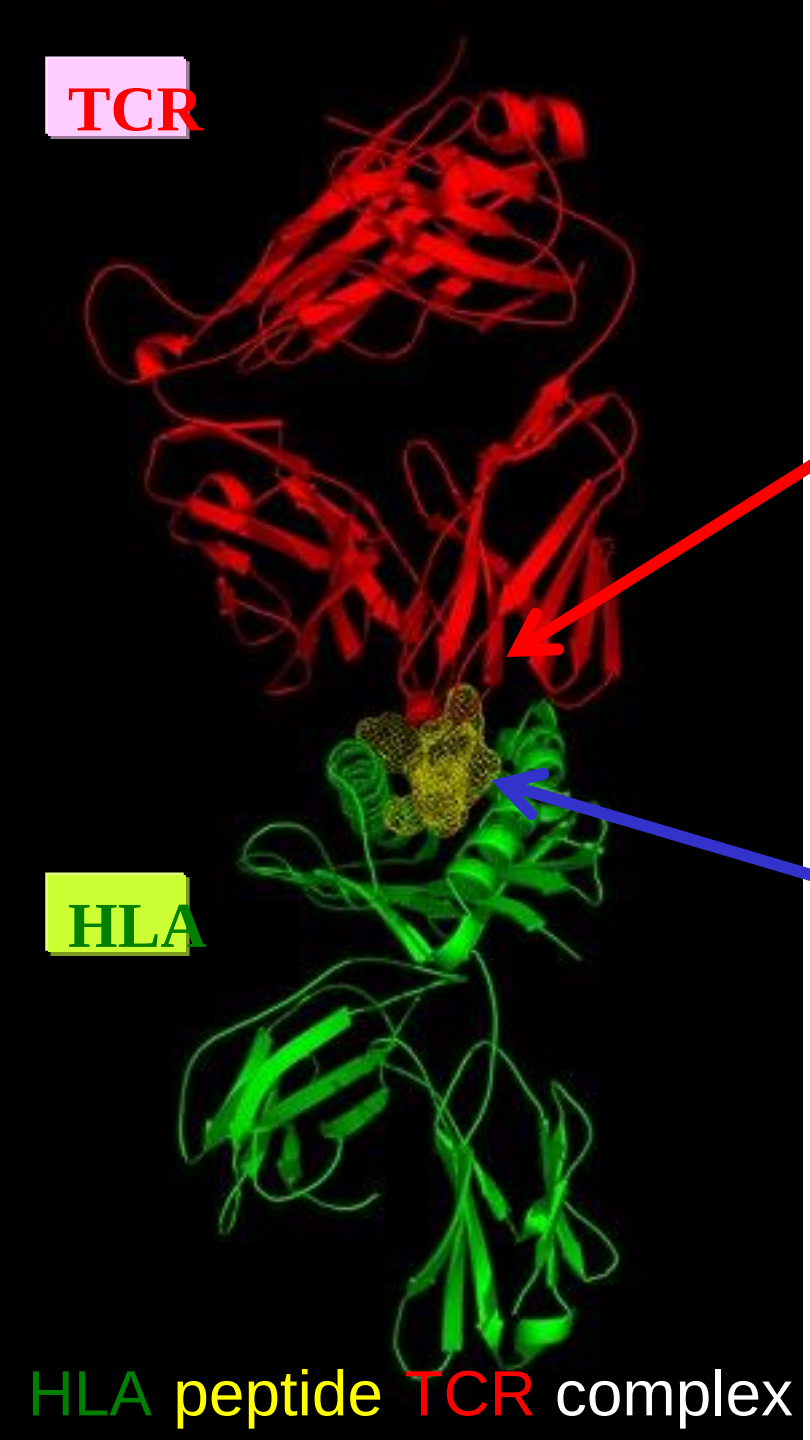
Hapten **p-i (TCR)** **p-i (HLA)**







Immune reaction **Pharmacological interaction**



p-i concept:

a) the drug binds first to the TCR (by non covalent bonds; not restricted to a HLA-allele)

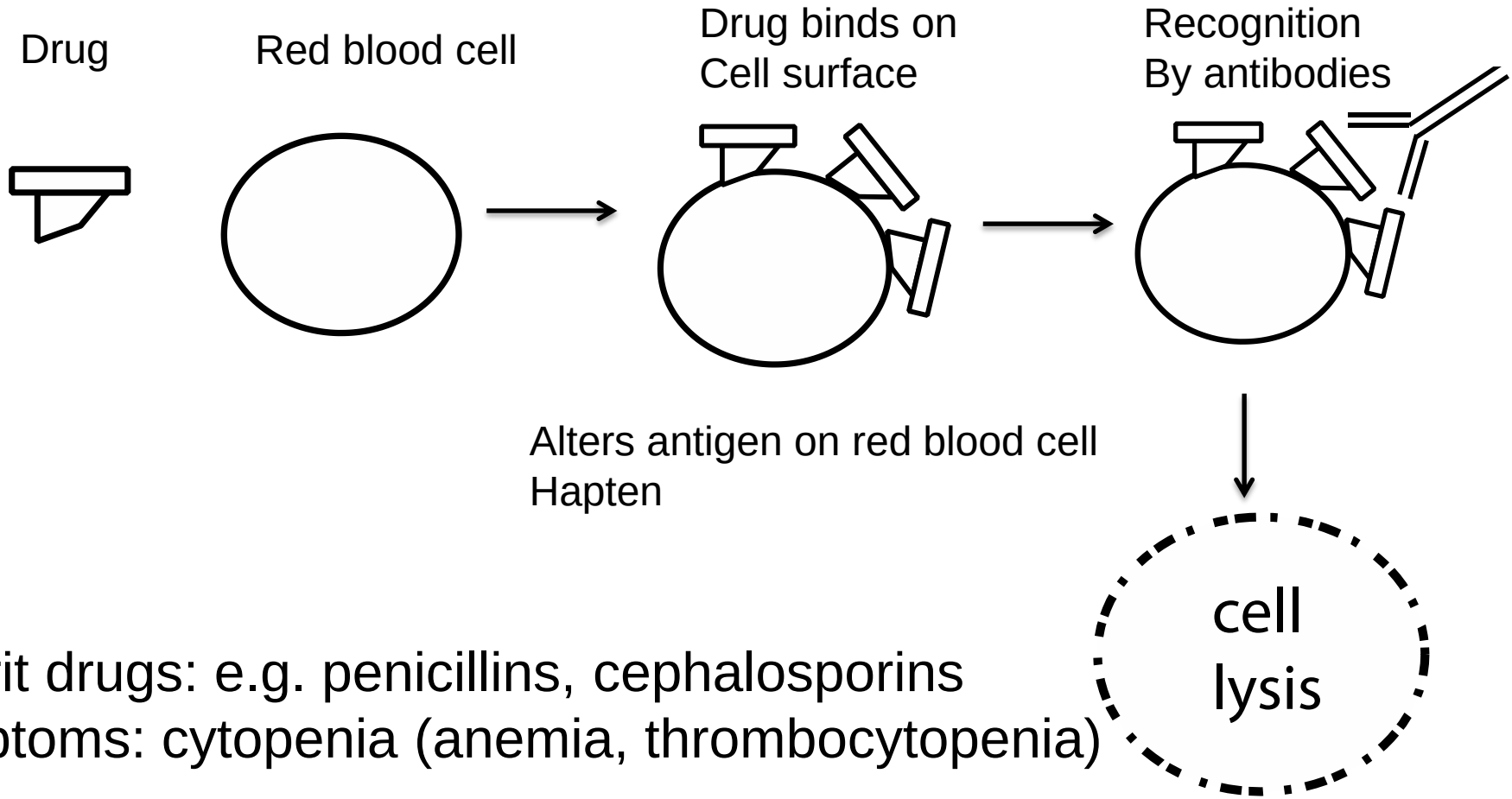
or

b) the drug binds first to the HLA molecule, and the HLA-peptide-drug complex is then recognized by the TCR

(HLA-class I restricted, CD8)

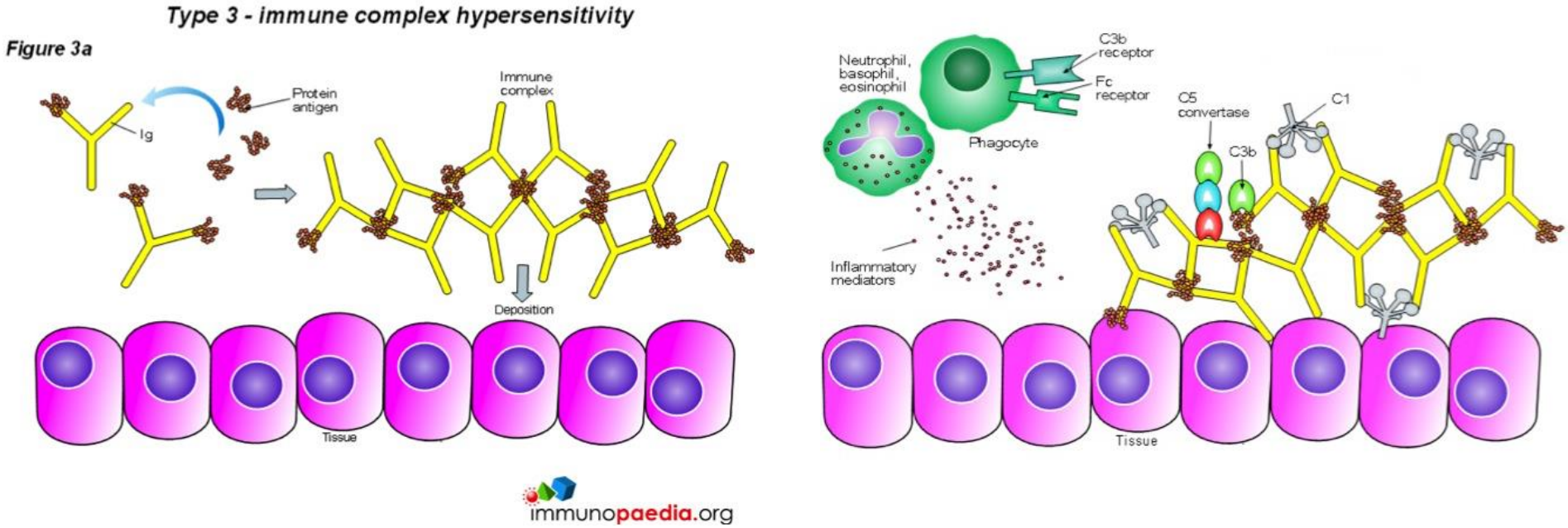
IgG mediated drug hypersensitivity (Typ II)

Haemolytic anaemia



Culprit drugs: e.g. penicillins, cephalosporins
Symptoms: cytopenia (anemia, thrombocytopenia)

IgG mediated drug hypersensitivity (Typ III)

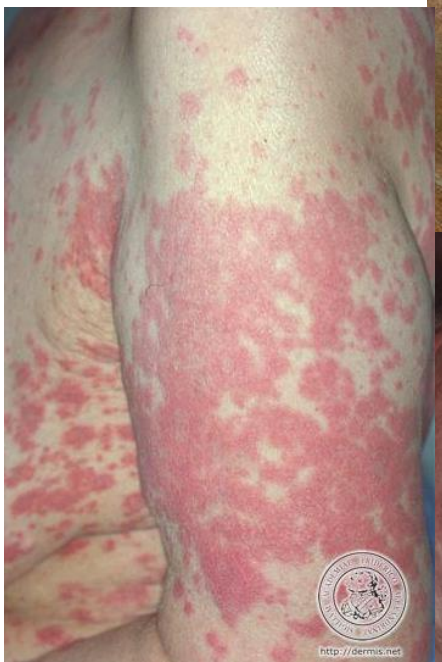


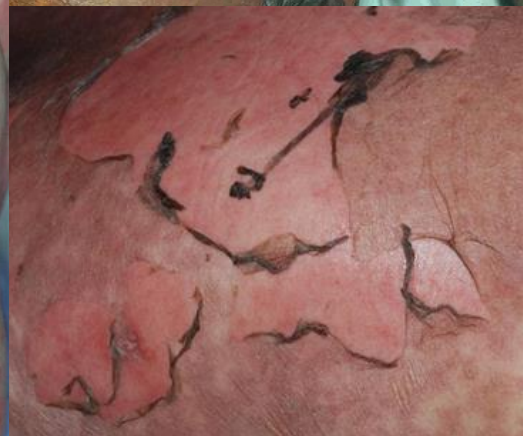
Immune complexes may deposit preferentially in joints →triggers an inflammatory response.

Clinic: vasculitis, skin, serum sickness, lungs, joints, fever

Symptoms of T cell mediated drug allergy

- Makulo-papular Exanthem
- bullous Exanthem
- Acute generalized exanthematous Pustulosis (AGEP)
- Stevens-Johnson Syndrome (SJS) toxic-epidermal Necrolysis (TEN)
- DRESS, Hepatitis, interstitial Nephritis, Pneumonitis





Contact Dermatitis

Contact Dermatitis

non-infectious reaction of the skin to external substances

<u>Allergic contact dermatitis</u>

T- Zell mediated immune response to contactallergens like:

- Nickel, lanolin, Peru balsam or potassium dichromate
- jewellery, medication cosmetics, dyes impregnating agents

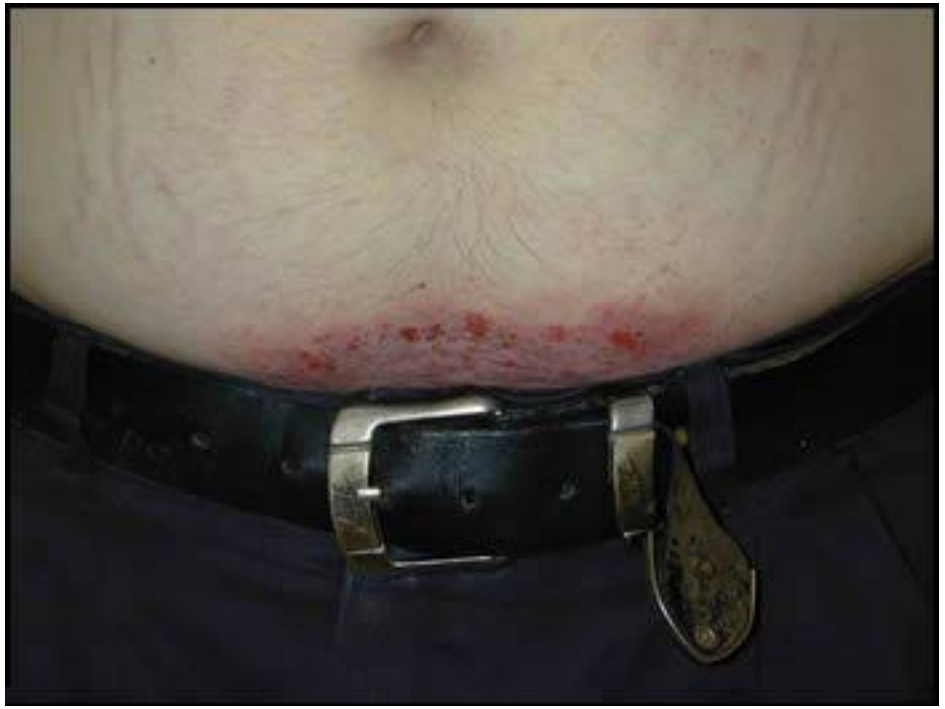
<u>Irritative contact dermatitis</u>

Non immune mediated response to physical, chemical irritants and physical influences

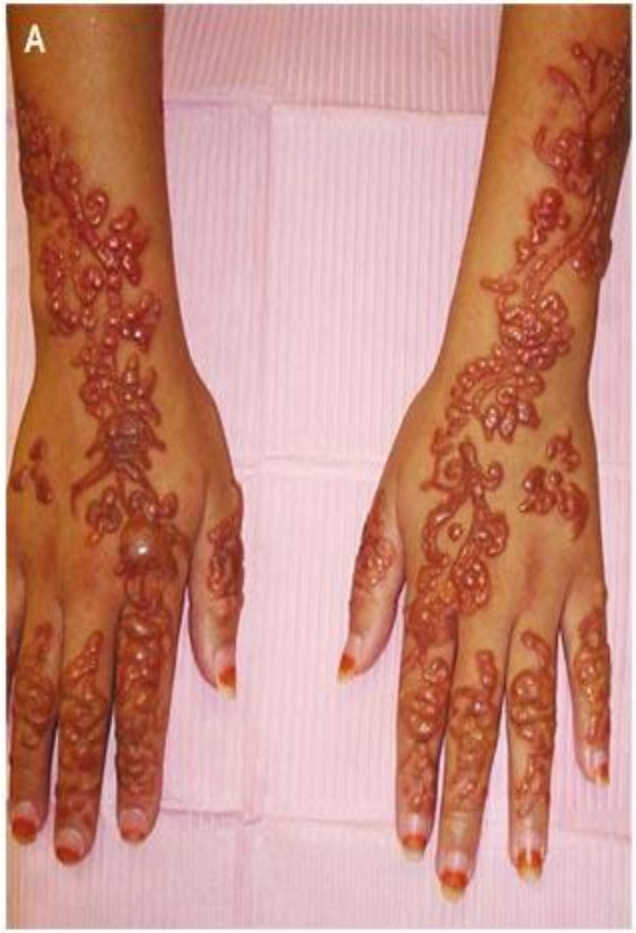
- rubbing, pressure, heat and cold or UV rays
- water, soap, disinfectants,

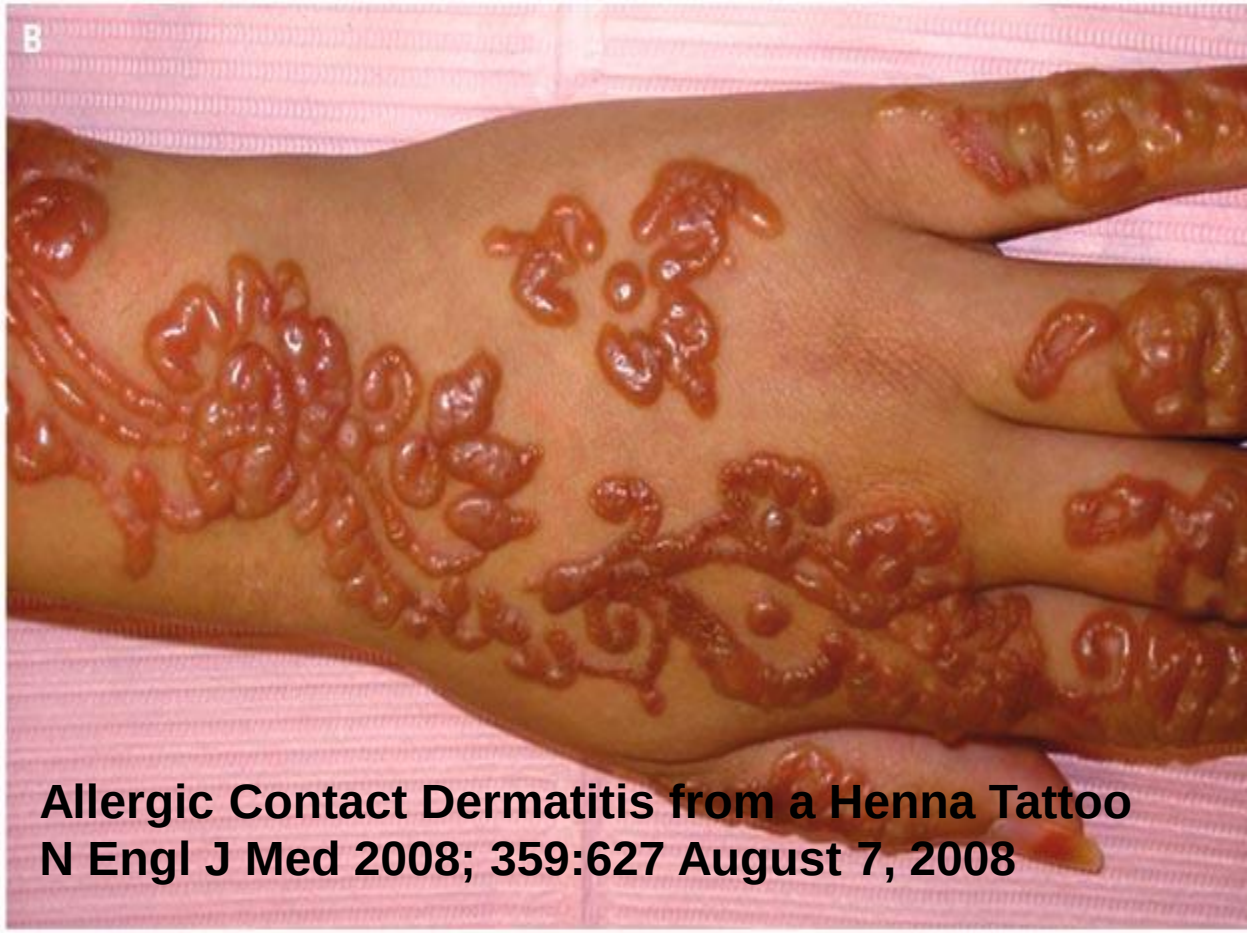
Allergic Contact Dermatitis

- The reaction usually occurs 24–48 hours after contact with the allergenic substance.
- The skin is inflamed and reddened, it may swell up and blisters or papules may appear.
- These symptoms are often combined with severe itching.
- The skin reaction appears at the site of the body where the skin came into contact with the irritant, but may also spread to nearby or remote regions of the skin.



Allergic Contact Dermatitis

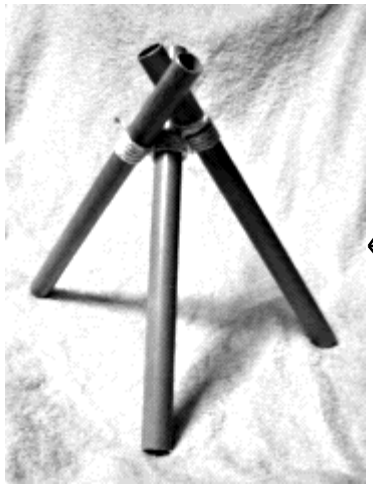


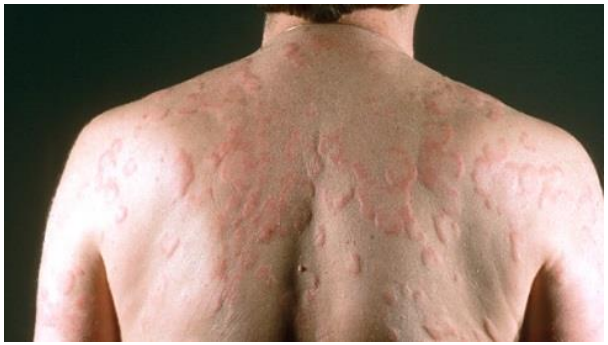


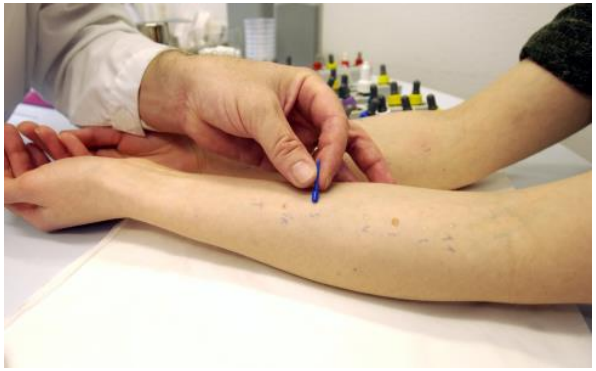
Allergic Contact Dermatitis from a Henna Tattoo
N Engl J Med 2008; 359:627 August 7, 2008

Diagnostics of allergic diseases

Diagnostics of allergic diseases





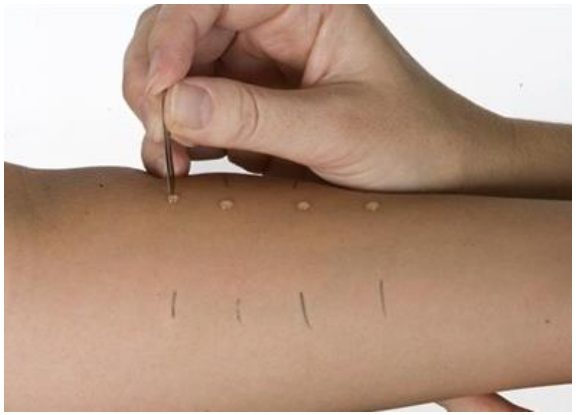


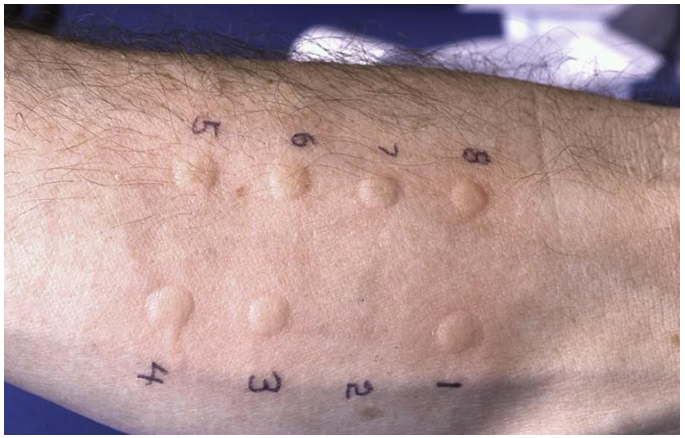
- Medical history
- Symptoms
- Tests

Diagnostics of allergic diseases

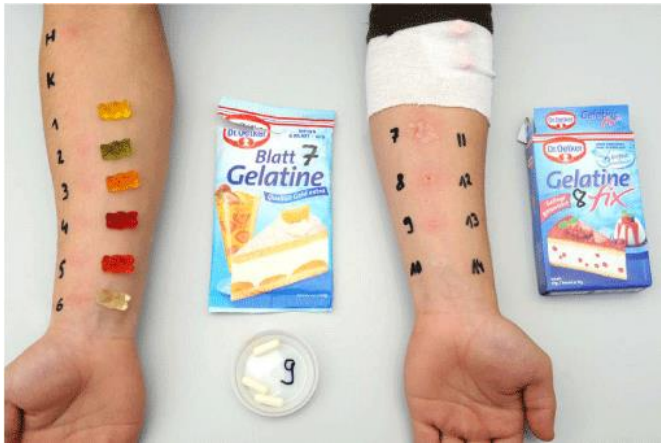
Typ I Hypersensitivity

Skin pricktest





Prick-to-prick Test

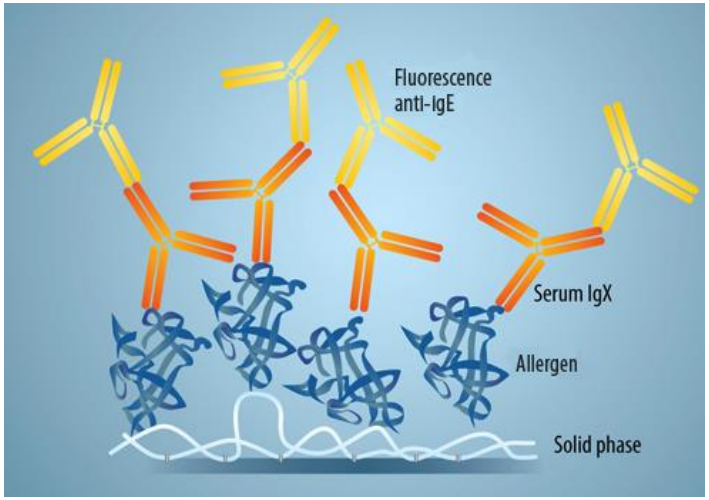


Diagnostics of allergic diseases

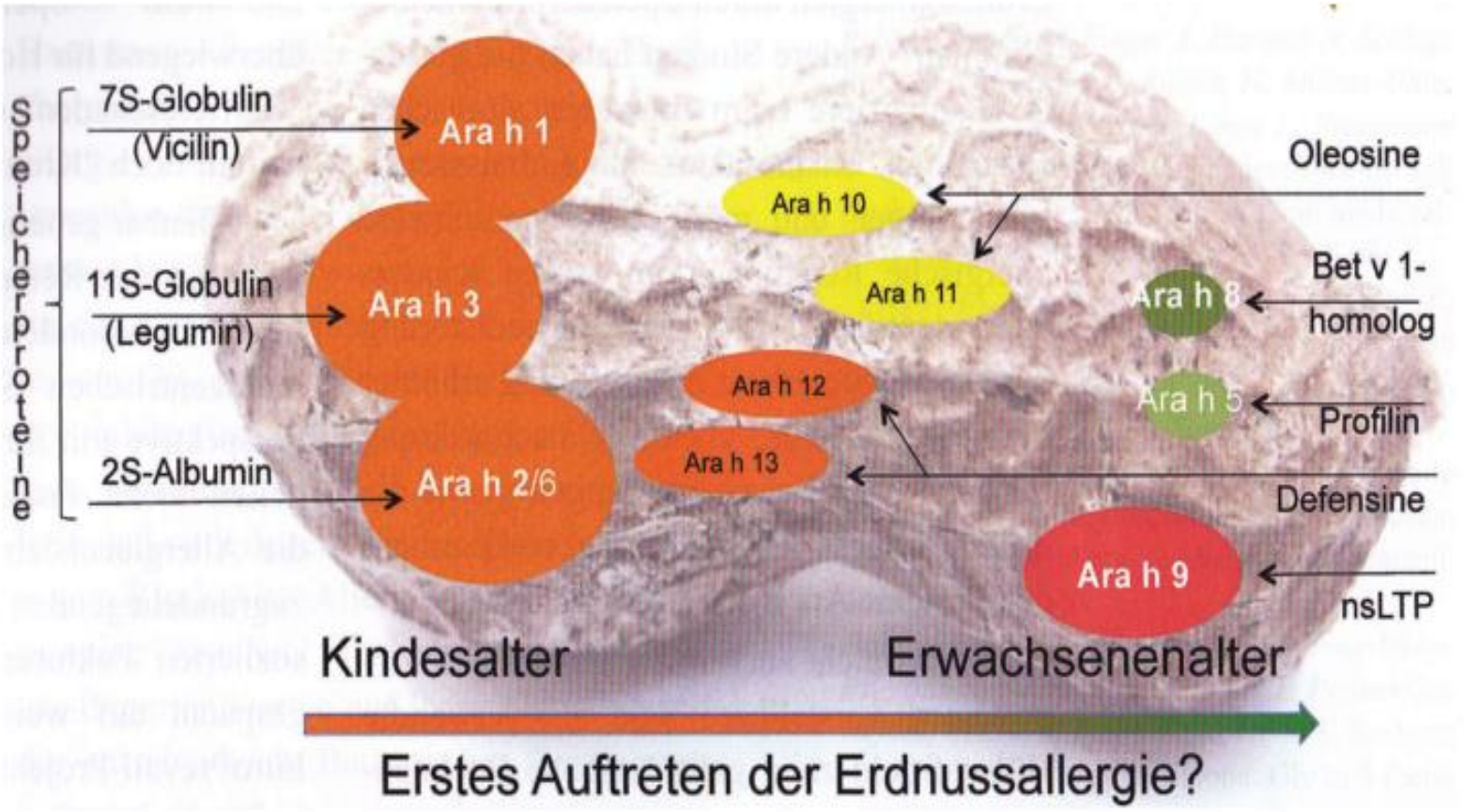
In-Vito Test and molecular allergy diagnostics

Type I Hypersensitivity

Serum IgE

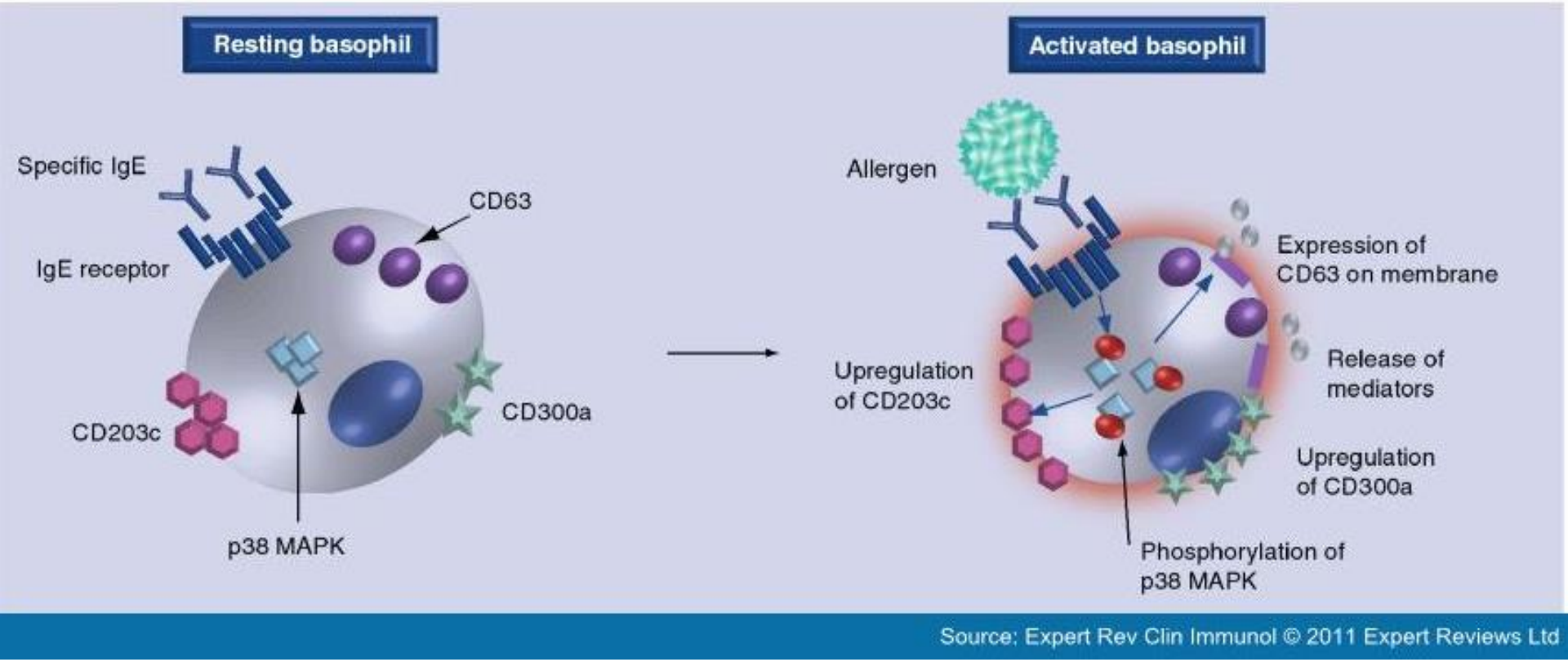


In-Vito Test and molecular allergy diagnostics

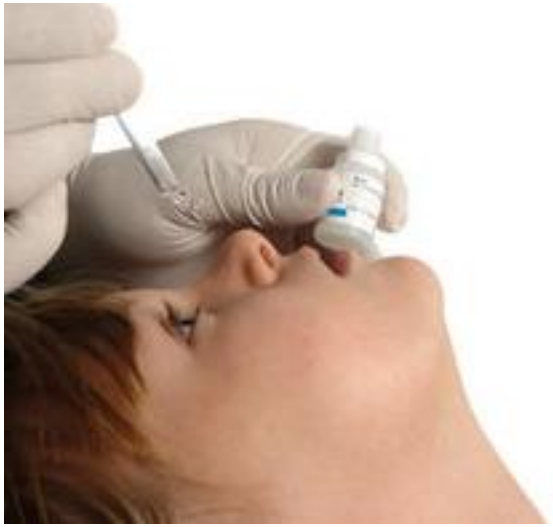


Diagnostics of allergic diseases

Basophil activation Test



Conjunctival provocation tests (CPT, allergen solution)



No standardization of CPT; no grading of ocular reactions

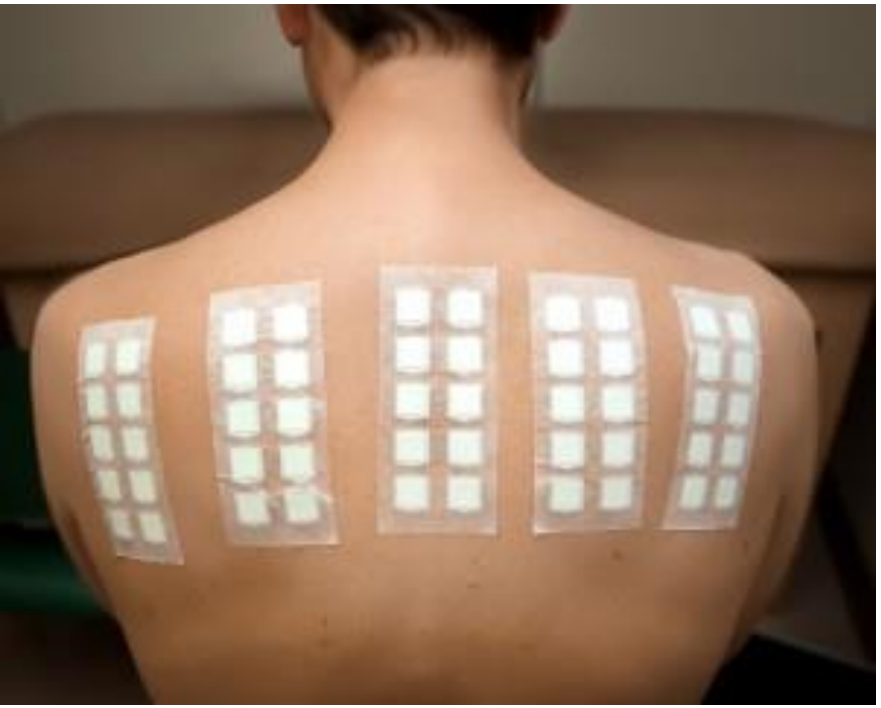
Digital image analysis possesses the potential of being an objective evaluation method compared to the wide-spread subjective

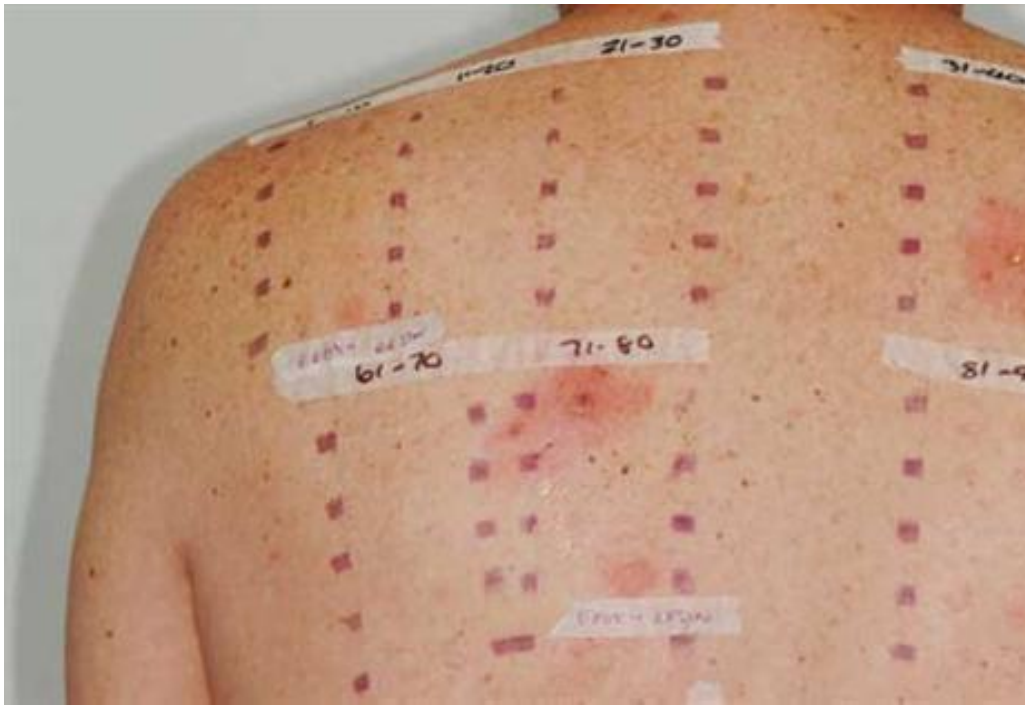
Dogan et al. Int Arch Allergy Immunol 2014;163:59–68

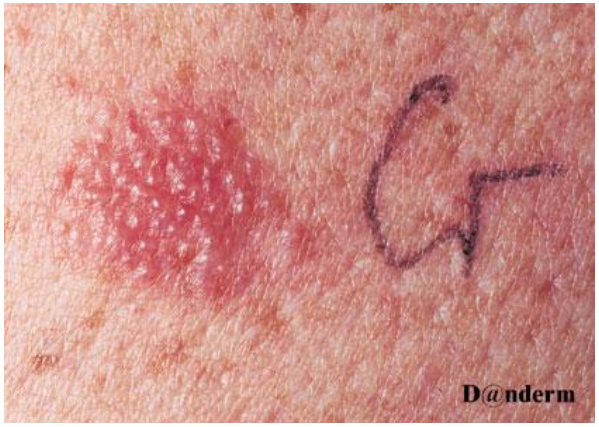
Oral provocation tests

Food challenge Tests

Patch Tests
Type IV Hypersenstivity





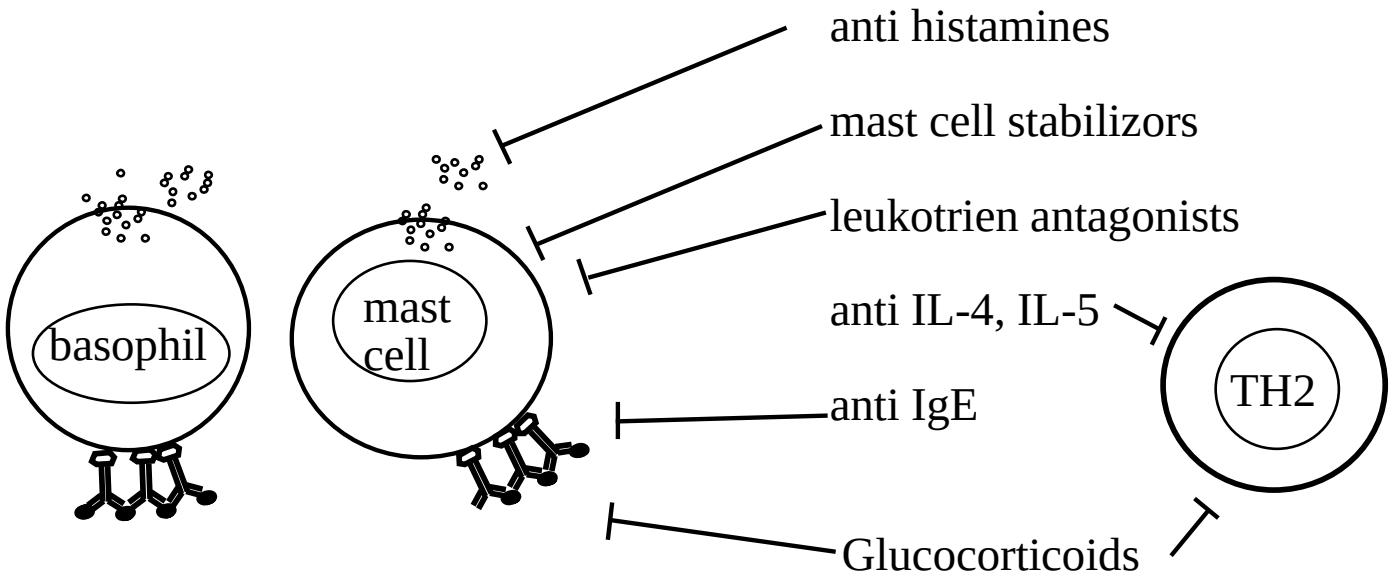


Therapy principles

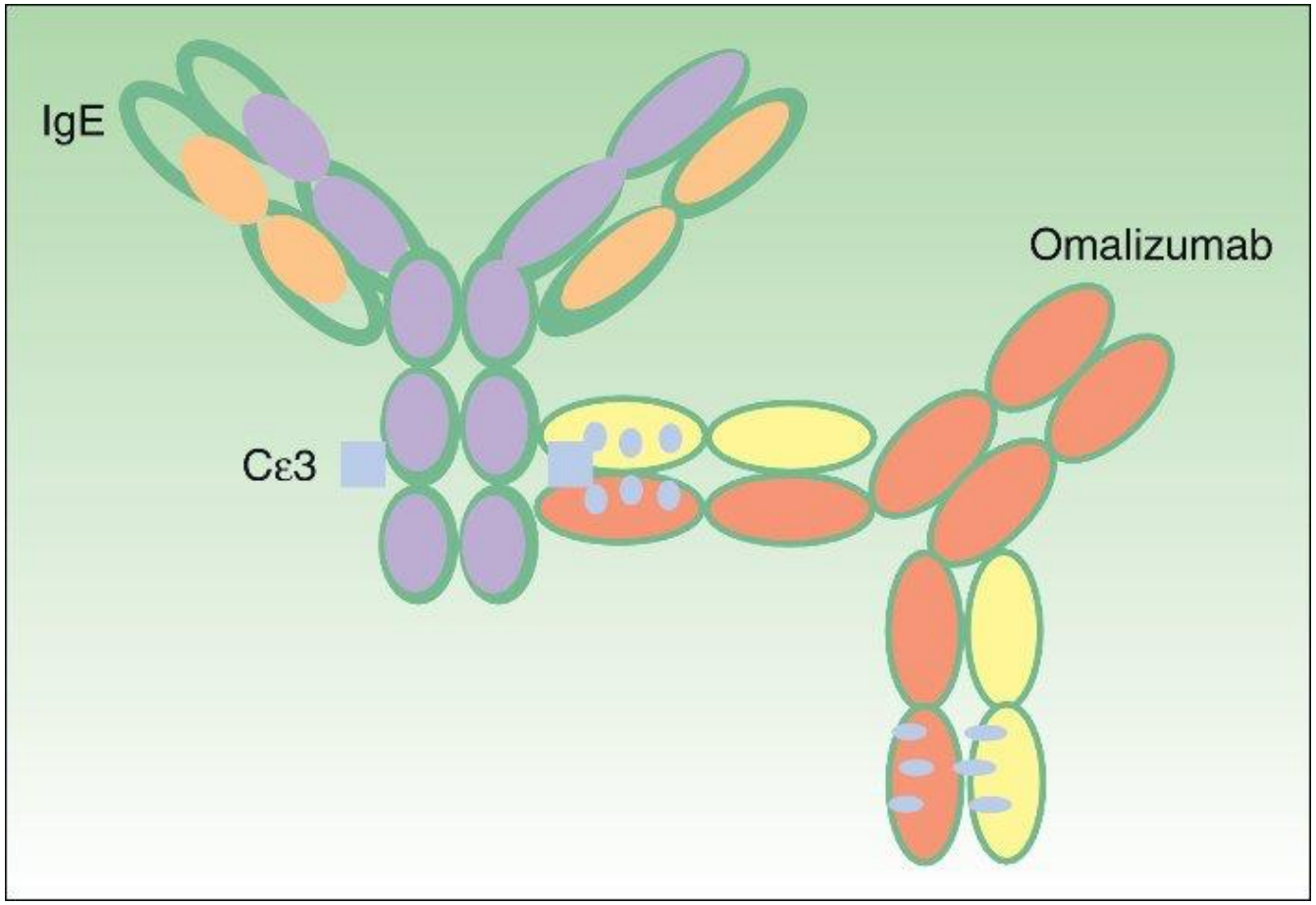
Therapy principles

1. Symptomatic therapy
- antihistamines
- corticosteroids
- leukotrien antagonists
- antiasthmatics (inhalativ medication)
- biologics (Omalizumab, anti-IgE), (Mepolizumab anti-IL5)

Inhibition of inflammatory mediatores released during ef fector phase:



Anti IgE therapy (omalizumab)



Binding of omalizumab to the ce3 domain of IgE.

Adapted from Francés et al. 2014 Actas Dermosifiliogr. 2014;105:45-52. - Vol. 105 Num.01

Therapy principles

Allergen-specific Immunotherapy alters course of disease

Bee keepers

Systemic reactions in 45% of beekeepers with <15 bee sting / year

No/less systemic reactions in Beekeepers with
> 200 bee sting / year

Why???

http://www.spiegel.de/fotostrecke/imkern-extrem-27-kilogramm-bienen-am-koerper-fotostrecke-70505.html

Milestones in Specific Immunotherapy

- 1911–1914 subcutaneous desensitization with pollen extracts

  Noon L: Prophylactic inoculation against hay fever. Lancet 1911;I:1572–3

  Freeman J: Further observations on the treatment of hay fever by Hypodermic inoculations of pollen vaccine. Lancet 1911;II:8141

  Freeman J: Further observations on the treatment of hay fever. Lancet 1914;II:1178

- 1930 Introduction of rush desensitization

  Freeman J: Rush inoculation with special reference to hay-fever treatment. Lancet 1930;I:744

- 1954 first double blind placebo controlled SIT study

  Frankland AW, Augustin R: Prophylaxis of summer hay fever & asthma: a controlled trial comparing crude grass-pollen extracts with the isolated main protein component. Lancet 1954;I:1055–7

- 1959 first study with semi-depot extracts

  Fuchs AM, Strauss MB: The clinical evaluation and the preparation and standardization of suspensions of a new water-insoluble ragweed pollen complex. J Allergy 1959;30:66

- 1969 first sublingual immunotherapy for foods and 1970 for inhalant allergens

  Morris D: Treatment of respiratory disease with ultra-small doses of antigens. Ann Allergy 1970;28: 494–500

Allergen-specific Immunotherapy

Reduktion allergischer Symptome

Calderon et al. JACI 2011;127:30-8

Radulovic et al. Allergy 2011;66:740-52

Asthma prevention

Douglas et al. Pediatrics 1968; 42: 793

Jacobsen et al. Allergy 2007;62:943-8

Möller et al. JACI 2002; 109: 251-256

Schmitt J et al. JACI 2015;136:1511-6

Subcutane Immuntherapy (SCIT)

Präsaisonal

Allergovit®, ALK 7®, PolVac®

- Kurzzeit
- 4-8 Injektionen
- Später Start
  - 2 Monate vor der Saison

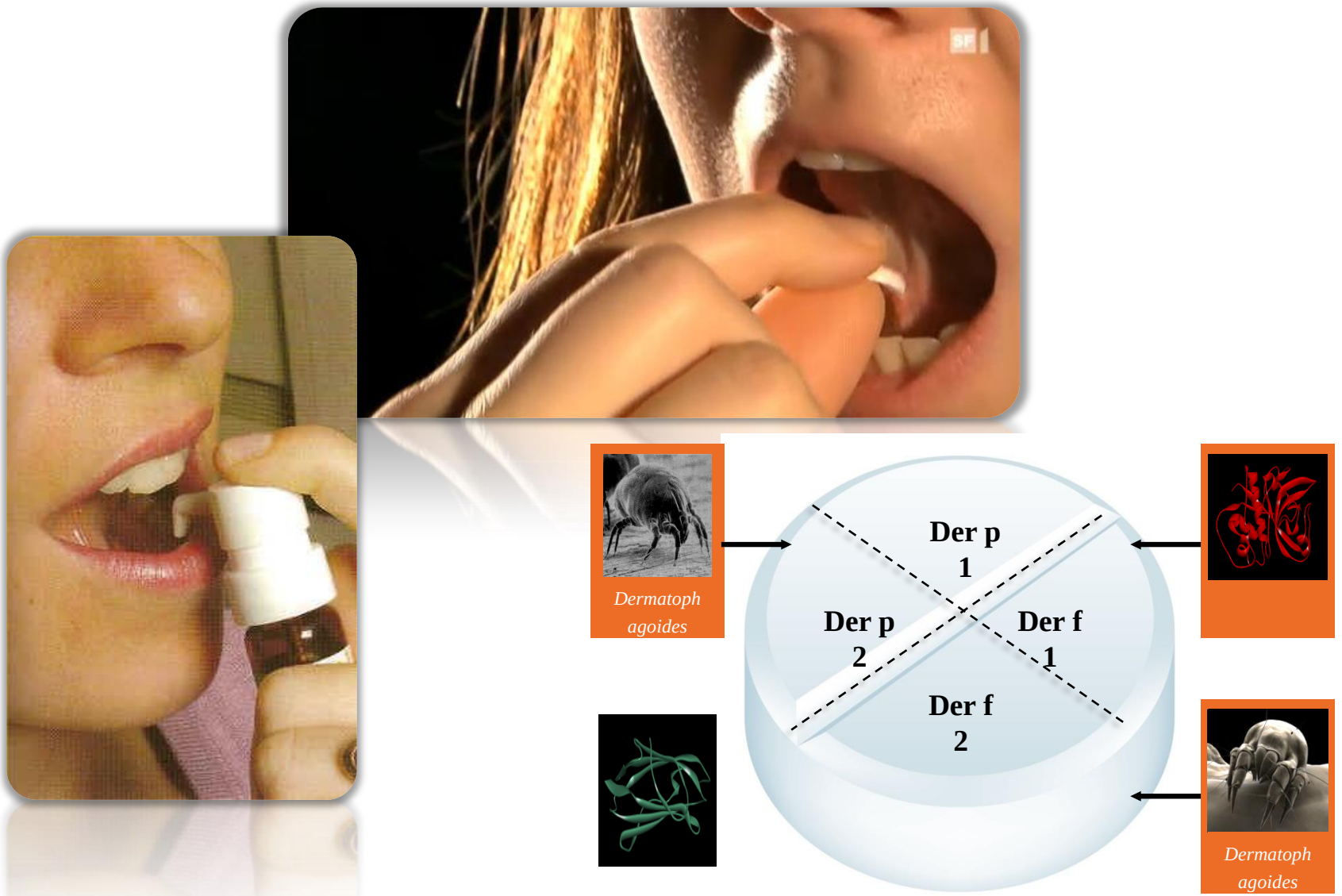
Perennial

ALK Alutard®
Novo-Helisen Depot®
Alyostal ®

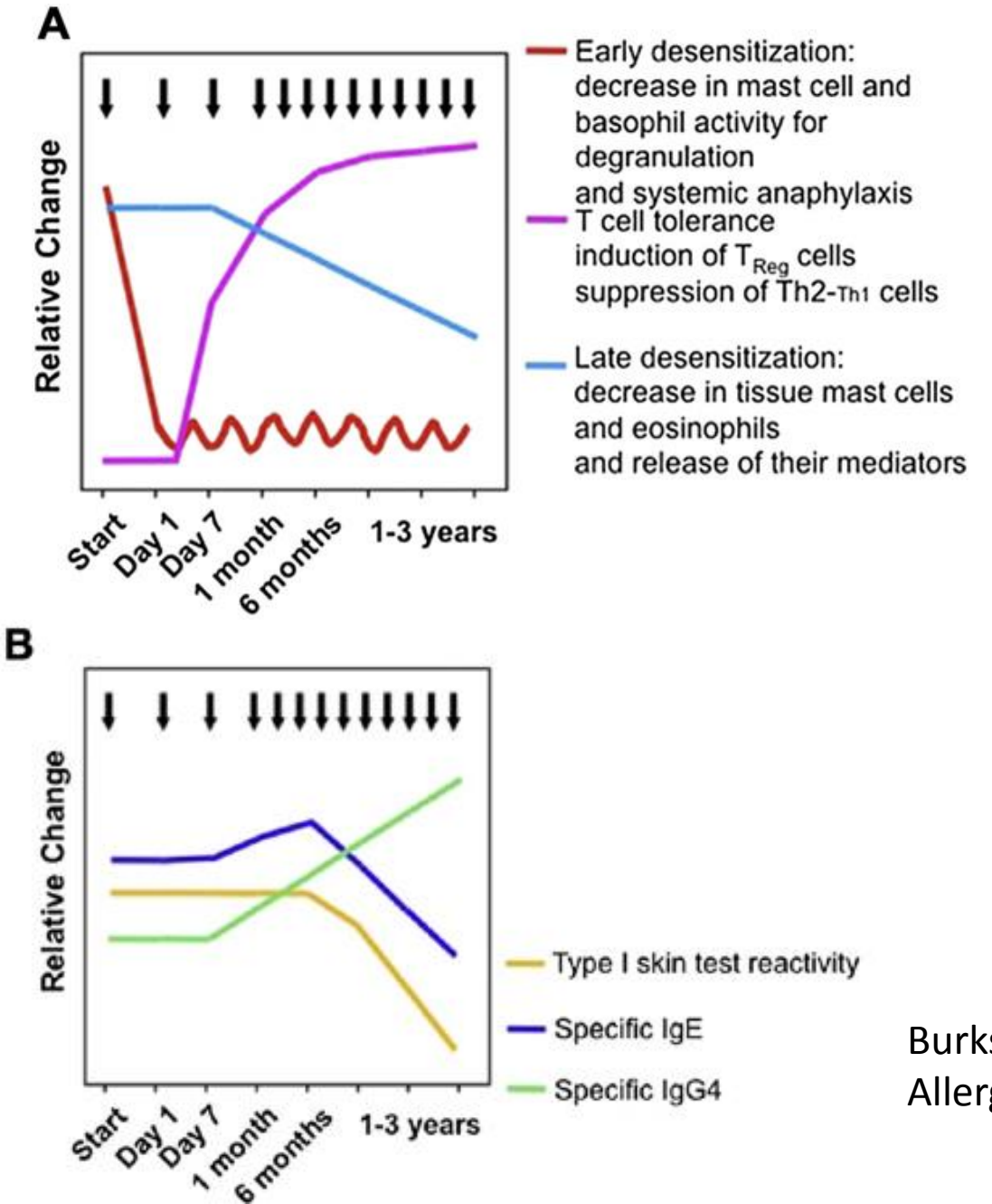
- ca. 45 Injektionen pro Jahr

Sublingual Immuntherapy SLIT

Passalacqua et al. JACI 2007;119:881-91



Mechanisms of SIT



Burks et al. J
Allergy Clin Immunol 2013;131:1288-96.

Summary

Definitions

Atopy: genetic determined readiness to react by IgE formation to substances taken up via aerogen or gastro-intestinal routes

Sensitization: immune reaction to a foreign substance (proven in skin tests, serology, cellular tests...)

Allergy: immune reaction to a non replicating (harmles) substance (protein, chemical, drug, metal), which leads to clinical symptoms like.

Sentisitation and Atopy = Allergy

Type 1 hypersensitivity

Key Players:

IgE

Allergen

Eosinophils

B cells

TH2

Cytokines
(IL-4, IL-5, IL-13)

APC

Chemokines

Mast cells