CORSO DI IMMUNOLOGIA

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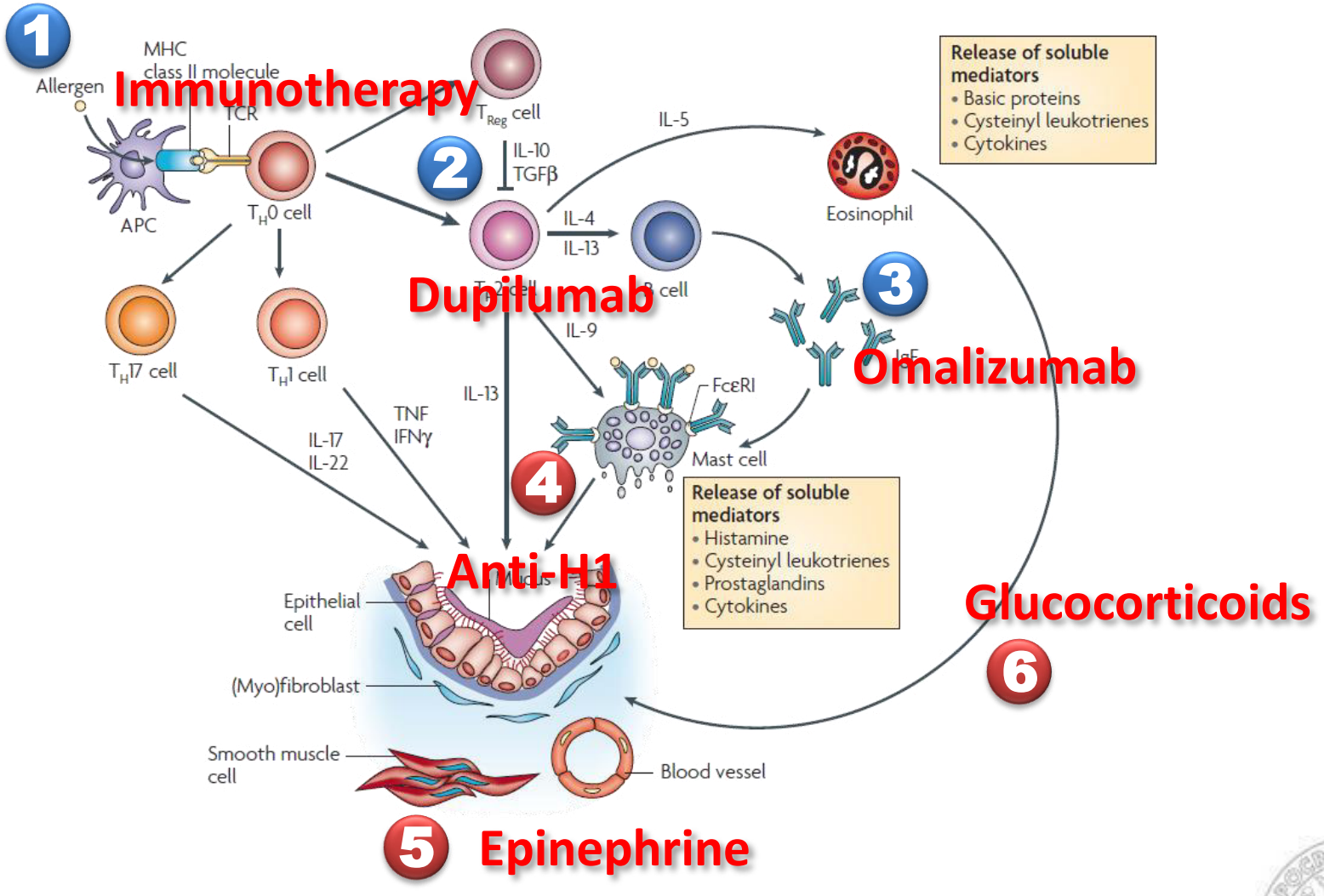
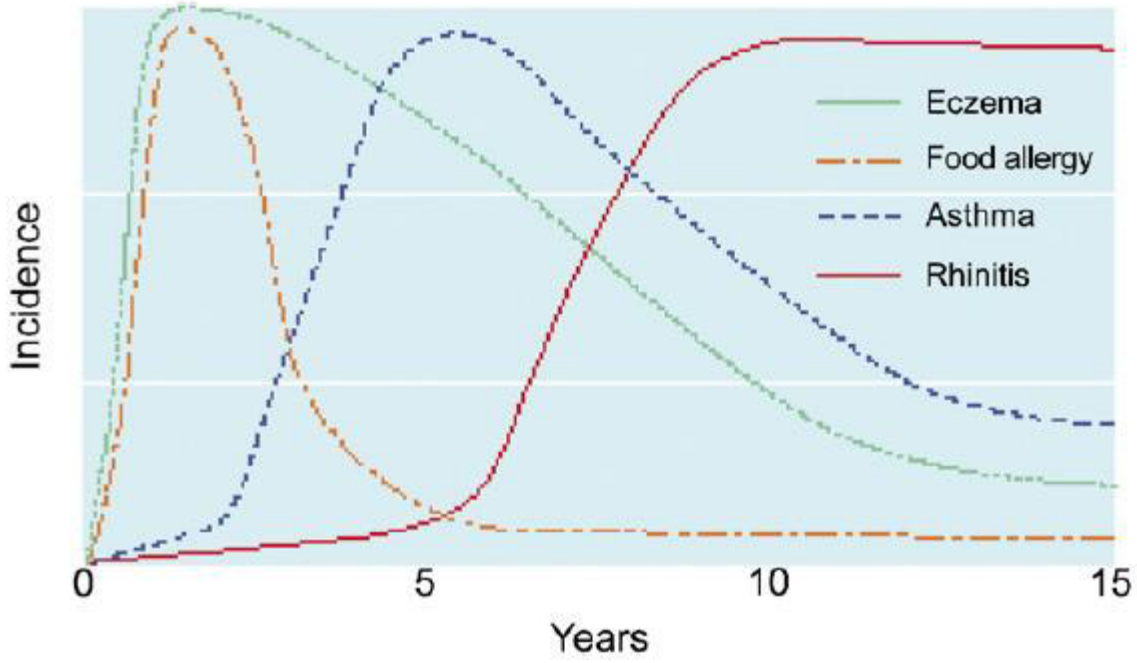
A summary of allergic mechanisms



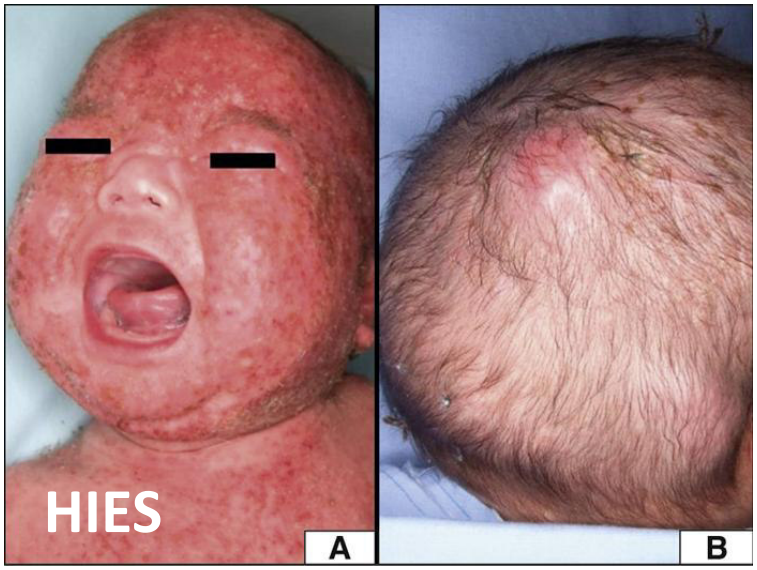
Holgate & Polosa, Nat Rev Immunol 2008;8:218

The atopic march



Spergel, Ann Allergy Asthma Immunol 2010;105:99


Omenn Syndrome


HIES
A
B

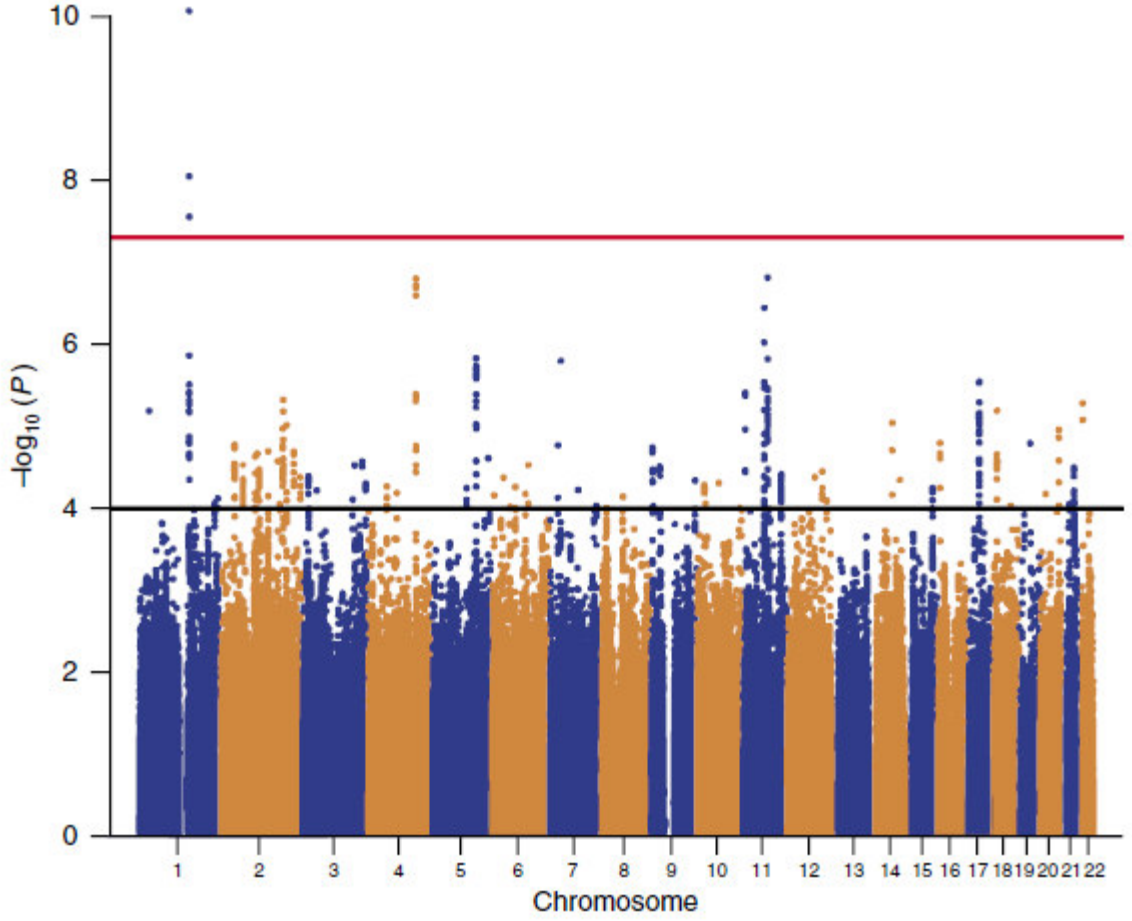

IPEX


Atopy


WAS

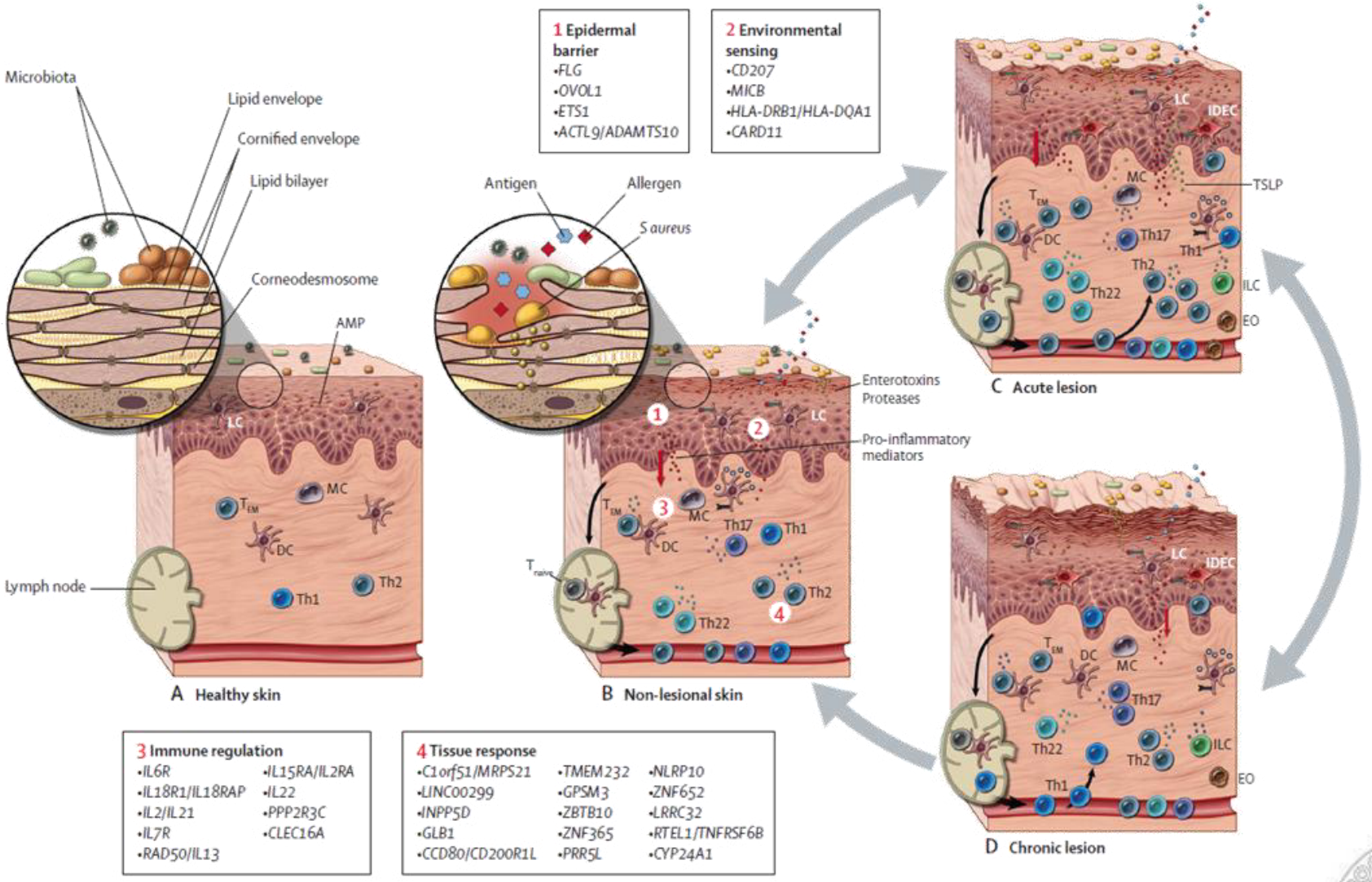
	Omenn Syndrome	Wiskott-Aldrich	Hyper-IgE Syndrome	IPEX	Atopic Eczema
Allergy	No	Food	Food (DOCK8)	Food	Yes
Auto-immunity	Yes	Yes	Yes	Yes	?
Immune deficiency	Severe	Yes	Yes	Mild	?
IgE levels	Very High	High	Very High	High	High
Eosinophils	High	High	High	Variable	High
IL-4 levels	Low	Low	Not Changed	Not Changed	High
Treg function	Defective	Defective	Defective	Absent	Defective?
Other	Oligoclonal T Cells	Low Platelets	Low Th17	Autoreactive T/B Cells	Reduced CD8 T Cells
Gene defect	RAG1/RAG2	WASP	STAT3/DOCK8	FOXP3	Various

Association results of the meta-GWAS on the atopic march



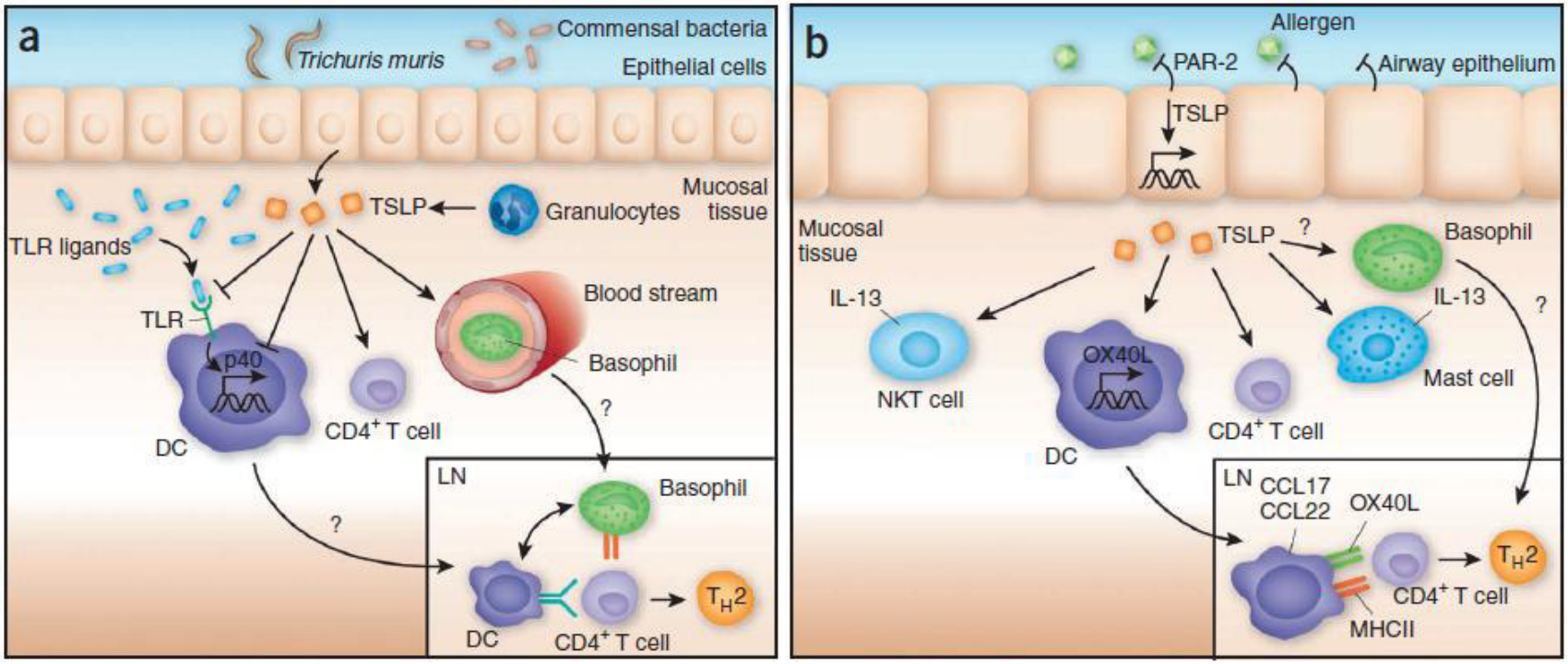
Marenholz et al, Nat Commun 2015;6:8804

Pathophysiological changes in atopic dermatitis



Weidinger & Novak, Lancet 2016;387:1109

TSLP induces Th2 cytokine responses after exposure to helminths and allergens



Ziegler & Artis, Nat Immunol 2010;11:289

TABLE II. Clinical and immunologic differences among 3 common forms of allergic disease

	Peanut-induced anaphylaxis	EoE	Delayed anaphylaxis to mammalian meat (alpha-gal syndrome)
Relevant allergens	Ara h 1, Ara h 2 (peanut)	Bos d 4, Bos d 5 (cow's milk) Wheat proteins	Alpha-gal*
Route of sensitization	Skin	Esophagus (?) Skin unlikely	Skin (Tick bites)
Risk factors	Eczema	Unknown	Outdoor activity Lipitor (?)
Serum IgE antibody	High-titer IgE to peanut proteins (5-500 IU/mL)	Low-titer or negative IgE to cow's milk proteins† (<0.1-2 IU/mL)	High-titer IgE to alpha-gal (often 10% to 30% of total IgE)
Treatment	Diet free of peanut Oral immunotherapy	Diet free of cow's milk with swallowed cromolyn 4 times daily‡	Diet free of mammalian products
Prevention	Prevent eczema Feed peanut from 3 mo	Not known	Avoid tick bites
Timing of reaction to foods	15-60 min to local and generalized swelling§	12-24 h	3-6 h after eating red meat

Platts-Mills et al. J Allergy Clin Immunol 2016;137:1662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PHYSICO-CHEMICAL PROPERTIES OF HUMAN REAGINIC ANTIBODY

IV. Presence of a Unique Immunoglobulin as a Carrier of Reaginic Activity[1]

KIMISHIGE ISHIZAKA, TERUKO ISHIZAKA AND MARGARET M. HORNBROOK

From the Children's Asthma Research Institute and Hospital, Denver, Colorado

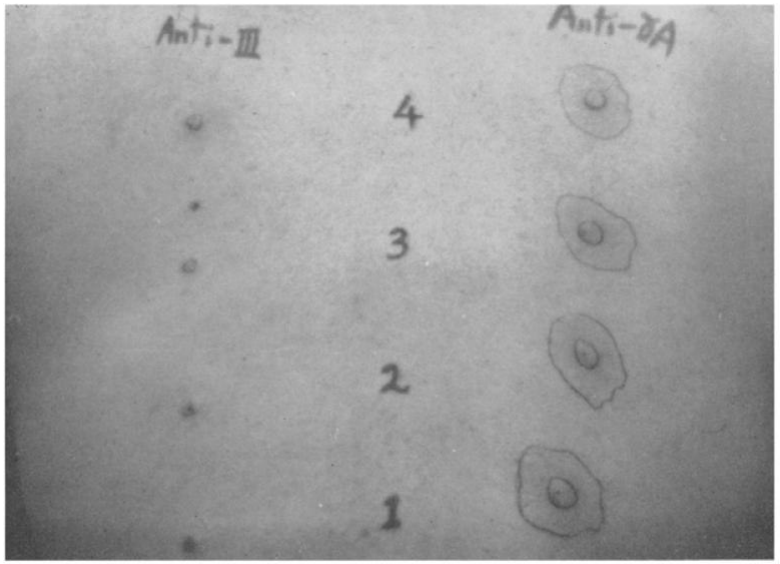
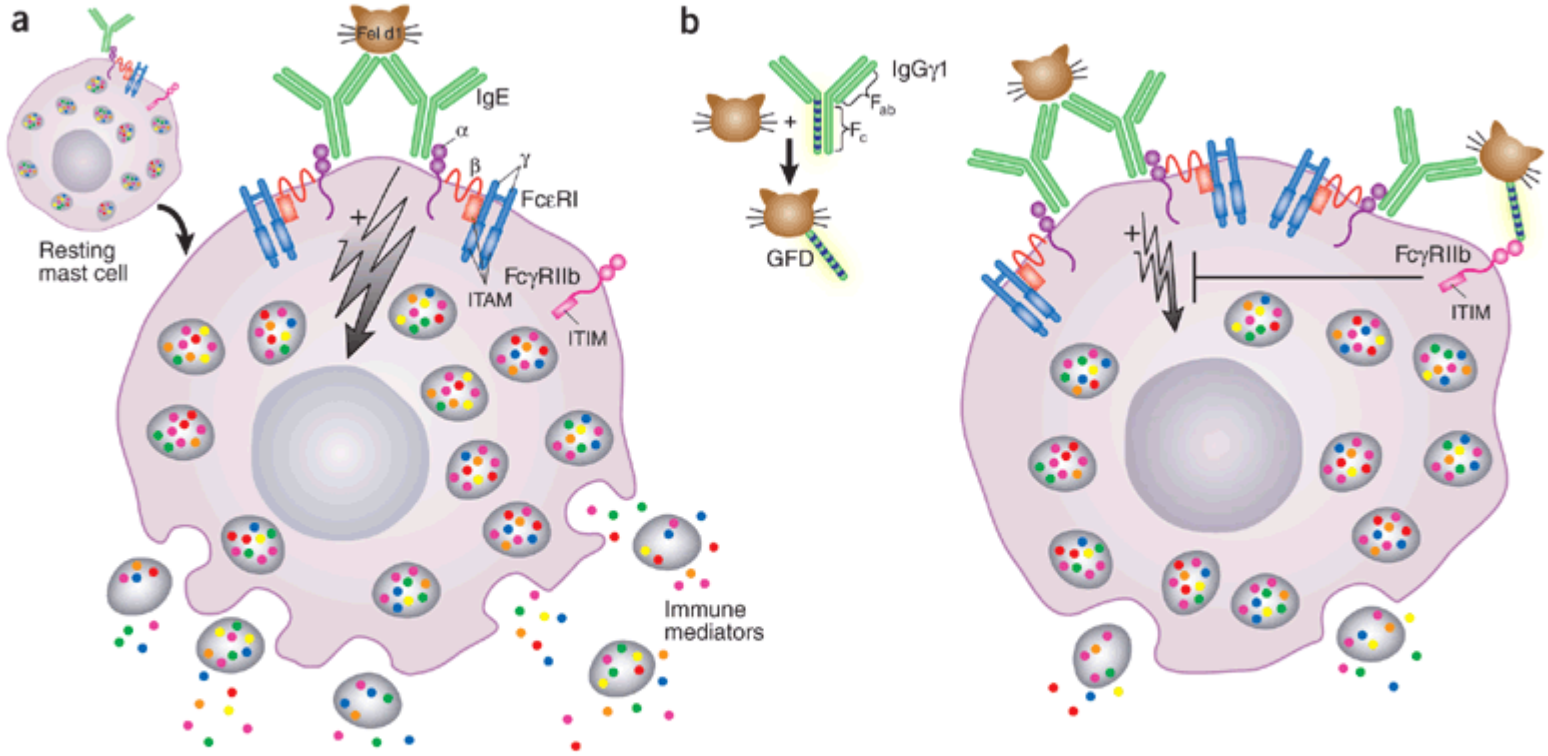
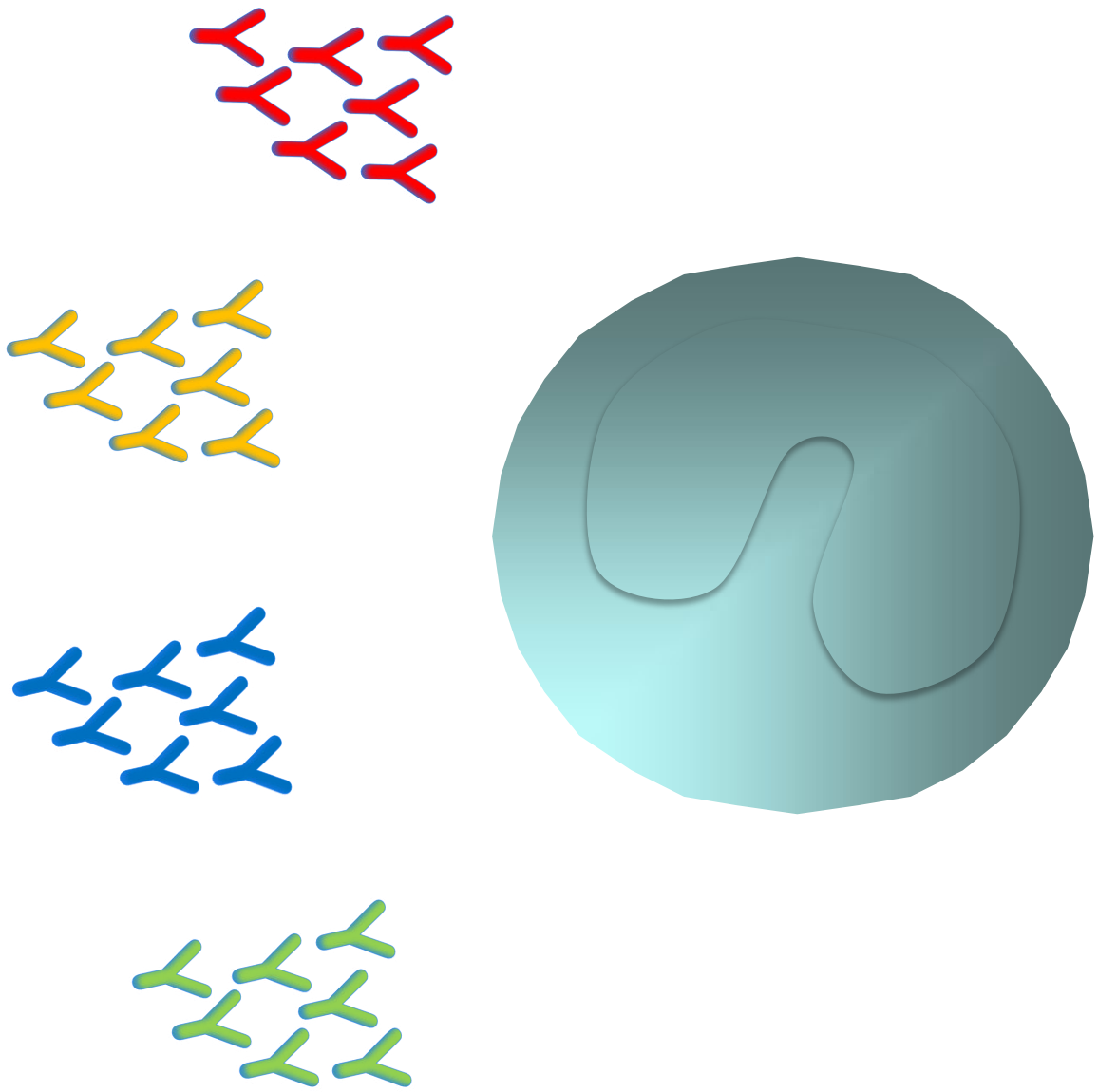


Figure 3. Prausnitz-Küstner reactions with supernatants obtained after the absorption of Fr. γA_1 (serum U) with anti-Fr. III (*left*) or with anti-γA (*right*). Skin sites 1 to 4 (*bottom* to *top*) received two-fold dilutions of the supernatants (*cf.* Table II).

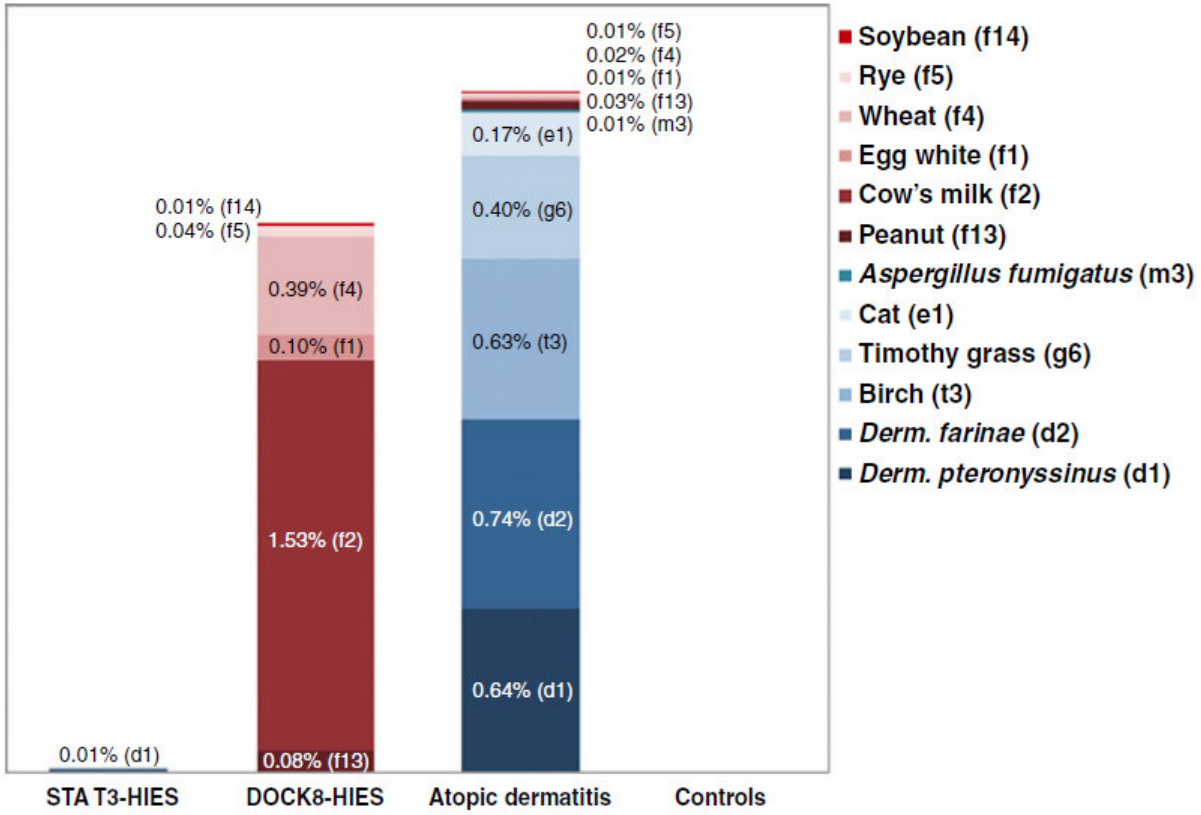
How allergen activates mast cells



Kalesnikoff & Galli, Nat Med 2005;11:381

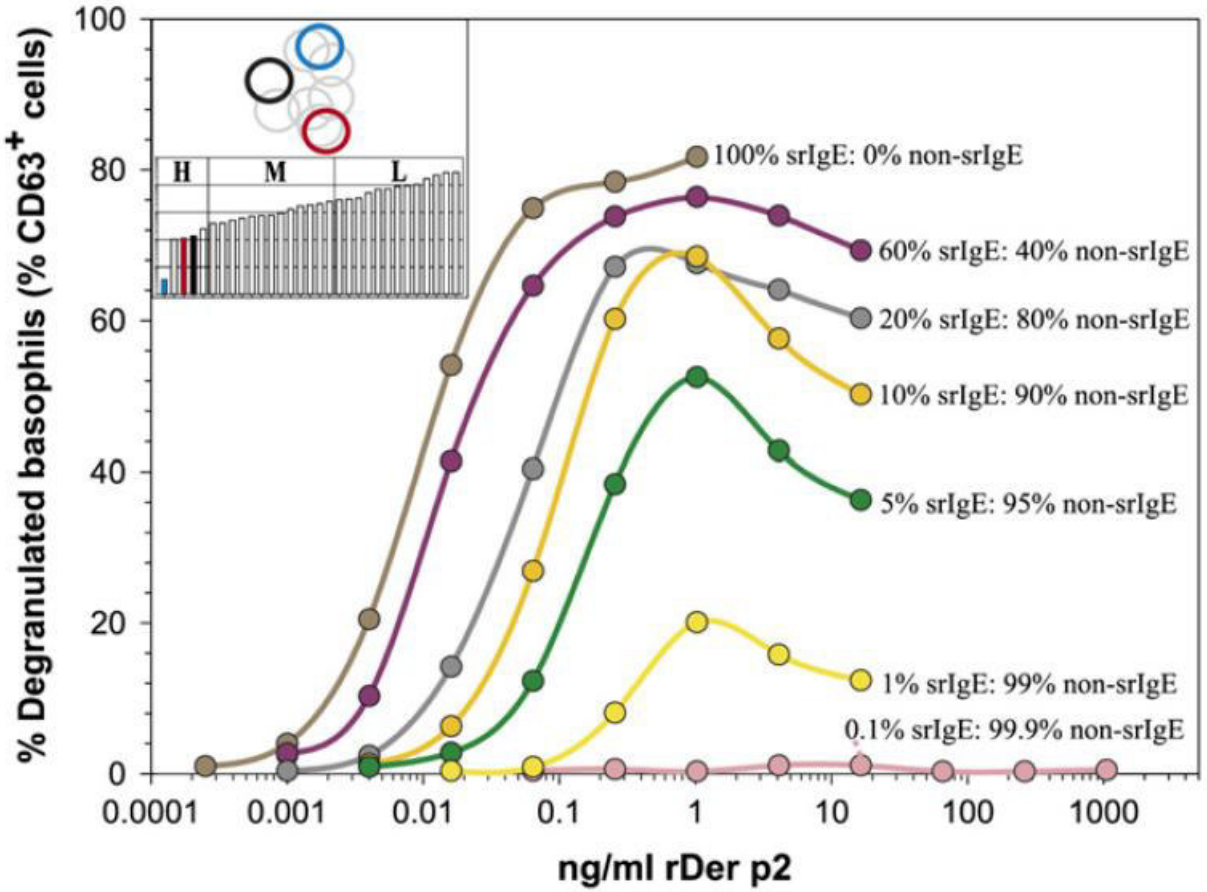


IgE-based sensitization patterns in patients with high IgE titers



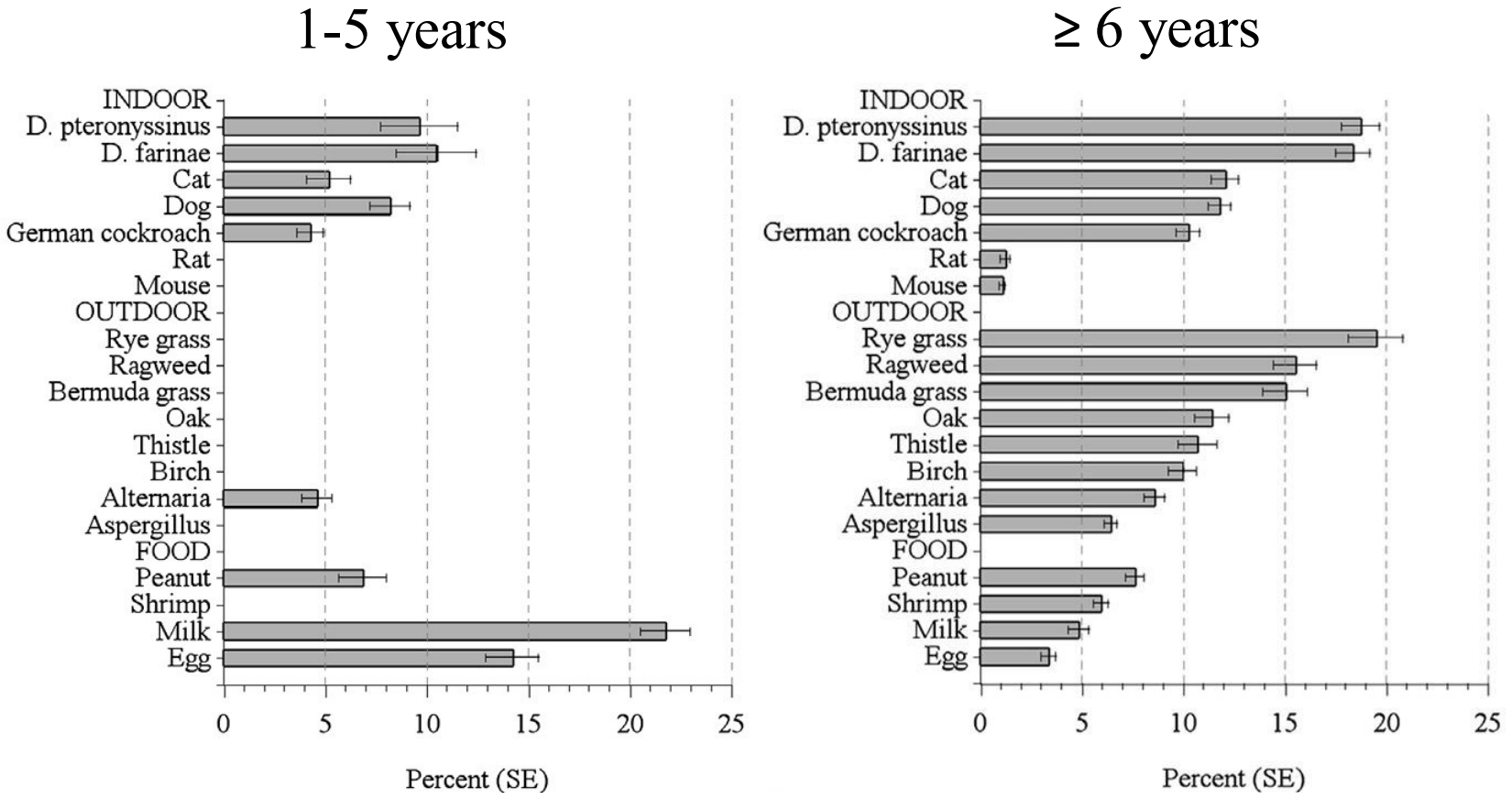
Boos et al, Allergy 2014;69:943

The basophil response to allergen depends on the relative density of specific IgE



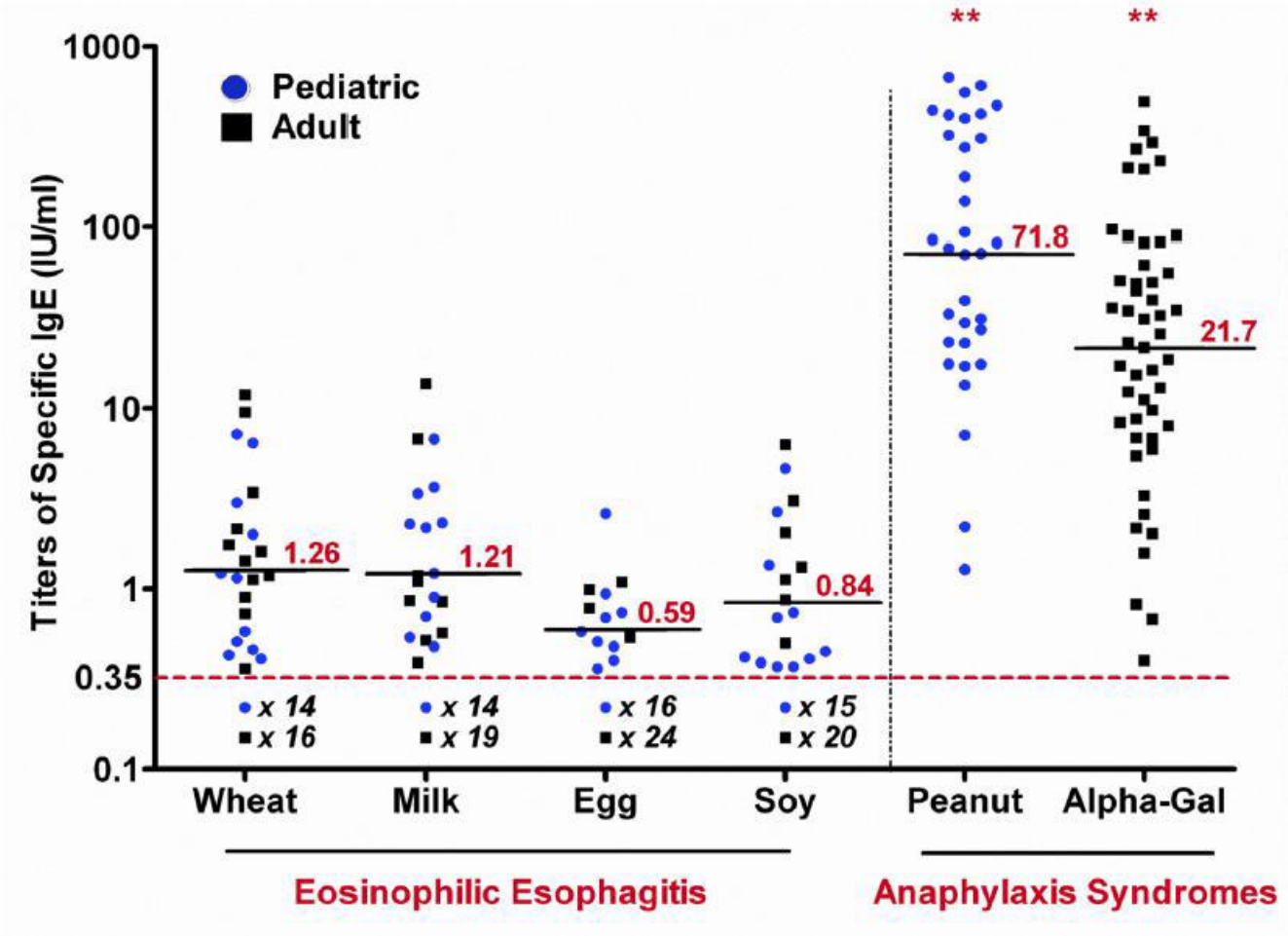
Christensen et al, J Allergy Clin Immunol 2008;122:298

Prevalence of allergic sensitization in the general population (NHANES 2005-06)



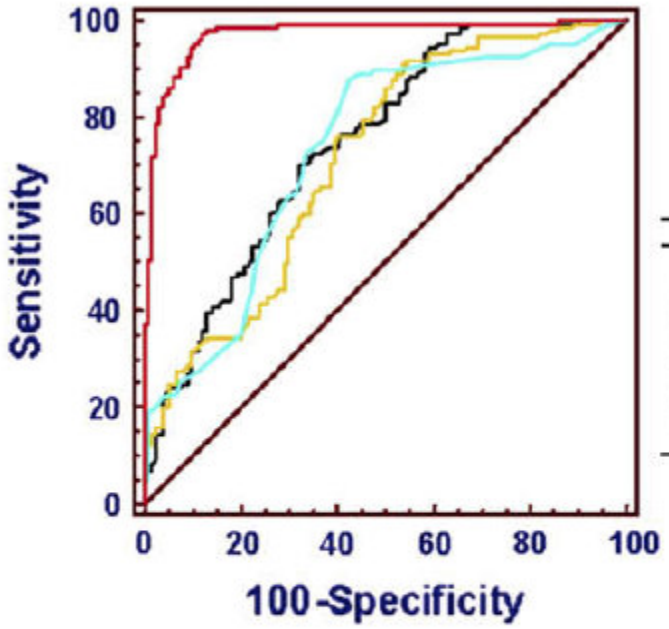
Salo et al, J Allergy Clin Immunol 2014;134:350

IgE titers and the risk of anaphylaxis



Platts-Mills et al. J Allergy Clin Immunol 2016;137:1662

Diagnostic value of the ratio of specific to total serum IgE

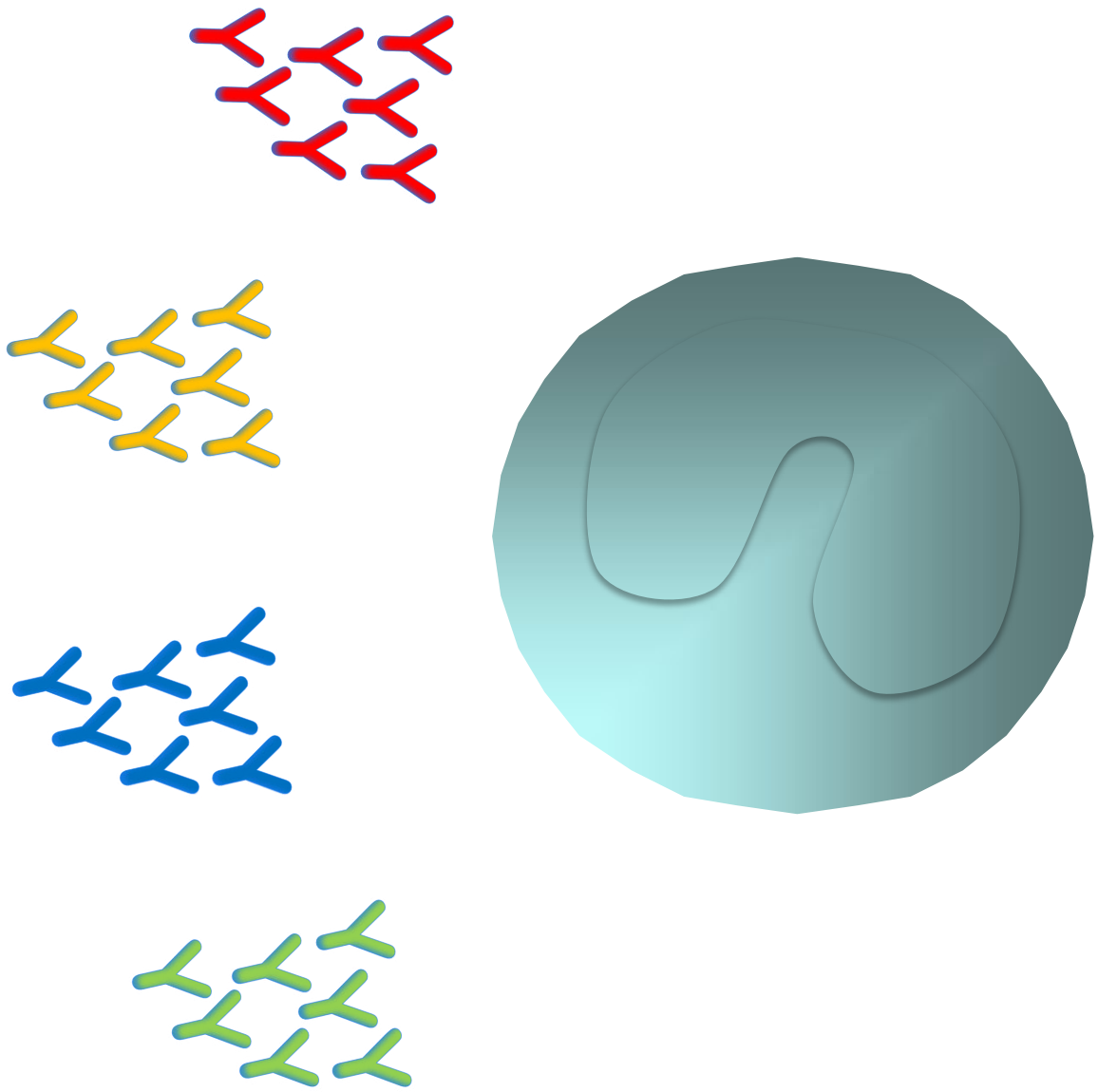


Serum total IgE
Serum specific IgE
Blood eosinophil counts
Ratio serum specific IgE and serum total IgE

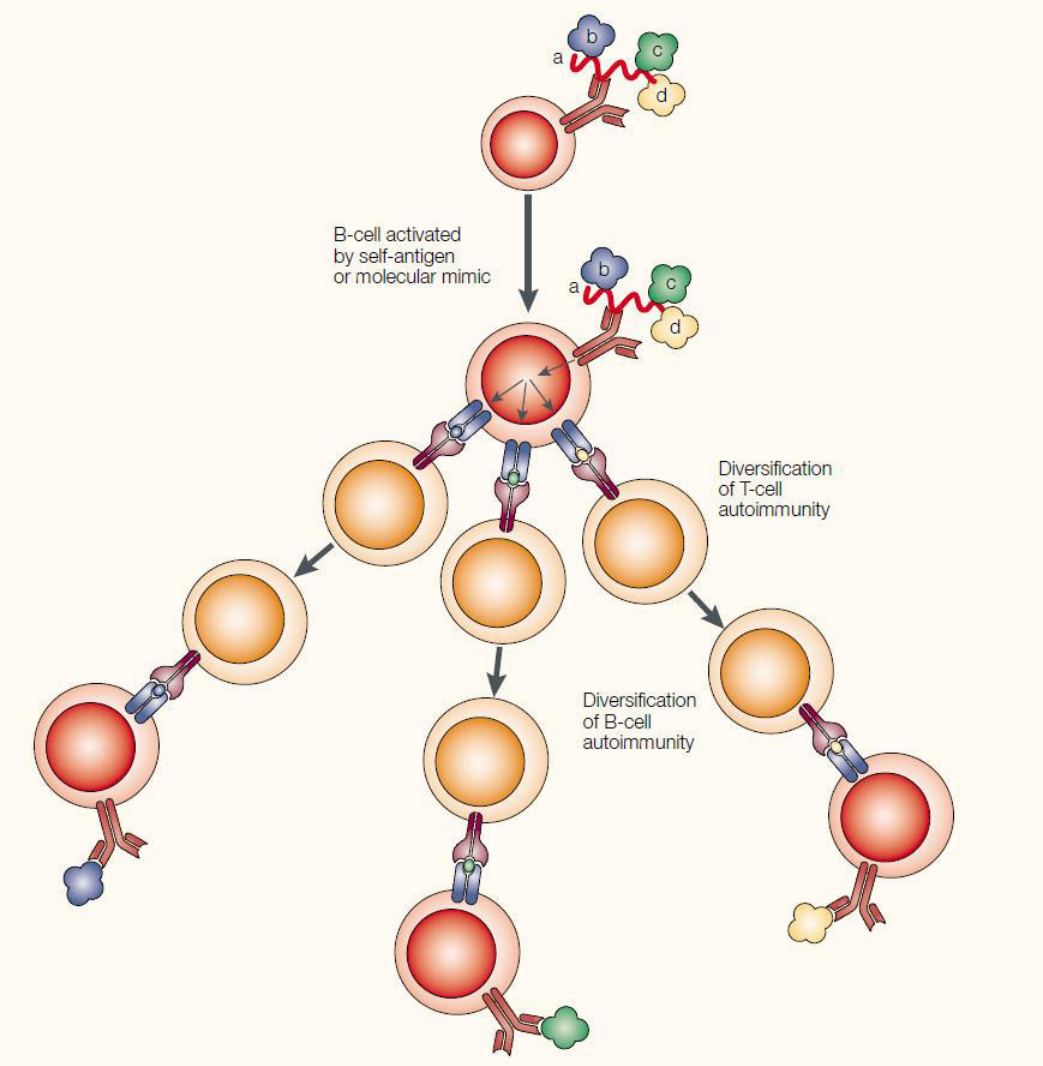
	Difference between areas	95%CI	*P*-value
serum t-IgE *vs.* serum s-IgE	0.031	-0.020 to 0.082	0.2
serum t-IgE *vs.* b-eos counts	0.014	-0.053 to 0.082	0.6
serum s-IgE *vs.* b-eos counts	0.016	-0.053 to 0.086	0.6
serum t-IgE *vs.* serum s-IgE/t-IgE[§] ratio	0.22	0.16 to 0.28	< 0.001
serum s-IgE *vs.* serum s-IgE/t-IgE[§] ratio	0.25	0.20 to 0.31	< 0.001
b-eos counts *vs.* serum s-IgE/t-IgE[§] ratio	0.24	0.17 to 0.30	< 0.001

FIG 1. ROC curves obtained with serum t-IgE levels (decision point, ≤133 kU/L; sensitivity, 69.7%; and specificity, 67.9%), serum s-IgE levels (decision point, 9.5 kAU/L; sensitivity, 91.0%; specificity, 46.3%), b-eos counts (decision point, 0.43 cells × 10^{-3} μL; sensitivity, 87.6%; specificity, 57.5%), and serum s-IgE/serum t-IgE ratios (decision point, 16.2%; sensitivity, 97.2%; specificity, 88.1%) by plotting sensitivity in patients with an effective response to ASI versus 100-specificity in patients with an ineffective response to ASI.

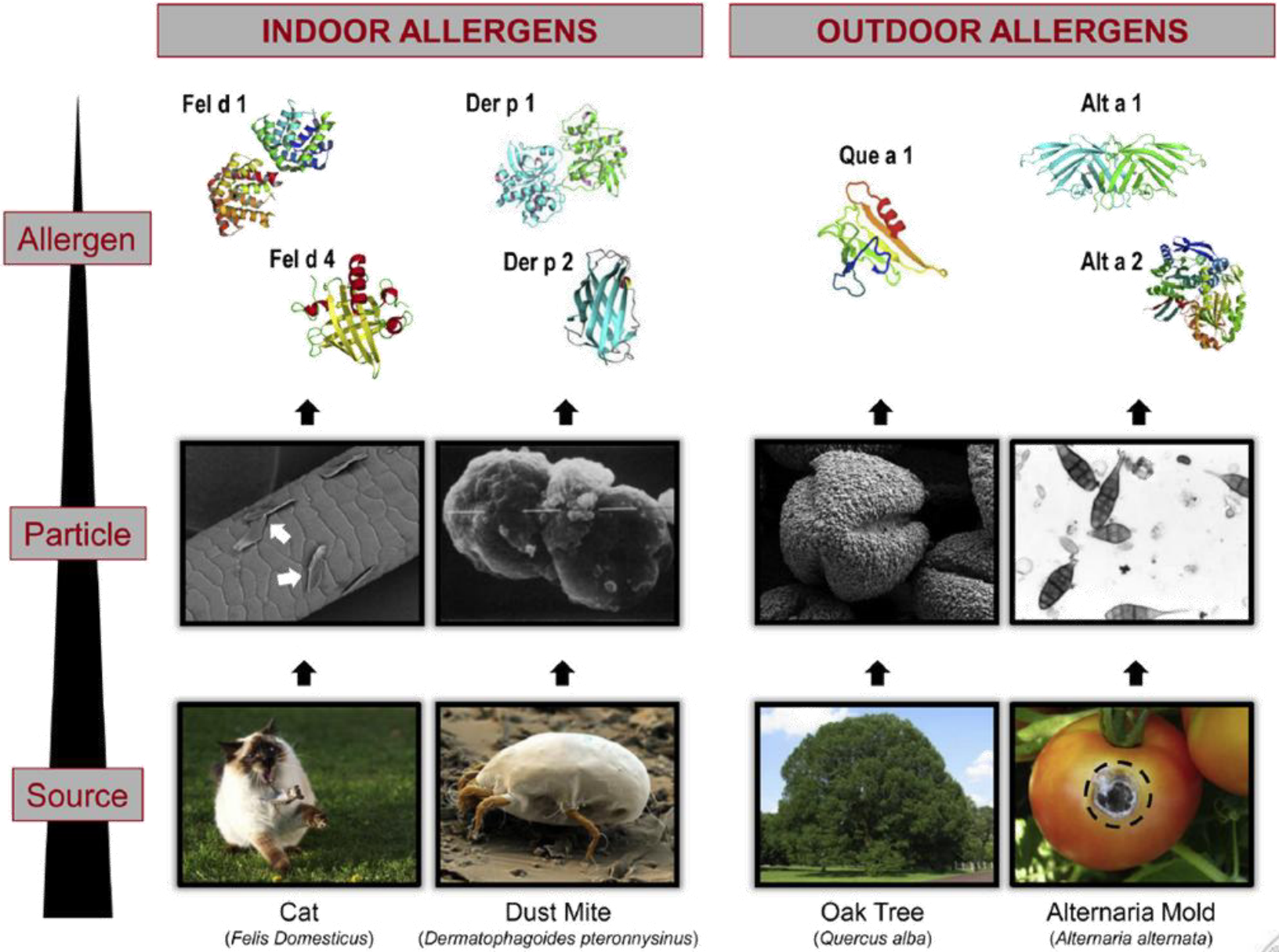
Di Lorenzo et al, J Allergy Clin Immunol 2009;123:1103



Mechanism of epitope spreading

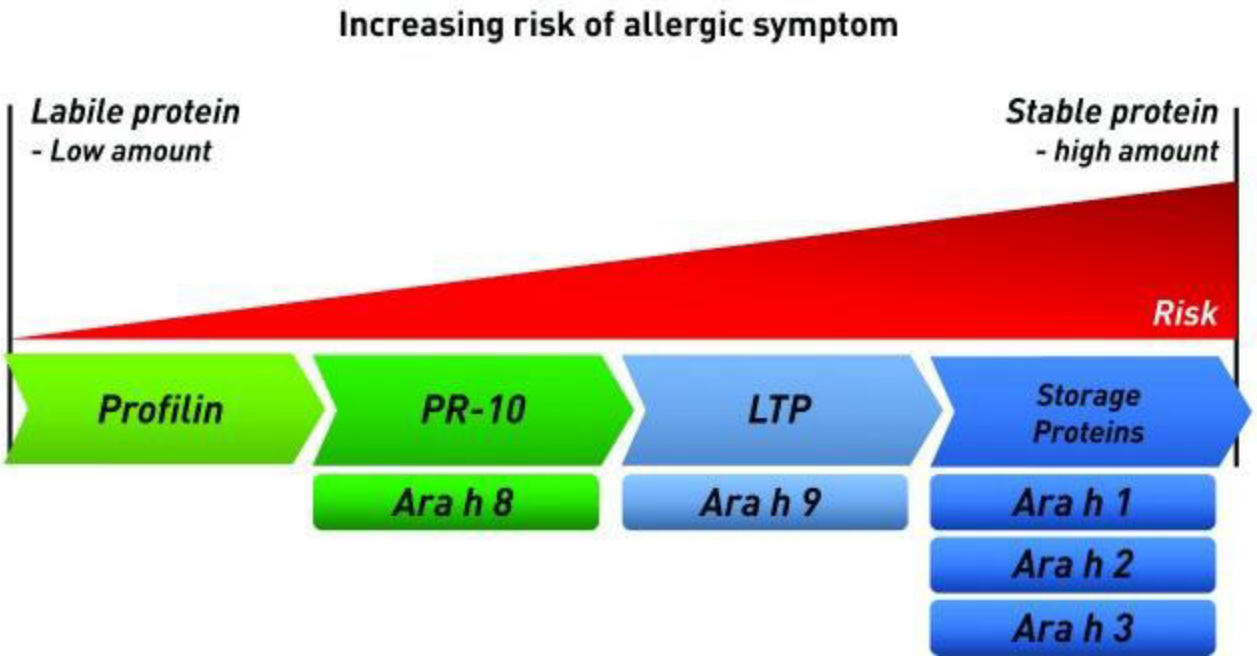


Shlomchick et al, Nat Rev Immunol 2001;1:147



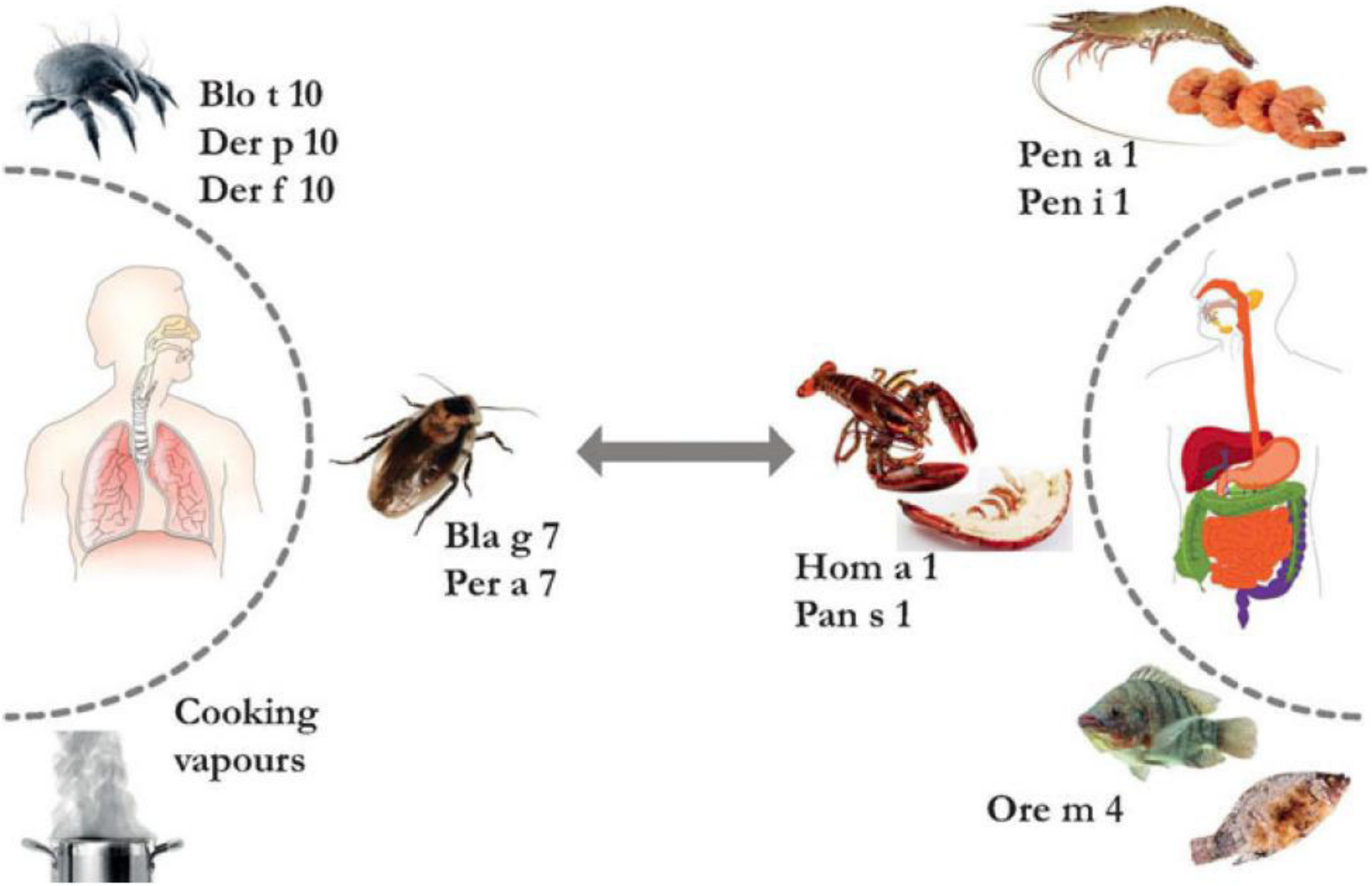
Platts-Mills et al. J Allergy Clin Immunol 2016;137:1662

Allergic risk associated with protein families



Reinhardt, clpmag.com/2014/05

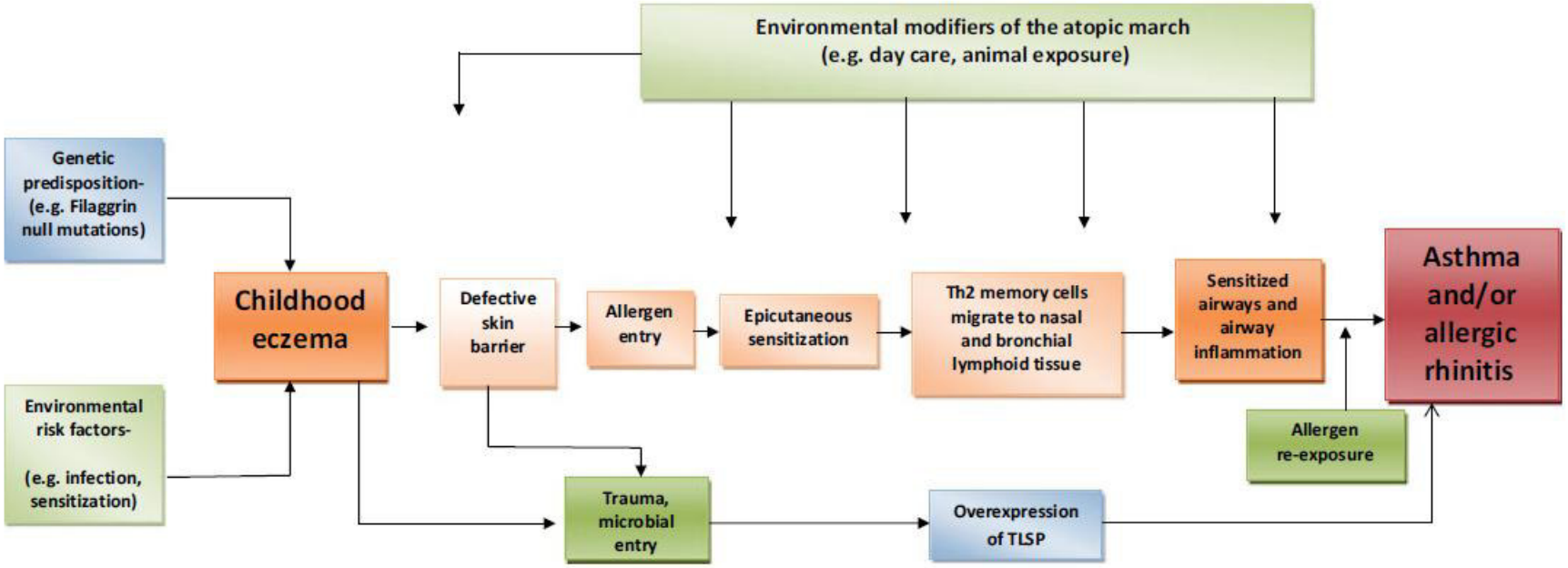
The importance of panallergens in multiple sensitizations



McKenna et al. Pediatr Allergy Immunol 2016;10.1111/pai.12589

Skin allergy testing

A proposed pathway for the atopic march



Dharmage et al, Allergy 2014;69:17