

Johns Hopkins Engineering

Immunoengineering

Allergy and Autoimmunity

Allergic Immune Response



JOHNS HOPKINS
WHITING SCHOOL
of ENGINEERING

Several Mechanisms for Allergic Reaction

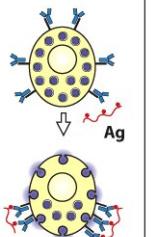
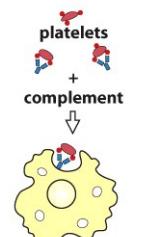
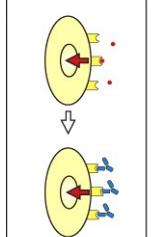
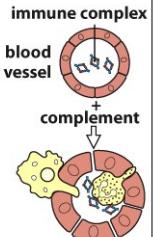
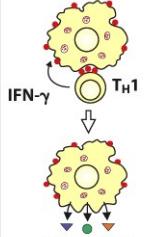
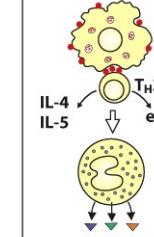
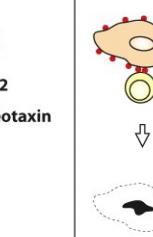
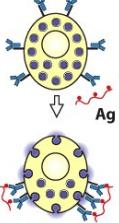
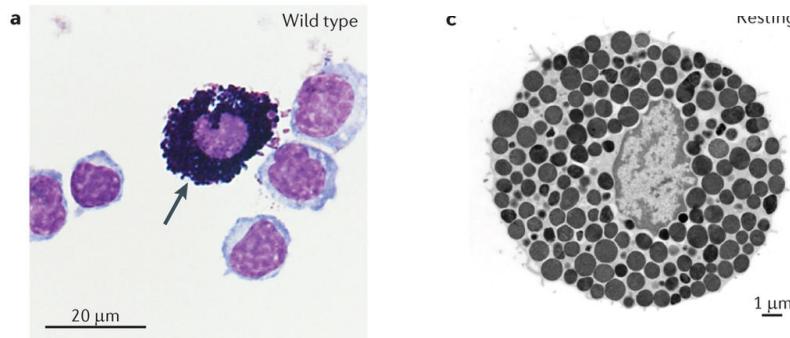
	Type I	Type II		Type III	Type IV		
Immune reactant	IgE	IgG		IgG	T_{H1} cells	T_{H2} cells	CTL
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Cell-surface receptor	Soluble antigen	Soluble antigen	Soluble antigen	Cell-associated antigen
Effector mechanism	Mast-cell activation	Complement, FcR^+ cells (phagocytes, NK cells)	Antibody alters signaling	Complement, phagocytes	Macrophage activation	IgE production, eosinophil activation, mastocytosis	Cytotoxicity
							
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies	Some drug allergies (e.g. penicillin)	Chronic urticaria (antibody against FcεRI alpha chain)	Serum sickness, Arthus reaction	Allergic contact dermatitis, tuberculin reaction	Chronic asthma, chronic allergic rhinitis	Graft rejection, allergic contact dermatitis to poison ivy

Figure 14.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Mast Cell Activation

Type I	
Immune reactant	IgE
Antigen	Soluble antigen
Effector mechanism	Mast-cell activation
	
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies

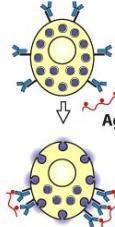


- Hematopoietic cells from bone marrow
- Migrate to tissues – particularly host-environment interfaces
- Many electron-dense secretory granules

Figure 14.1 Janeway's Immunobiology, 8ec

Wernersson, Sara, and Gunnar Pejler. "Mast cell secretory granules: armed for battle." *Nature Reviews Immunology* 14.7 (2014): 478-494.

Mast Cell Secretory Granules

Type I	
Immune reactant	IgE
Antigen	Soluble antigen
Effector mechanism	Mast-cell activation 
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies

- **Lysosomal Enzymes:** E.g. Cathepsin, β -hexosaminidase
- **Biogenic Amines:** E.g. Histamine, Serotonin, Dopamine
- **Cytokines:** E.g. TNF, IL-4, IL-6
- **Growth Factors:** E.g. bFGF, VEGF,
- **Proteoglycans:** E.g. Serglycin
- **Proteases:** E.g. Tryptase, Chymase, Granzyme B
- **Granular Membrane-associated Proteins:** E.G. Syntaxin, LC3-II
- **Other:** E.g. antimicrobial peptides, Heparanase

Figure 14.1 Janeway's Immunobiology, 8ec

Mast Cell Secretory Granules - Proinflammatory

Type I	
Immune reactant	IgE
Antigen	Soluble antigen
Effector mechanism	Mast-cell activation
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies

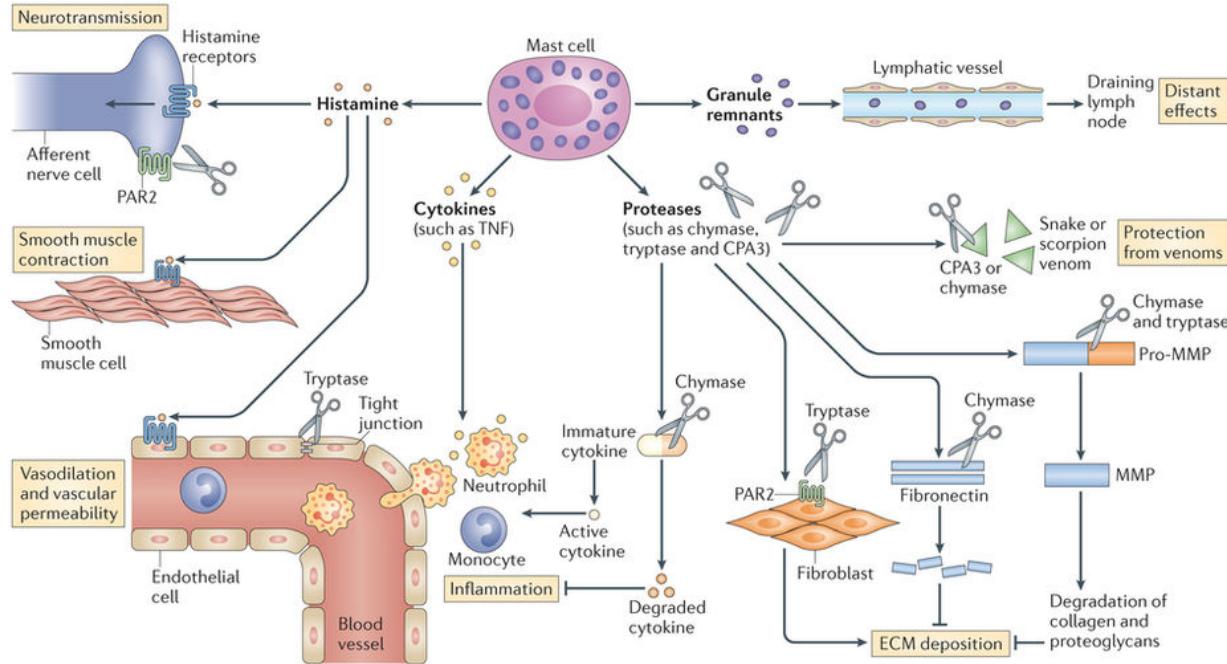


Figure 14.1 Janeway's Immunobiology, 8ec

Nature Reviews | Immunology

Wernersson, Sara, and Gunnar Pejler. "Mast cell secretory granules: armed for battle." Nature Reviews Immunology 14.7 (2014): 478-494.

Protective Mast Cell Function

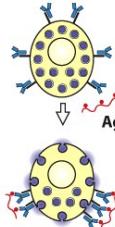
	Type I
Immune reactant	IgE
Antigen	Soluble antigen
Effector mechanism	Mast-cell activation 
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies

Table 3 | Impact of mast cell granule compounds on disease models as determined by studies of knockout mice

Disease model	Role of mast cells*	Role of mast cell granule compound	Proposed mechanism	Refs
Bacterial infection	Protective	• Protective: mMCP4 and mMCP6 • Detrimental: histamine	• mMCP4: TNF degradation • mMCP6: neutrophil recruitment • Histamine: suppression of phagocytosis	86,129,132
Venom defence	Protective	Protective: CPA3 and mMCP4	Degradation of toxic peptides	124–126
Kidney fibrosis (unilateral ureteral obstruction)	Protective	Protective: mMCP4	Degradation of fibronectin	145
Trichinella spiralis infection	Protective	Protective: mMCP1 and mMCP6	• mMCP1: promotes parasite expulsion • mMCP6: contributes to eosinophil recruitment	85,133
Post-traumatic spinal cord damage	Protective	Protective: mMCP4	Degradation of cytokines (including CCL2, IL-6 and IL-13)	119
Post-traumatic brain inflammation	Protective	Protective: mMCP4	Not known	118
Kidney inflammation or fibrosis (immune complex-mediated glomerulonephritis)	Protective	Detrimental: mMCP4	Angiotensin II formation	147

Figure 14.1 Janeway's Immunobiology, 8ec

Detrimental Mast Cell Function

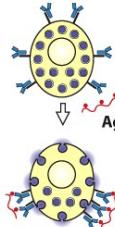
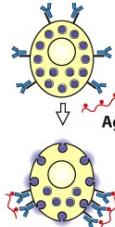
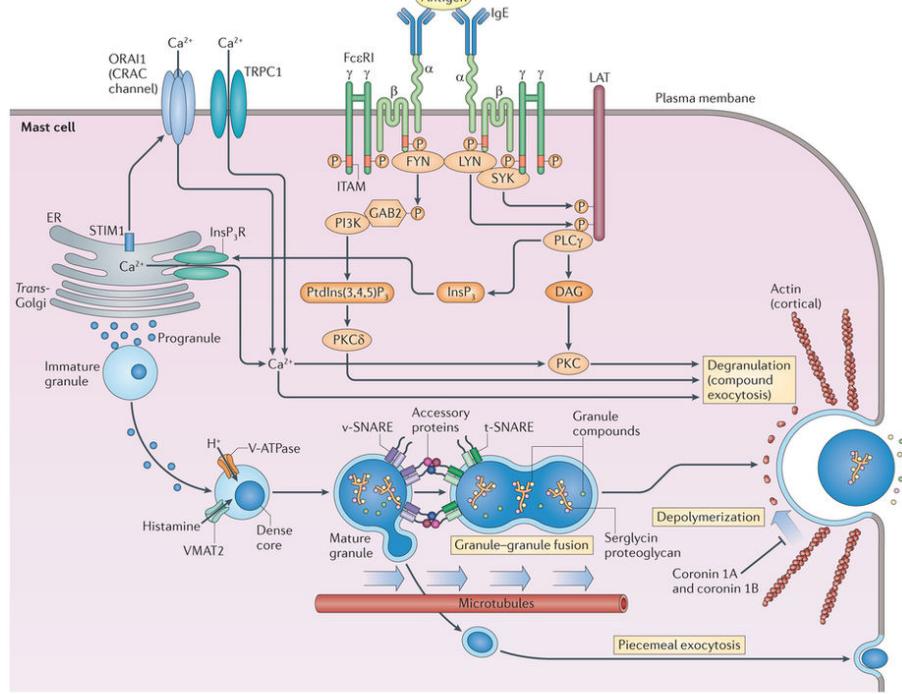
Type I					
Immune reactant	IgE				
Antigen	Soluble antigen				
Effector mechanism	Mast-cell activation				
					
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies				
Abdominal aortic aneurysm formation		Detrimental	Detrimental: mMCP4 and mMCP6	<ul style="list-style-type: none"> • Pro-angiogenic effects • Elastase degradation • Activation of cysteine proteases • Cytokine induction 	95
Experimental colitis		Detrimental	Detrimental: mMCP6	Stimulation of chemokine and cytokine expression	97
Asthma		Detrimental	<ul style="list-style-type: none"> • Protective: mMCP4 • Detrimental: histamine 	Degradation of IL-33	113,114,198
Burn injury		Detrimental	Detrimental: mMCP4 and mMCP5	Degradation of tight junctions	58,94
Lung fibrosis (bleomycin)		Detrimental	Detrimental: mMCP4	Not known	96
Arthritis		Detrimental [#]	Detrimental: mMCP6, mMCP4 and histamine	<ul style="list-style-type: none"> • mMCP6: aggrecan degradation (via MMP3 and MMP13 activation) • Effects of mMCP4 and histamine unknown 	137–140,144
Experimental autoimmune encephalitis		Detrimental [#]	Protective: histamine	Histamine deficiency reduces the production of pro-inflammatory cytokines and reduces brain inflammation	199
Skin blistering (bullous pemphigoid)		Detrimental	Detrimental: mMCP4	<ul style="list-style-type: none"> • Degradation of hemidesmosomes • MMP9 activation 	104

Figure 14.1 Janeway's Immunobiology, 8ec

Wernersson, Sara, and Gunnar Pejler. "Mast cell secretory granules: armed for battle." *Nature Reviews Immunology* 14.7 (2014): 478-494.

Mast Cell Secretory Granules

Type I	
Immune reactant	IgE
Antigen	Soluble antigen
Effector mechanism	Mast-cell activation
	
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies



Nature Reviews | Immunology

Figure 14.1 Janeway's Immunobiology, 8ec

Wernersson, Sara, and Gunnar Pejler. "Mast cell secretory granules: armed for battle." Nature Reviews Immunology 14.7 (2014): 478-494.

Mast cell activation leading to allergic symptoms

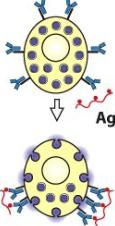
Type I	
Immune reactant	IgE
Antigen	Soluble antigen
Effector mechanism	Mast-cell activation
	
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies

Figure 14.1 Janeway's Immunobiology, 8ec

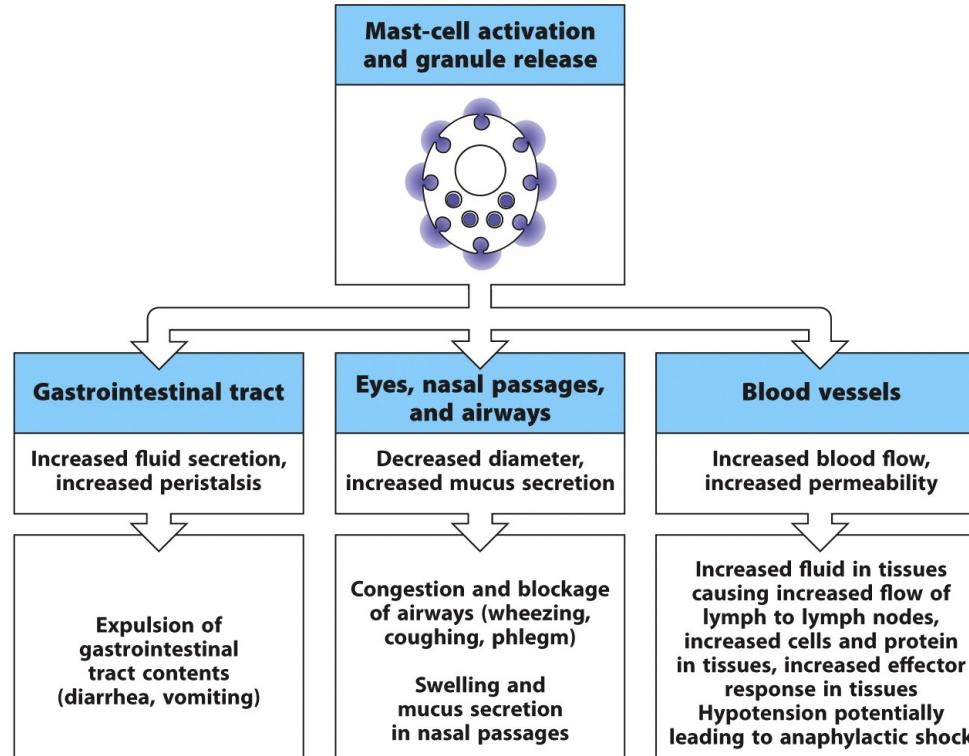
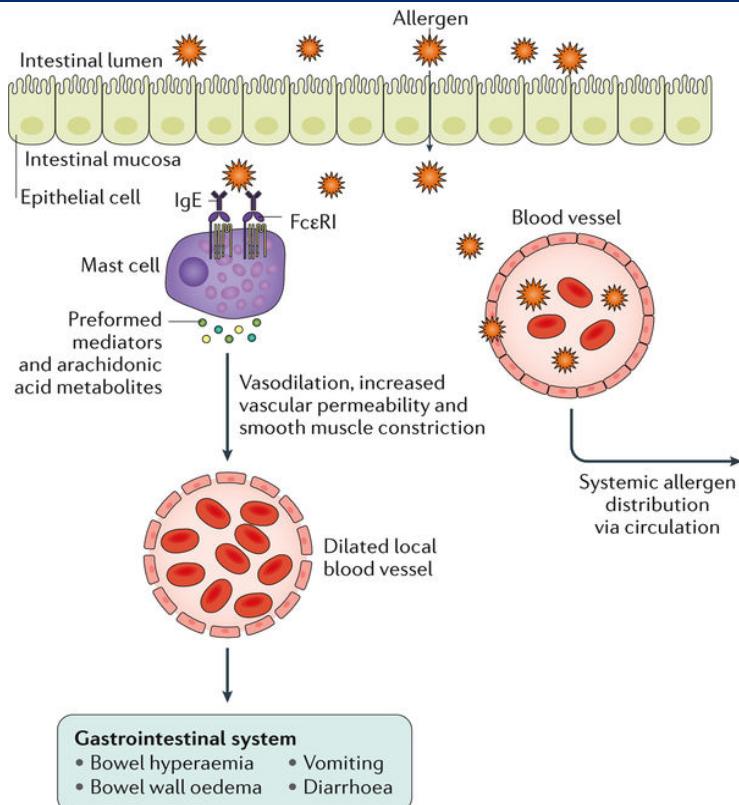


Figure 14.10 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Food Allergy Example



Cardiovascular system

- Vasodilation
- Plasma leak
- Myocardial depression
- Arrhythmias
- Shock
- Tachycardia
- Hypotension

Integumentary system

- Urticaria
- Flushing
- Generalized pruritus
- Angio-oedema

Respiratory system

- Bronchoconstriction
- Dyspnoea
- Laryngeal oedema (stridor)
- Cough, wheeze and/or hoarseness
- Rhinorrhoea and/or sneeze
- Periorificial, nasal and/or oropharyngeal pruritus
- Mucus production

Central nervous system

- Altered mental status
- Anxiety
- Dizziness and/or loss of consciousness

Peripheral nervous system

- Itch
- Conjunctival erythema and tearing
- Uterine cramping (lower back pain) in women

Development of IgE antibodies

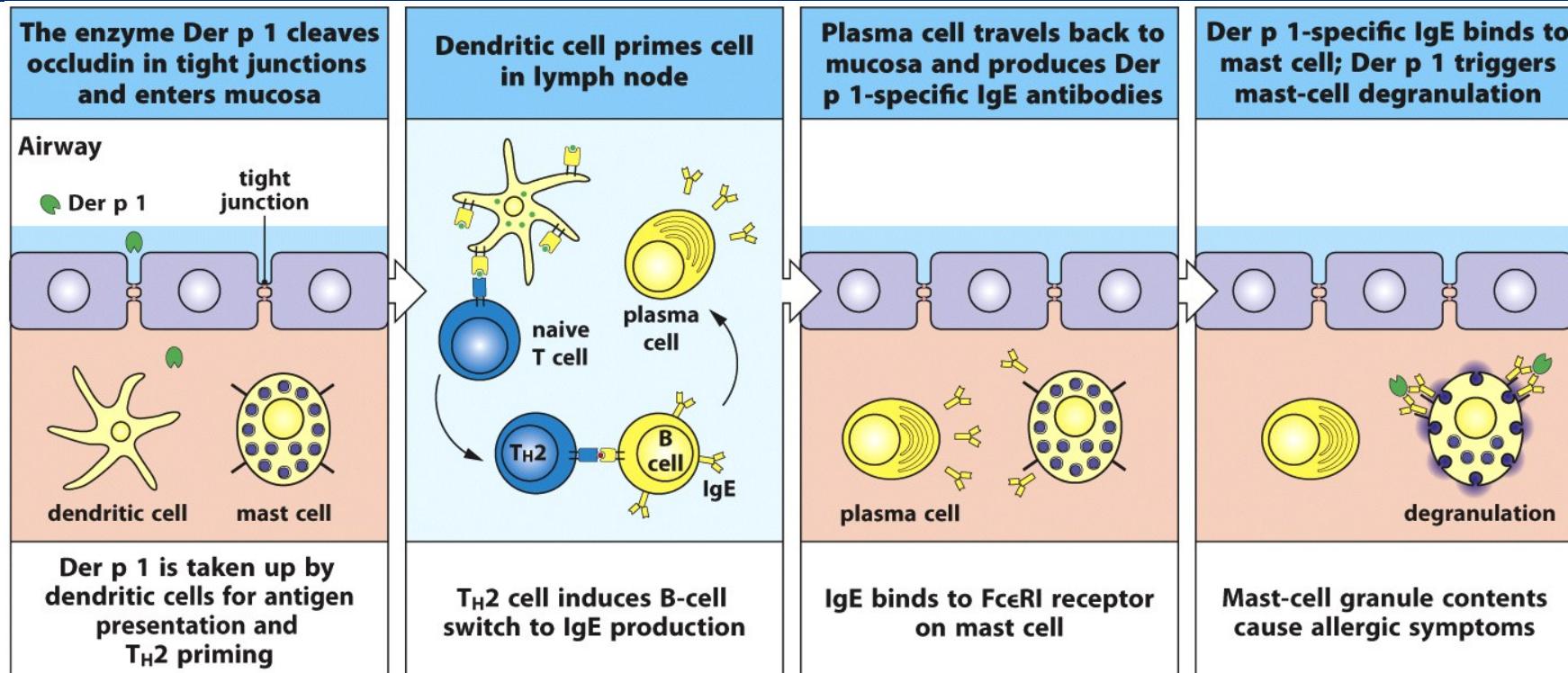


Figure 14.3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Positive-feedback Reaction

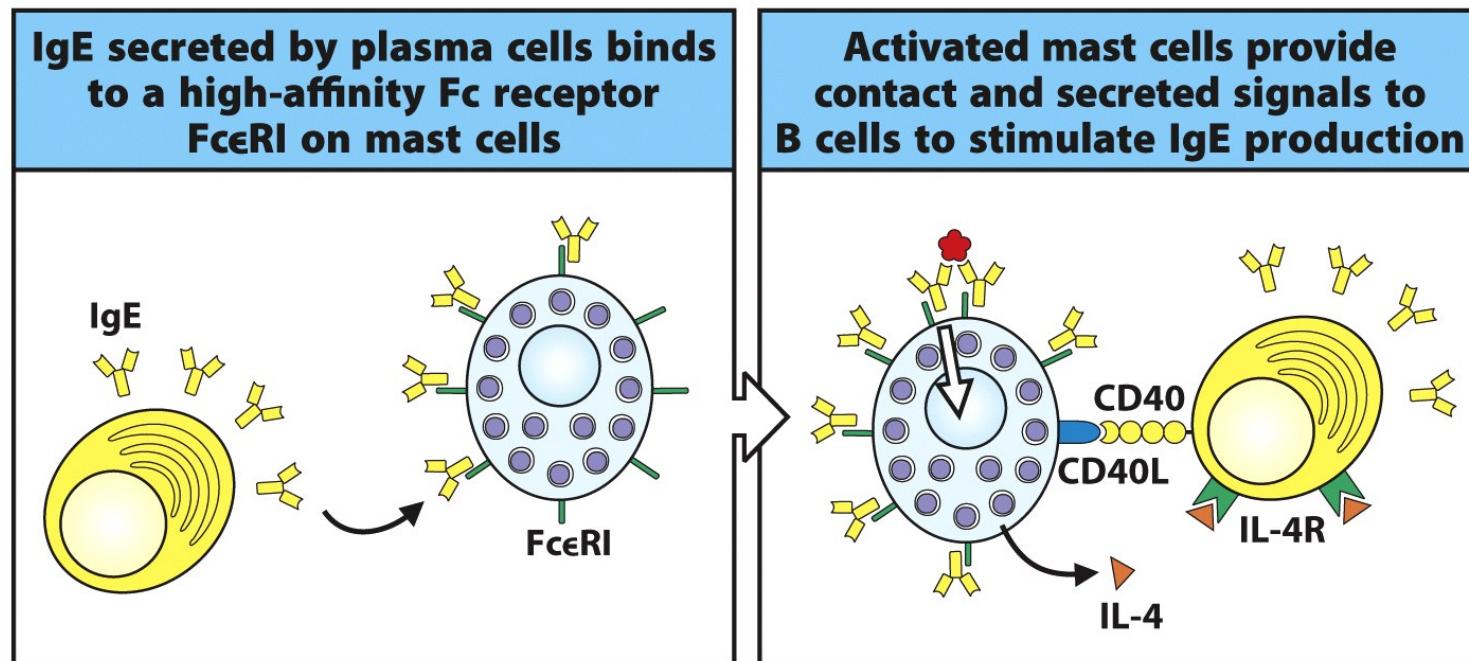


Figure 14.4 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Th2 T cells where do they come from?

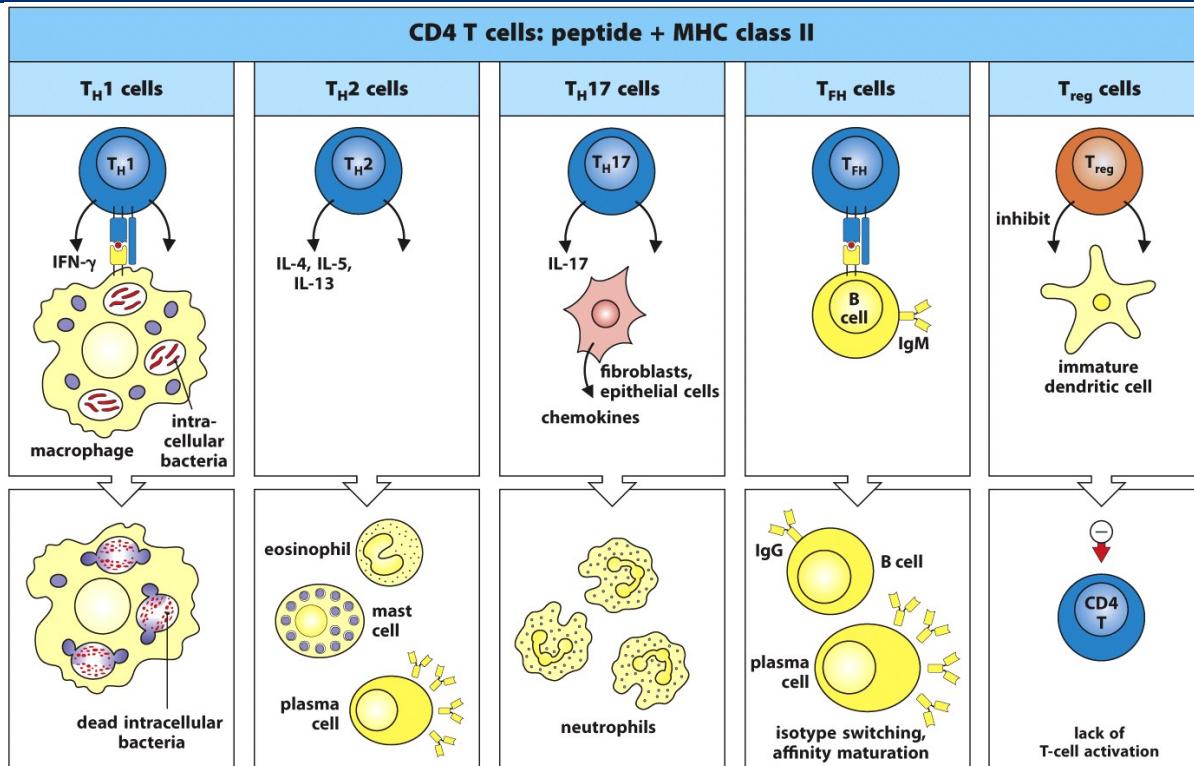
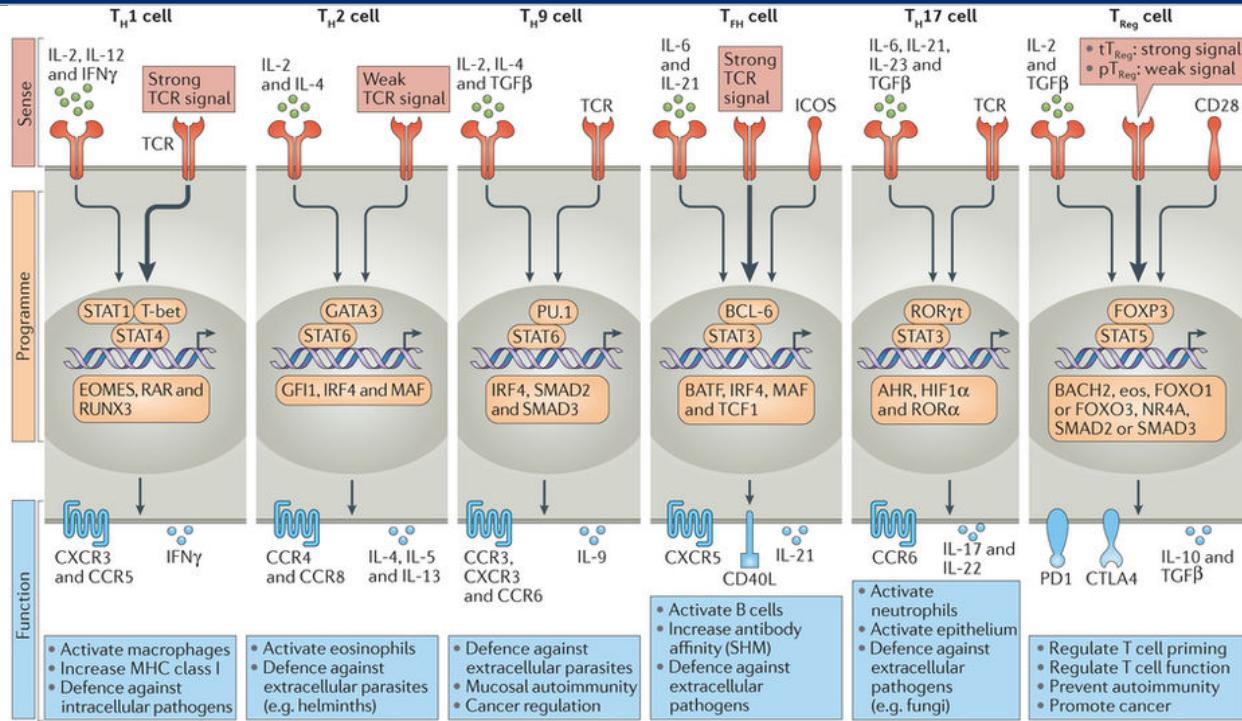


Figure 9.28 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Th2 T cells where do they come from?



Nature Reviews | Immunology

DuPage, Michel, and Jeffrey A. Bluestone. "Harnessing the plasticity of CD4+ T cells to treat immune-mediated disease." *Nature Reviews Immunology* 16.3 (2016): 149-163.

Th1 vs. Th2 Induction – Antigen Presenting Cells

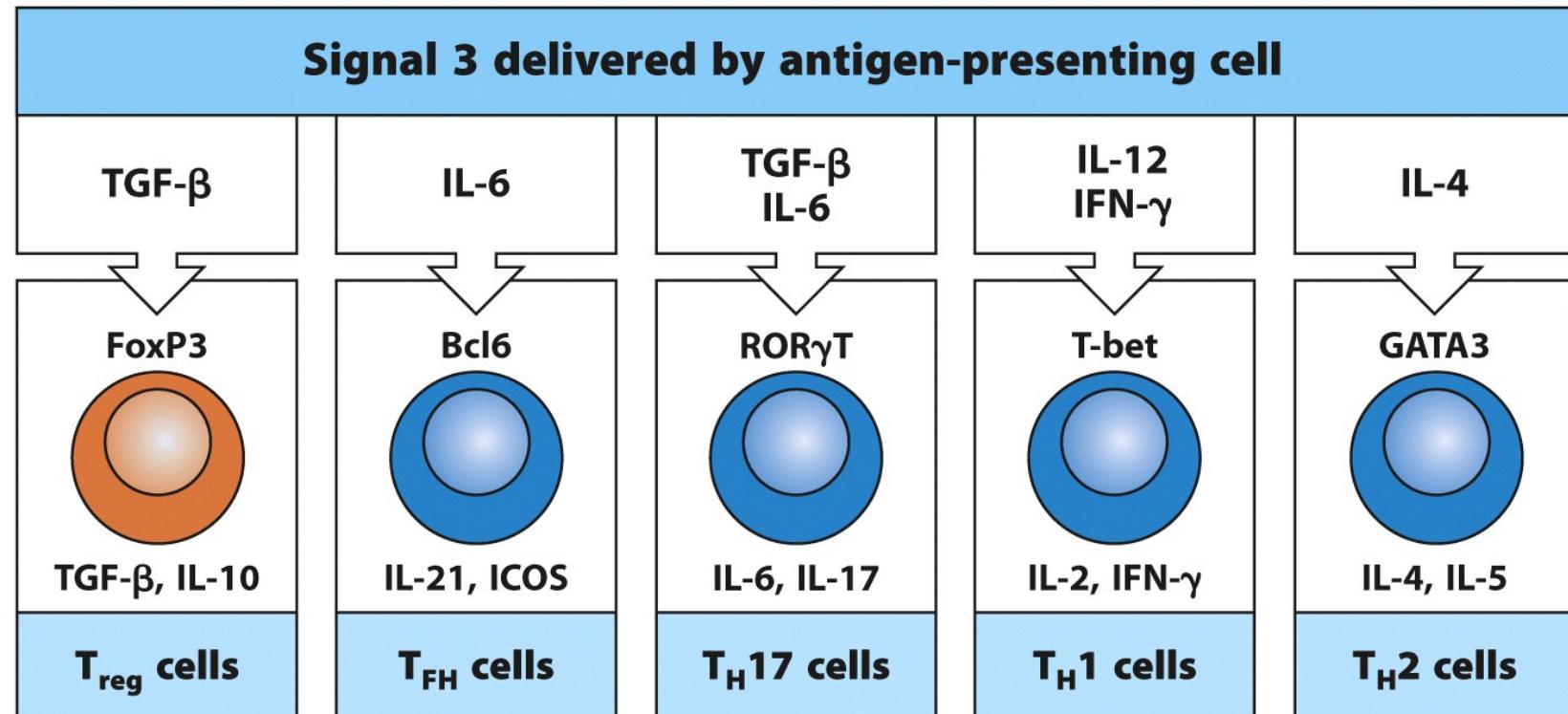


Figure 9.29 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Th1 vs. Th2 Induction

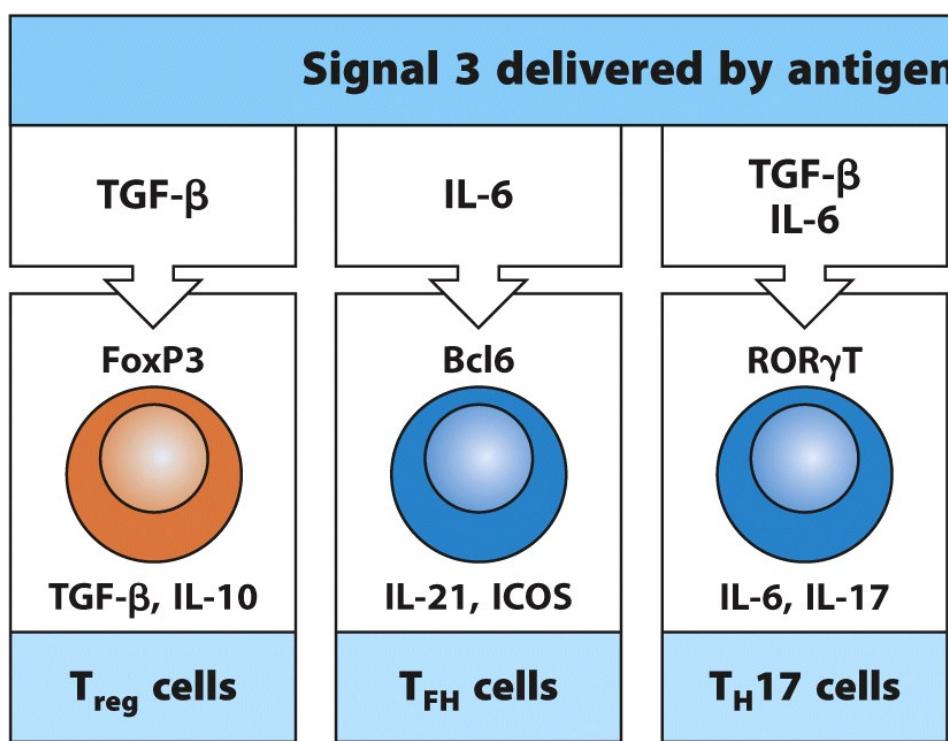


Figure 9.29 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

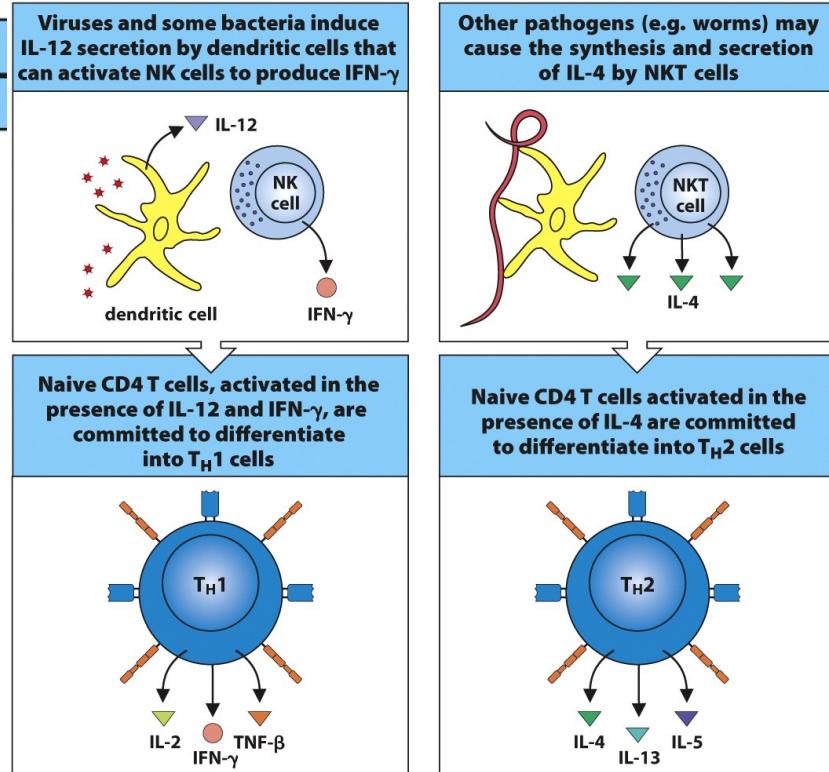


Figure 11.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Th1 vs. Th2 Induction

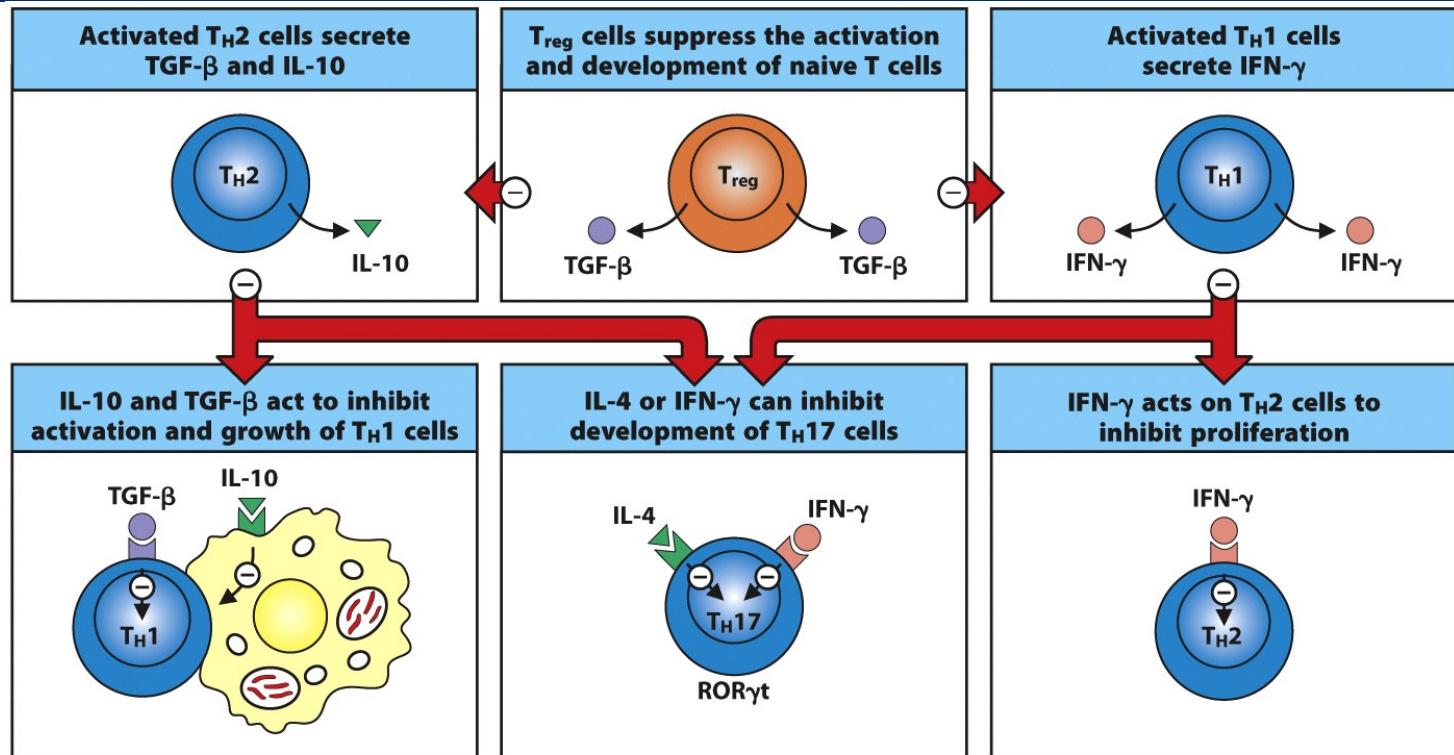
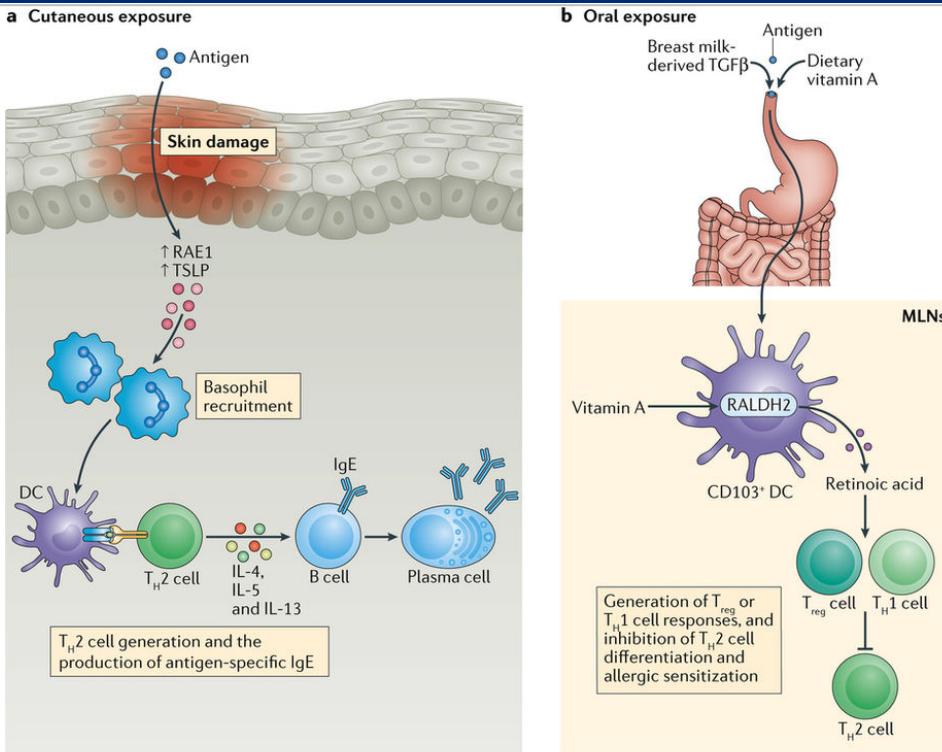


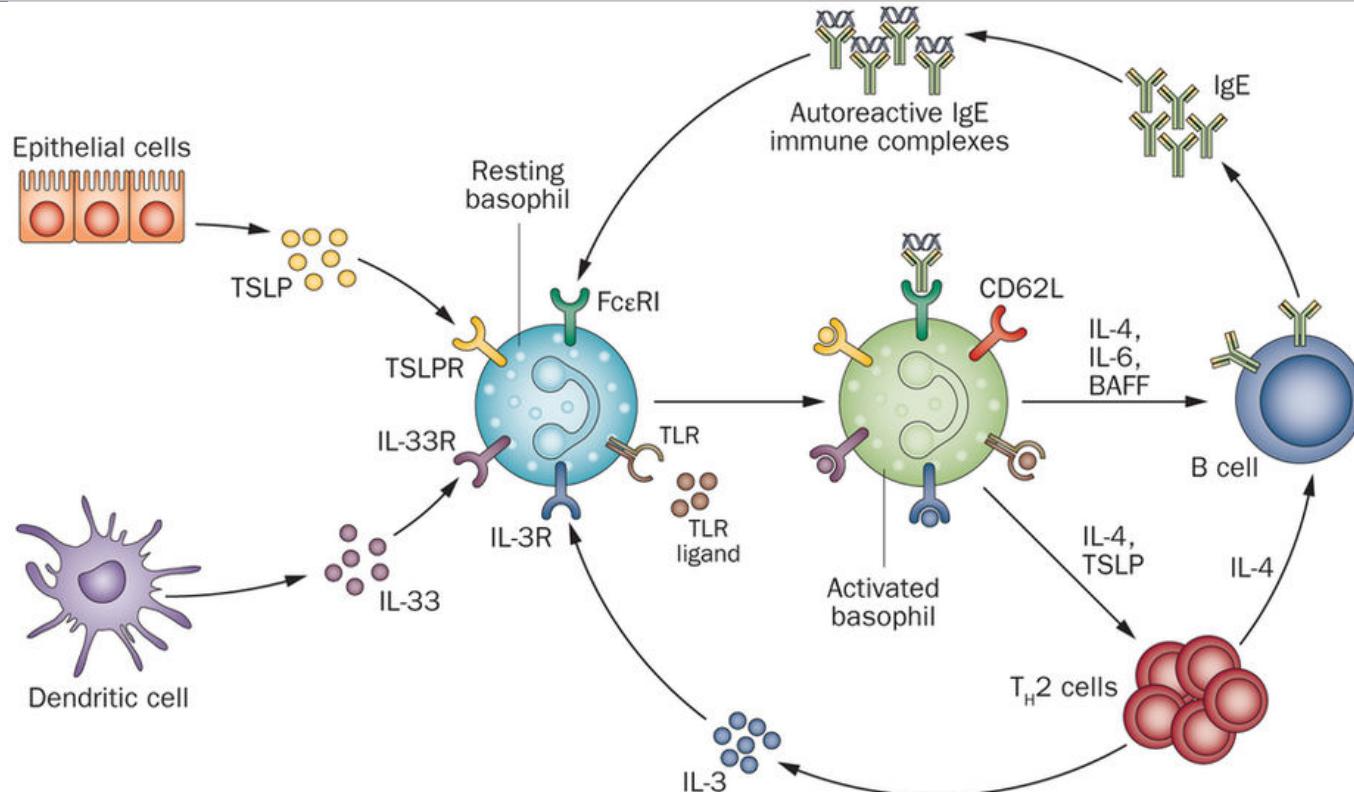
Figure 11.7 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Th1 vs. Th2 Induction – Exposure Route



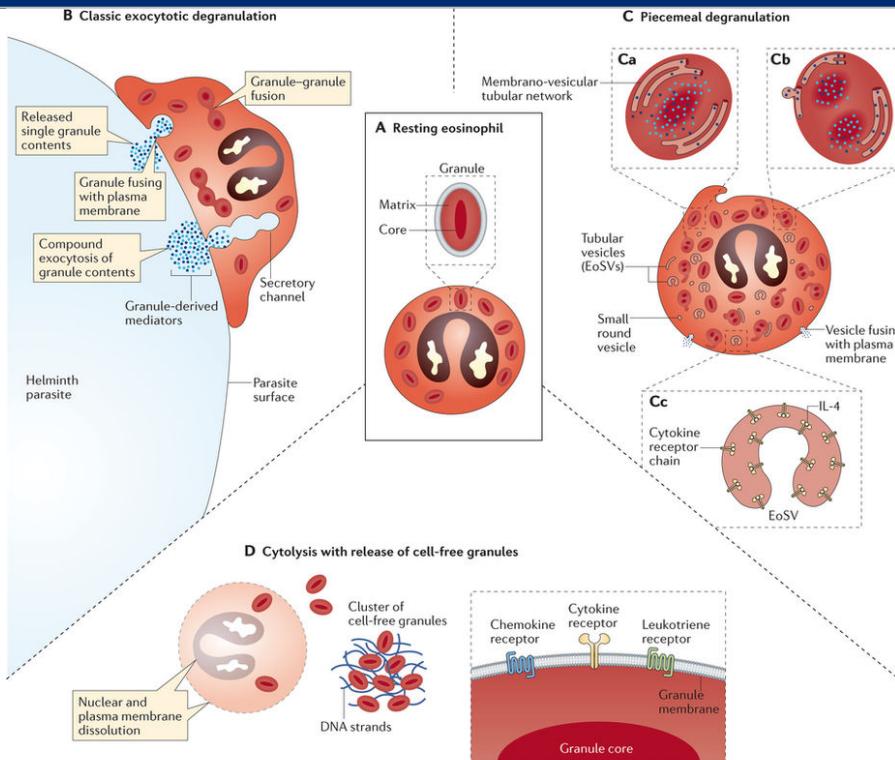
Nature Reviews | Immunology

Brief Introduction to Basophils



Sharma, Meenu, and Jagadeesh Bayry. "Autoimmunity: basophils in autoimmune and inflammatory diseases." *Nature Reviews Rheumatology* 11.3 (2015): 129-131.

Brief Introduction to Eosinophils



Nature Reviews | Immunology

Several Mechanisms for Allergic Reaction

	Type I	Type II		Type III	Type IV		
Immune reactant	IgE	IgG		IgG	T _H 1 cells	T _H 2 cells	CTL
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Cell-surface receptor	Soluble antigen	Soluble antigen	Soluble antigen	Cell-associated antigen
Effector mechanism	Mast-cell activation	Complement, FcR ⁺ cells (phagocytes, NK cells)	Antibody alters signaling	Complement, phagocytes	Macrophage activation	IgE production, eosinophil activation, mastocytosis	Cytotoxicity
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies	Some drug allergies (e.g. penicillin)	Chronic urticaria (antibody against FcεRI alpha chain)	Serum sickness, Arthus reaction	Allergic contact dermatitis, tuberculin reaction	Chronic asthma, chronic allergic rhinitis	Graft rejection, allergic contact dermatitis to poison ivy

Figure 14.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Several Mechanisms for Allergic Reaction

	Type I	Type II	Type III	
Immune reactant	IgE	IgG	IgG	
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Cell-surface receptor	Soluble antigen
Effector mechanism	Mast-cell activation	Complement, Fc γ R $^+$ cells (phagocytes, NK cells)	Antibody alters signaling	Complement, phagocytes
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies	Some drug allergies (e.g. penicillin)	Chronic urticaria (antibody against Fc ϵ RI alpha chain)	Serum sickness, Arthus reaction

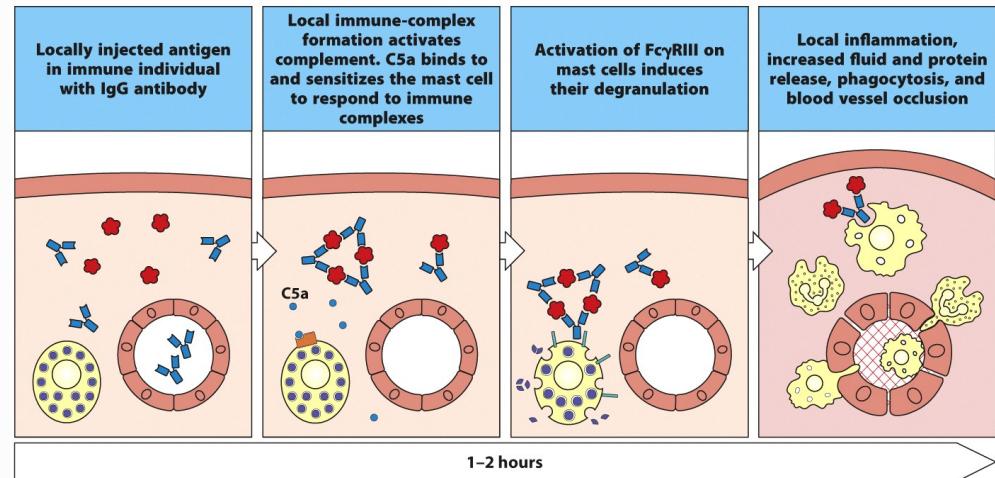


Figure 14.20 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Figure 14.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Several Mechanisms for Allergic Reaction

	Type I	Type II		Type III	Type IV		
Immune reactant	IgE	IgG		IgG	T _H 1 cells	T _H 2 cells	CTL
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Cell-surface receptor	Soluble antigen	Soluble antigen	Soluble antigen	Cell-associated antigen
Effector mechanism	Mast-cell activation	Complement, FcR ⁺ cells (phagocytes, NK cells)	Antibody alters signaling	Complement, phagocytes	Macrophage activation	IgE production, eosinophil activation, mastocytosis	Cytotoxicity
Example of hypersensitivity reaction	Allergic rhinitis, allergic asthma, atopic eczema, systemic anaphylaxis, some drug allergies	Some drug allergies (e.g. penicillin)	Chronic urticaria (antibody against FcεRI alpha chain)	Serum sickness, Arthus reaction	Allergic contact dermatitis, tuberculin reaction	Chronic asthma, chronic allergic rhinitis	Graft rejection, allergic contact dermatitis to poison ivy

Figure 14.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Entry and Dose Effect Reaction and Symptoms

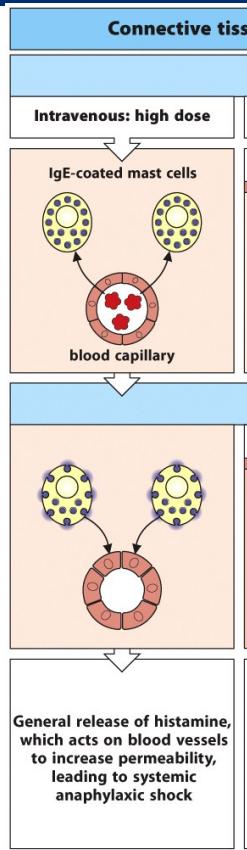


Figure 14.14 Janeway's Immunobi

Entry and Dose Effect Reaction and Symptoms

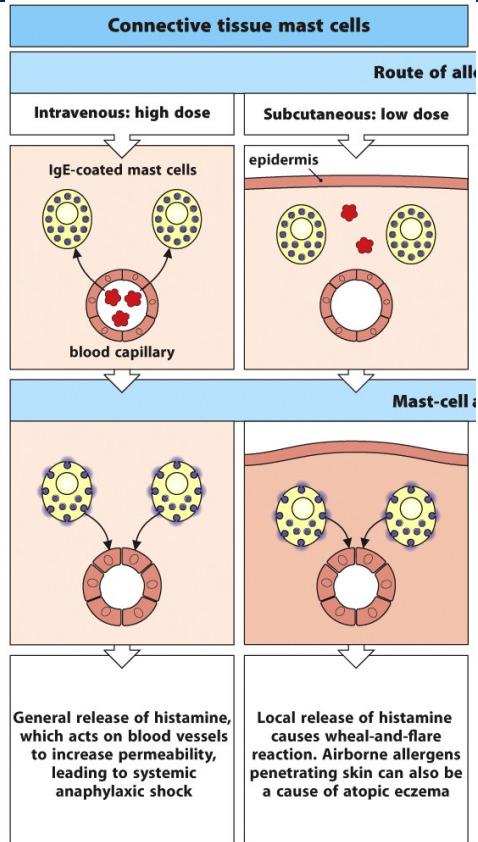


Figure 14.14 Janeway's Immunobiology, 8ed. (© Garland Science 2

Entry and Dose Effect Reaction and Symptoms

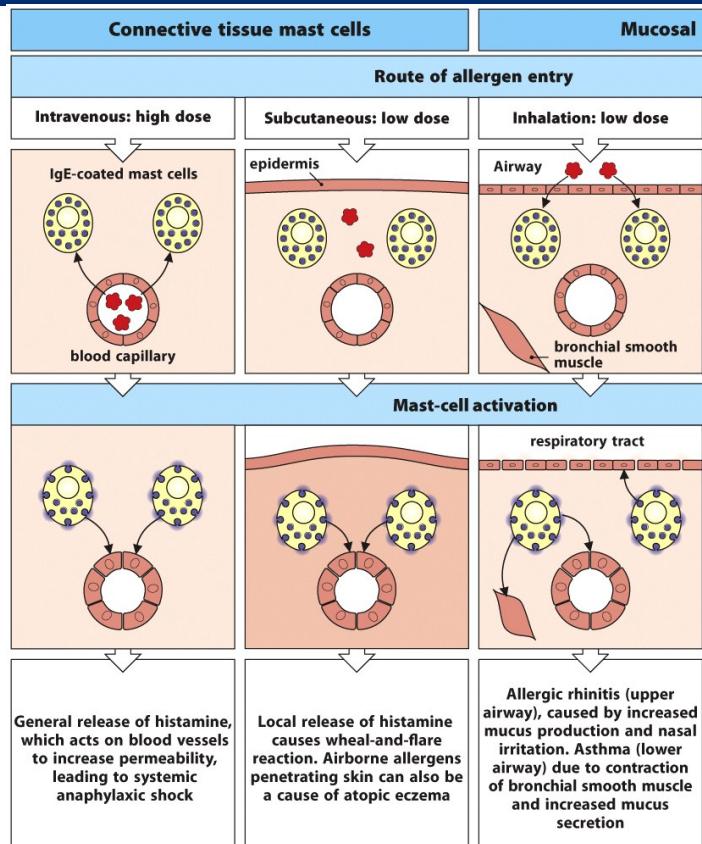


Figure 14.14 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Entry and Dose Effect Reaction and Symptoms

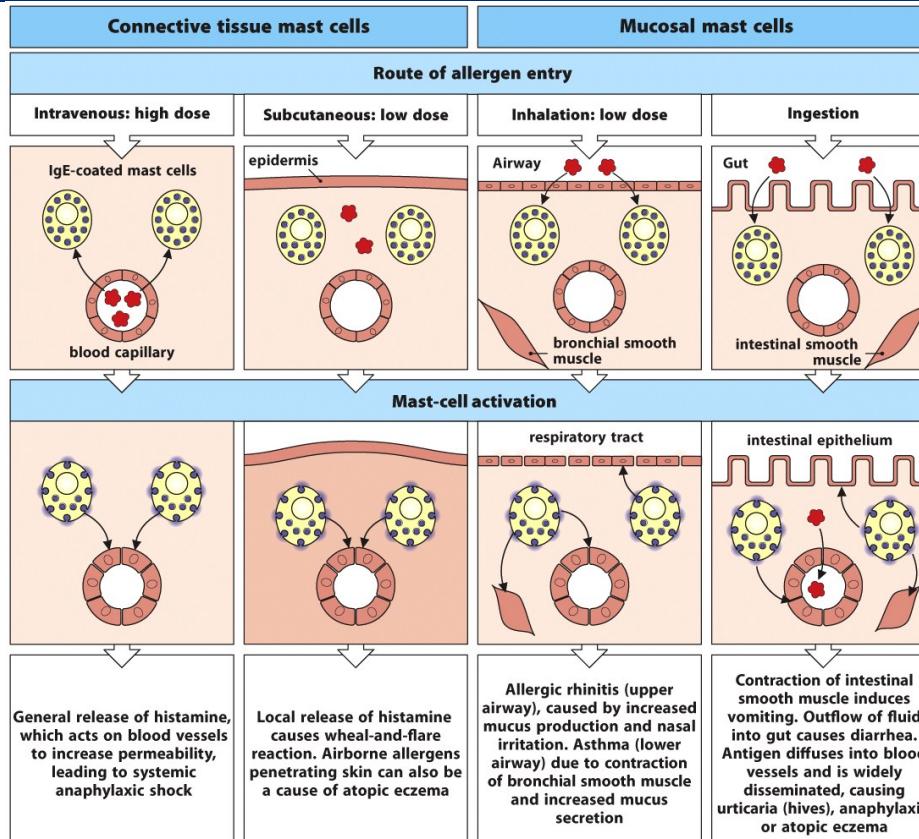


Figure 14.14 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Timing Associated with Allergic Response

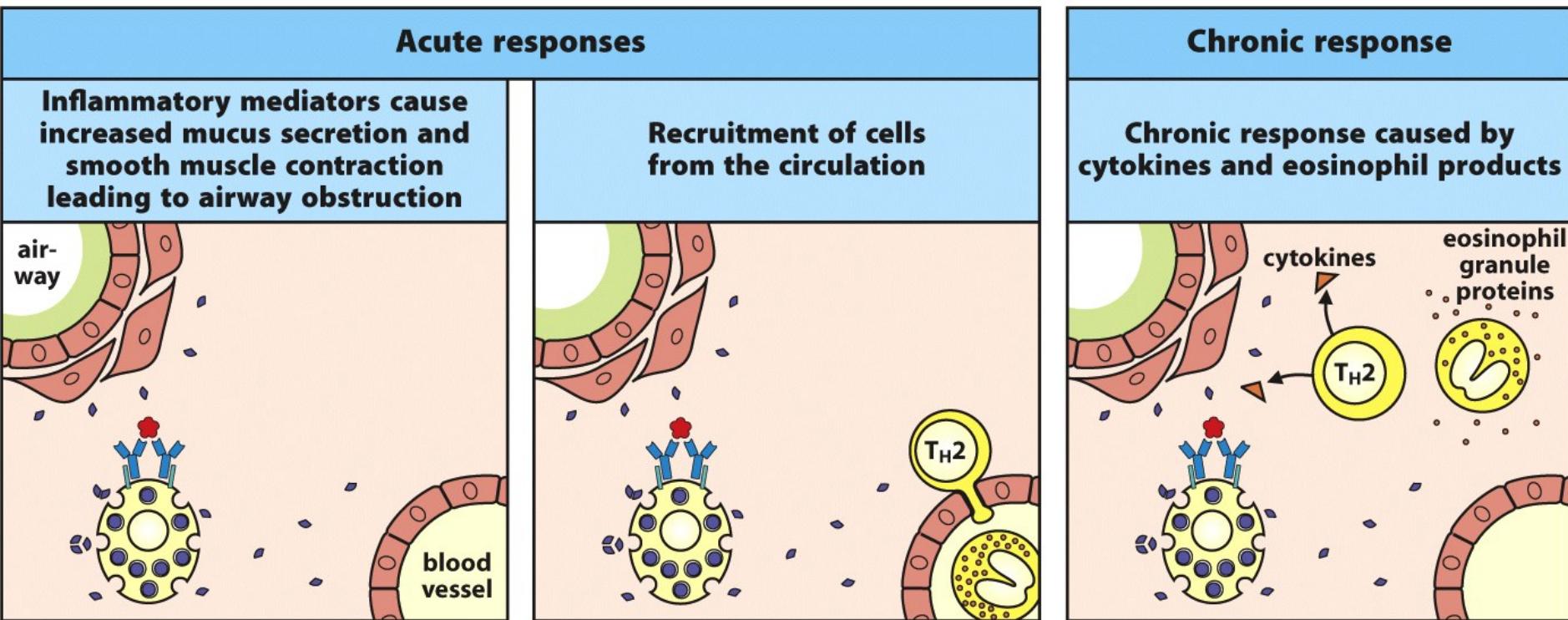


Figure 14.15 Janeway's Immunobiology, 8ed. (© Garland Science 2012)



JOHNS HOPKINS
WHITING SCHOOL
of ENGINEERING