

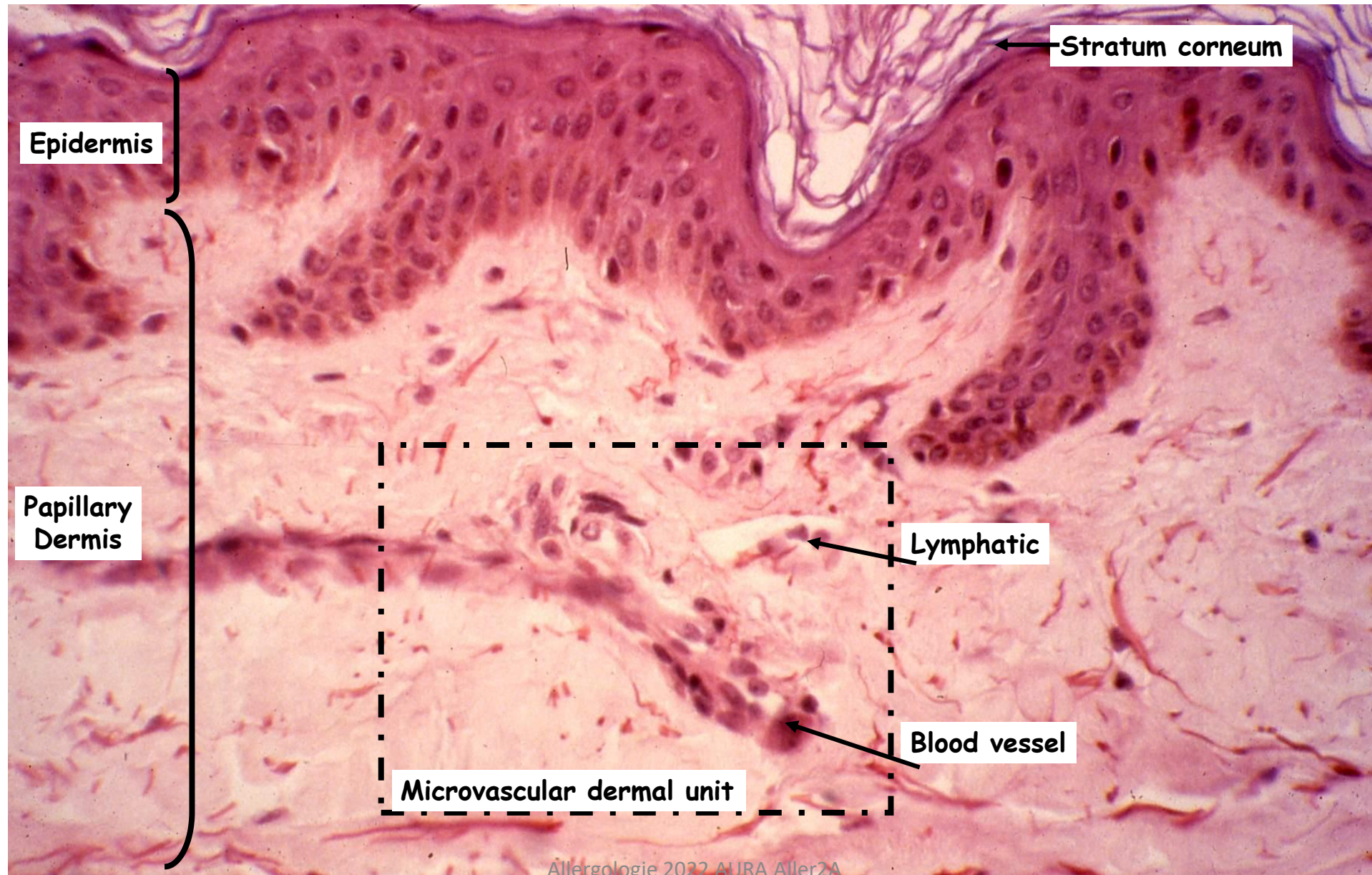
# Hypersensibilités et allergies cutanées

**Audrey NOSBAUM, Florence HACARD, Marc VOCANSON,  
Frédéric BERARD, Jean-François NICOLAS**

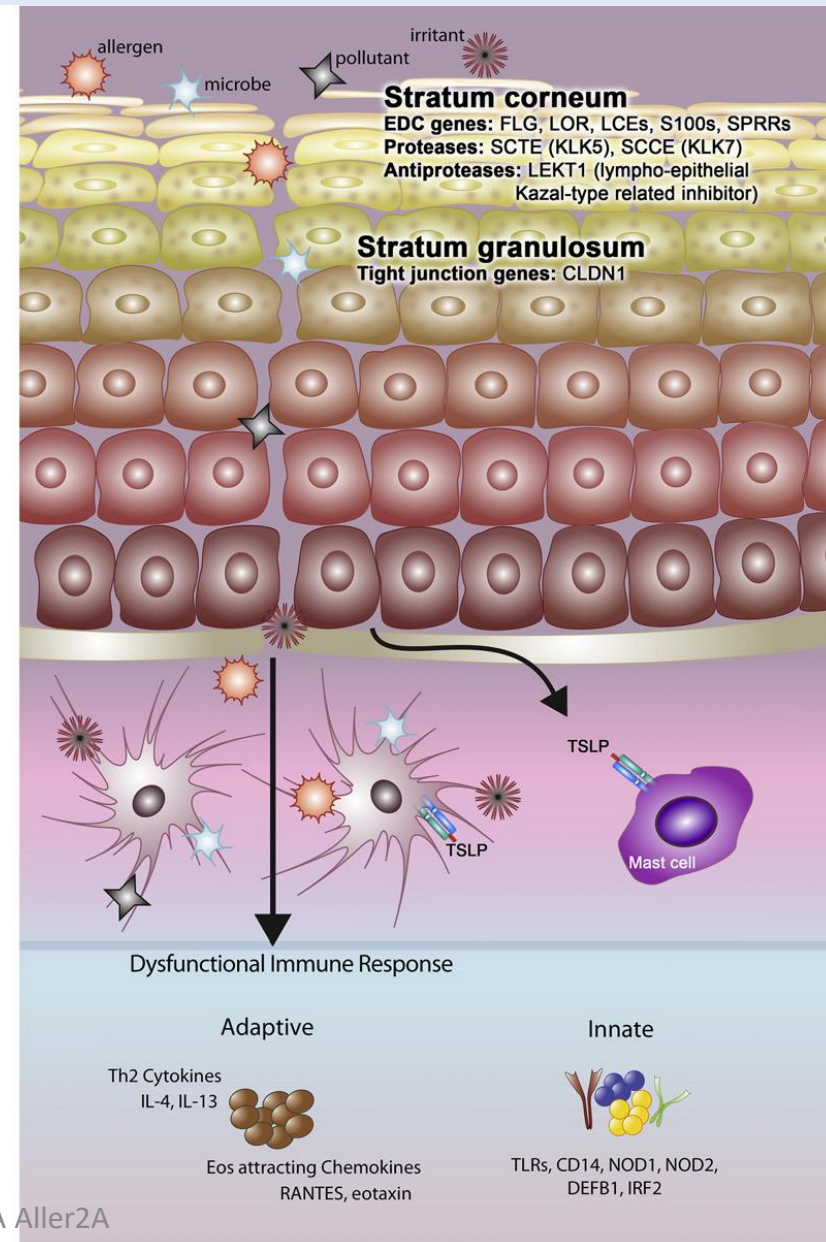
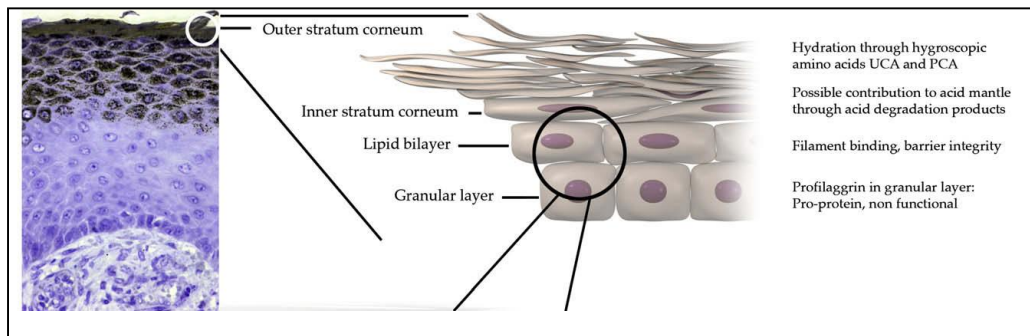
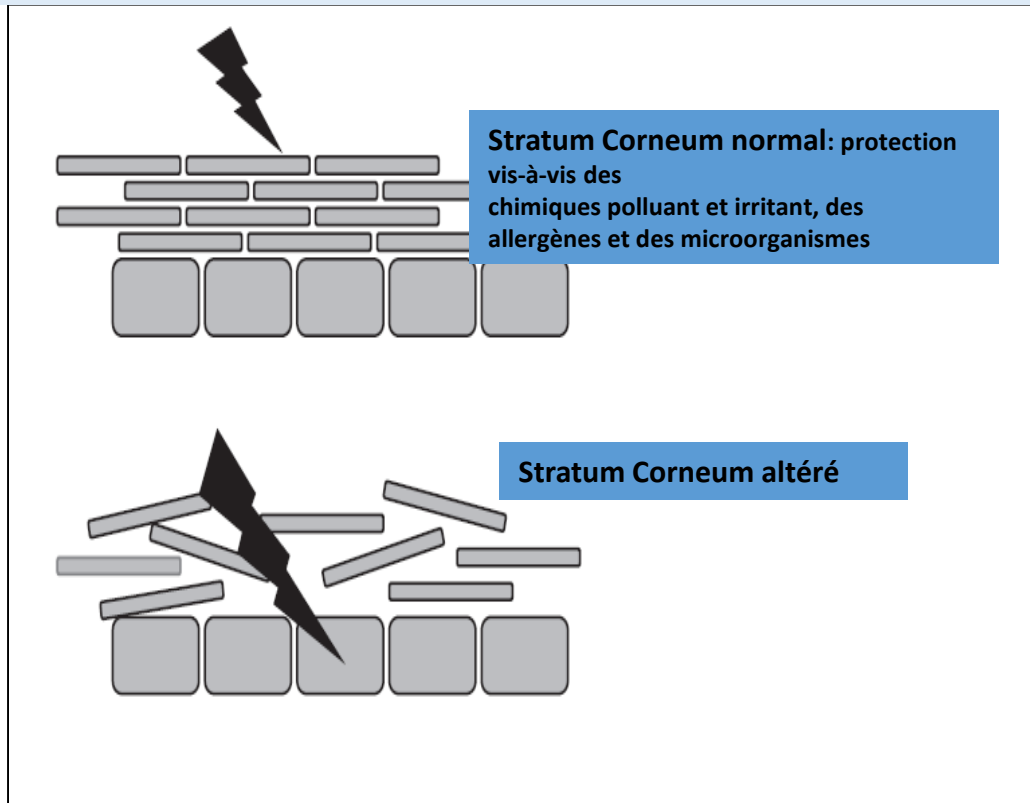
Allergologie et Immunologie Clinique,  
INSERM U1111-CIRI, CHU Lyon-Sud



# Skin anatomy and physiology



# ECZEMAS – Impairment of epidermal barrier



# Hypersensitivity reactions

## 1. Immunology definition – Gell & Coombs

Hypersensitivity reactions = inappropriate and damaging immune response to an antigen caused by adaptive immunity (Igs and/or T cells)

- Allergic diseases
- Autoimmune diseases

## 2. Allergy définition

Hypersensitivity reactions = inappropriate and damaging immune response to a molecule caused by both innate and/or adaptive immunity

- Allergic HS
- Non allergic HS



# Hypersensibilité (HS)



HS adaptative  
Allergique

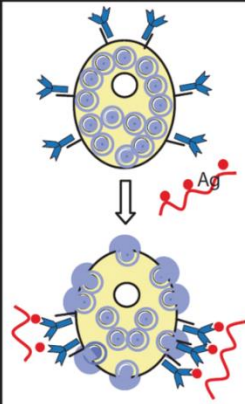
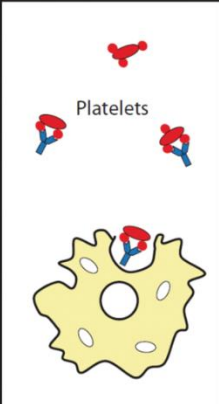
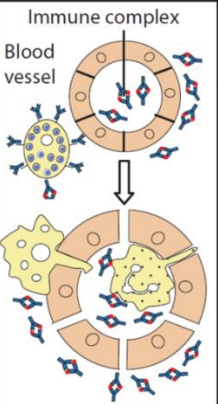
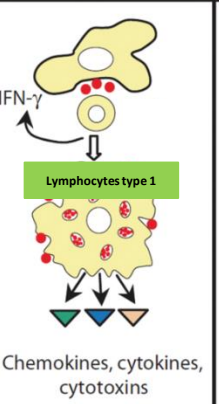
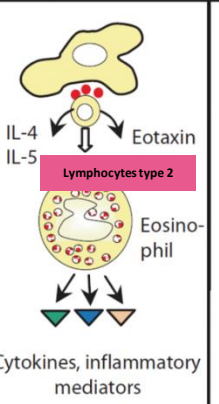
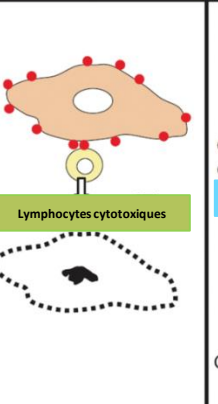
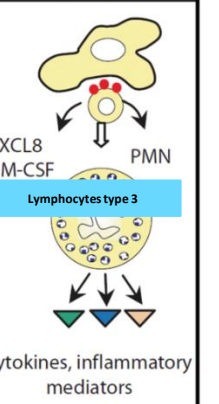


HS innée  
Non Allergique



# Hypersensibilités

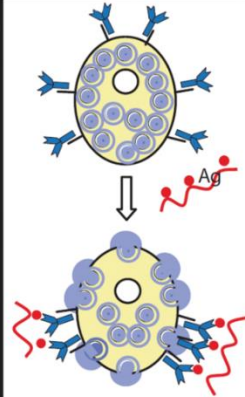
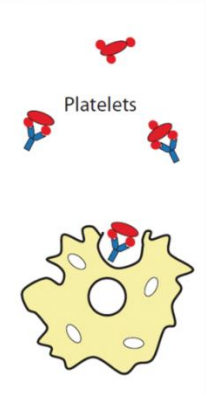
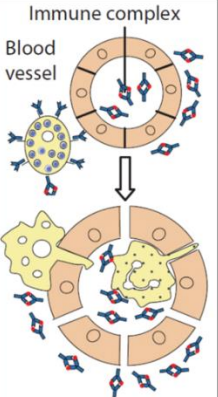
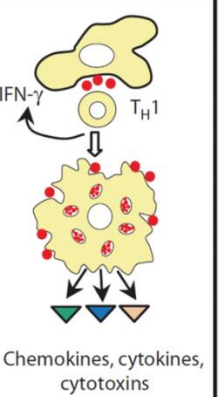
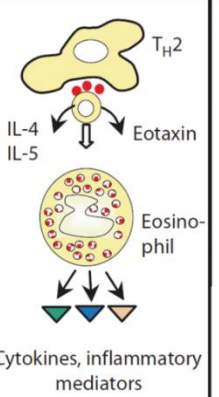
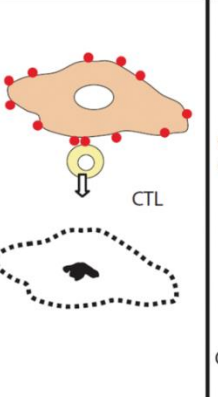
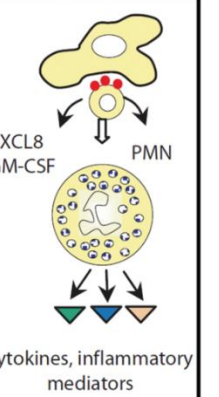
## Classification de Gell & Coombs

	Antibody			T cells			
	Type I	Type II	Type III	Type IVa	Type IVb	Type IVc	Type IVd
Immune reactant	IgE	IgG	IgG	IFN- $\gamma$ , TNF- $\alpha$ <b>Type 1</b>	IL-5, IL-4/IL-13 <b>Type 2</b>	Perforin/ granzyme B <b>Cytotoxic</b>	IL-17, IL-22 <b>Type 17/3</b>
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Soluble antigen	Antigen presented by cells or direct T-cell stimulation	Antigen presented by cells or direct T-cell stimulation	Cell-associated antigen or direct T-cell stimulation	Soluble antigen presented by cells or direct T-cell stimulation
Effector	Mast cell activation	FcR+ cells (phagocytes, NK cells)	FcR+ cells Complement	Macrophage activation	Eosinophils	T cells	Neutrophils
							
Maladies autoimmunes et allergiques	Anaphylaxie Rhinite allergique Asthme (crise)	Réaction transf. Anémie hémol. Thyroidite Myasthénie	Maladie sérique Lupus érythémateux	IDR tuberculine Rejet de greffe Polyarthrite Diabète	Asthme chron. Rhinite chron.	Rejet de greffe Diabète SEP	Polyarthrite Sclérose en plaque Mal. de Crohn
Dermatoses autoimmunes et allergiques	Urticaire contact	Pemphigus Pemphigoïde Urticaire chroni.	Vascularites	Psoriasis	Dermatite atopique	Vitiligo Pelade Eczéma contact	Psoriasis
Allergies médicaments	Choc anaphylactique	Cytopénies medic.	Vascularites immuno-allerg.	Exanthème médic.	DRESS	Lyell Stevens-Johnson	Pustulose exanthématique aigüe généralisée



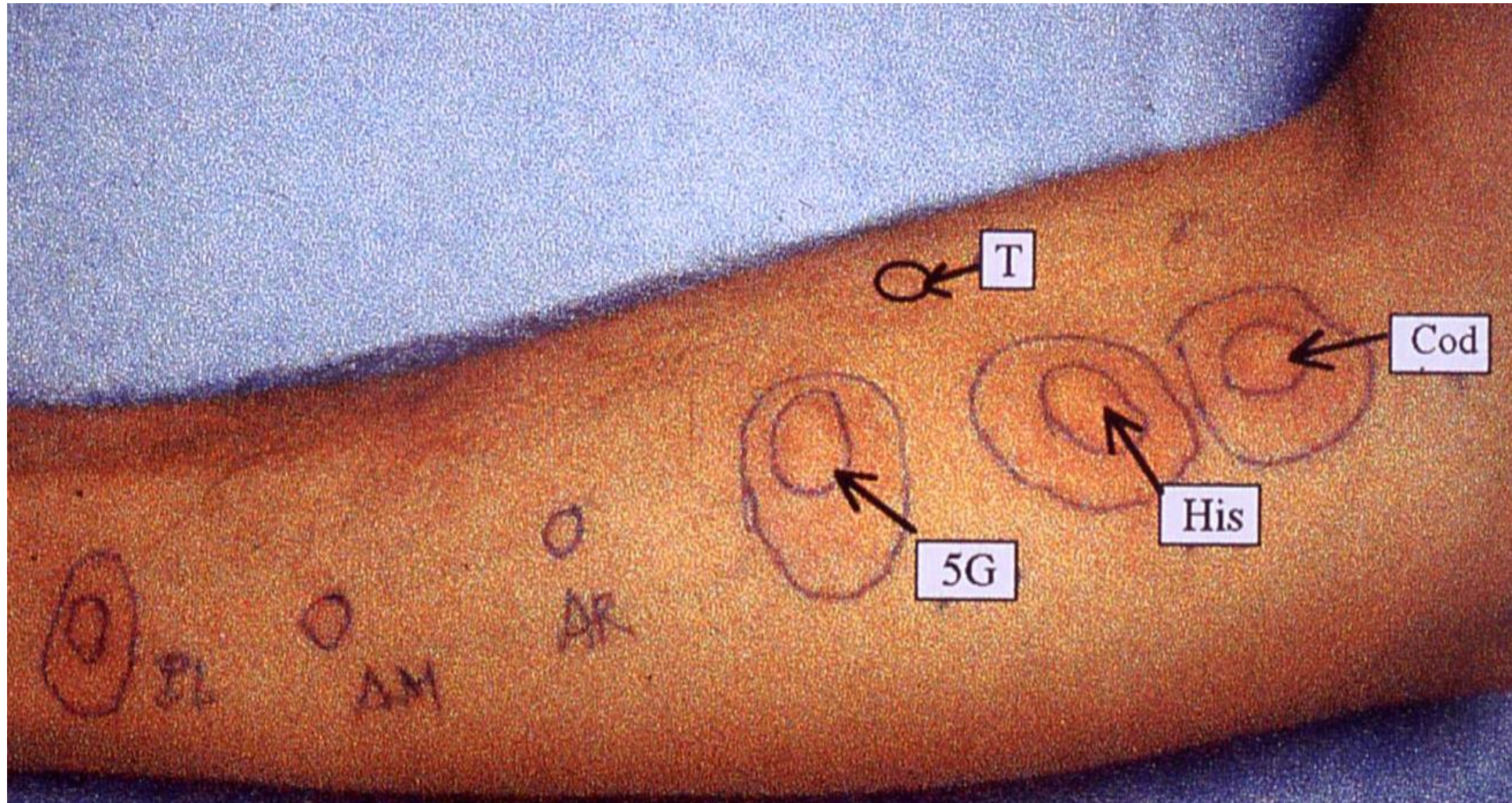
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# HSI allergique et non allergique



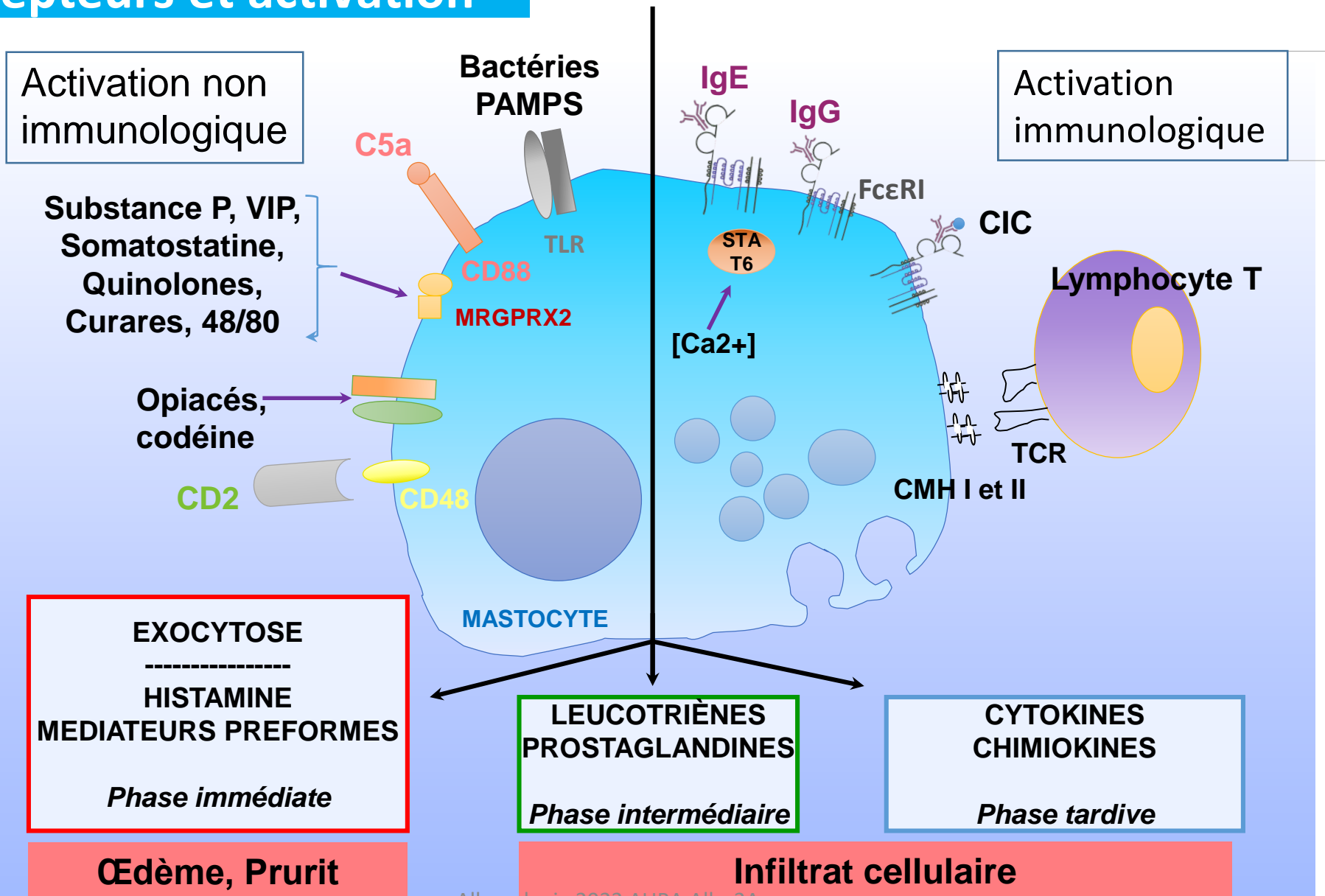
Tests cutanés aux pneumallergènes chez un patient atopique





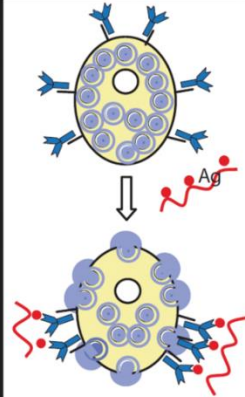
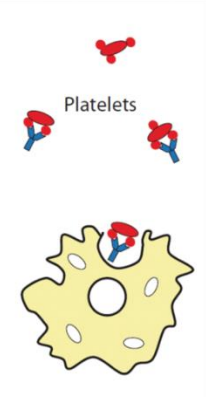
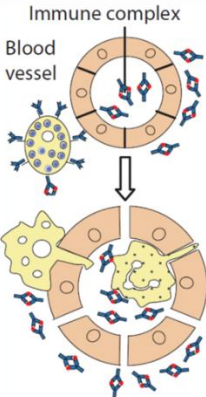
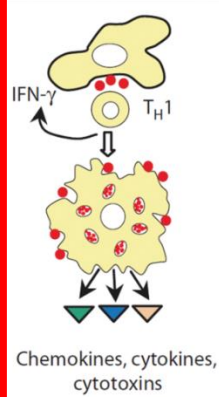
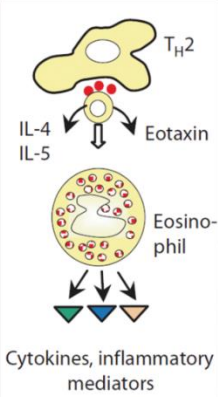
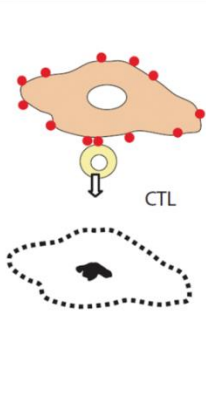
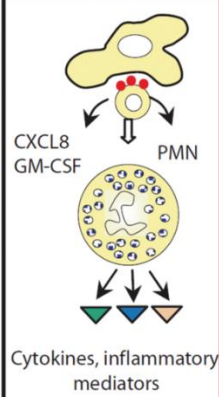
# MASTOCYTES

## Récepteurs et activation



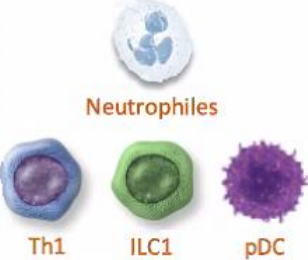


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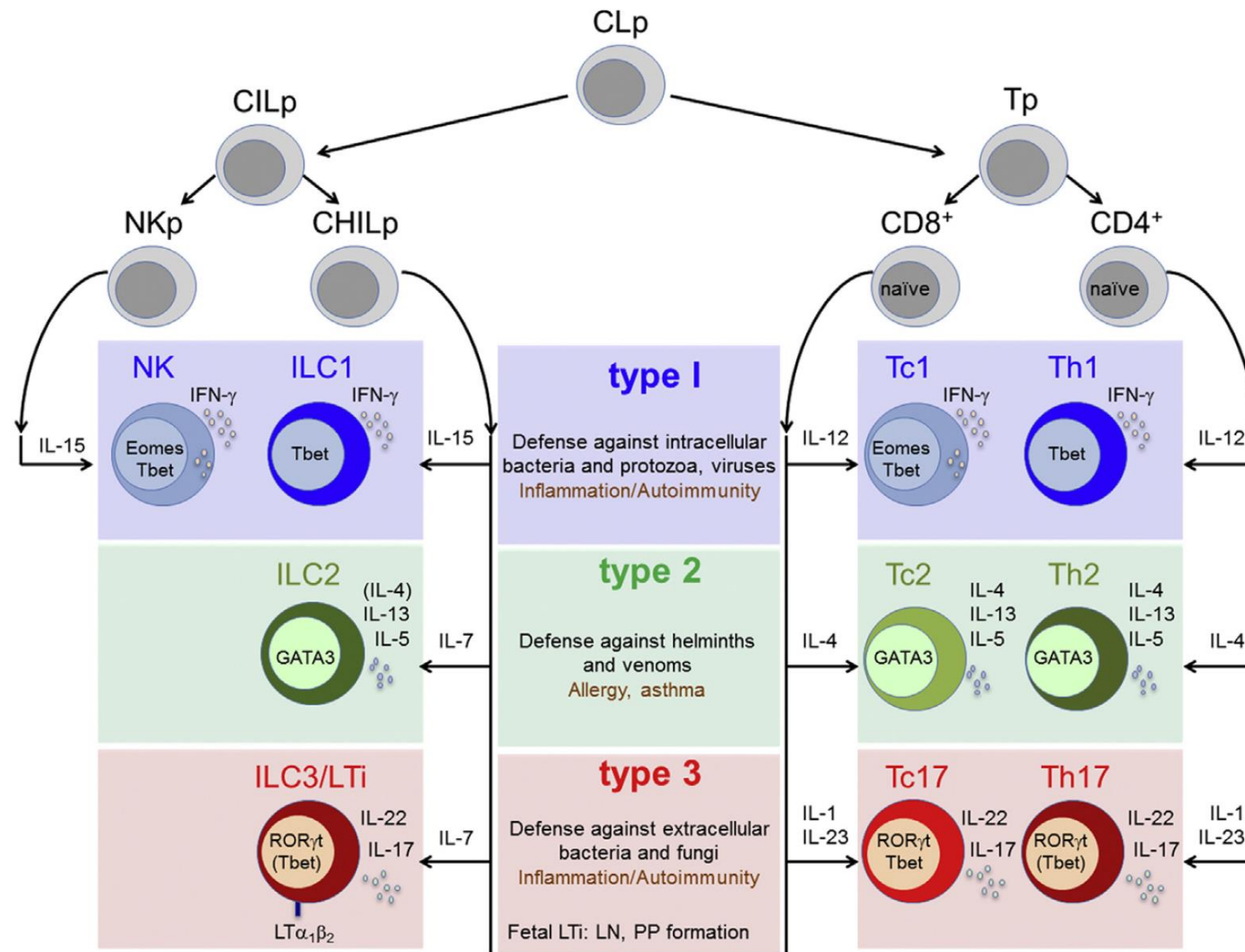


# Inflammation type 1, type 2, type 17

Voies Inflammatoires	Type 1	Type 2	Type 3
<b>Cellules Immunitaires<sup>1,2</sup></b>	 <p>Neutrophiles Th1 ILC1 pDC</p>	 <p>Th2 cell ILC2 Mast cell T<sub>fh</sub> Basophiles Eosinophiles</p>	 <p>Neutrophiles Th17 Th22 ILC3</p>
<b>Cytokines<sup>1-3</sup></b>	<p>IL-17 IFN<math>\gamma</math> IL-6 IL-12 IL-2 TNF</p>	<p>IL-4 IL-5 IL-13 IL-31</p>	<p>IL-17 IL-6 IL-22 IL-23</p>
<b>Cibles<sup>1,3</sup></b>	<p>Virus Bactéries intracellulaires Cancer</p>	<p>Allergènes Parasites</p>	<p>Bactéries extracellulaires -Mycoses</p>
<b>Exemples de pathologies<sup>4-6</sup></b>	<p><b>Maladies auto-immunes</b> Lupus Lichen Vitiligo-Pelade</p>	<p><b>Pathologies de type 2</b> Dermatite Atopique Rhinite Allergique Asthme Polypose Nasale Oesophagite à éosinophiles Allergie alimentaire</p>	<p><b>Maladies auto-immunes</b> Psoriasis Psoriatic arthritis <b>Lupus</b></p>

Kaiko GE, et al. *Immunology*. Eyerich K, Eyerich S. *J Eur Acad Dermatol Venereol*. Raphael I, et al. *Cytokine*. 2015 Nakayama T, et al. *Annu Rev Immunol*. 2017. Coates LC, et al. *Semin Arthritis Rheum*. 2016 Gandhi NA, et al. *Expert Rev Clin Immunol*. 2017

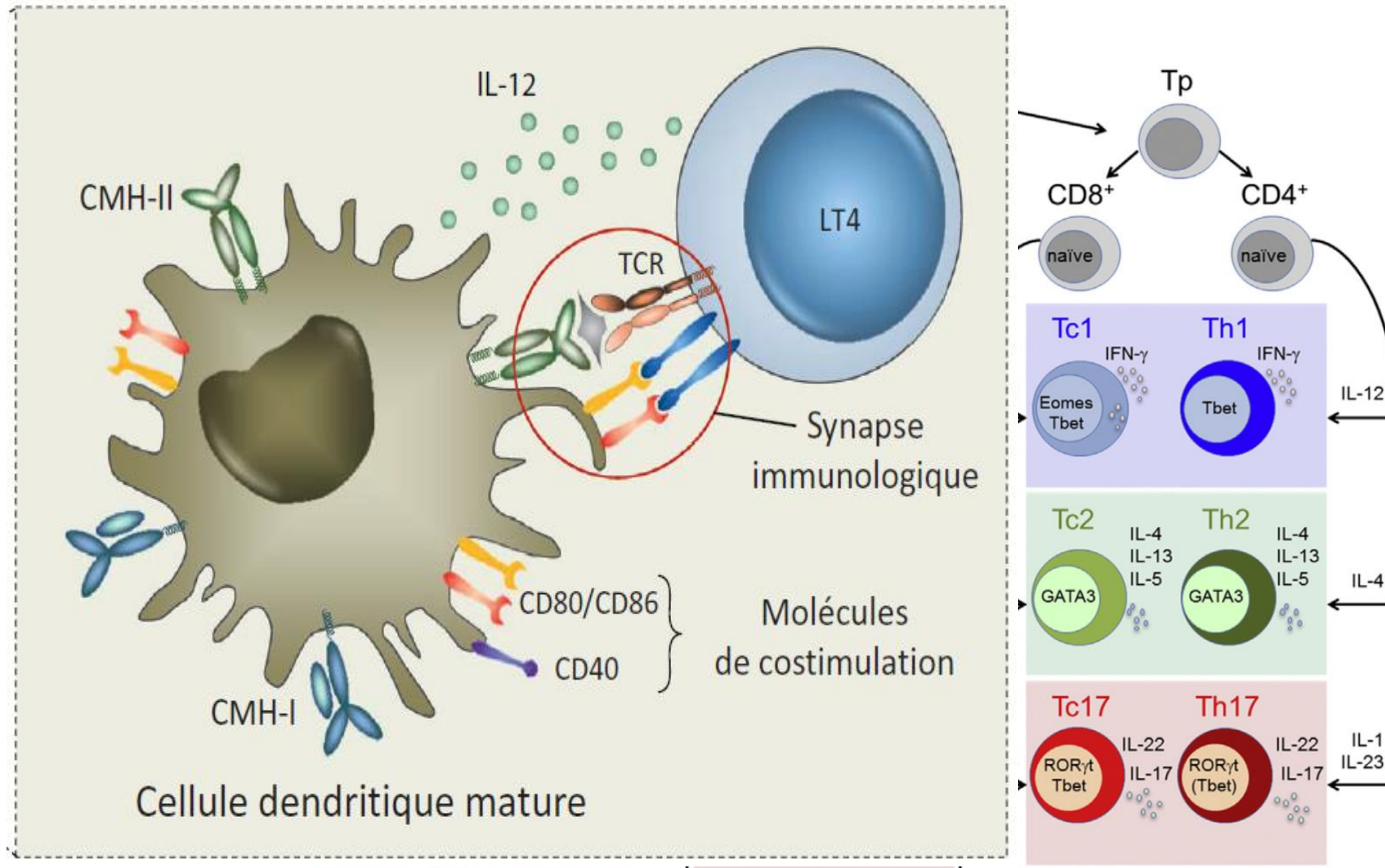




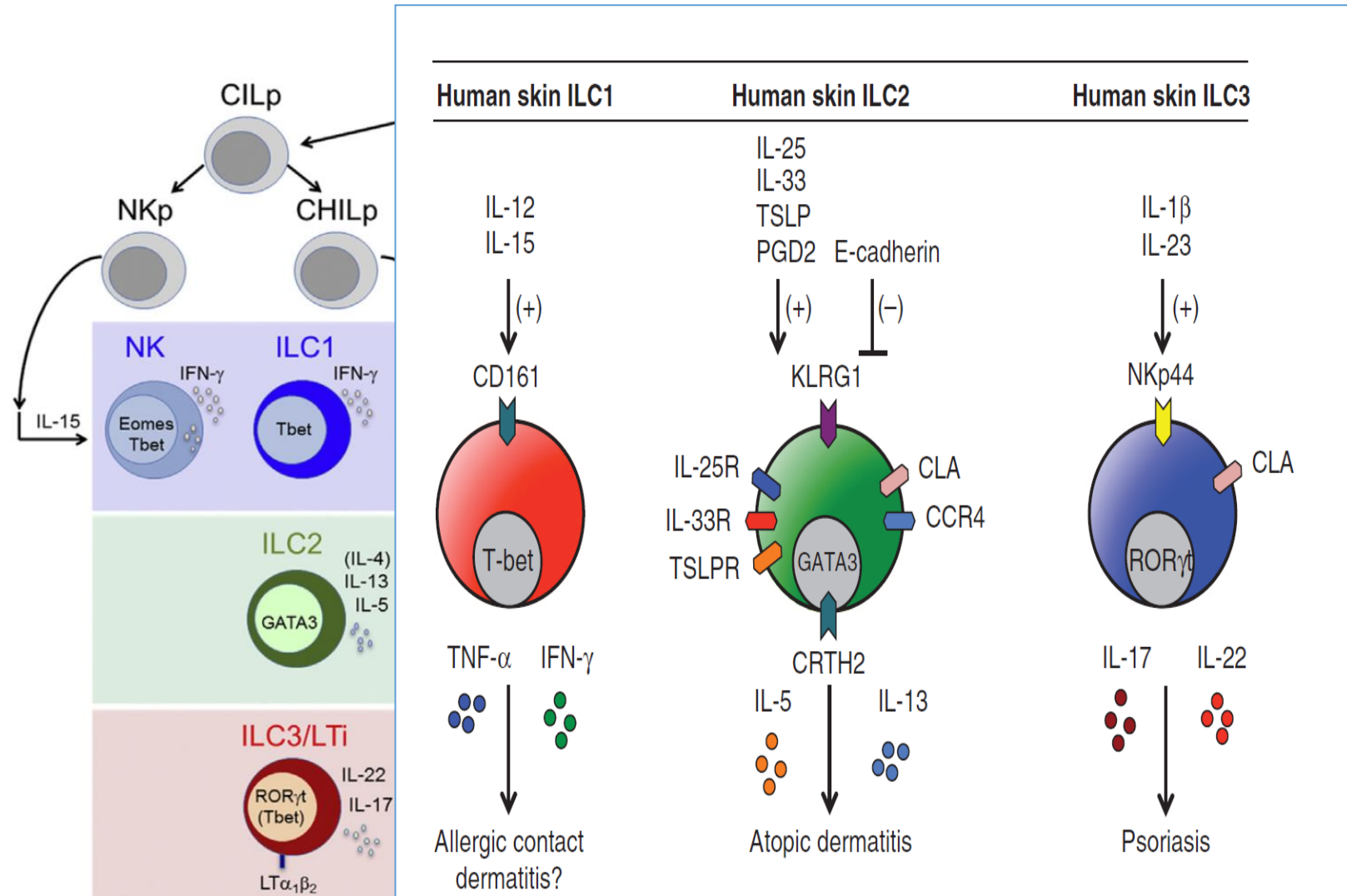
**FIG 1.** The 3 major types of innate and adaptive cell-mediated effector immunity. Type 1 immunity is composed of T-bet<sup>+</sup> IFN- $\gamma$ -producing CD4<sup>+</sup> T<sub>H</sub>1 cells and ILC1s and T-bet<sup>+</sup>Eomes<sup>+</sup>CD8<sup>+</sup> T<sub>C</sub>1 and NK cells. Type 2 immunity is composed of GATA-3<sup>+</sup>CD4<sup>+</sup> T<sub>H</sub>2 cells, CD8<sup>+</sup> T<sub>C</sub>2 cells, and ILC2s, which produce IL-4, IL-5, and IL-13. Type 3 immunity is composed of ROR $\gamma$ t (RORC)<sup>+</sup>CD4<sup>+</sup>T<sub>H</sub>17 cells, CD8<sup>+</sup> T<sub>C</sub>17 cells, and ILC3s, producing IL-17, IL-22, or both. *CILp*, Common innate lymphoid precursor; *CLp*, common lymphoid precursor; *LN*, lymph node; *LTi*, lymphoid tissue inducer; *PP*, Peyer patch; *Tp*, T-cell progenitor.



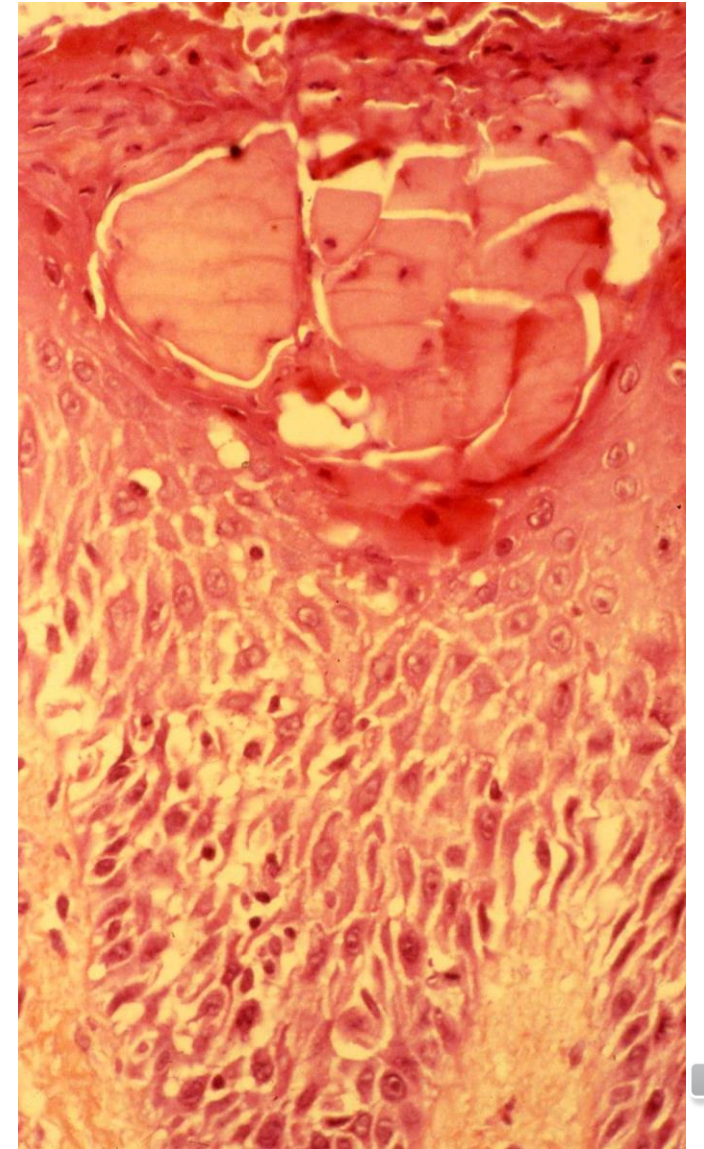
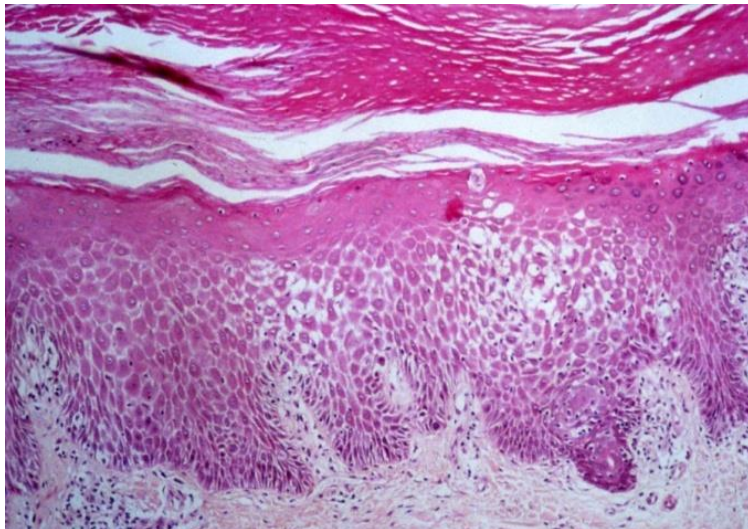
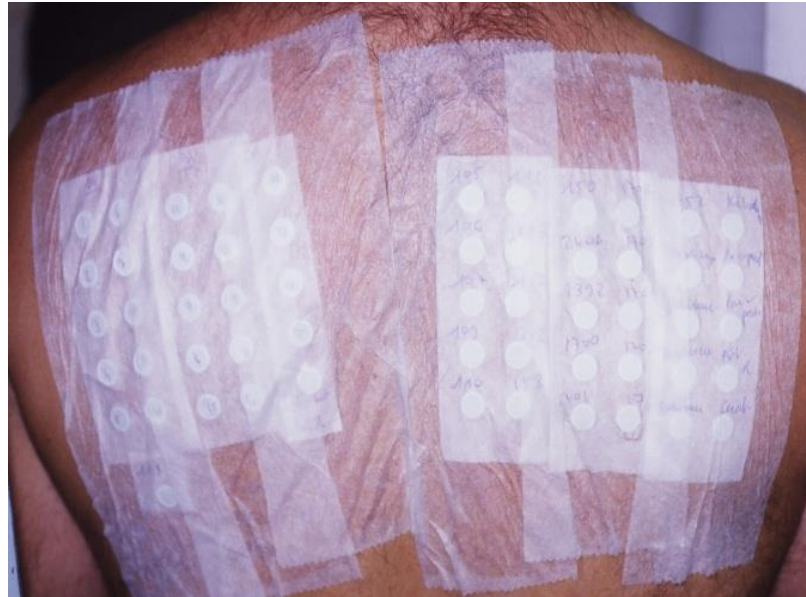
# The 3 major types of innate and adaptative cell-mediated immunity



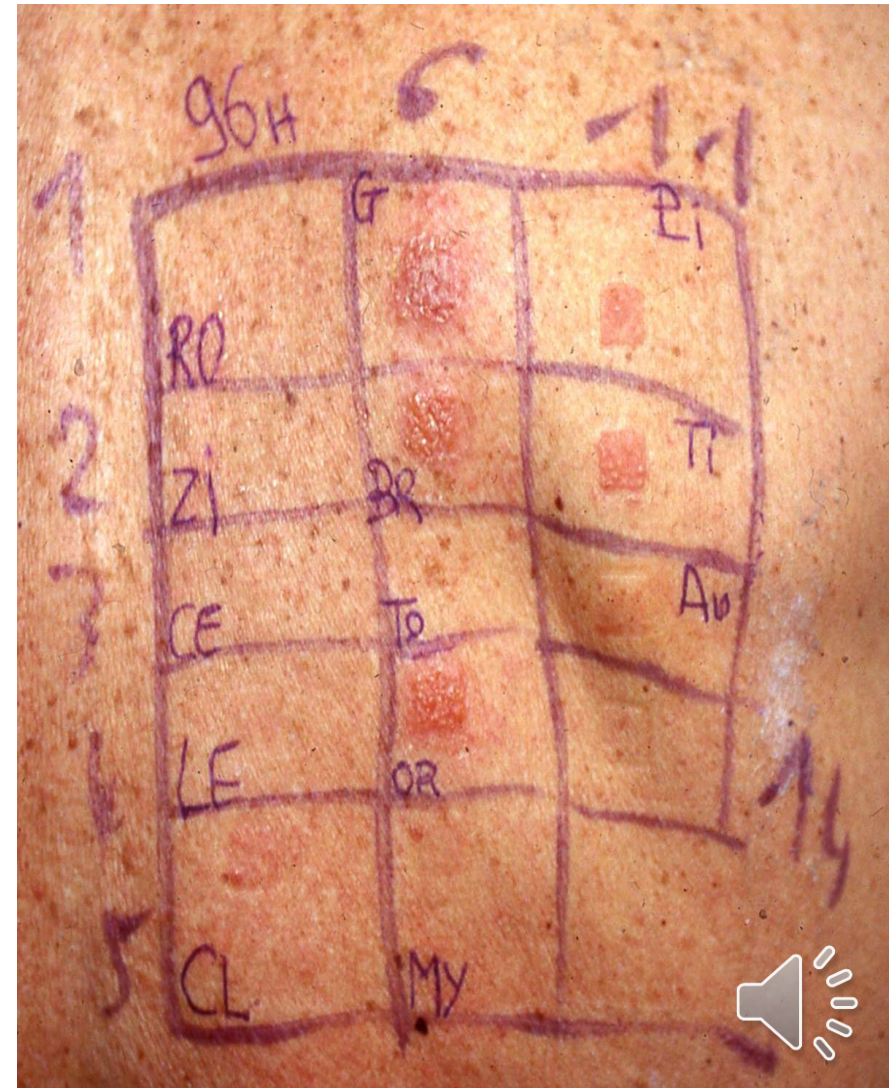
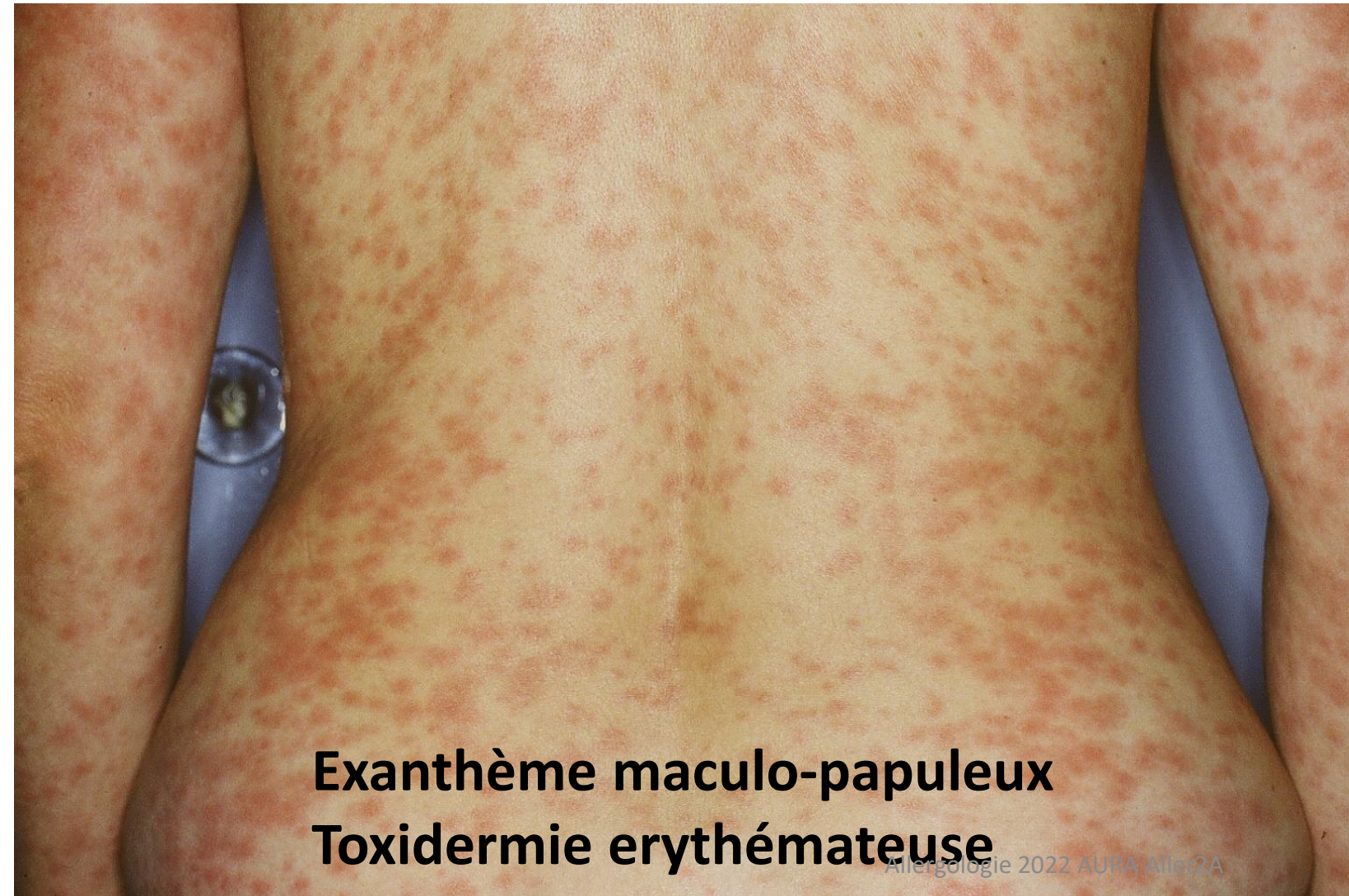
# The 3 major types of innate and adaptative cell-mediated immunity



# Type IV hypersensitivity - Type 1



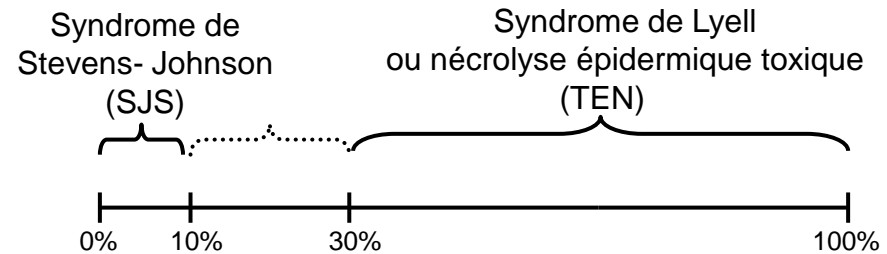
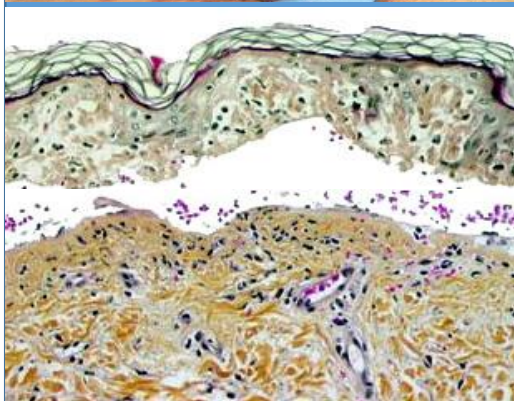
# Type IV hypersensitivity - Type 1





# Type IV hypersensitivity - Type 1 cytotoxic

## Nécrolyse épidermique toxique – Sd de Stevens-Johnson – Sd de Lyell

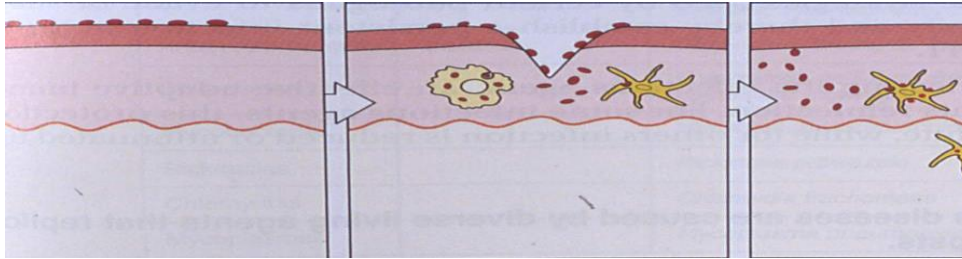


- **Physiopathologie:** apoptose kératinocytaire médiée par les LT
- **Incidence:** 1 à 3 cas/million/an.
- **Délai :** 1 à 21 jours
- **Clinique:**
  - Altération de l'état général, fièvre
  - Erosions muqueuses (>2 sites)
  - Décollements cutanés superficiels (S. de Nikolski +)
- **Biologie:** lymphopénie fréquente
- **Atteinte viscérale:** rénale, pulmonaire, digestive, foie
- **Histologie:** nécrolyse épidermique totale
- **Médicaments:** allopurinol+++, lamotrigine, carbamazépine, sulfaméthoxazole, AINS (oxicams), nevirapine,...
- **Mortalité:** 30-35% (estimée par le SCORTEN)

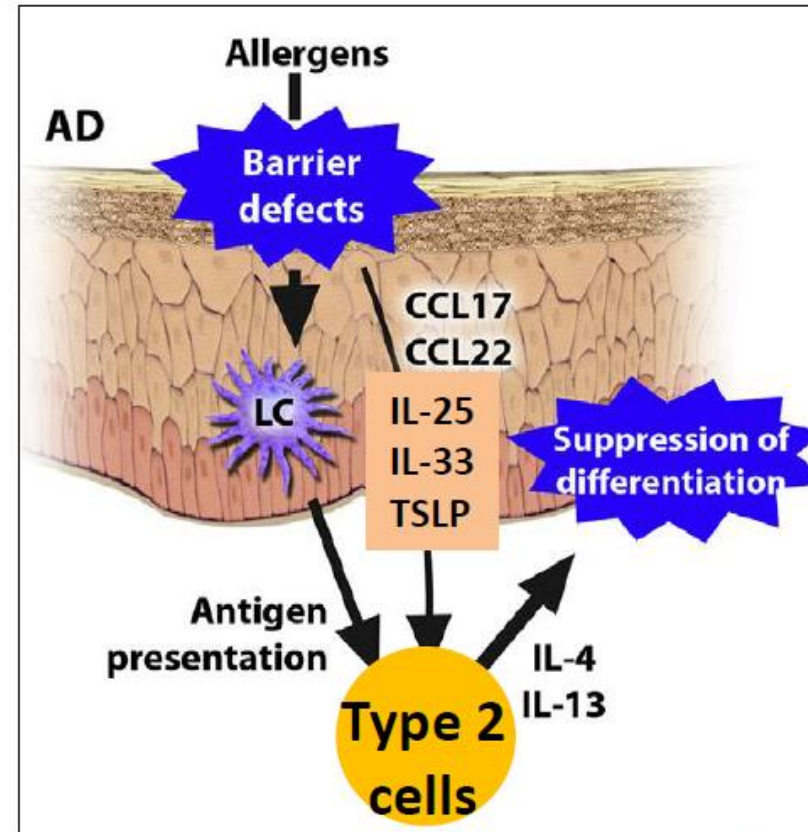


# Type IV hypersensitivity - Type 2 DERMATITE ATOPIQUE

Type 2



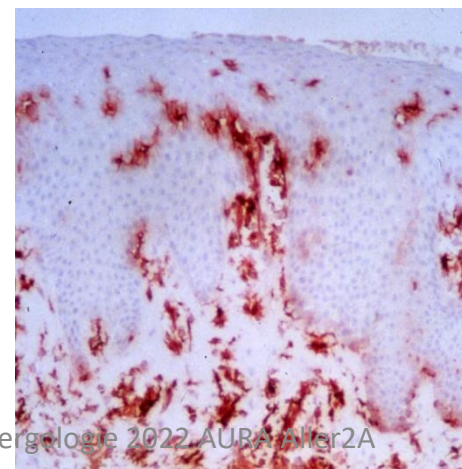
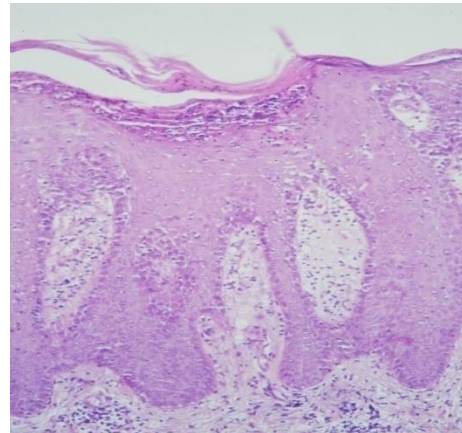
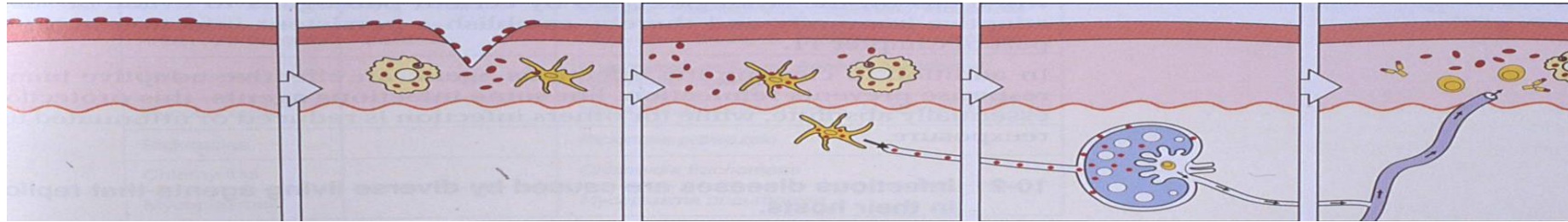
## Type 2 phenotype



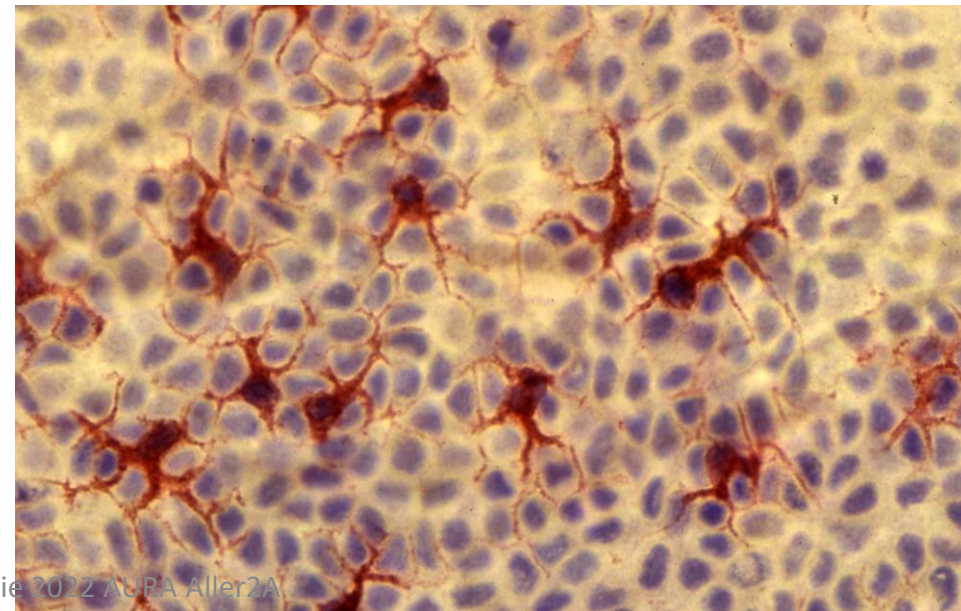
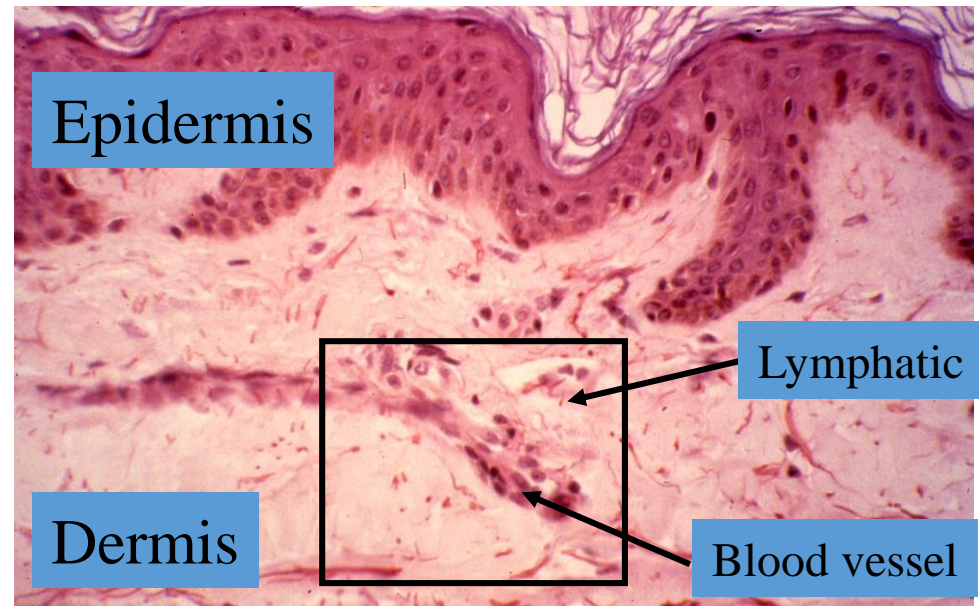
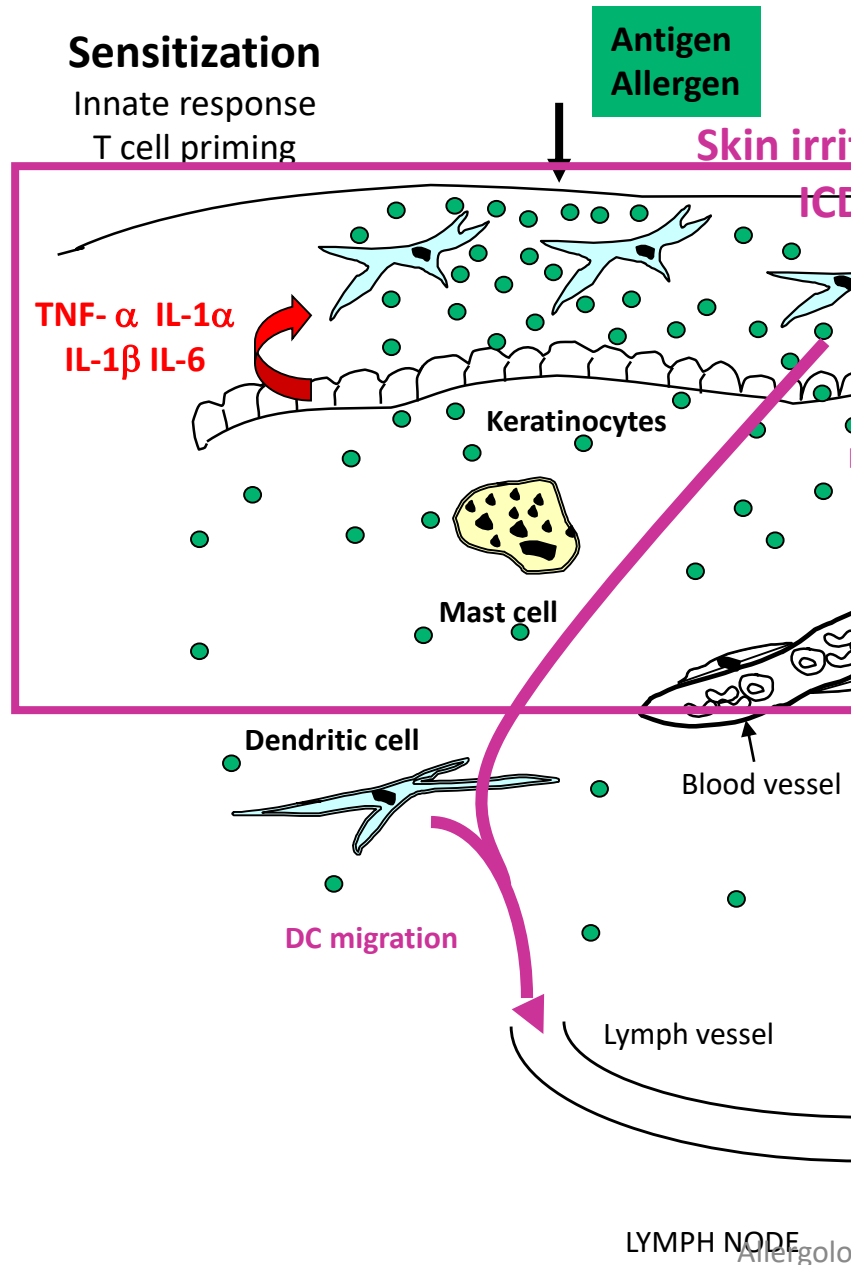
## Type 2 inflammation Type 2 immunity



# Type IV hypersensitivity - Type 3 Psoriasis



# Immunology of eczemas



# Pathophysiology of skin inflammation

**EARLY (6-24h)**

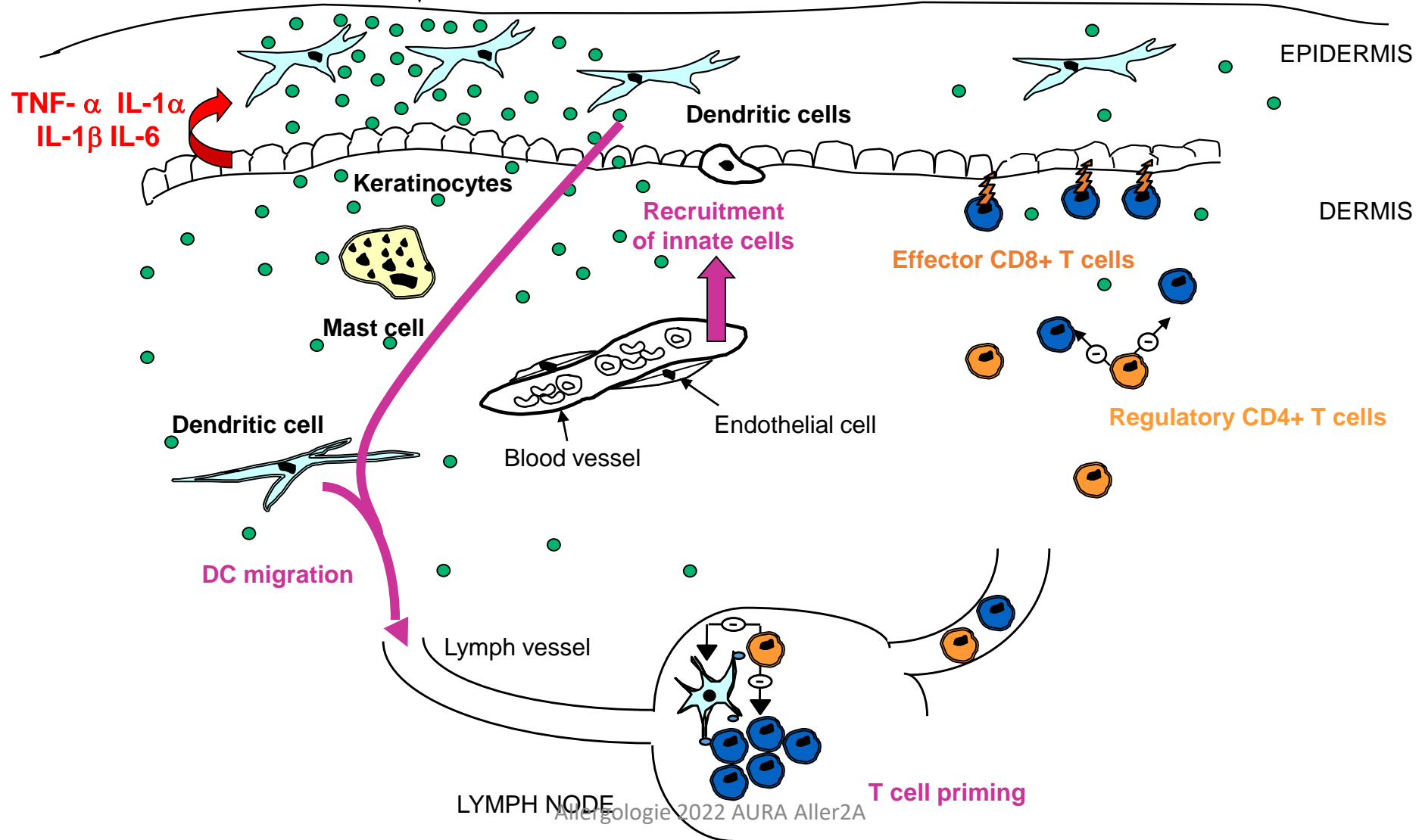
## Sensitization

Innate response  
T cell priming

**ANTIGEN (hapten, protein)**  
- Environmental antigen  
- Vaccine antigen

## Elicitation

Effector T cell response  
Skin inflammation



# Pathophysiology of skin inflammation

**LATE (48-72h)**

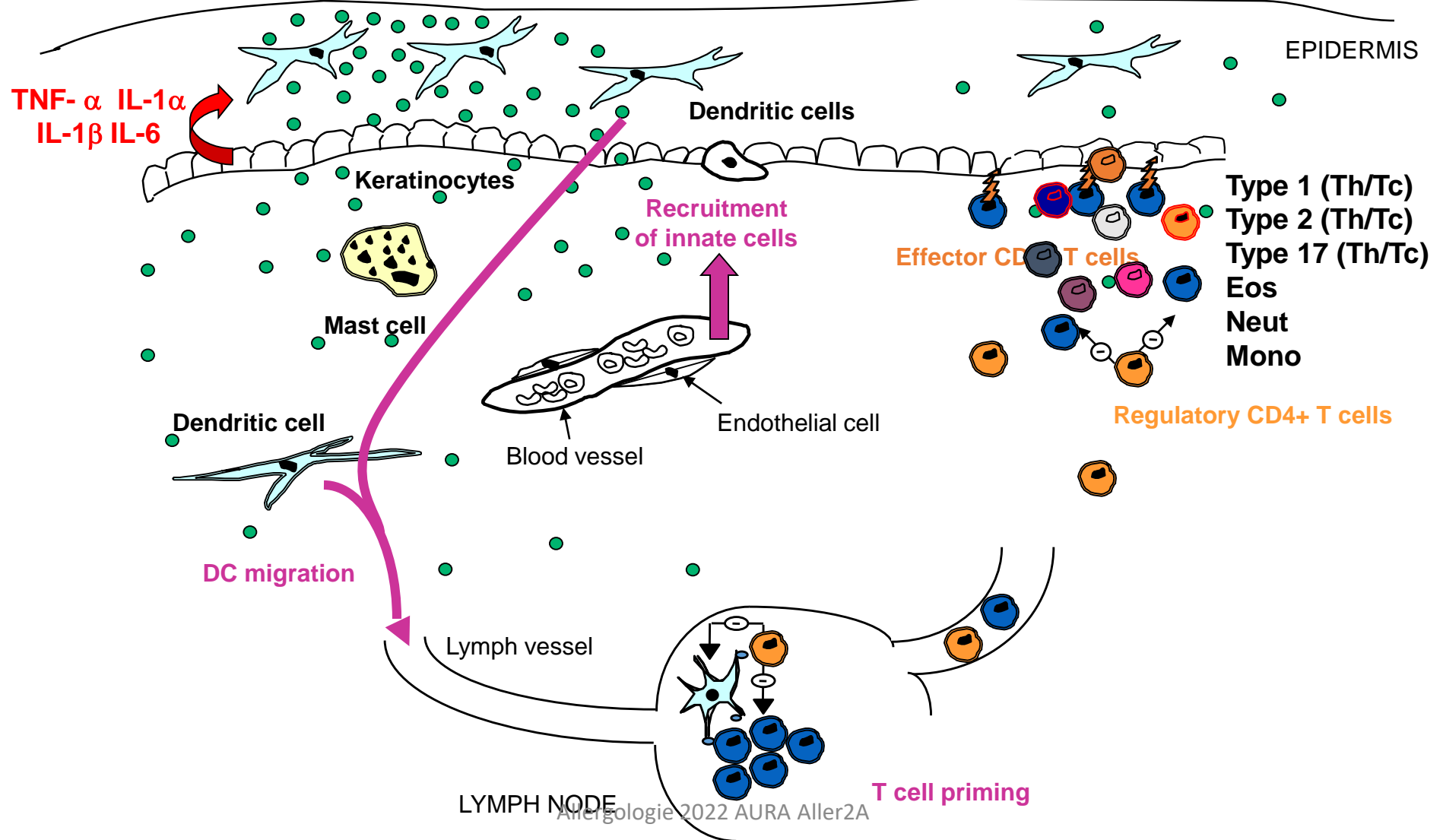
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Innate response  
T cell priming

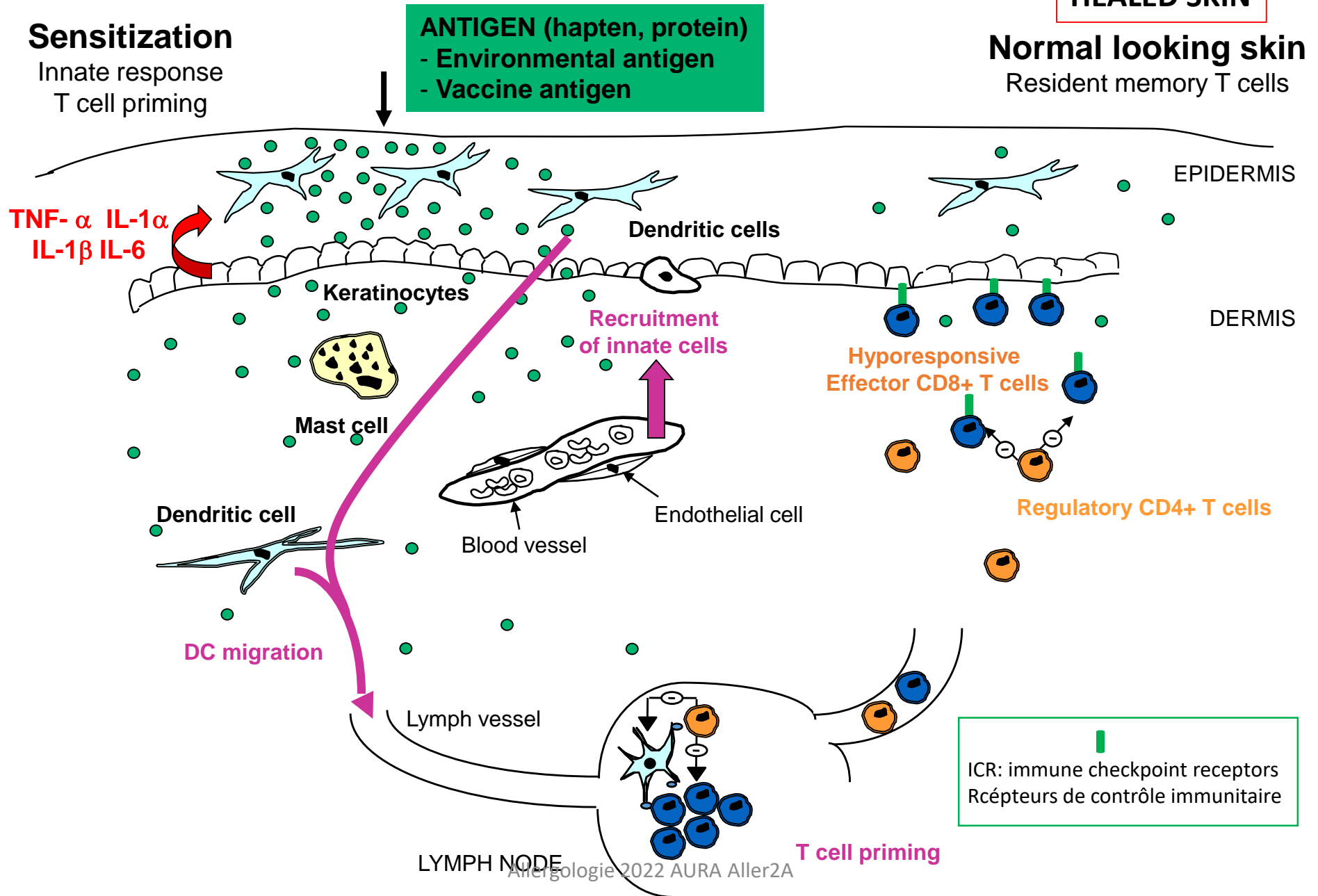
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## Elicitation

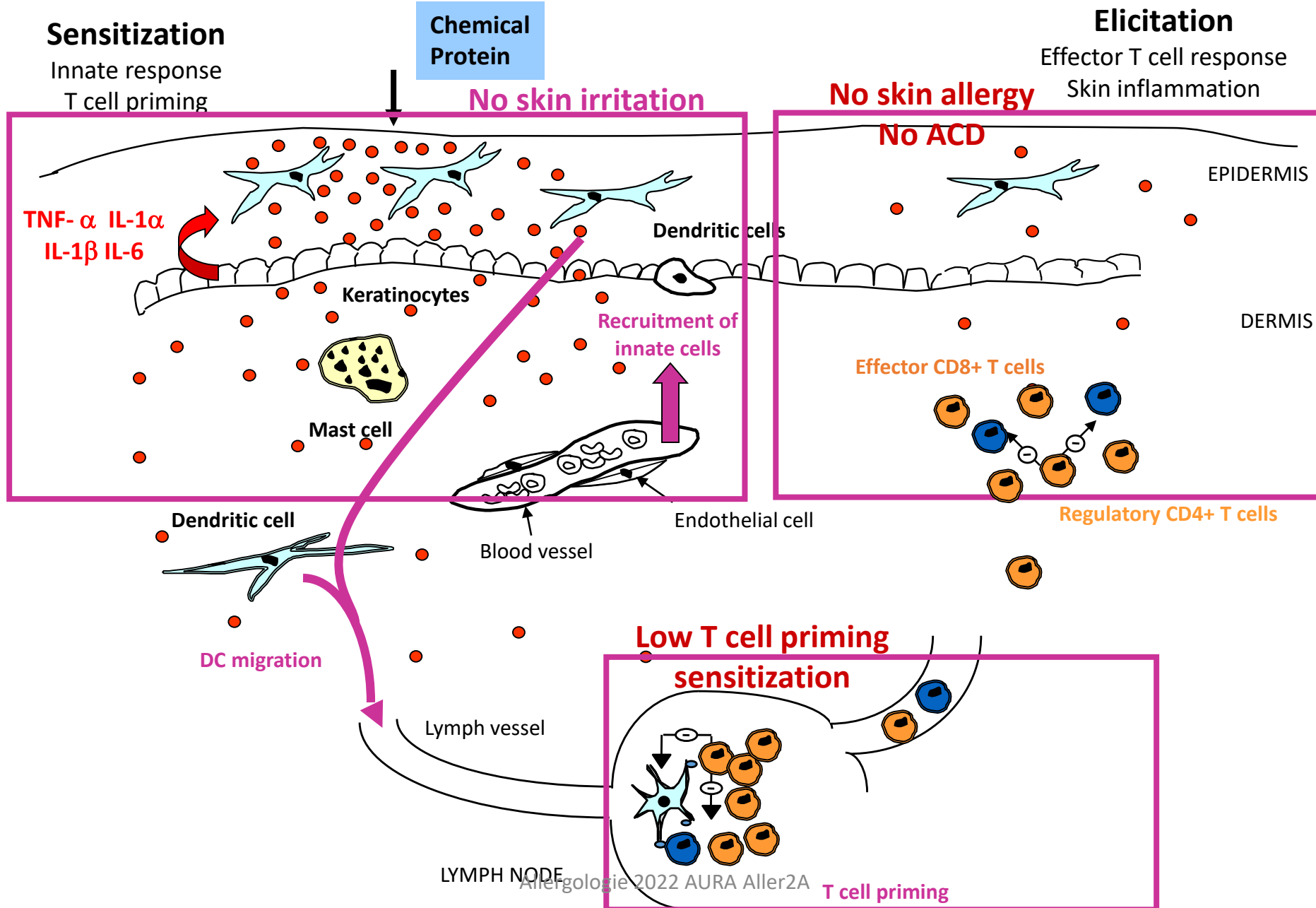
Effector T cell response  
Skin inflammation



# Pathophysiology of skin inflammation



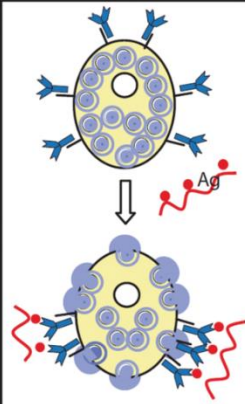
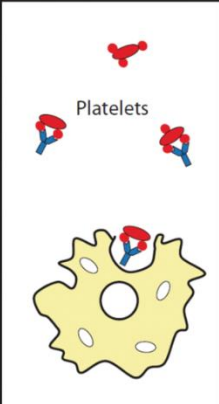
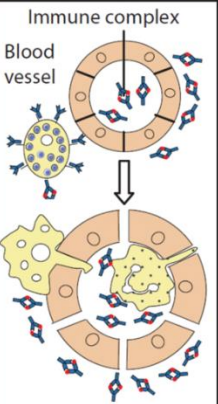
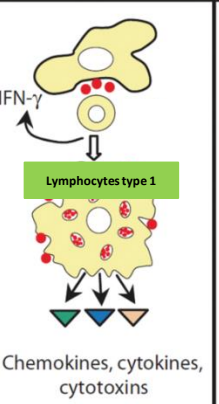
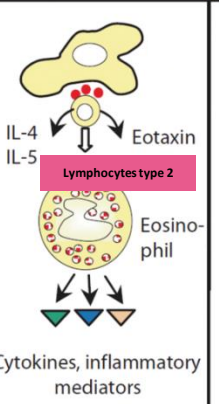
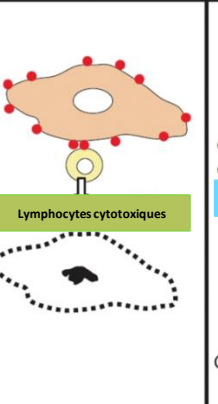
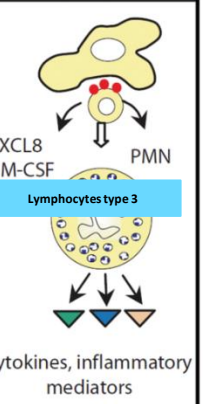
# Non allergic individual





# Hypersensibilités

## Classification de Gell & Coombs

	Antibody			T cells			
	Type I	Type II	Type III	Type IVa	Type IVb	Type IVc	Type IVd
Immune reactant	IgE	IgG	IgG	IFN- $\gamma$ , TNF- $\alpha$ <b>Type 1</b>	IL-5, IL-4/IL-13 <b>Type 2</b>	Perforin/ granzyme B <b>Cytotoxic</b>	IL-17, IL-22 <b>Type 17/3</b>
Antigen	Soluble antigen	Cell- or matrix-associated antigen	Soluble antigen	Antigen presented by cells or direct T-cell stimulation	Antigen presented by cells or direct T-cell stimulation	Cell-associated antigen or direct T-cell stimulation	Soluble antigen presented by cells or direct T-cell stimulation
Effector	Mast cell activation	FcR+ cells (phagocytes, NK cells)	FcR+ cells Complement	Macrophage activation	Eosinophils	T cells	Neutrophils
							
Maladies autoimmunes et allergiques	Anaphylaxie Rhinite allergique Asthme (crise)	Réaction transf. Anémie hémol. Thyroidite Myasthénie	Maladie sérique Lupus érythémateux	IDR tuberculine Rejet de greffe Polyarthrite Diabète	Asthme chron. Rhinite chron.	Rejet de greffe Diabète SEP	Polyarthrite Sclérose en plaque Mal. de Crohn
Dermatoses autoimmunes et allergiques	Urticaire contact	Pemphigus Pemphigoïde Urticaire chroni.	Vascularites	Psoriasis	Dermatite atopique	Vitiligo Pelade Eczéma contact	Psoriasis
Allergies médicaments	Choc anaphylactique	Cytopénies medic.	Vascularites immuno-allerg.	Exanthème médic.	DRESS	Lyell Stevens-Johnson	Pustulose exanthématique aigüe généralisée



# D.I.U Immunopathologie

Pour tout renseignement:  
audrey.nosbaum@chu-lyon.fr

Approche clinicobiologique  
transversale de  
l'immunologie appliquée en  
pathologie humaine

## 4 modules communs

- Module 1 : Bases fondamentales (20-21/10/2022)
- Module 2 : Immunopathologie générale & explorations biologiques (17-18/11/2022 et 01-02/12/2022)
- Module 3 : Immunothérapie (15-16/12/2022)
- Module 4 : Maladies inflammatoires systémiques (5-6/01/2023)

## 3 modules au choix parmi :

- Module 5 : Néphrologie (26-27/01/2023)
- Module 6 : Pneumologie (02-03/03/2023)
- Module 7 : Hématologie (23-24/03/2023)
- Module 8 : Dermatologie (06-07/04/2023)
- Module 9 : Neurologie (27-28/04/2023)
- Module 10 : Infectiologie (11-12/05/2023)
- Module 11 : Hépto-gastroentérologie/Endocrinologie (01-02/06/2023)
- Module 12 : Oncologie (08-09/06/2023)



**Volume horaire total ~ 100 heures**

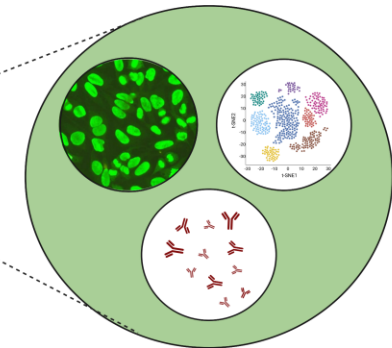
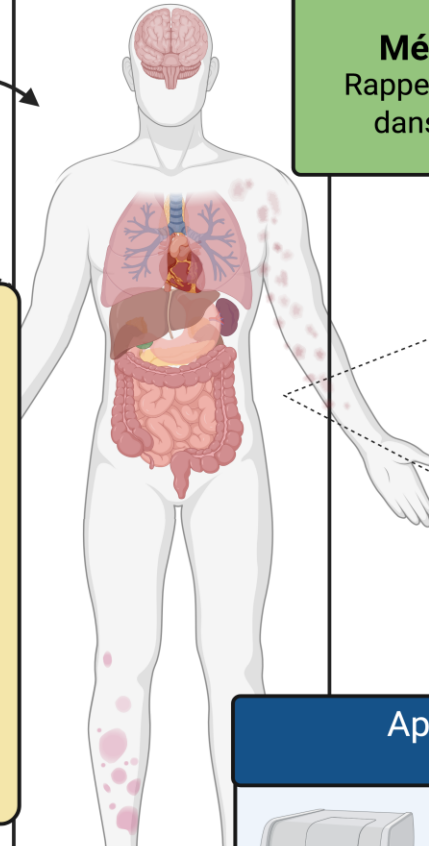
**Modules : du 20 octobre 2022 au 09 juin 2023**



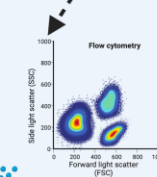
**Examens :**

- Tronc commun : Lecture Critique d'Article (19-20 janvier 2023)
- Modules spécifiques : Un article ou module à commenter (23 juin 2023)

**Mécanismes physiopathologiques**  
Rappel des principes fondamentaux impliqués  
dans les différents cadres nosologiques



## Applications diagnostiques et thérapeutiques



Biothérapies  
et thérapies  
ciblées

Vaccins, CAR-T cells...





# Département Allergologie et Immunologie Clinique



Clinical Research Unit



INSERM translational research team



Allergy & Clinical Immunology Department

Allergologie 2022 AURA Allergo

