Jagten på bigift specifikke antistoffer fra biavlere

Vestsjællandske Biavlerforeninger

31. januar 2026

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ALK

Agenda

- Who am I and why am I here?
- Introduction to allergy
- PhD project
- Isolating antigen specific memory B cells
- Blocking patient IgE with IgG4 cocktails

Who am I?

- 2017-2019: MSc in Biotechnology and Chemical Engineering at Aarhus University
- 2020-2023: PhD project in collaboration with Aarhus University and ALK Abelló
- 2023-current: Scientist in Global Research Drug Development @ ALK Abelló

And why am I here?

- I recruited beekeepers as subjects in my PhD research and did a talk at Hørsholm beekeeper association

What is type I hypersensitivity?

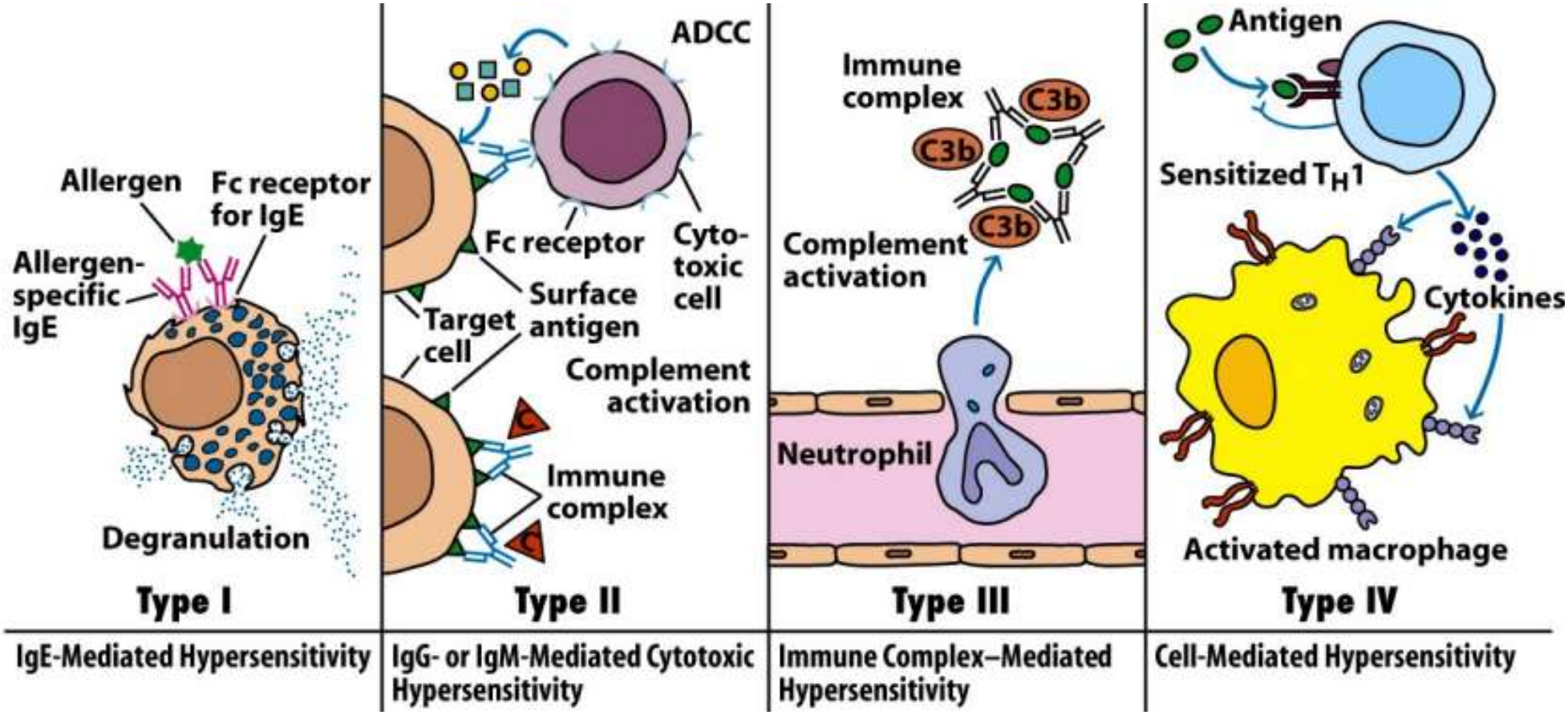

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Figure 15-1
Kuby IMMUNOLOGY, Sixth Edition
© 2007 W. H. Freeman and Company

What is type I hypersensitivity?

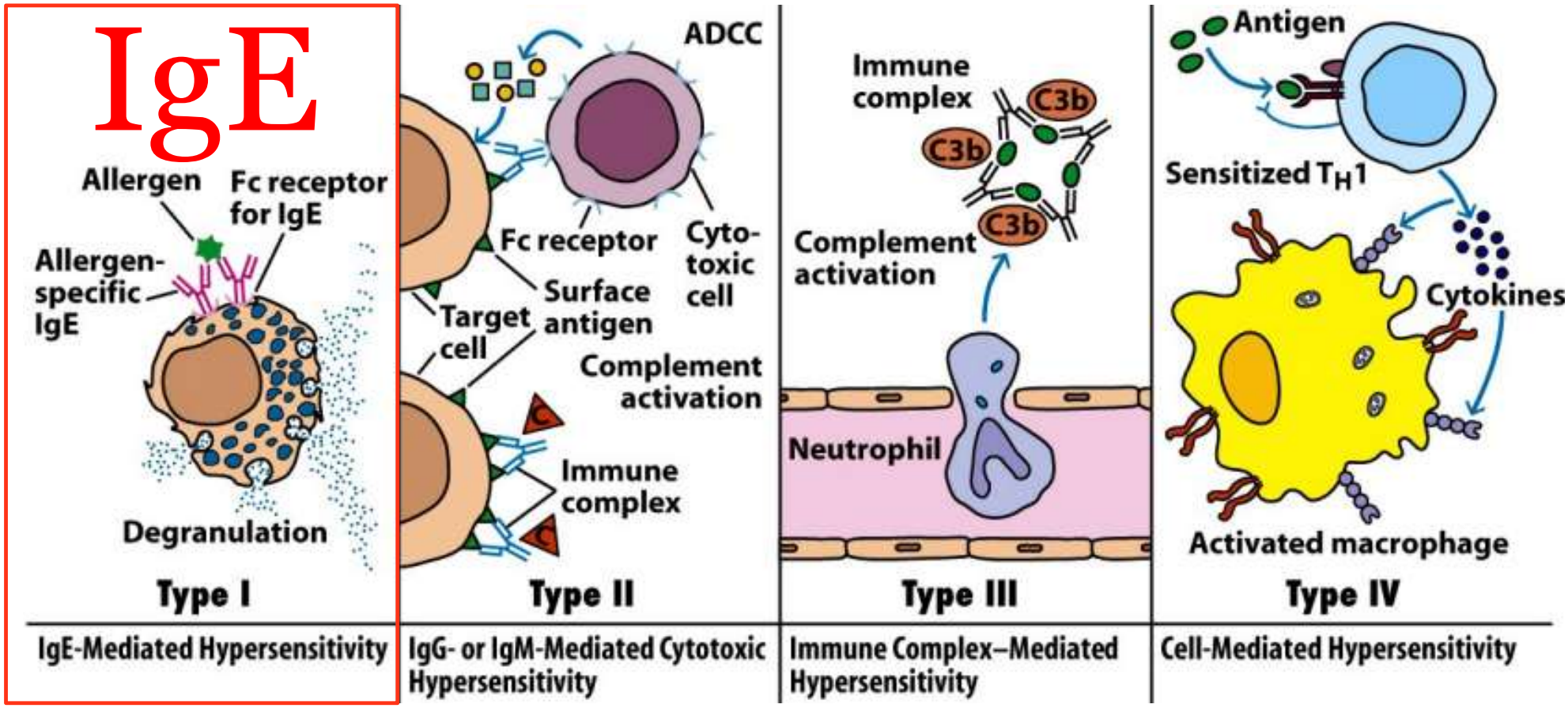

Figure 15-1
Kuby IMMUNOLOGY, Sixth Edition
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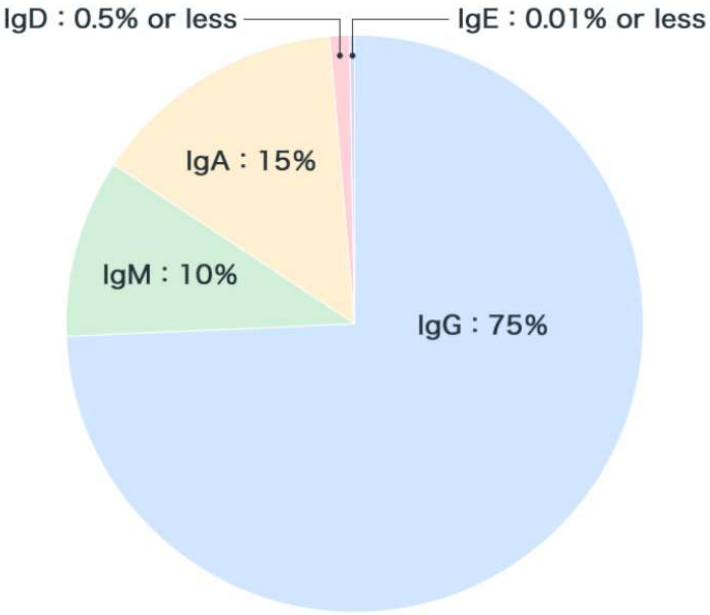
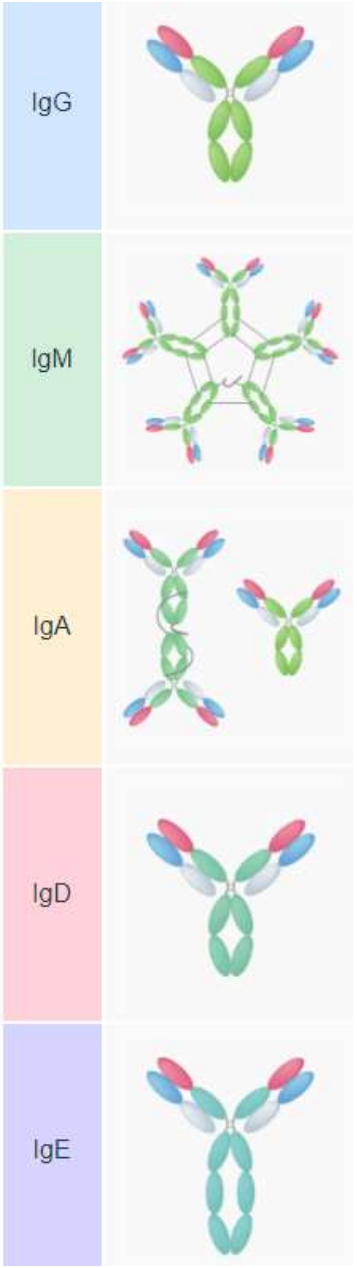
What is IgE?

- Five overall immunoglobulin/antibody (Ig) isotypes in humans

What is IgE?

- Five overall immunoglobulin/antibody (Ig) isotypes in humans
- IgE is the rarest antibody isotype in circulation





How does type I hypersensitivity develop?

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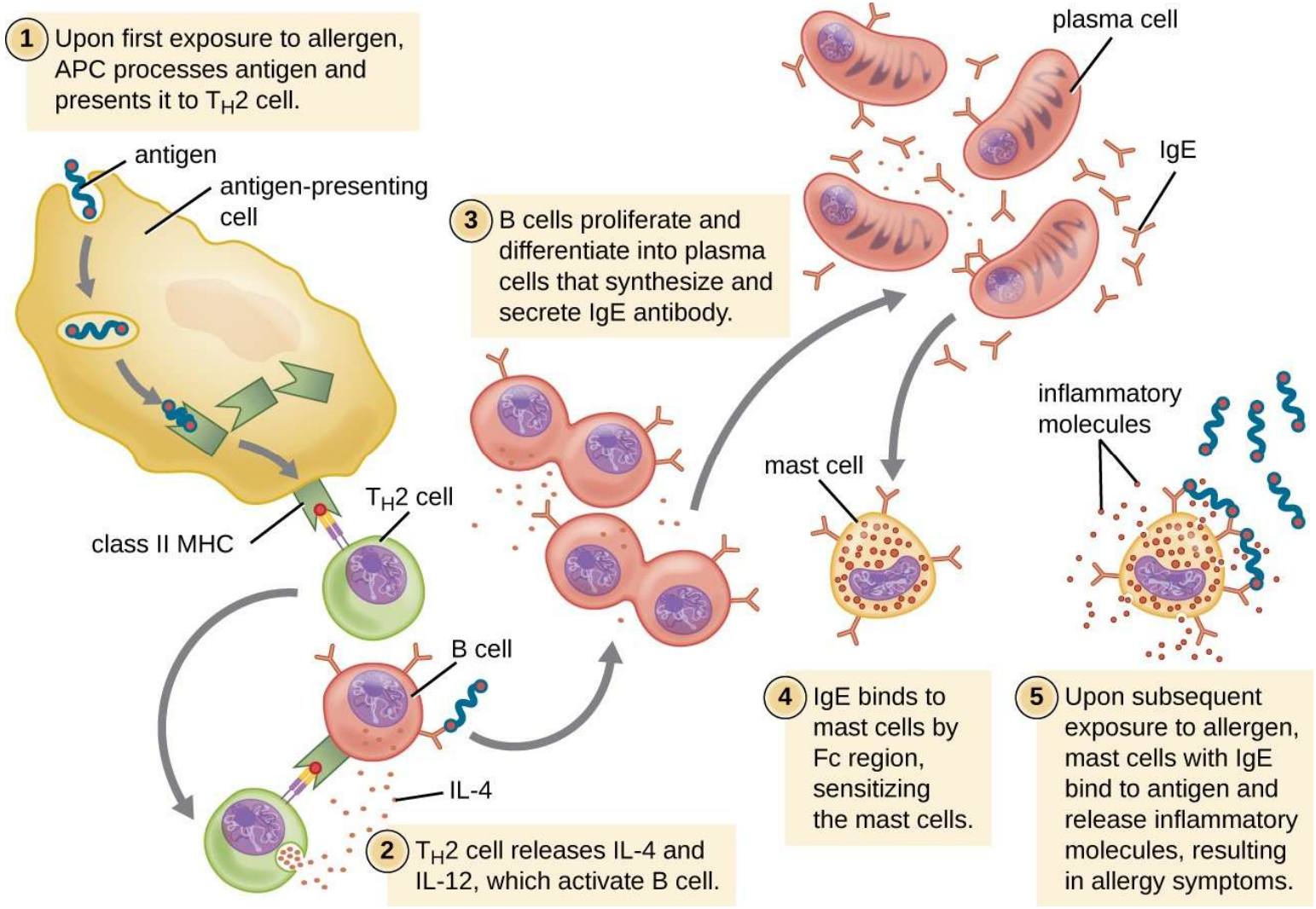

Oregon state University website

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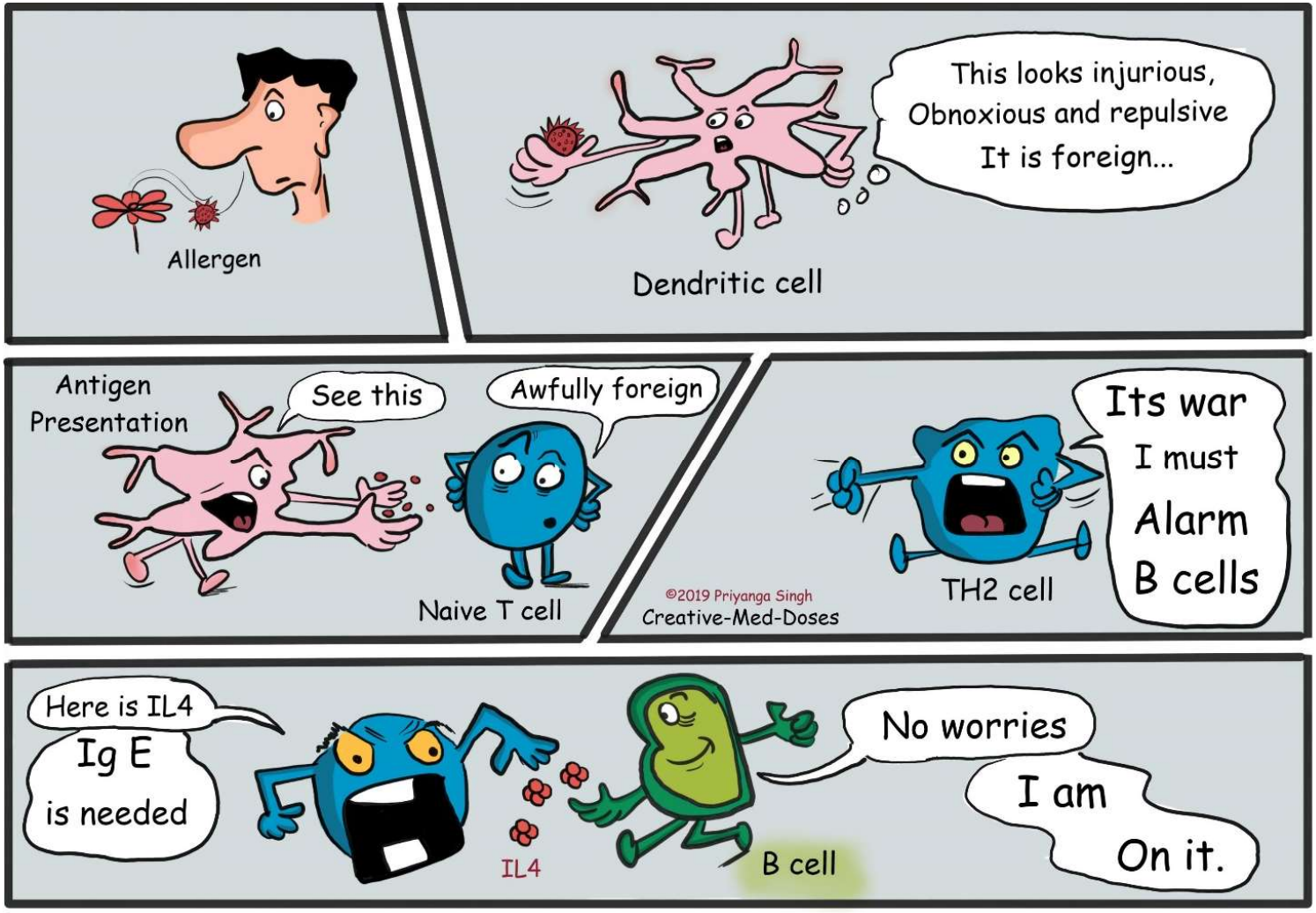

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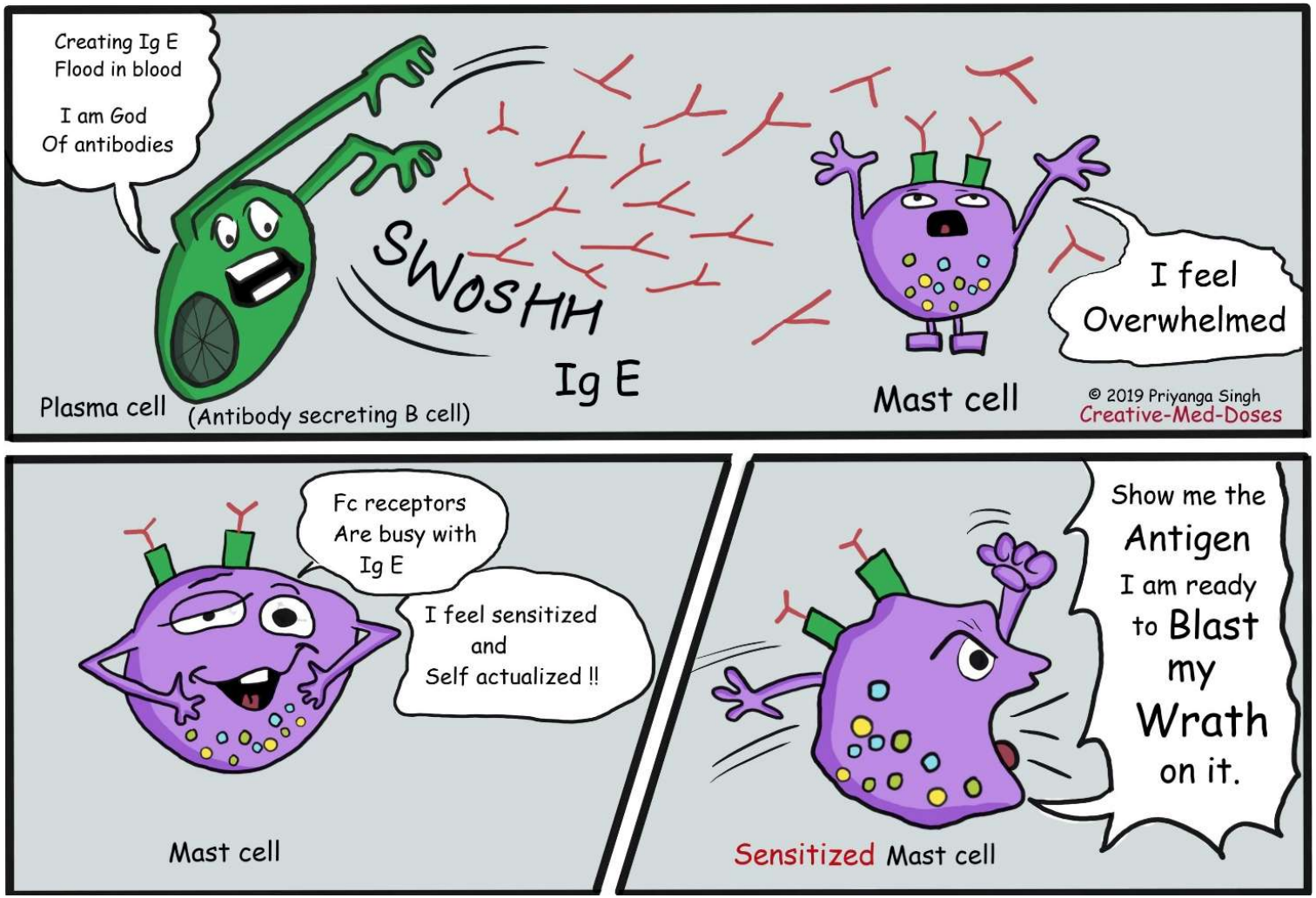

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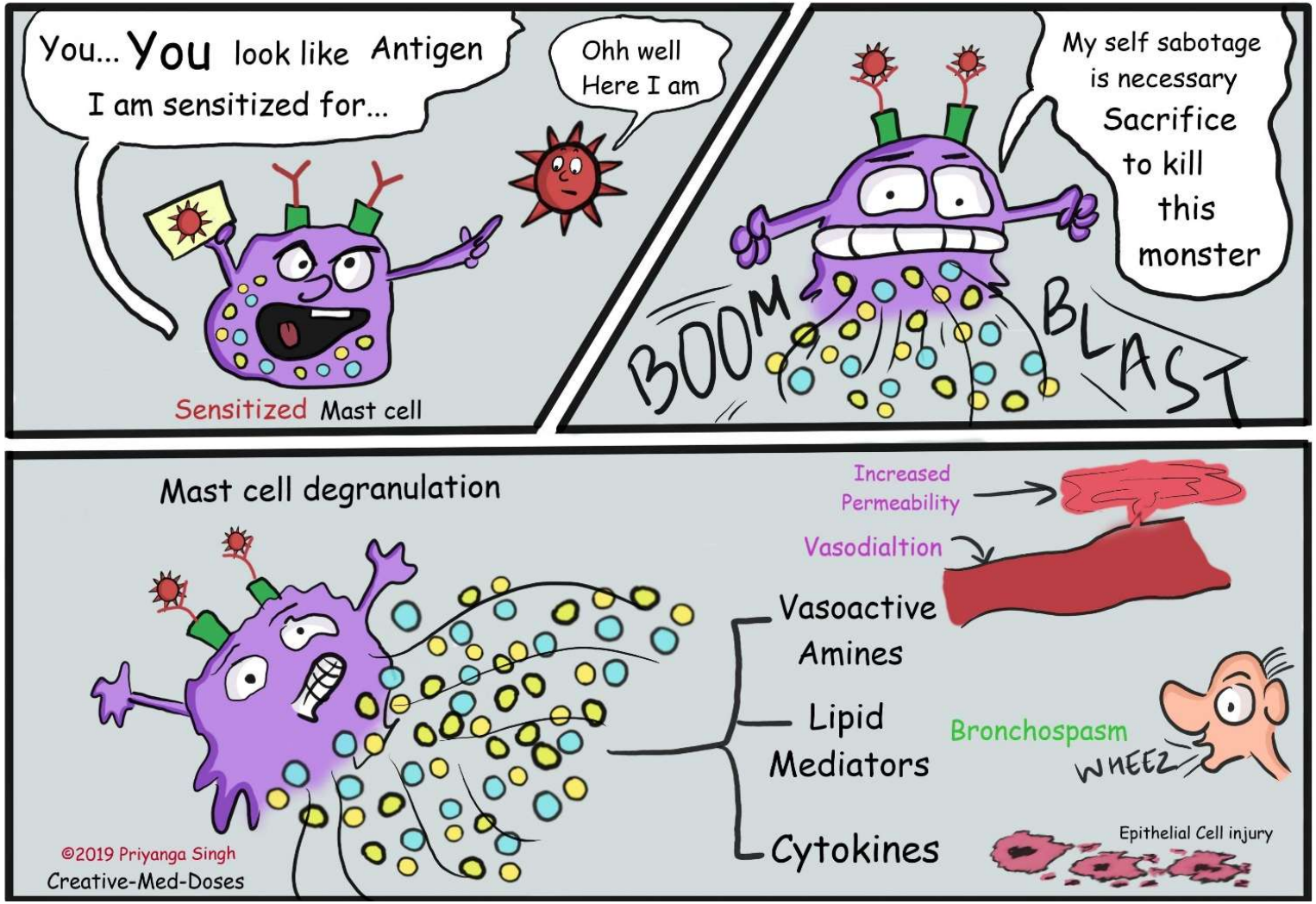
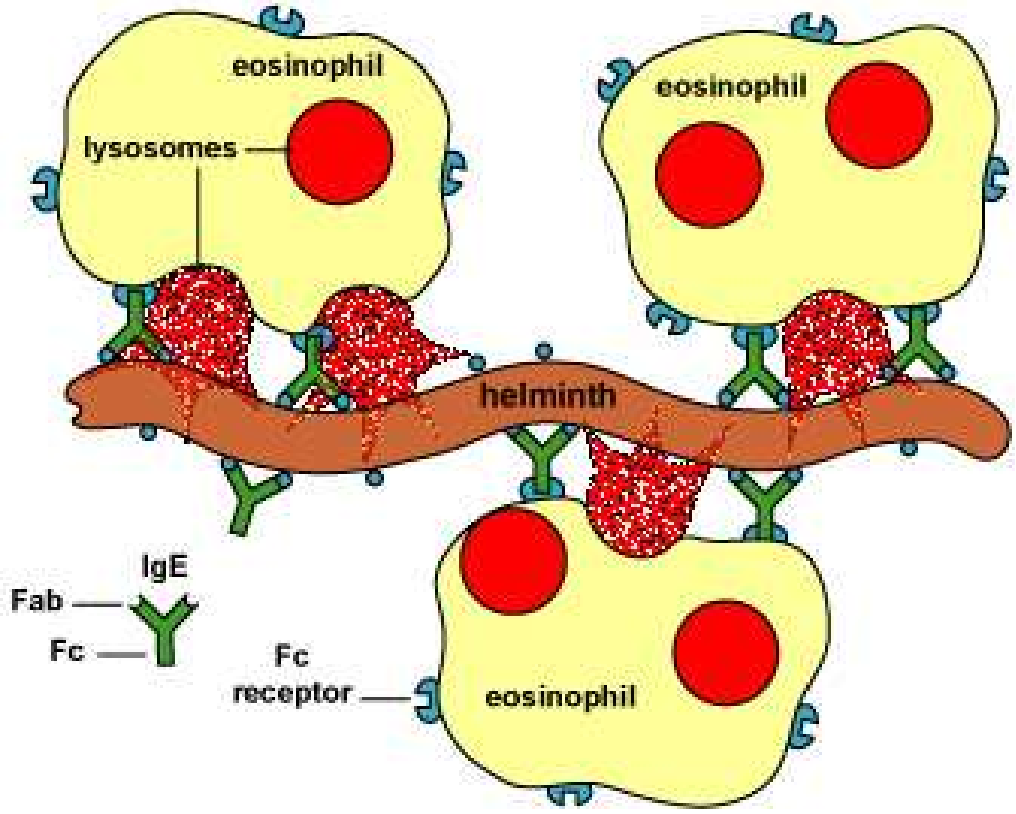


Type I hypersensitivity potential use

- Fight parasite and helminth infections



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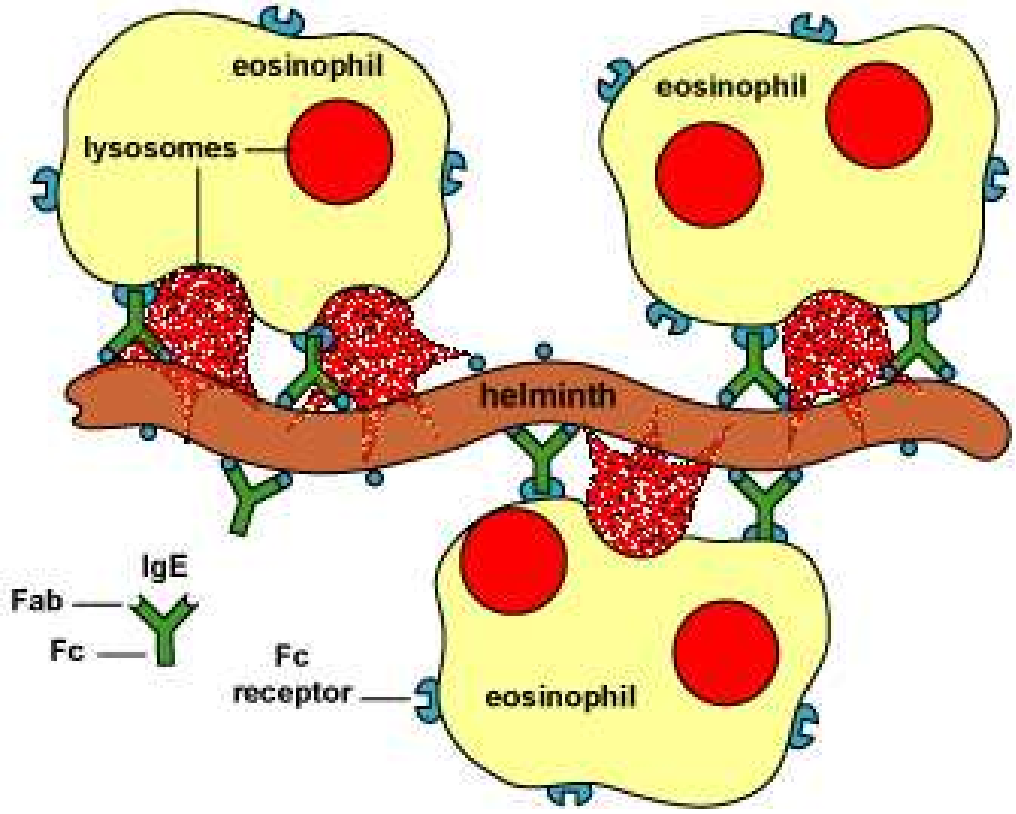
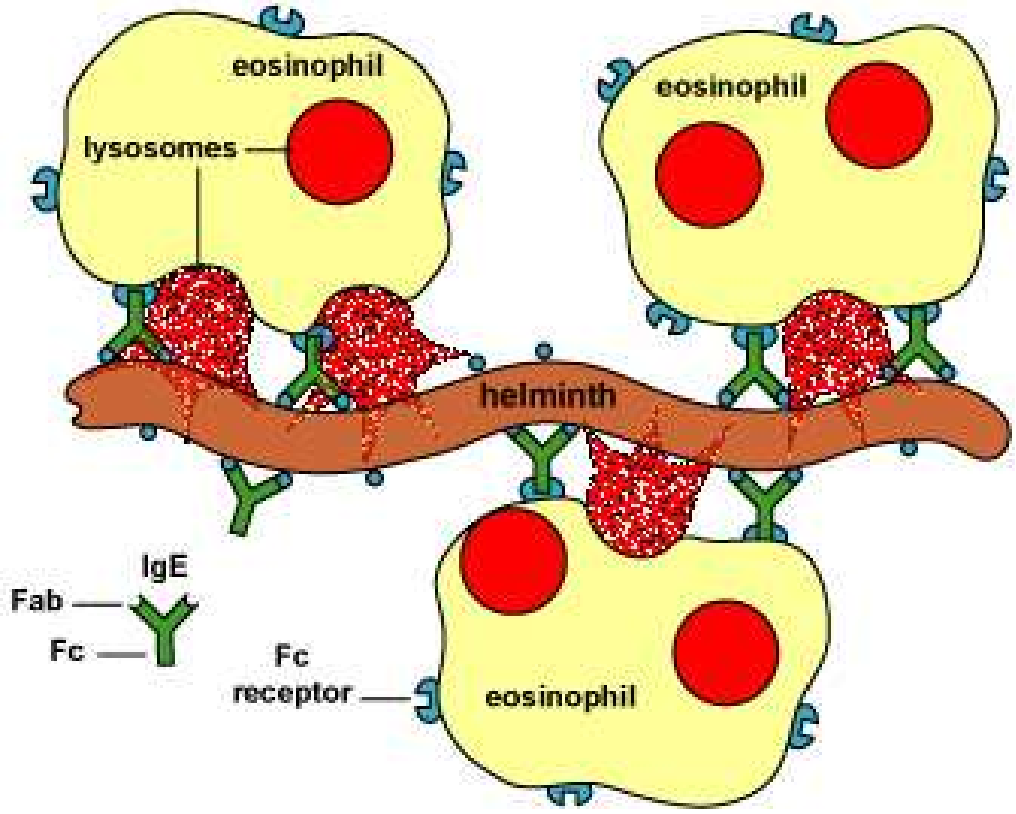


Type I hypersensitivity potential use

- Fight parasite and helminth infections
- Parasites not a problem in developed countries
- IgE does not have a clear purpose in humans in developed countries



Type I hypersensitivity prevalence

31,8% of adults reported to have some form of seasonal or food allergy

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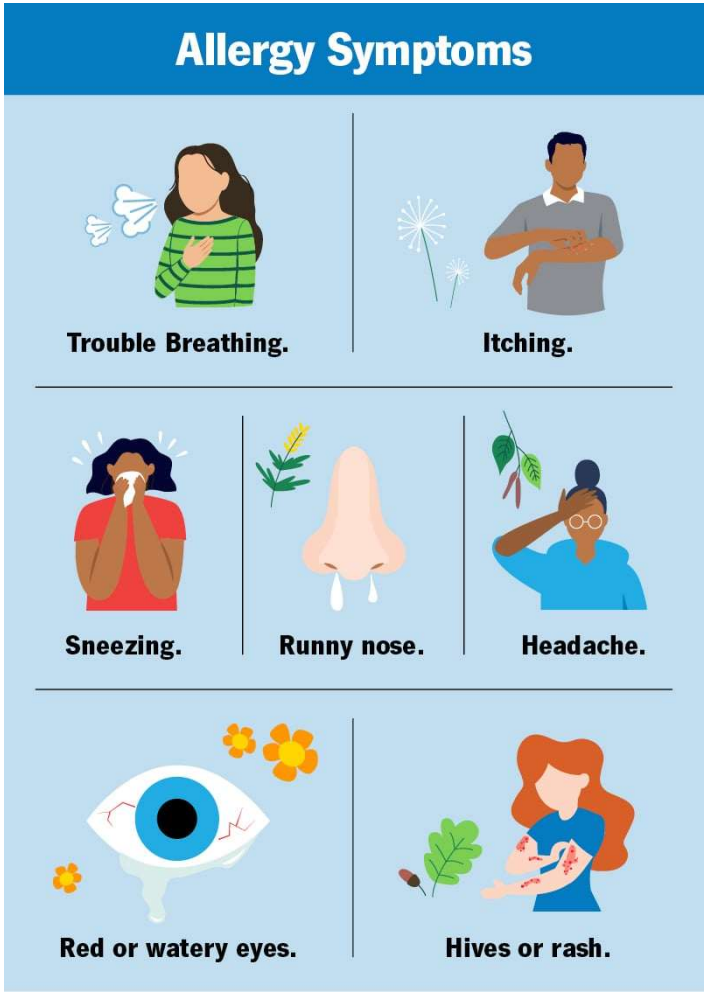
National Center for Health Statistics, National Health Interview Survey, 2021

Type 1 allergy symptoms

- Local reactions
- Mild systemic reactions



Cleveland clinic website

Type 1 allergy symptoms

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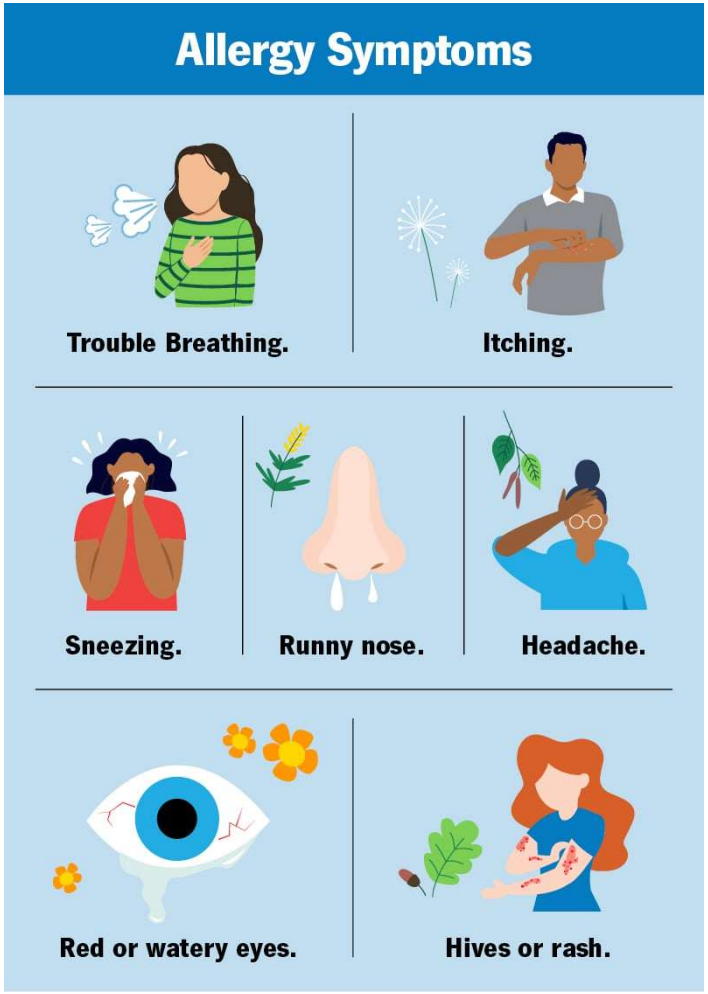
- Decrease cognitive function, productivity and general quality of life (Canonica et al., 2008)



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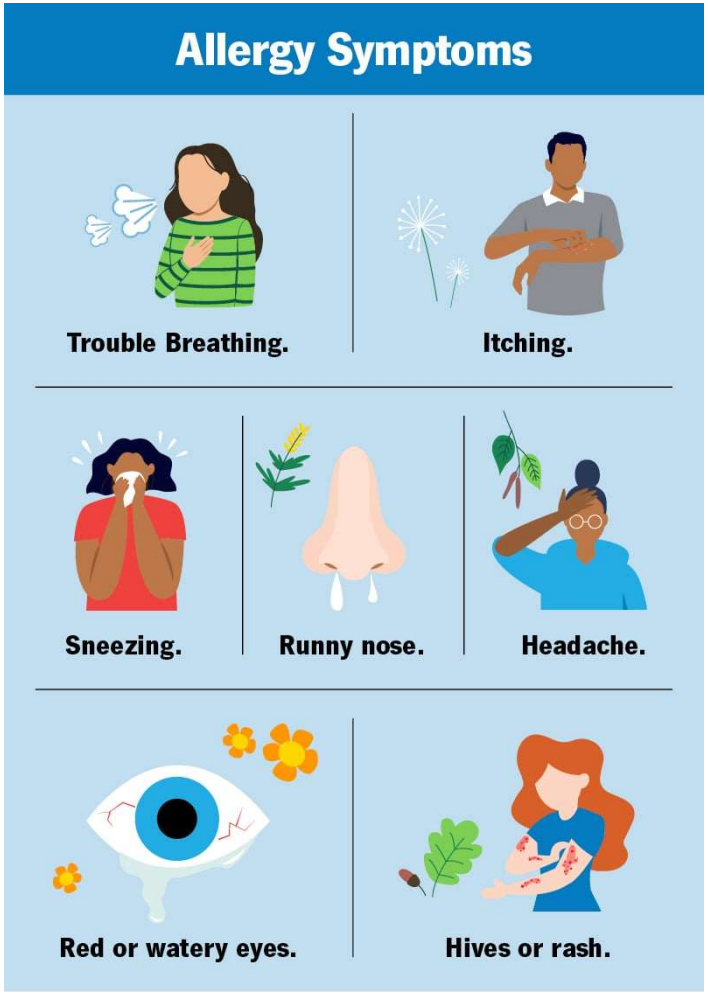
- Symptomatic treatment using antihistamines and corticosteroids



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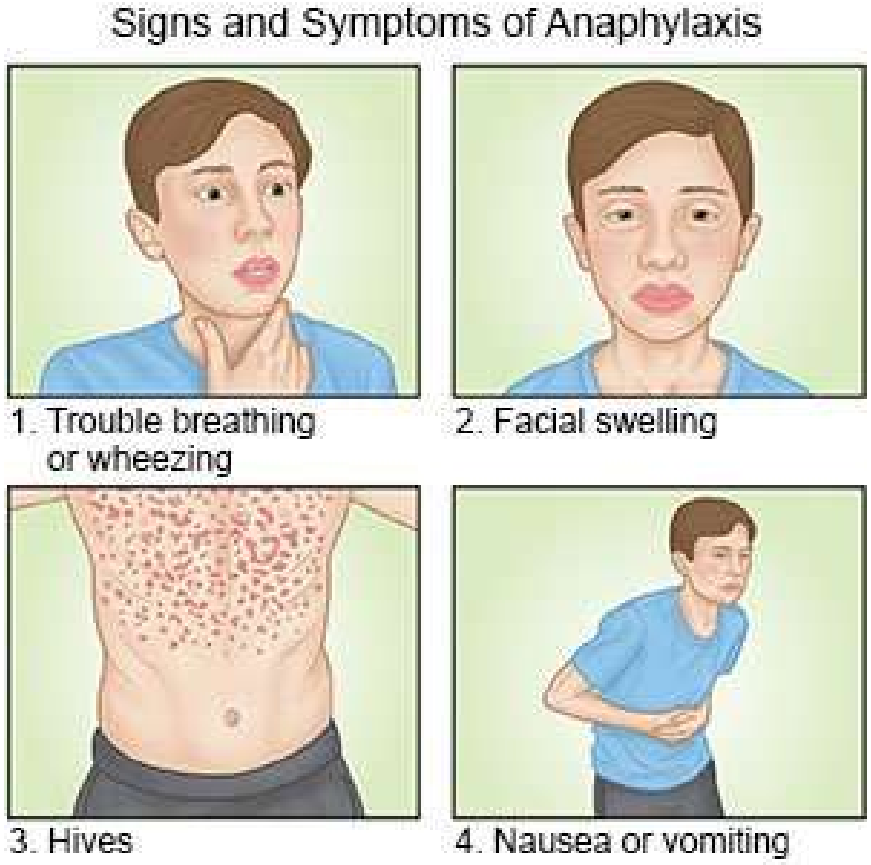
Type 1 allergy symptoms

- Severe systemic reactions often from food and insect venom allergies

"Anaphylaxis causes the immune system to release a flood of chemicals that can cause you to **go into shock — blood pressure drops** suddenly and the **airways narrow**, **blocking breathing**.

Signs and symptoms include a **rapid, weak pulse**; a **skin rash**; and **nausea** and **vomiting**" – Mayo clinic



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- Acute treatment using epinephrine injection

Honeybee venom allergy at a glance

1. Prevalence: 0,3-3,4% of general population and 32% of beekeepers [1] [2] [3]

[1] R. Boyle, M. Elremeli, J. Hockenhull, M. Cherry, M. D. M. Bulsara and J. Oude Elberink, "Venom immunotherapy for preventing allergic reactions to insect stings," *Cochrane database of systematic reviews,* 2012.
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[4] Köhler, J. *et al.* Component resolution reveals additional major allergens in patients with honeybee venom allergy. *J. Allergy Clin. Immunol.* (2014) doi:10.1016/j.jaci.2013.10.060.
[5] Spillner, E., Blank, S. & Jakob, T. Hymenoptera allergens: From venom to 'venome'. *Frontiers in Immunology* (2014) doi:10.3389/fimmu.2014.00077.

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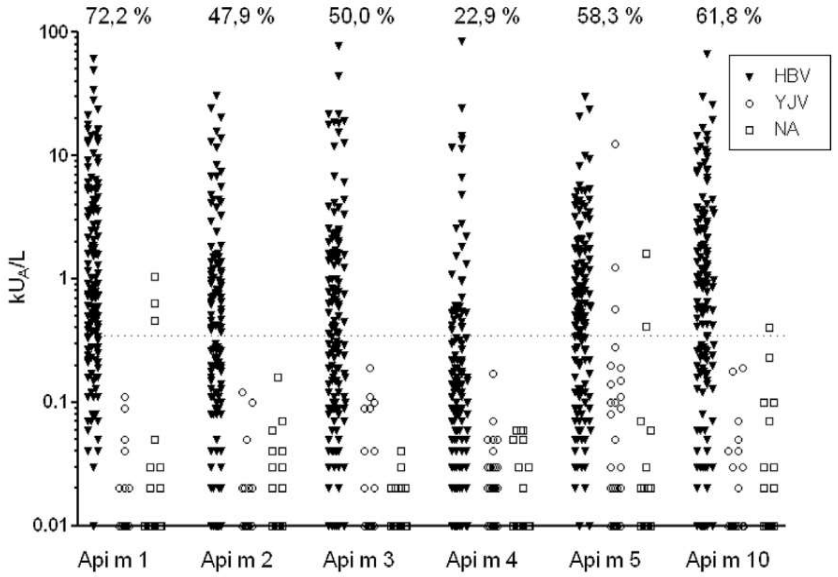

FIG 1. IgE immunoreactivity of individual patient sera with recombinant allergens. IgE reactivity to HBV allergens of sera from patients with HBV allergy (n = 144), patients with YJV allergy (n = 40), and HBV-exposed but nonallergic control subjects (*NA*; n = 40). The lower-end cutoff of the CAP-FEIA (<0.35 kU$_A$/L) is represented as a *dotted line*.

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3. Api m 1 is the most abundant major allergen [5]

Allergen	Name/function	MW (kDa)	% DW
BEES (*Apis mellifera, A. cerana, A. dorsata*)			
Api m 1, Api c 1, Api d 1	Phospholipase A2	17	12
Api m 2	Hyaluronidase	45	2
Api m 3	Acid phosphatase	49	1–2
Api m 4	Melittin	3	50
Api m 5	Allergen C/DPP IV	100	<1
Api m 6	Protease inhibitor	8	1–2
Api m 7	Protease	39	?
Api m 8	Carboxylesterase	70	?
Api m 9	Carboxypeptidase	60	?
Api m 10	CRP/icarapin	55	<1
Api m 11.0101	MRJP 8	65	?
Api m 11.0201	MRJP 9	60	?
Api m 12	Vitellogenin	200	?

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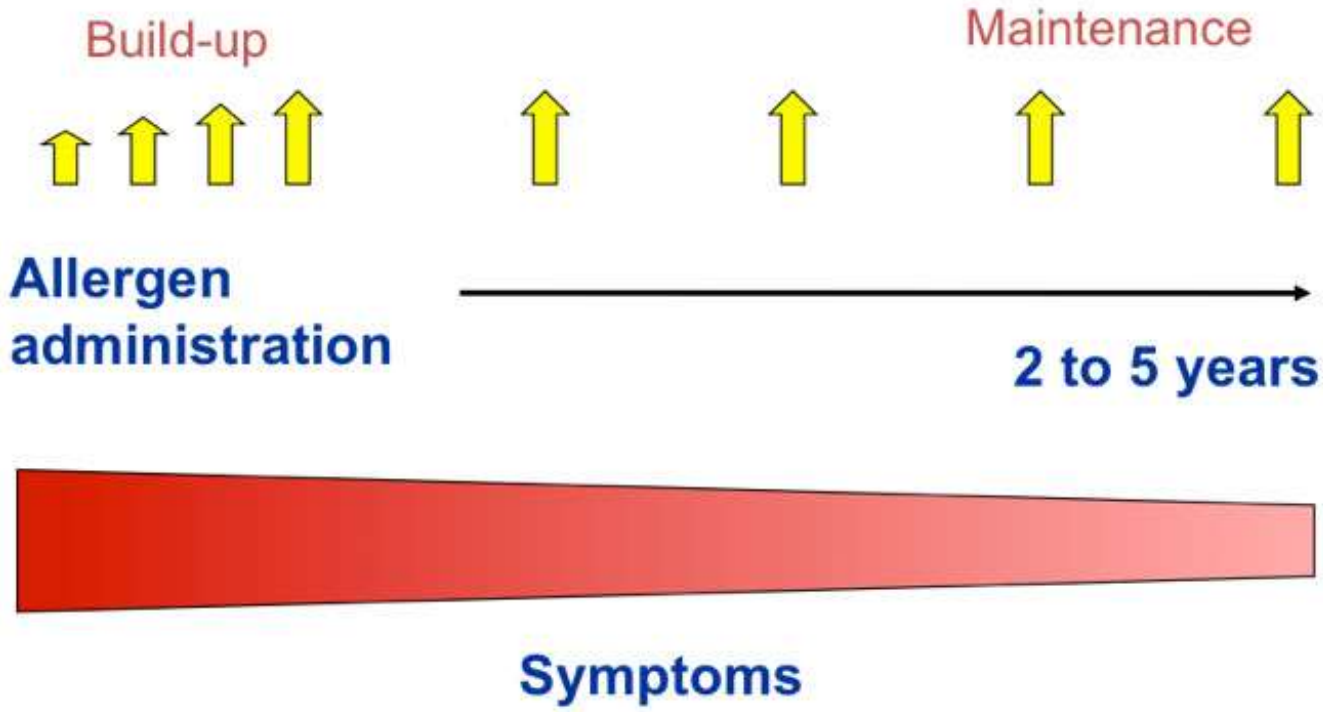
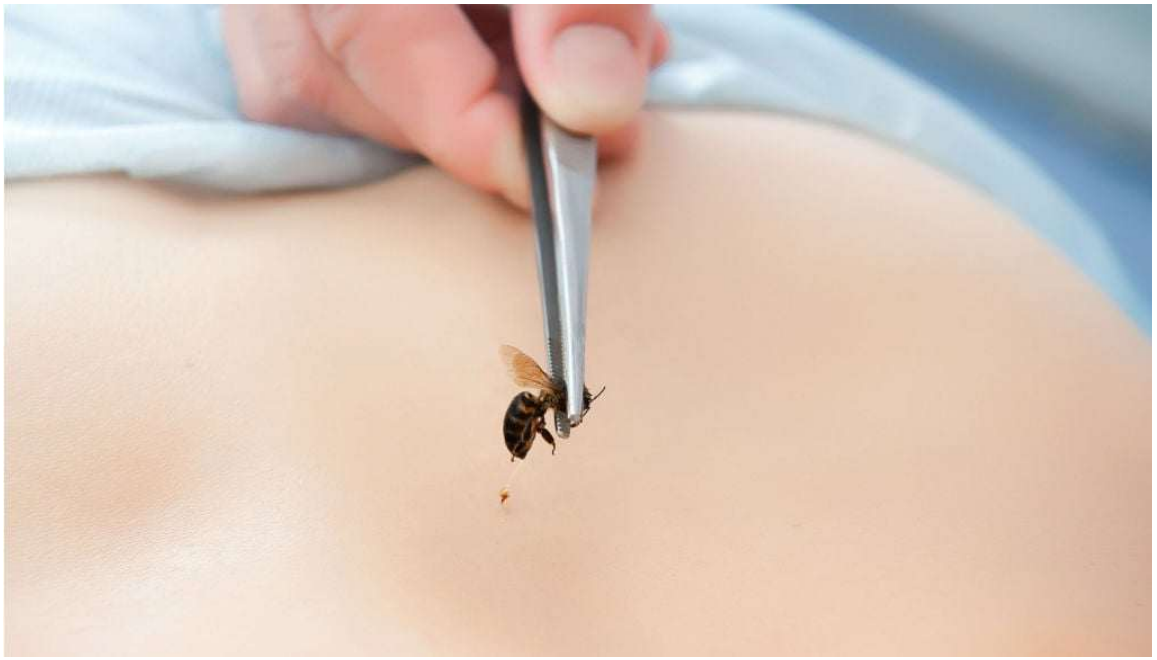
Allergy immunotherapy (AIT)

- Culprit allergen extracts administered subcutaneously or sublingually
- In clinical practice since 1911 (L. Noon 1911)



Honeybee venom immunotherapy (VIT)

- 5-year treatment duration



G Sturm et al., 2018

Honeybee venom immunotherapy (VIT)

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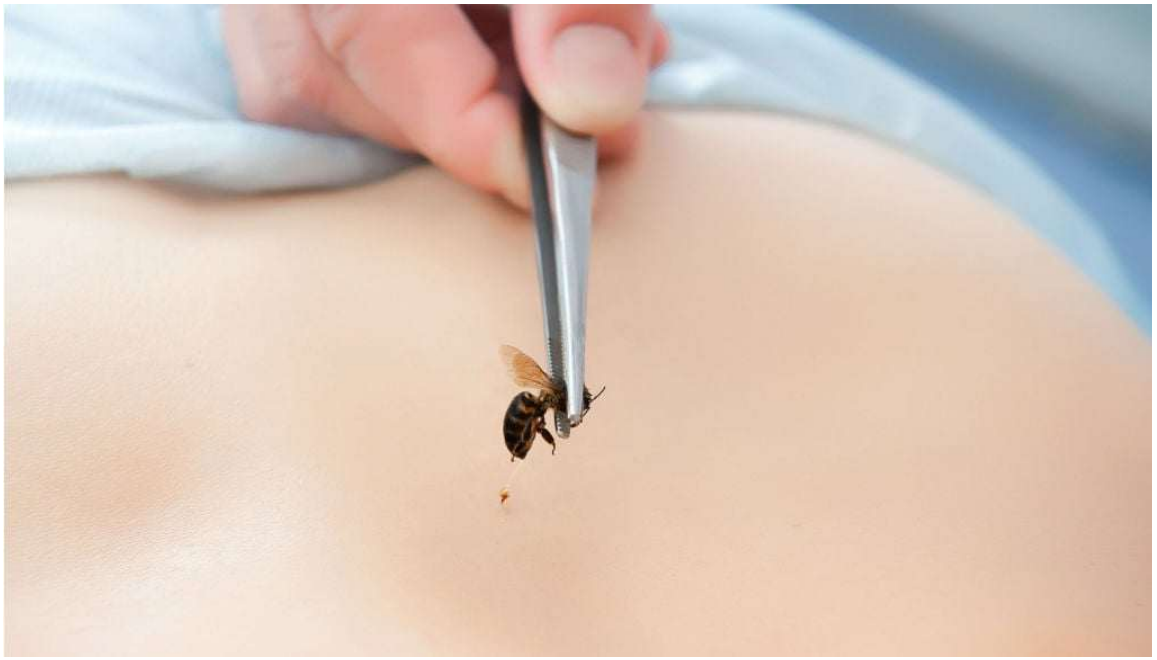
- Around 80% treatment success (95% for wasp VIT)



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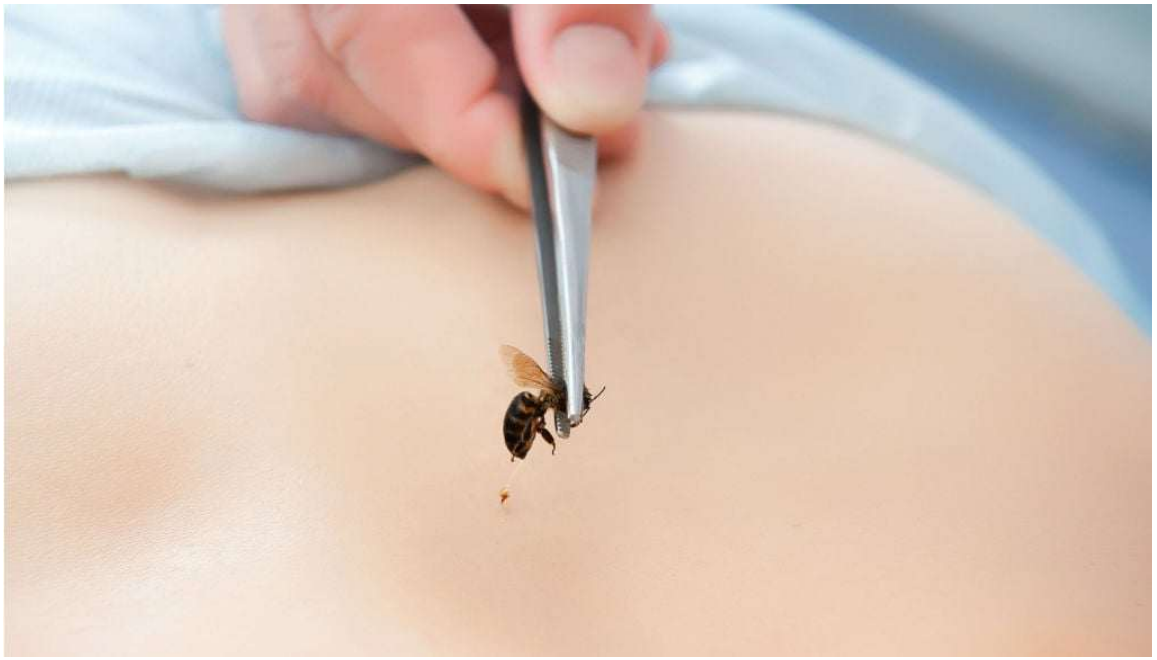

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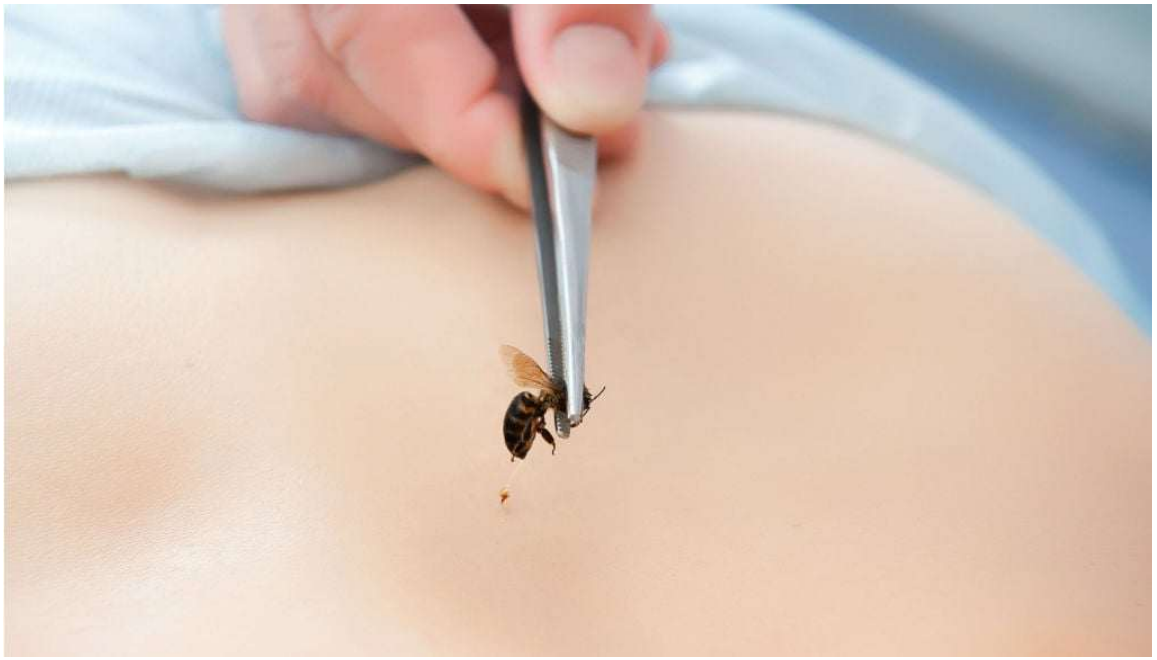

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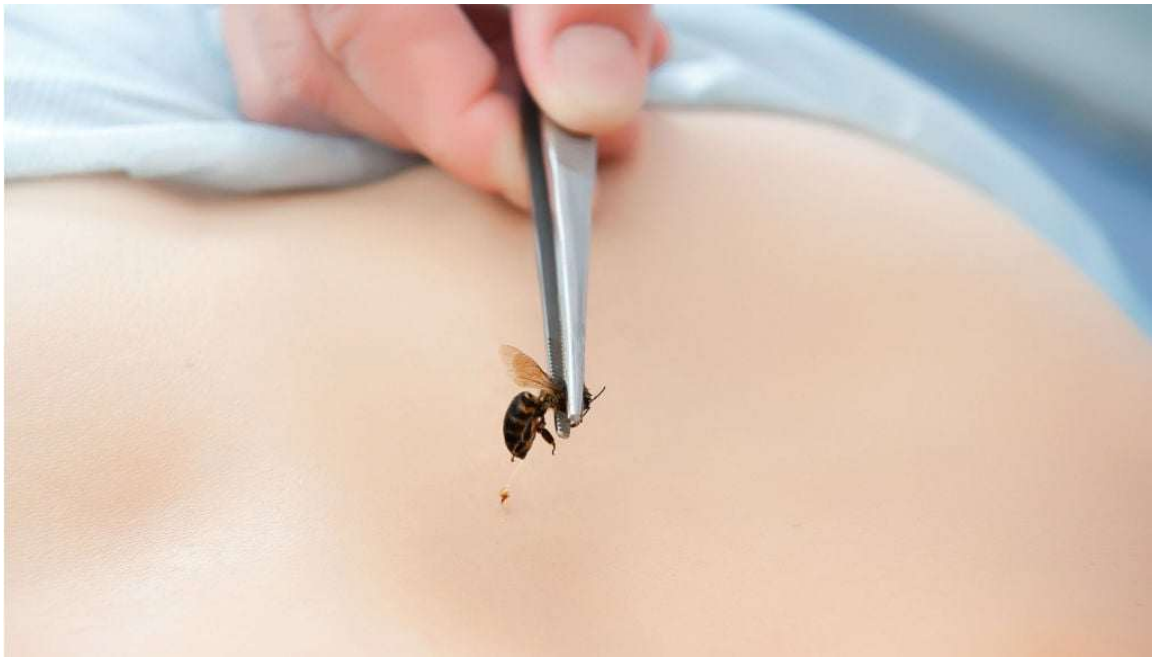
- Honeybee VIT works – but not as well as wasp VIT!



G Sturm et al., 2018

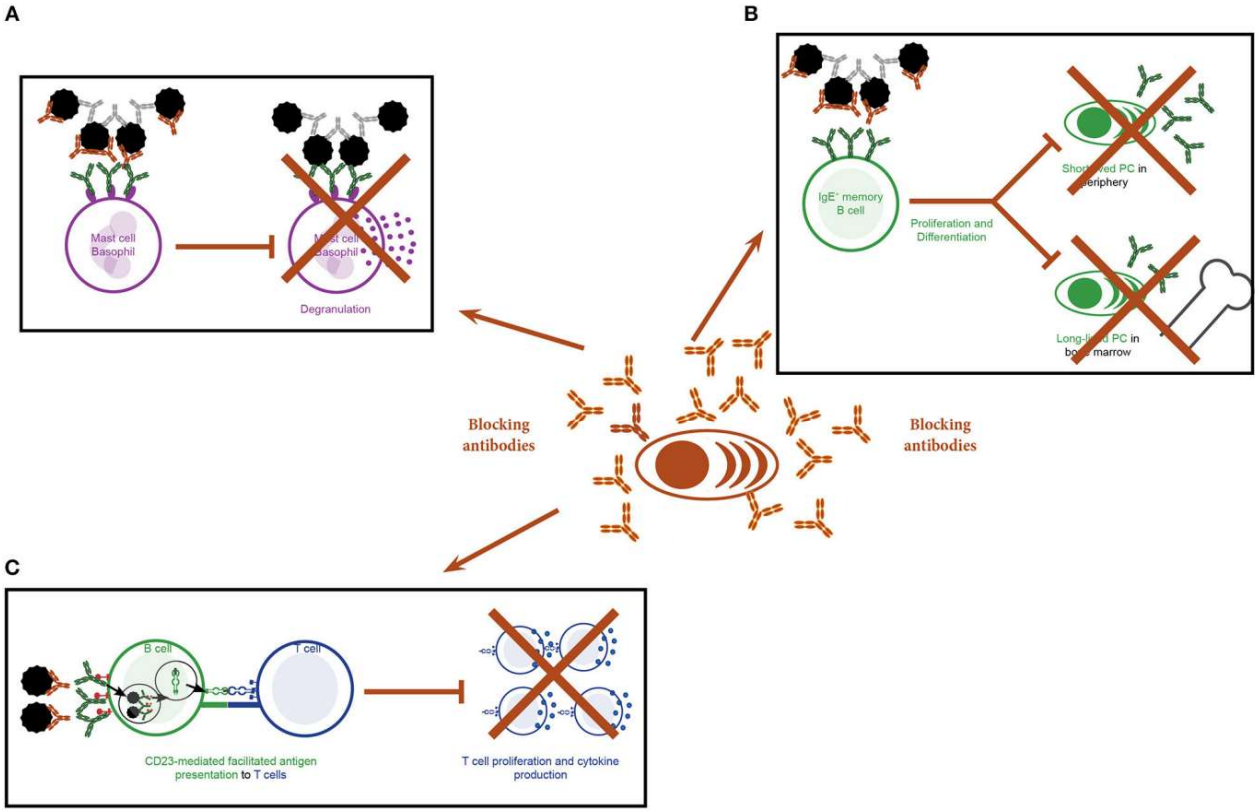
Passive immunotherapy

- Administer allergen specific IgG antibodies to block sIgE epitopes

Dorna et al 2019

Passive immunotherapy

- Administer allergen specific IgG antibodies to block sIgE epitopes
- sIgG will block sIgE epitopes and mimic serologically what happens during AIT



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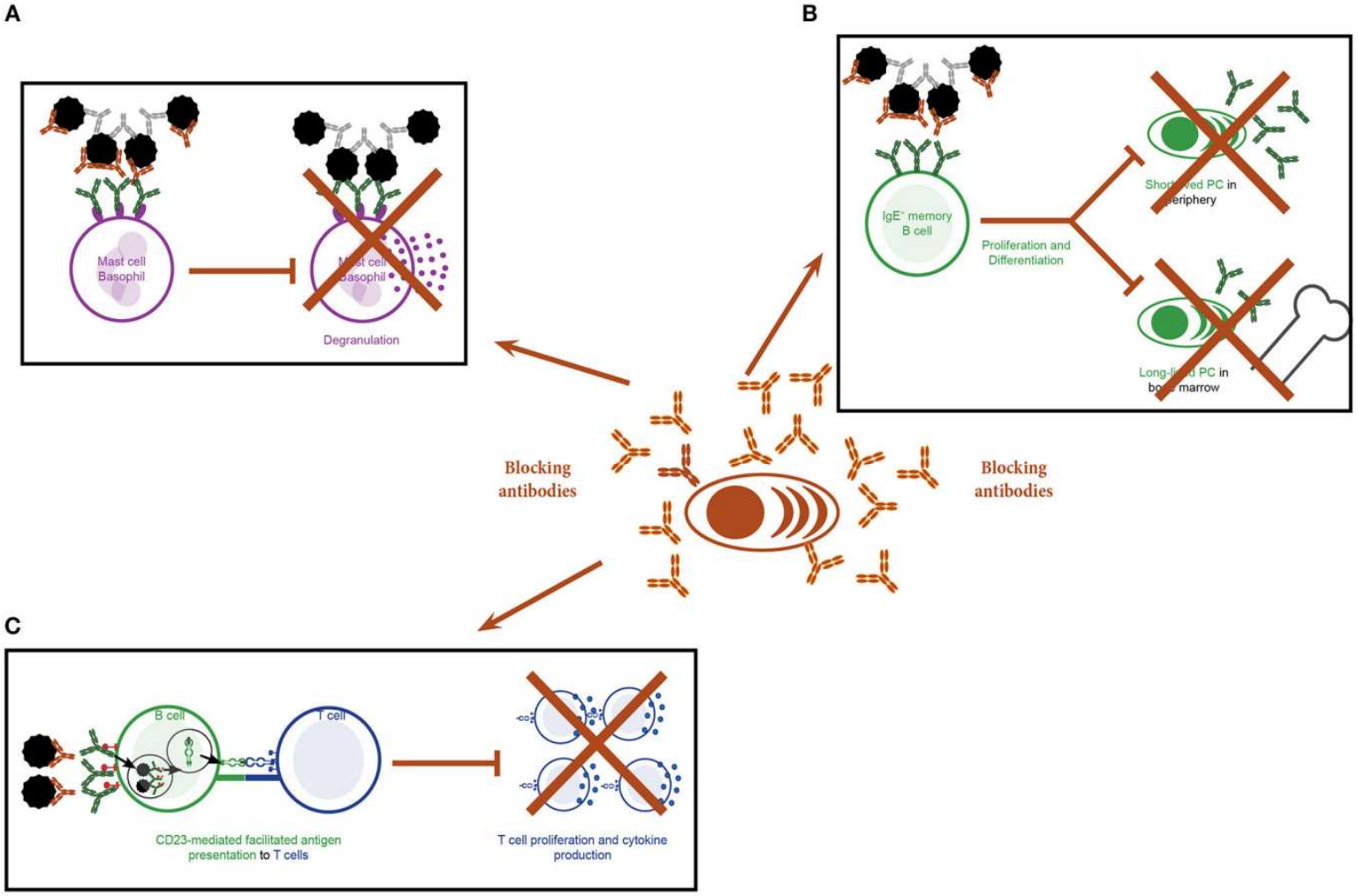

Dorna et al 2019

Project aim

The aim of this PhD project was to generate **fully human monoclonal antibodies** specific for honeybee venom major allergens **Api m 1, 2, 3, 5,** and **10**.

Selected antibodies, in therapeutic **IgG4 format**, will be tested for their ability to block binding of honeybee venom allergen specific IgE to cognate allergens, for use as a **potential passive immunotherapy** against honeybee venom allergy.

How to find allergen specific antibodies?

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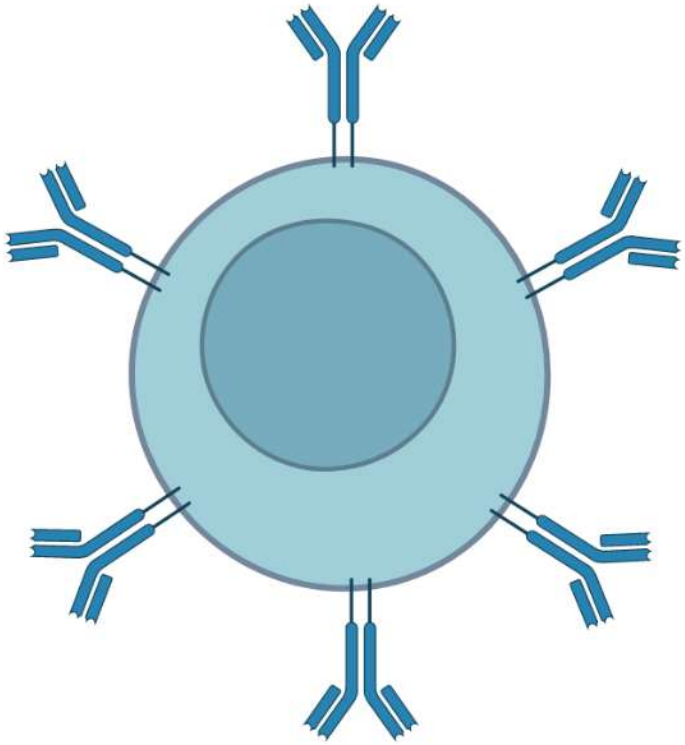
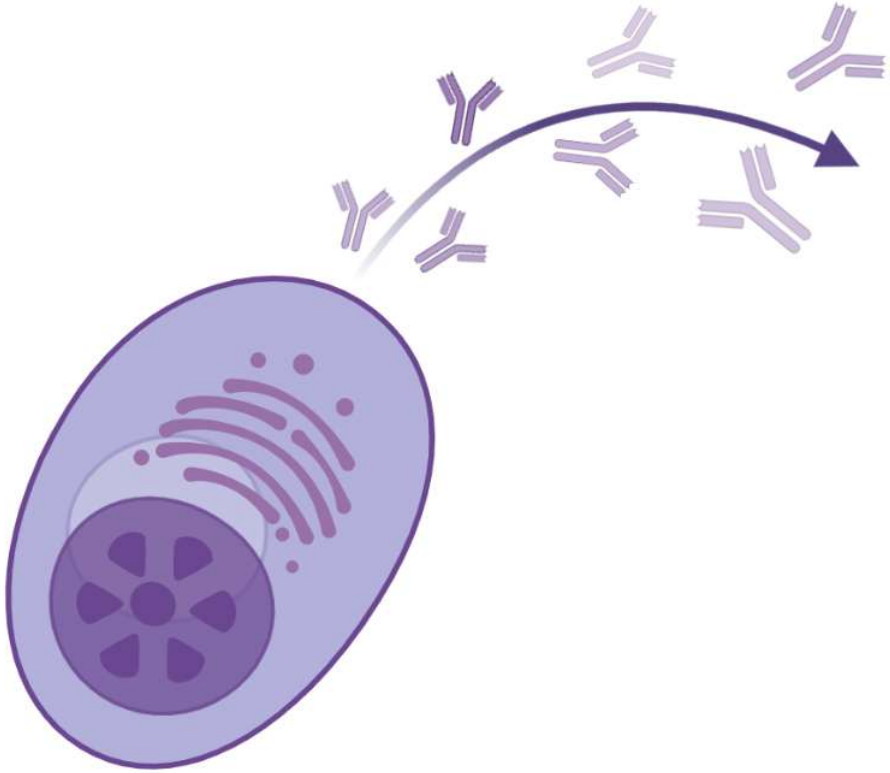


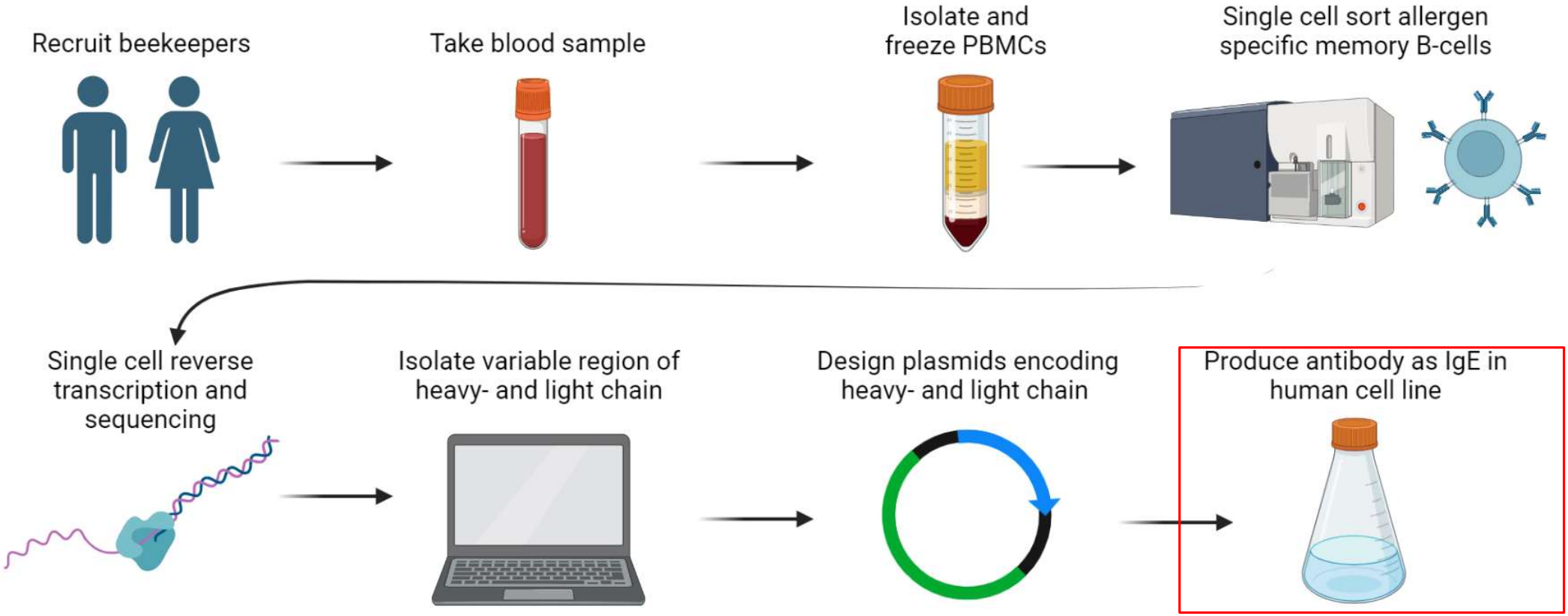
Memory B cell



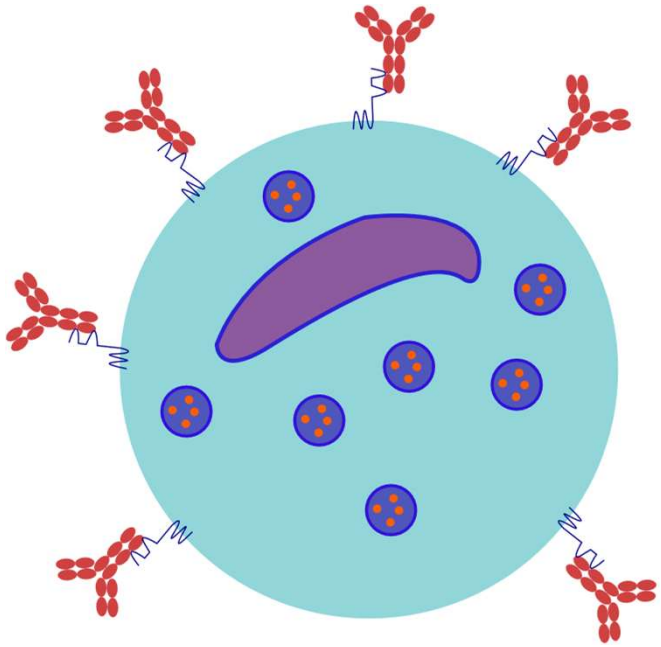
Plasma cell

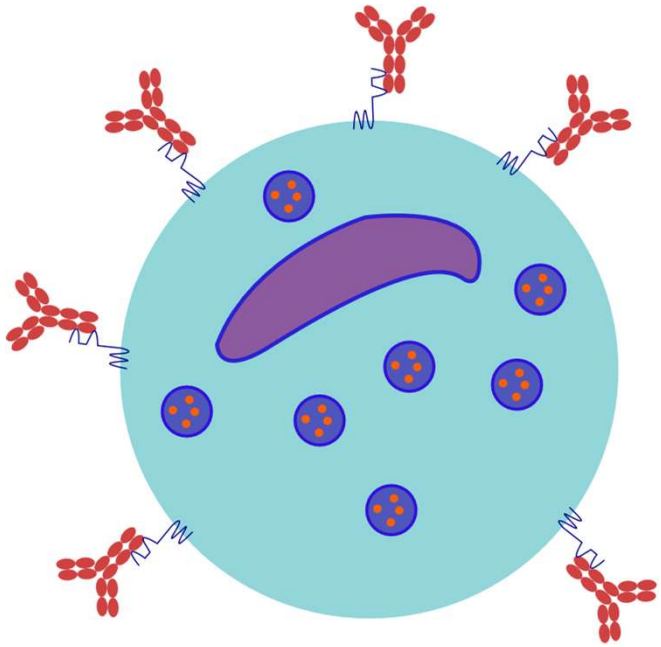
How to find allergen specific antibodies?

Isolating honeybee venom specific memory B cells



Inhibition of basophil activation





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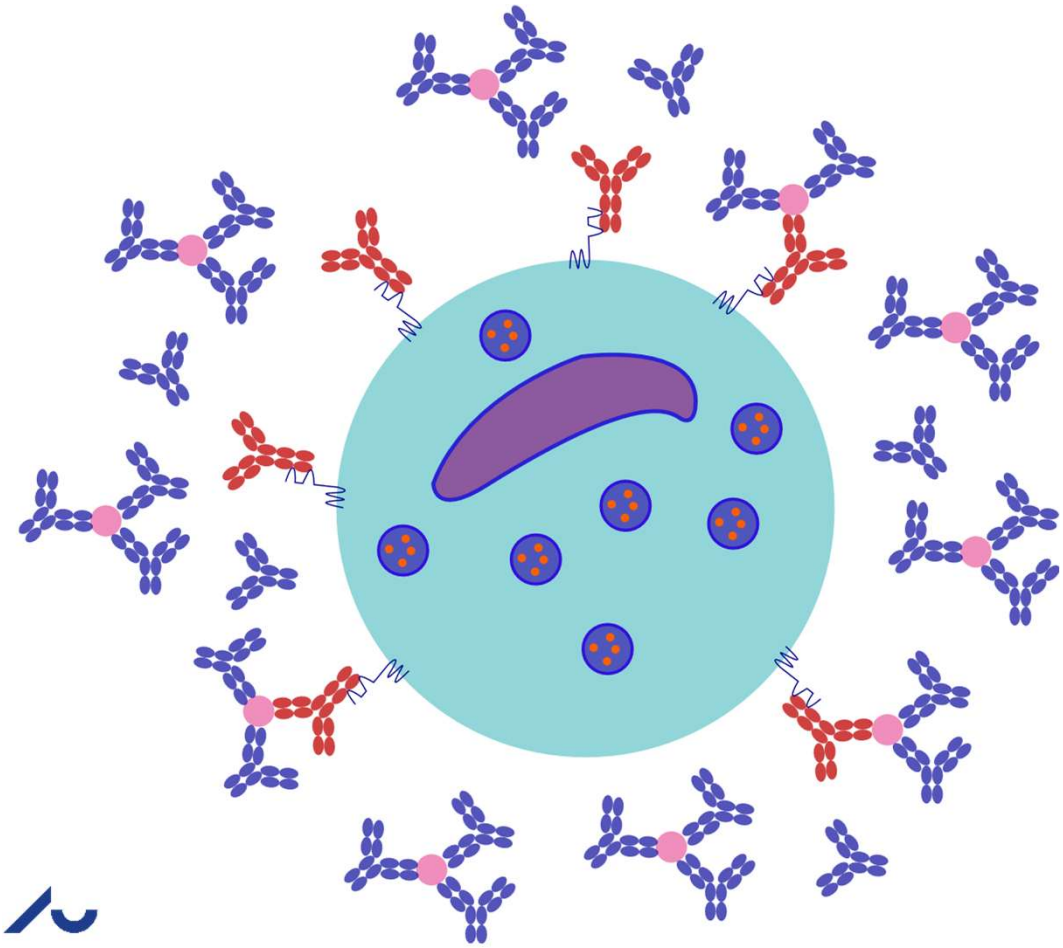

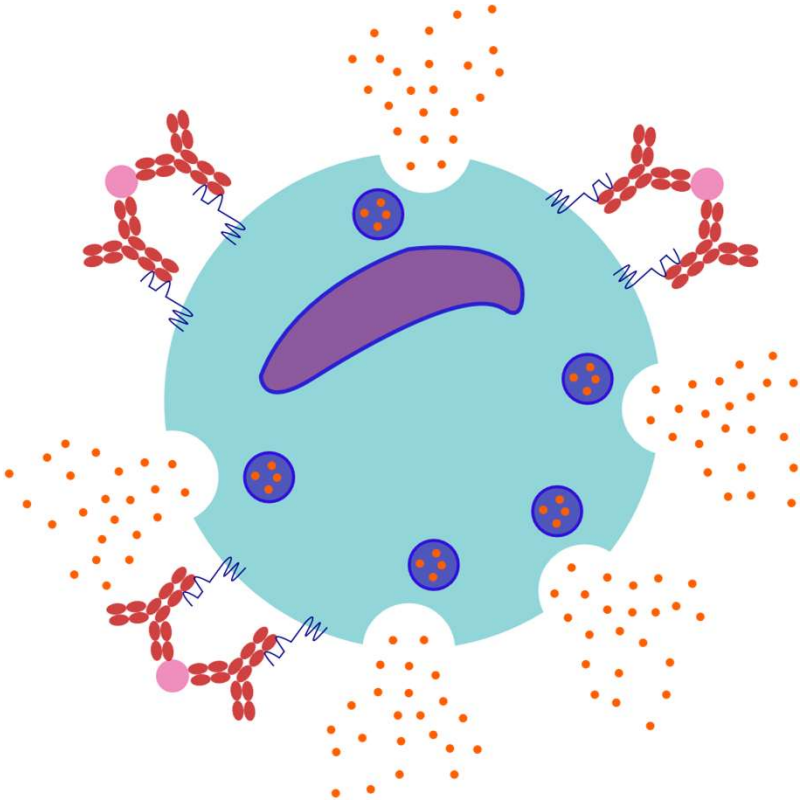

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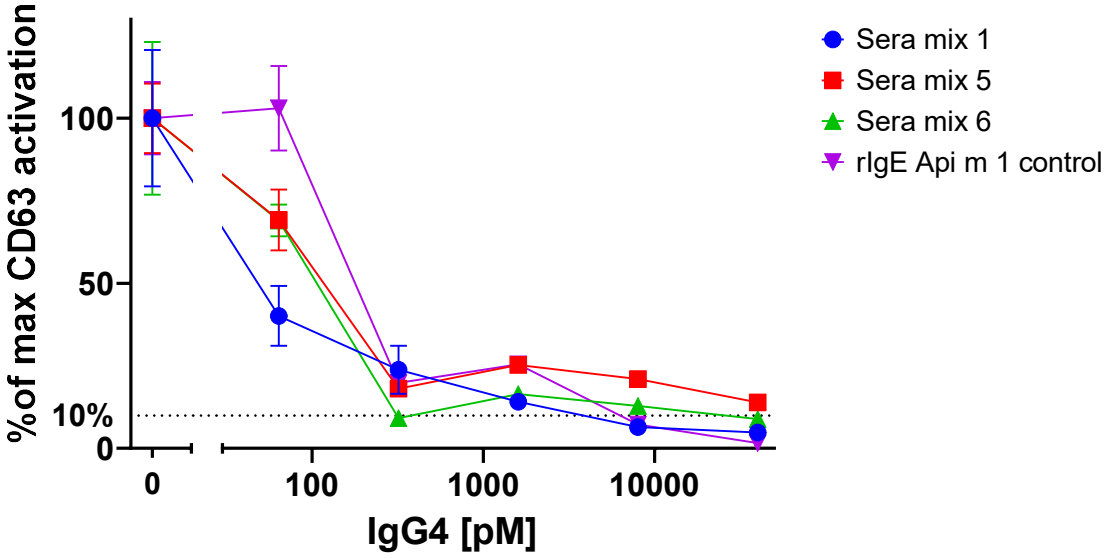
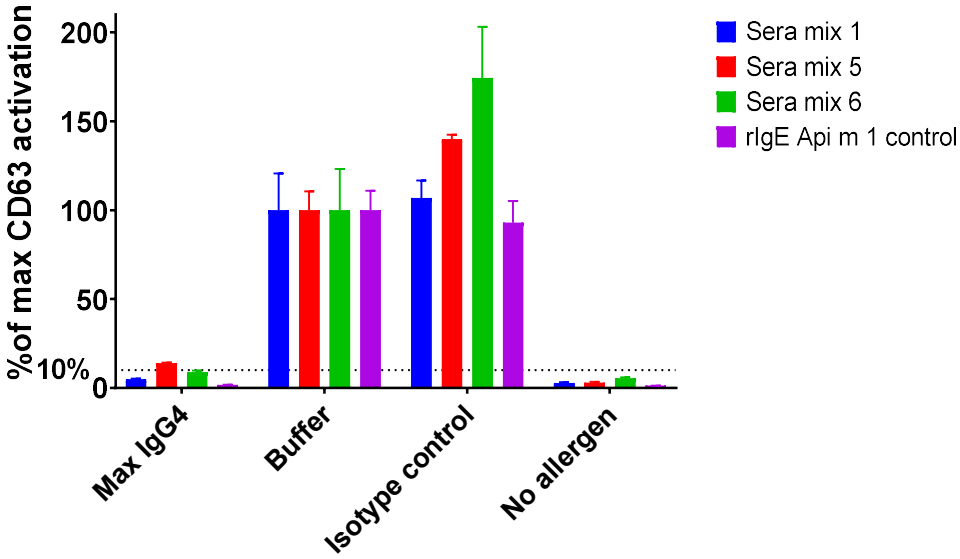
Passive patient sera sensibilization BAT blocking





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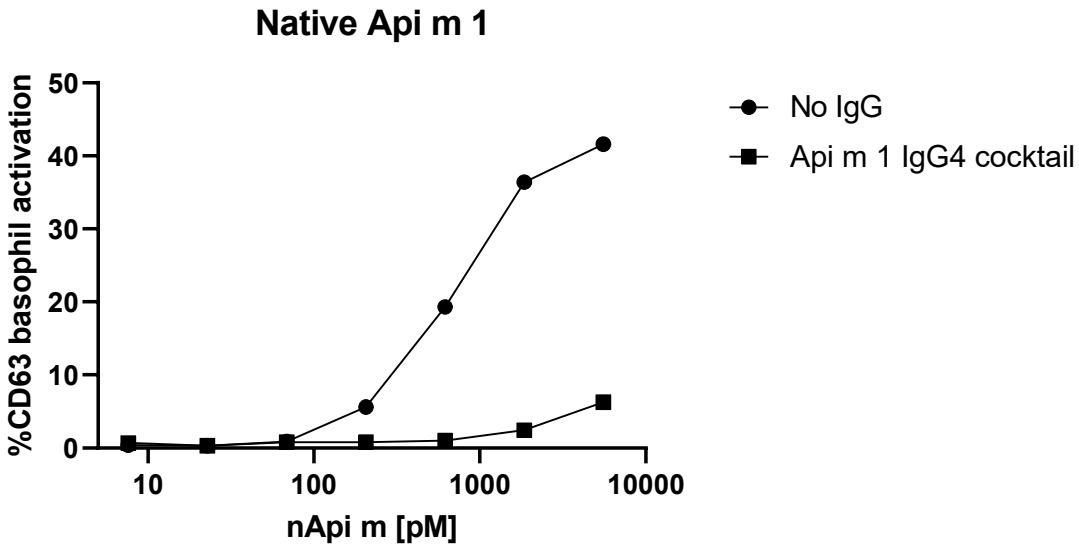
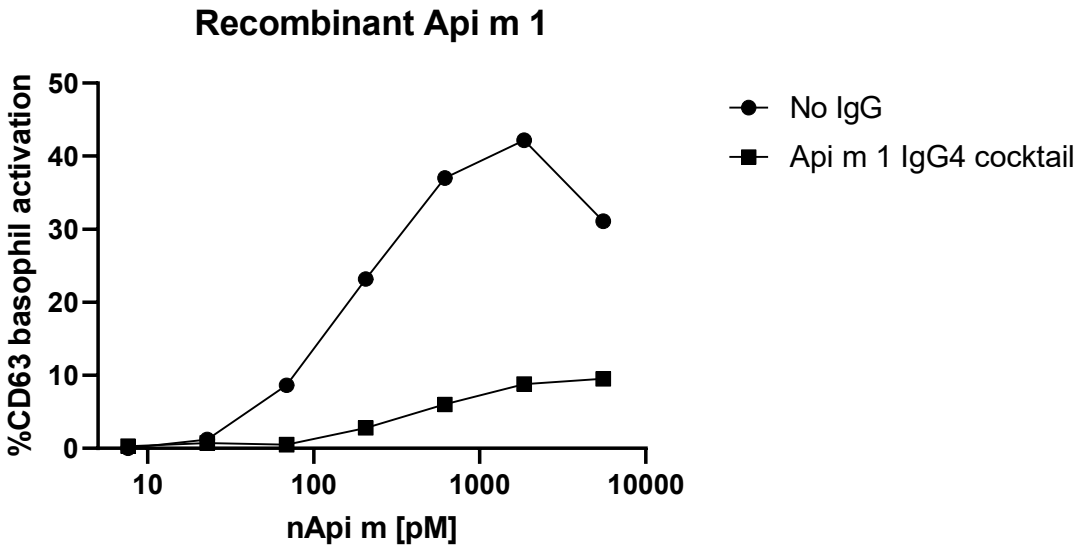
Full blood BAT inhibition (r)Api m 1





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Thank you for your attention