

Allergologie AURA

Module 1 « Immunologie de l'Allergie »

12 décembre 2024

Le système immunitaire en action

Induction et régulation

de l'inflammation cutanée

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Team “Epidermal Immunity & Allergy”

Research activities

Main Features

- High prevalence
 - 10% of children (AD)
 - 1st occupational disease (ACD)
- Benign to very severe
- Localized acute or chronic lesions
- **Delayed-type allergy / Specific T cells**
- Breakdown of tolerance

Allergens

- Chemicals/haptens & proteins
- Endowed with antigenic & adjuvant properties
- Skin or systemic route

Objectives

- Decipher the pathophysiology
- Develop new diagnostic/predictive assays
- Develop new therapeutic strategies to restaure skin tolerance



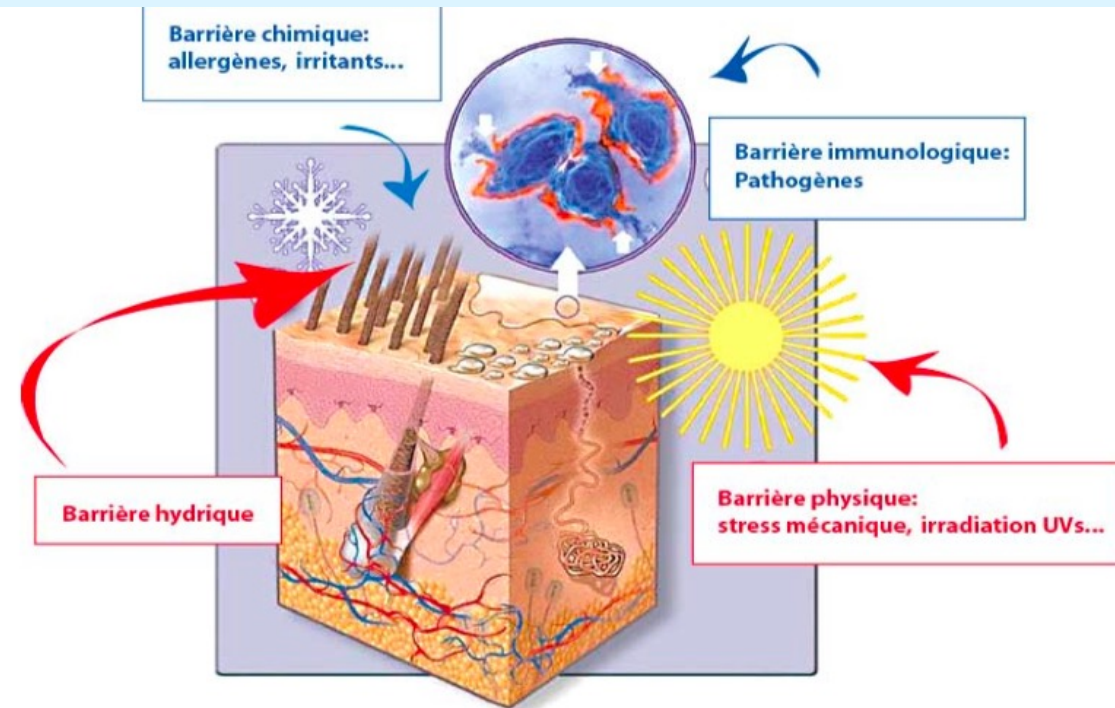
PLAN

- Bases immunologiques de la réponse à l'interface cutanée
- Induction & régulation de l'inflammation cutanée : *exemple de l'eczéma de contact*

PLAN

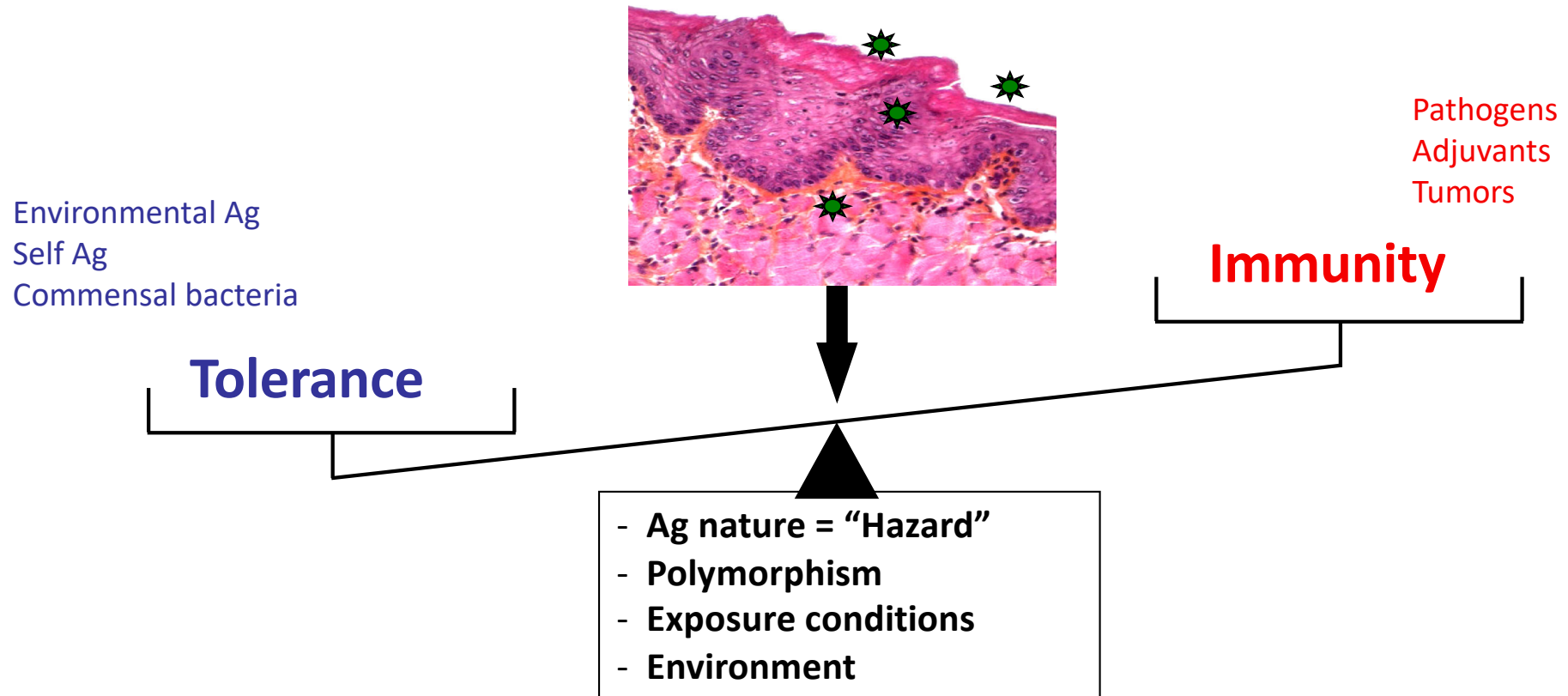
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The skin: the multitasking organ



- Skin area=1.8 m²
- Being constantly exposed to potential hazards -> maintain homeostasis
- Examples of the non-immune functions of the skin:
 - Physical and biochemical barrier
 - Sensory-receptive area
 - Ensures hydratation
 - Allows synthesis of vitamins, hormones

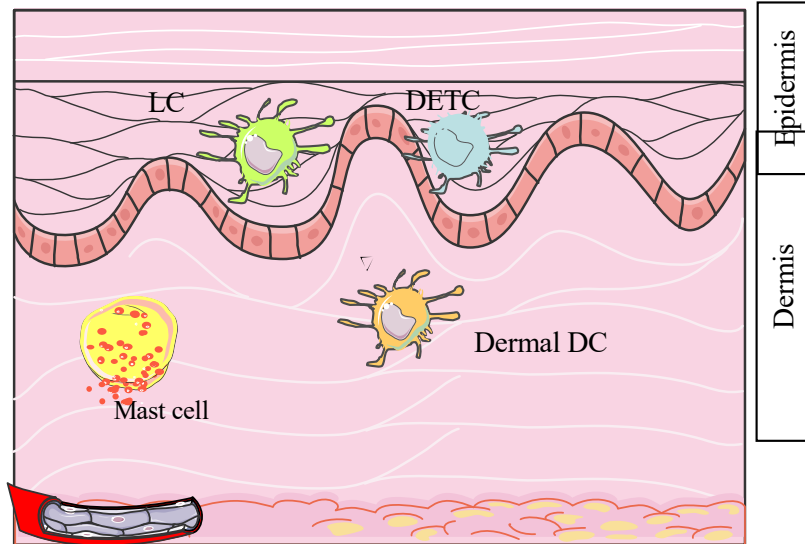
The skin: an immuno-protective organ



- Serves as an immuno-protective organ that actively defends deeper body tissues against infectious agents. Privileged site for vaccination
- Maintains self-tolerance, preventing allergens and inhibiting autoimmunity⁶

Induction of systemic immunity upon skin exposure/immunization

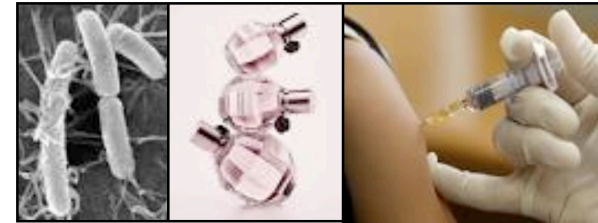
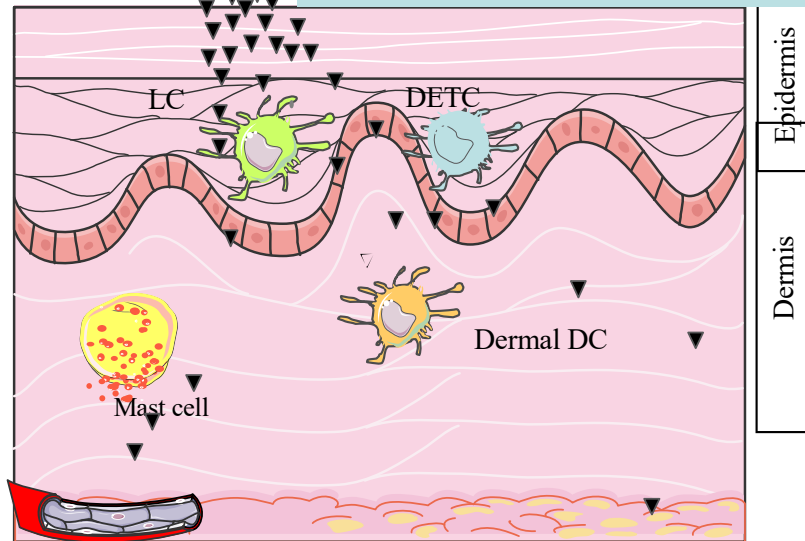
Skin exposure, immunization



Induction of systemic immunity upon skin exposure/immunization

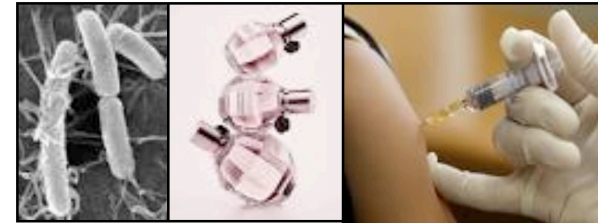
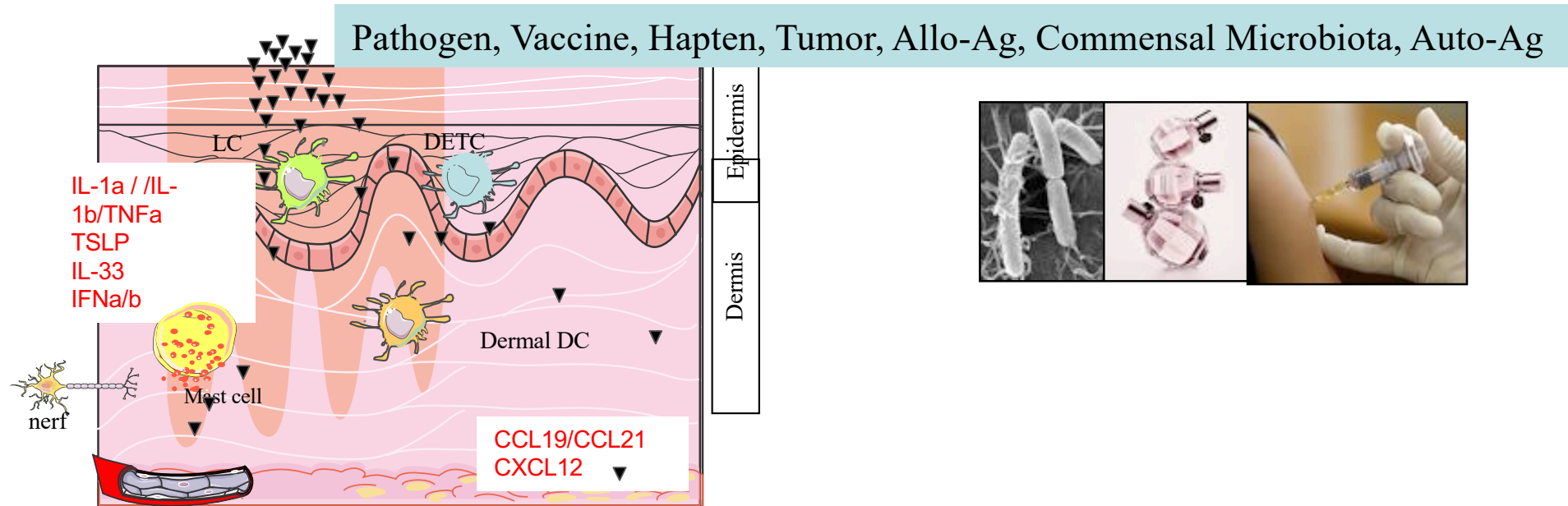
Skin exposure, immunization

Pathogen, Vaccine, Hapten, Tumor, Allo-Ag, Commensal Microbiota, Auto-Ag



Induction of systemic immunity upon skin exposure/immunization

Skin exposure, immunization



Innate immunity -> 1st line of defence
Release of inflammatory mediators

Inflammation

General scheme

4 major inflammatory components

Inducers

**Microbes,
Allergens
AlloAg**

Tissue damage

Cell-derived
Plasma-derived
ECM-derived

Sensors

P(athogen)AMPs

TLR, NLR...

D(amage)AMPs

TLR, NLR, RAGE...

Nociceptors

Mediators

Cellular

Neutrophils, Eosinophils,
Monocytes/Macrophages,
T & B cells...

Molecular

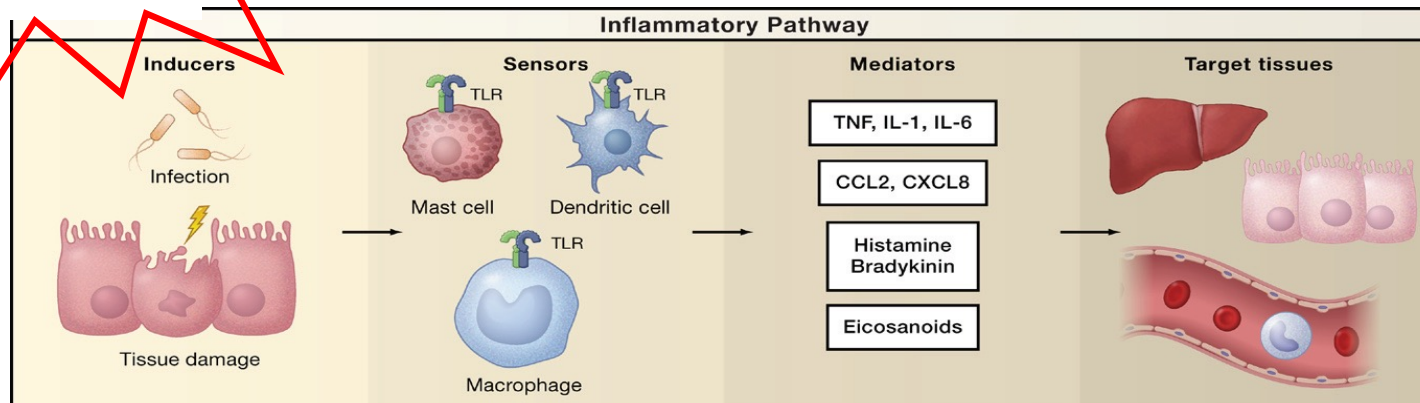
Cytokines and chemokines,
Vasoactive amines or peptides
Complement fragments
lipide mediators
proteolytic enzymes

Target tissues

**Redness/Oedema
Heat/Pain**

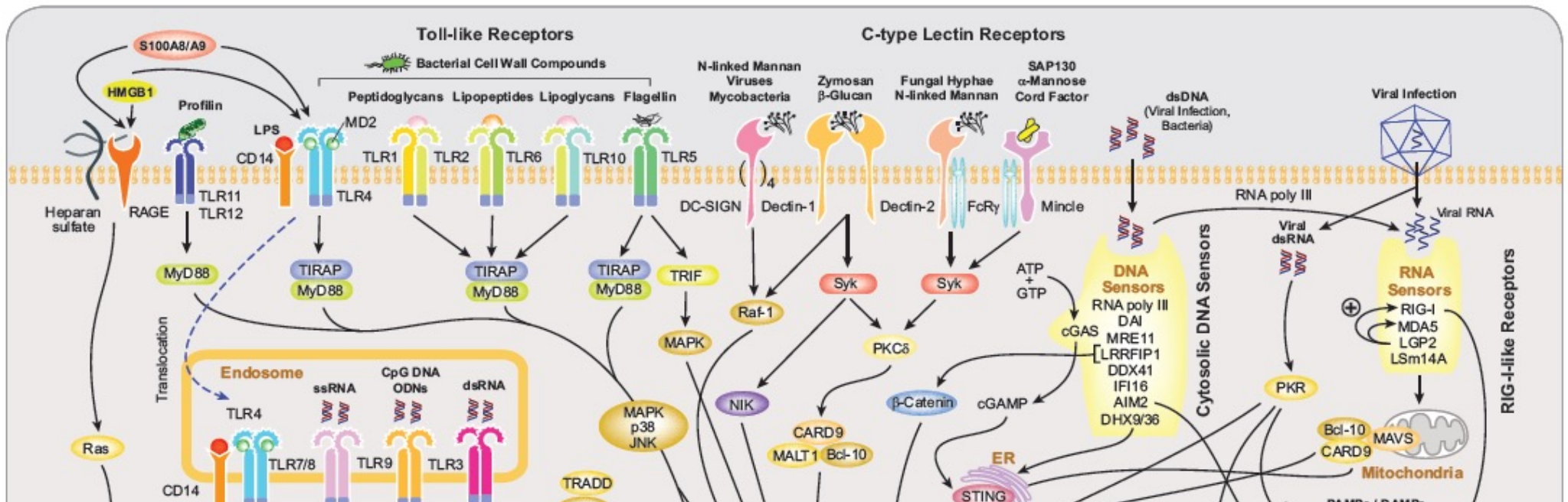
Loss of function

**DANGER
Hypothesis**



Pathogen recognition receptors (PRRs)

- Microbial Pattern Recognition Receptors: TLR, RLR, NLR, CLR signaling (examples)

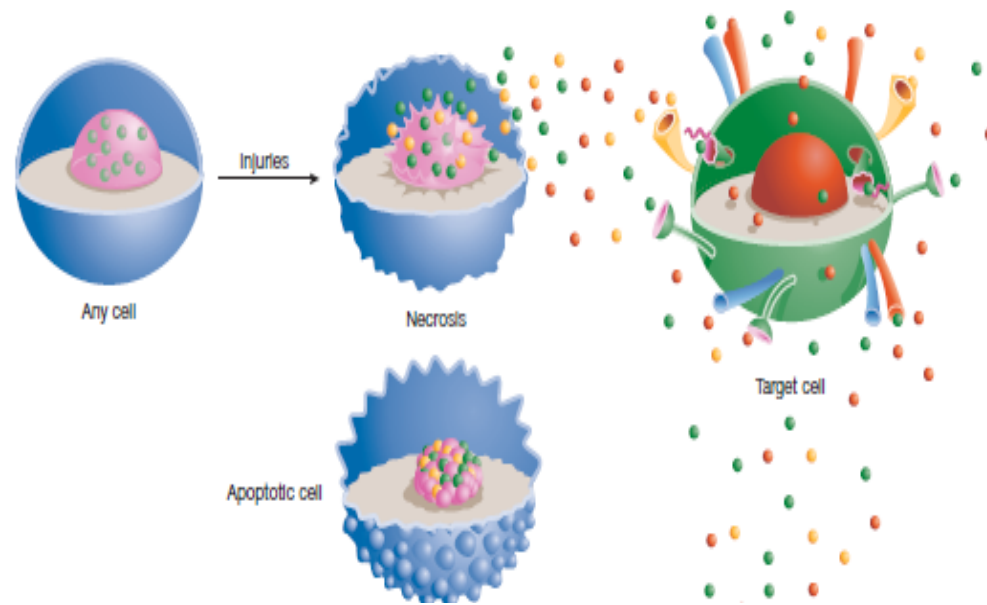


- Recognition of specific structures (polysach, nucleic acids, nucleotides lipoproteins, glycolipids)
- Cell compartment localisation, tissue-specific expression
- Cell intrinsic → infected cells, cell extrinsic → not infected cells; but most of PAMPs are detected by both
- Recognition of functional features (enzymatic activities, pore-forming toxins)

Inflammation

PAMPs – DAMPs and their sensors

Intracellular DAMPs



DAMP	Adjuvant activity
HMGB1	<i>In vivo</i> : adjuvant activity of purified molecule; adjuvant activity shown by selective depletion <i>In vitro</i> : DC activation
Uric acid (MSU)	<i>In vivo</i> : adjuvant activity shown by injection of purified molecule and selective depletion <i>In vitro</i> : DC activation
Chromatin, nucleosomes and DNA	<i>In vivo</i> : DC maturation induced by purified molecule <i>In vitro</i> : DC activation induced by chromatin-IgG complexes
HSPs	<i>In vivo</i> : tumour immunogenicity enhanced by overexpressed molecule or addition of purified molecule (HSP70); DC migration to lymph nodes induced by purified molecule (gp96) <i>In vitro</i> : DC maturation (gp96 and HSP70)
Adenosine and ATP	<i>In vivo</i> : exacerbation or abrogation of bronchial asthma by purified molecule or specific inhibition, respectively <i>In vitro</i> : DC maturation
Galectins	<i>In vivo</i> : ND <i>In vitro</i> : DC maturation
Thioredoxin	ND
S100 proteins	ND
Cathelicidins	<i>In vitro</i> : DC maturation; DC activation induced by LL37-self-DNA complex
Defensins	<i>In vivo</i> : adjuvant activity by co-administration of purified molecule <i>In vitro</i> : DC maturation
N-formylated peptides	<i>In vivo</i> : ND <i>In vitro</i> : DC chemotaxis

Inflammation

PAMPs – DAMPs and their sensors

Extracellular DAMPs

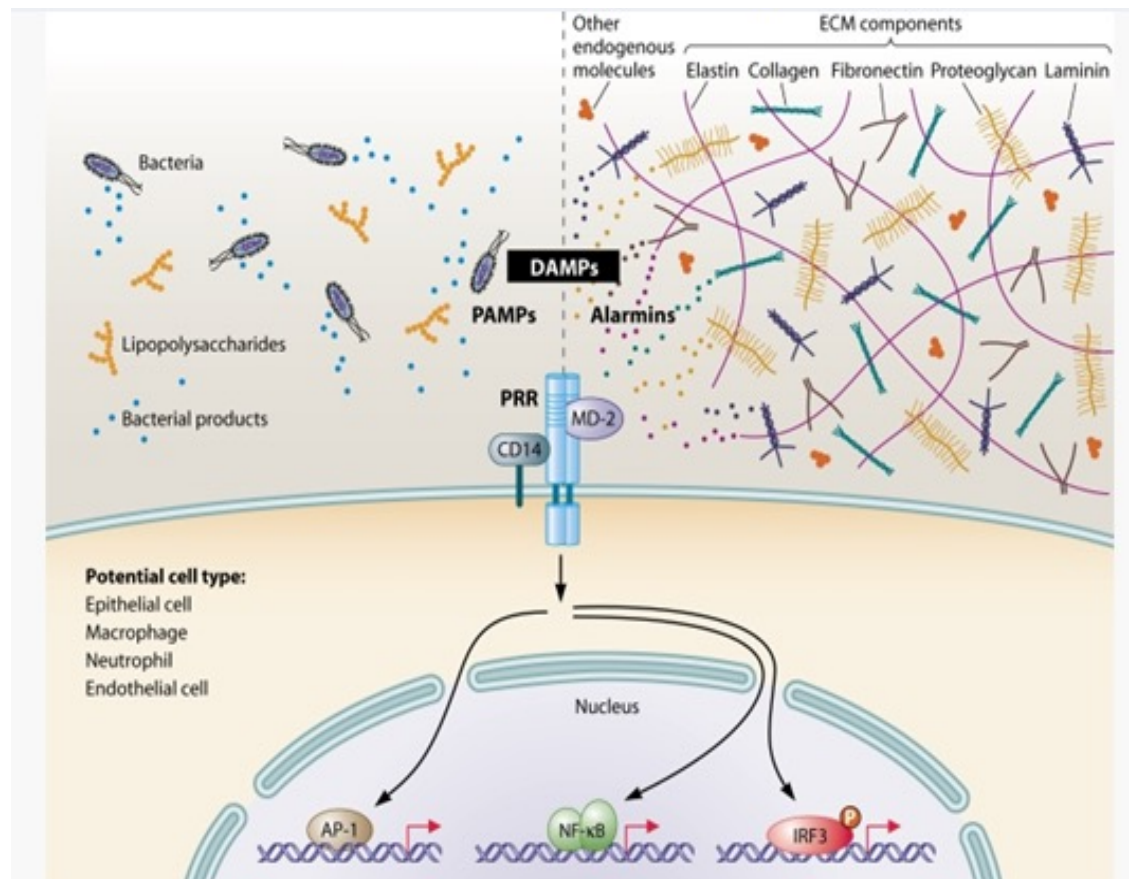
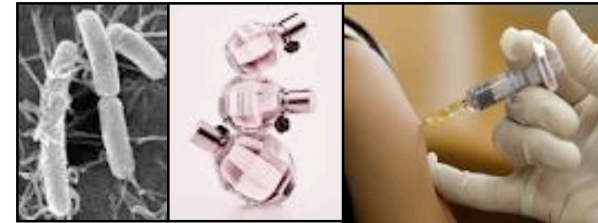
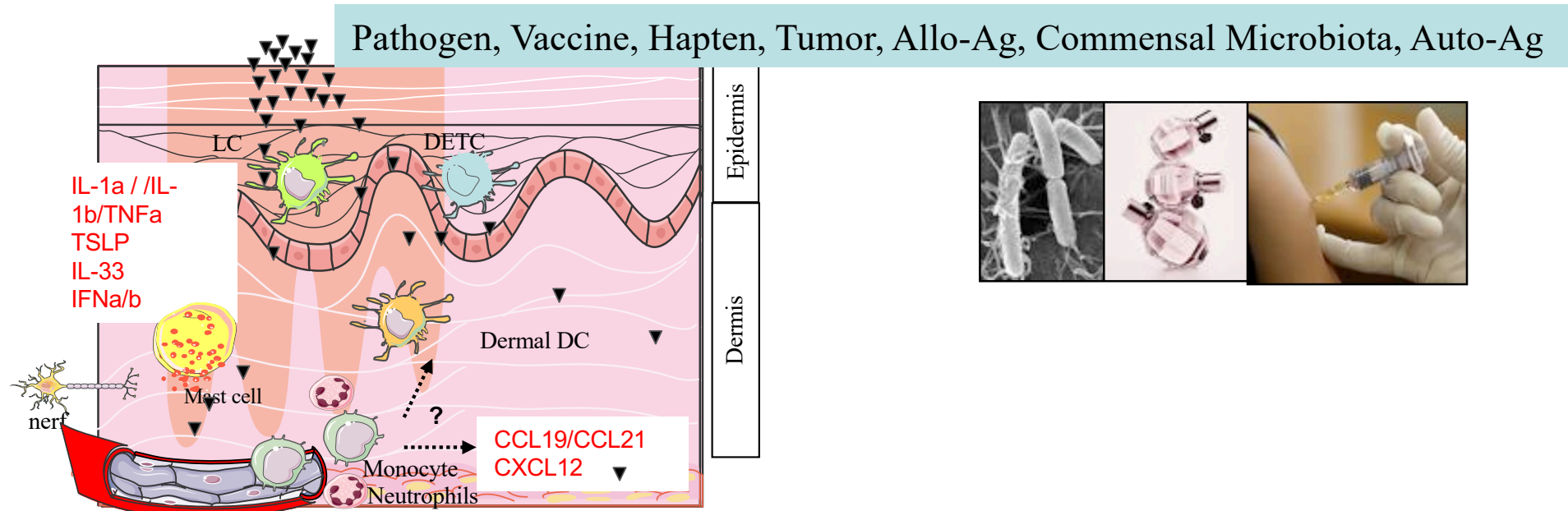


Table 2 | Adjuvant and pro-inflammatory activity of extracellular DAMPs

DAMP	Adjuvant activity
Hyaluronic acid	<i>In vivo</i> : inhibition of Langerhans-cell maturation by blocking peptide; adjuvant activity by administration of purified molecule <i>In vitro</i> : DC maturation
Heparan sulphate	<i>In vitro</i> : DC maturation
Fibrinogen	<i>In vitro</i> : DC maturation
Collagen-derived peptides	<i>In vivo</i> : ND <i>In vitro</i> : DC maturation
Fibronectin	<i>In vitro</i> : DC maturation
Elastin-derived peptides	<i>In vivo</i> : ND <i>In vitro</i> : ND
Laminin	<i>In vivo</i> : ND <i>In vitro</i> : ND

Induction of systemic immunity upon skin exposure/immunization

Skin exposure, immunization



Innate immunity -> 1st line of defence

Release of inflammatory mediators

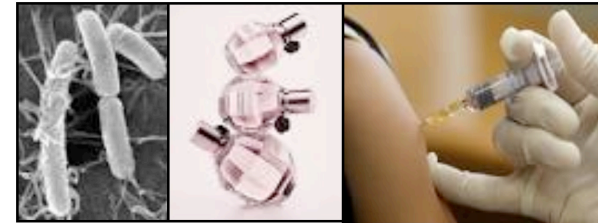
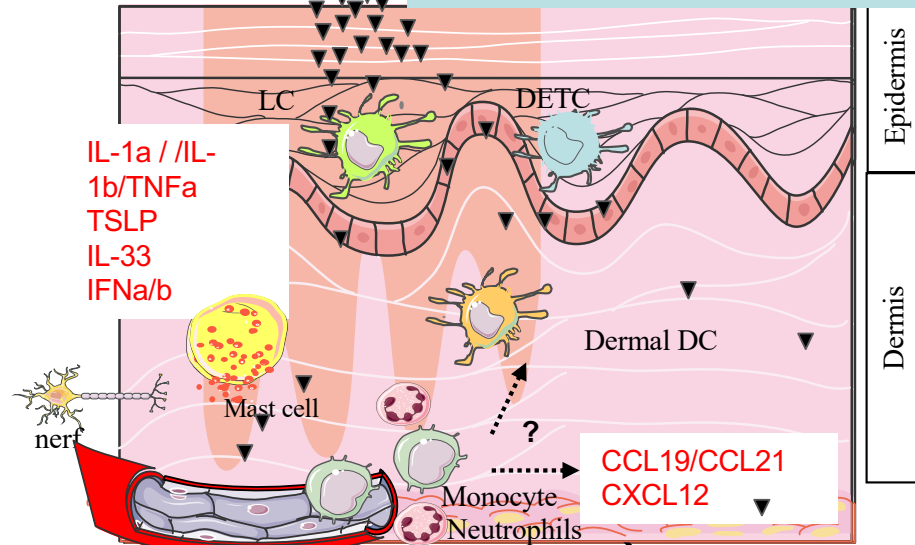
Coordinated cross-talk between epithelial and immune cells

Infiltration of blood leucocytes

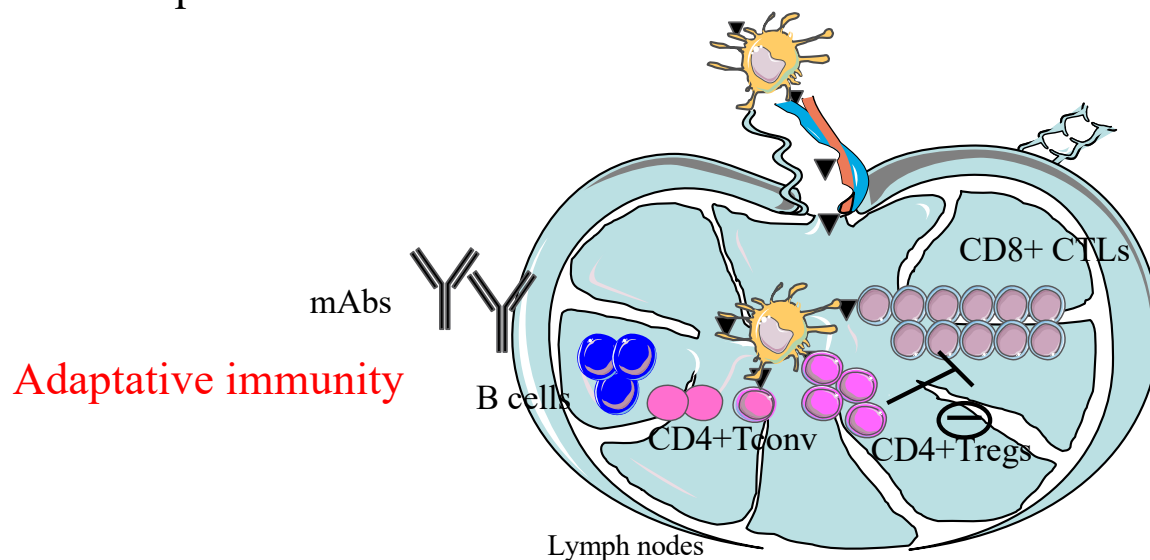
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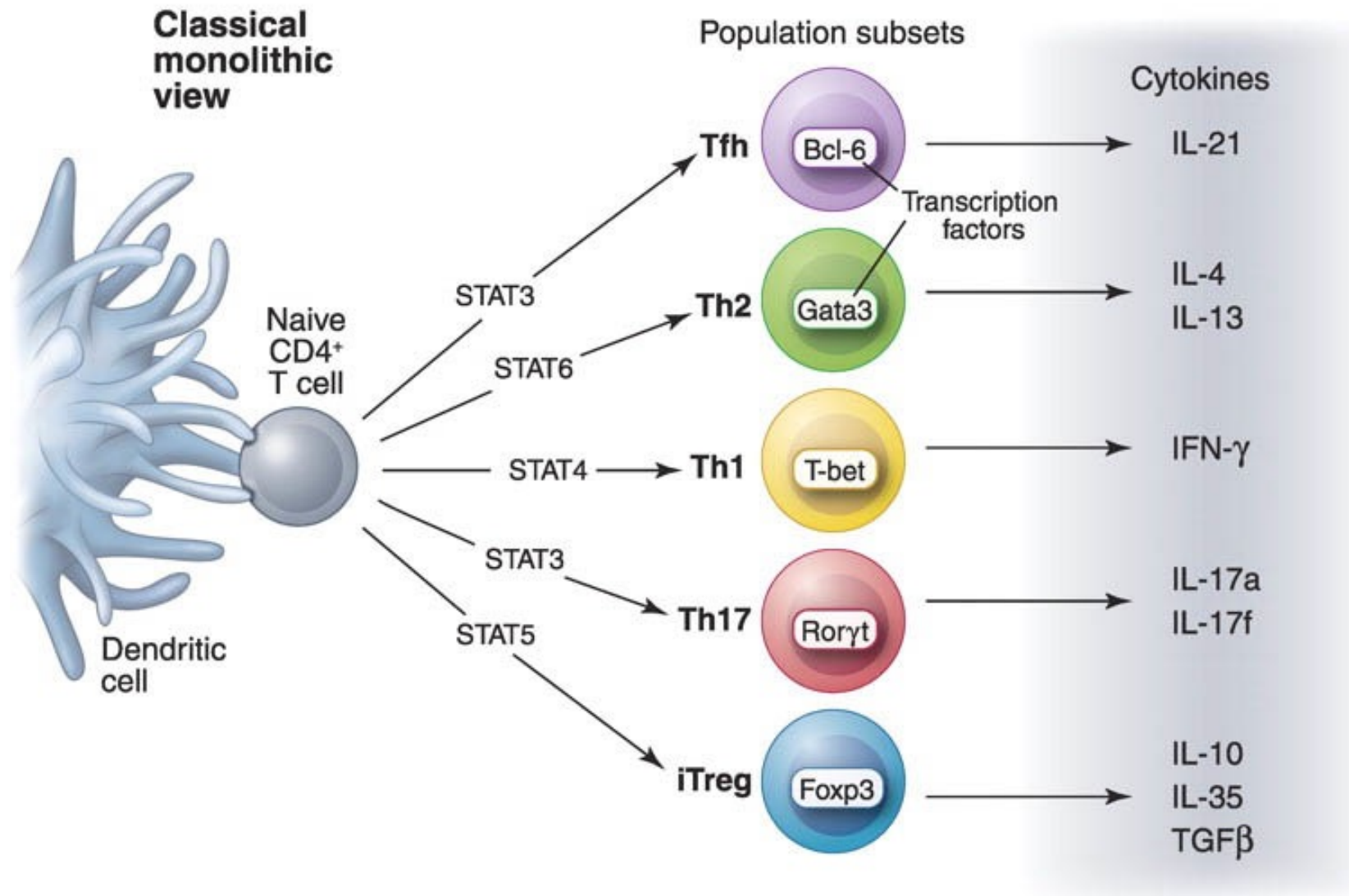


Innate response



Antibody production
Effector CD4+ & CD8+ T cells
Memory T cells, B cells & plasma cells

Distinct T cells



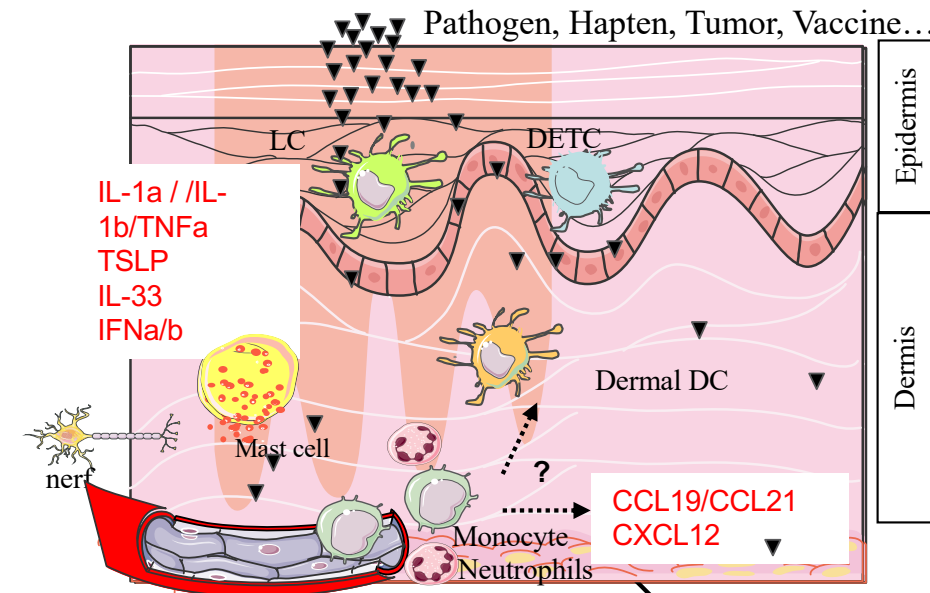
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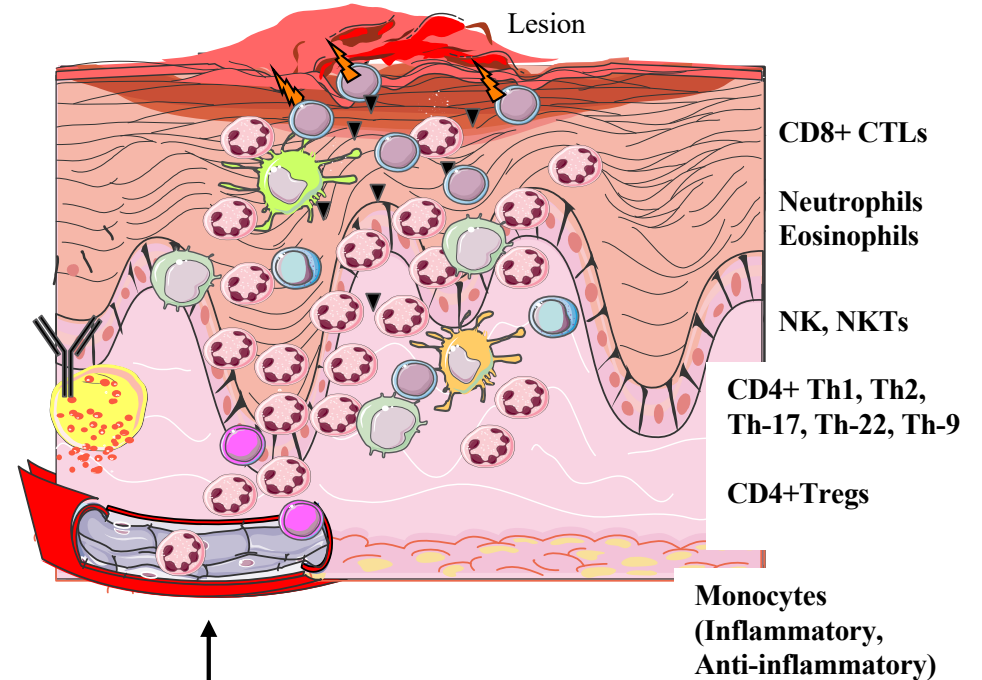
Persistence / Re-exposure → delayed-response (days)

Skin inflammation, elimination of infected cells

Tissue response/repair

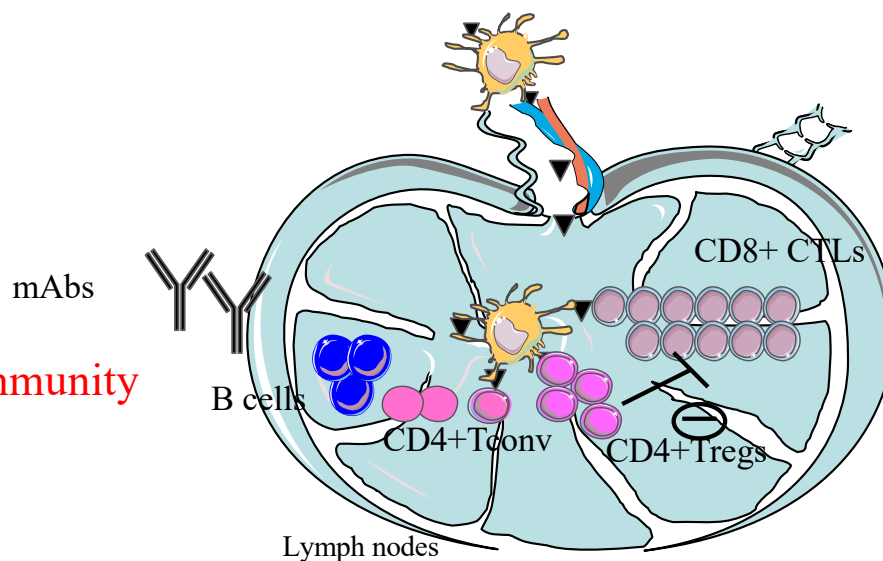


Innate response



Effector & memory response → 2nd line of defence

Adaptative immunity

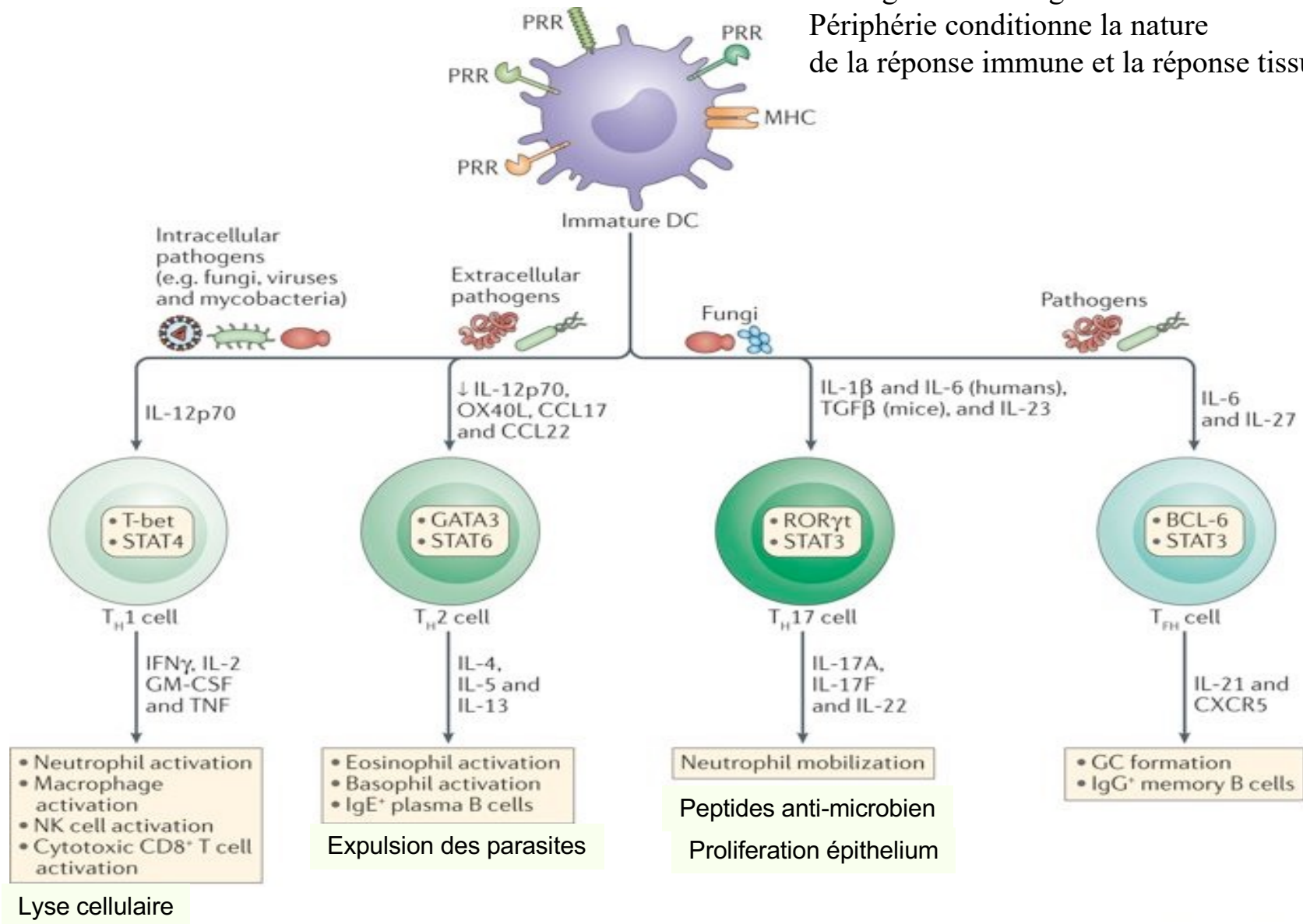


Different mode of recognition by the innate immunity

→ different layers of sensing by the immune system

→ different effector response

L'intégration des signaux de la Périphérie conditionne la nature de la réponse immune et la réponse tissulaire



PLAN

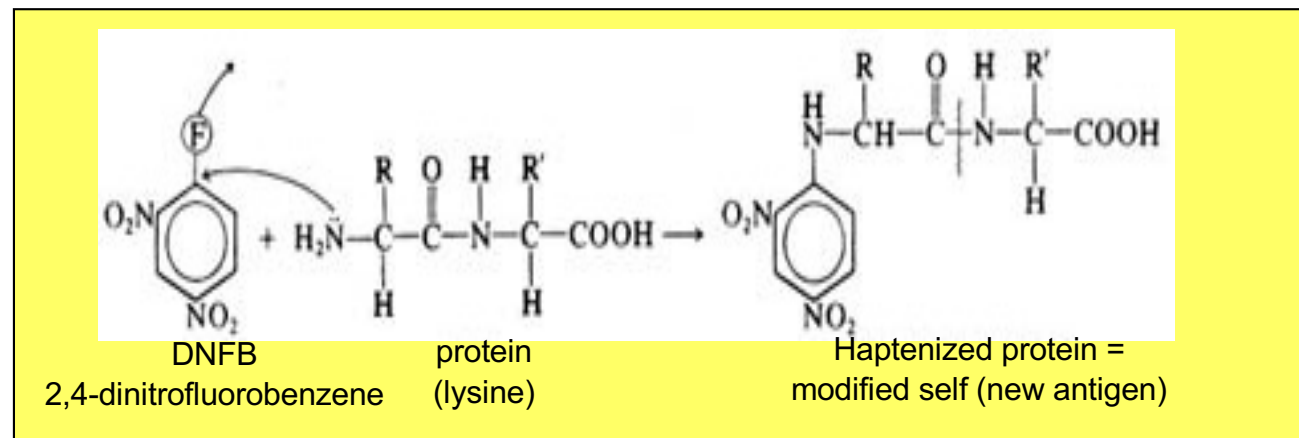
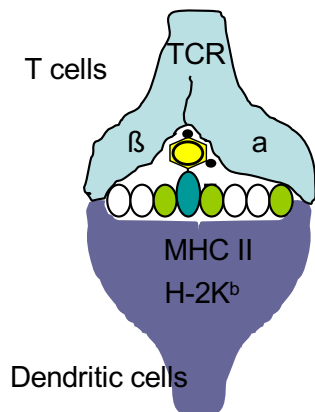
- Bases immunologiques de la réponse à l'interface cutanée
- Induction & régulation de l'inflammation cutanée : exemple de l'eczéma de contact

Allergic Contact Dermatitis (ACD): Generalities



Features

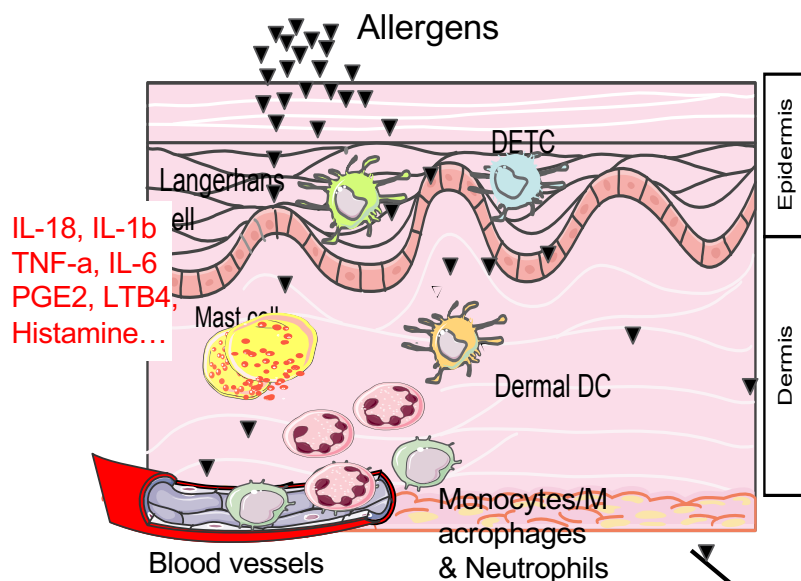
- High prevalence, 1st occupational disease
- Repeated exposure to environmental allergens (cosmetics, jewels, drugs...)
- Breakdown of skin tolerance
- Delayed-type allergy:
→ infiltration and activation of allergen-specific T cells



Presentation of haptened peptides

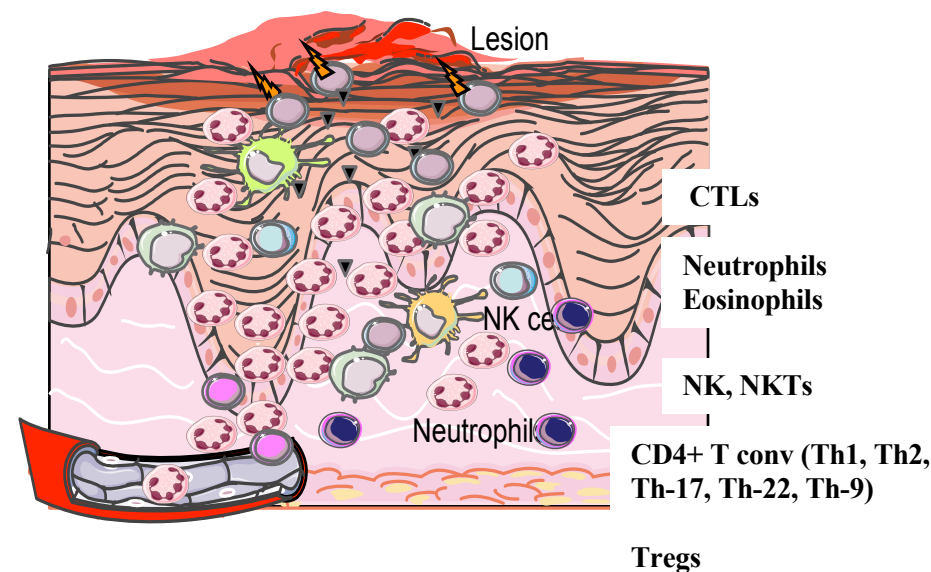
1- Sensitization phase

Innate immunity/ T cell priming

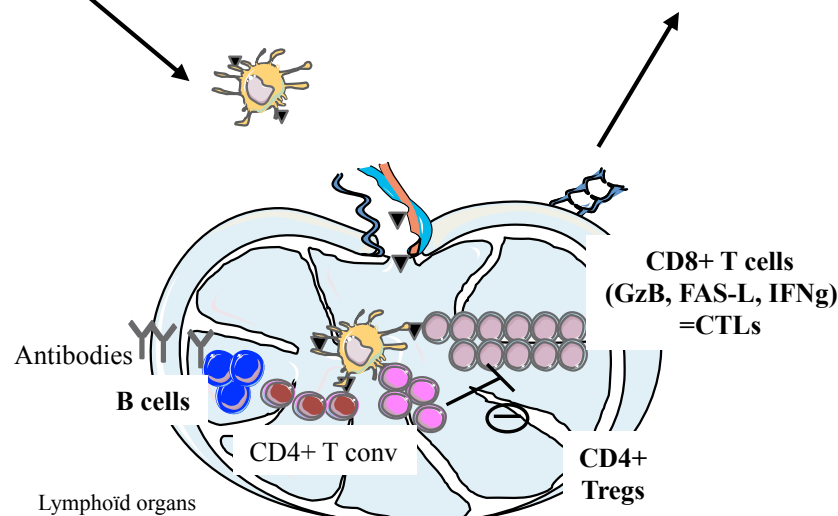


2- Elicitation phase

Effector response/ Polymorphic recruitment



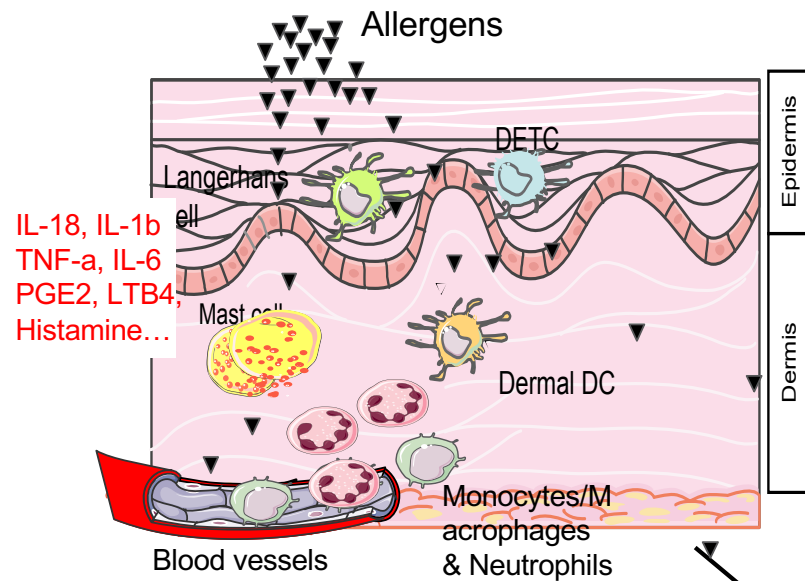
**Monocytes
(Inflammatory,
Anti-inflammatory)**



BOUR et al. *Eur J Immunol*, 1995
 KRASTEVA et al. *J Immunol*, 1998
 KEHREN et al. *J Exp Med*, 1999
 AKIBA et al. *J Immunol*, 2002
 SAINT-MEZARD et al. *J Immunol*, 2003
 AKIBA et al. *J Invest Dermatol*, 2004
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 ROUZAIRE et al. *Eur J Immunol*, 2012
 GOUBIER et al. *J Invest Dermatol*, 2013
 CORTIAL et al. *Nanomedicine*, 2015
 GAMRADT *J Allergy Clin Immunol* 2019

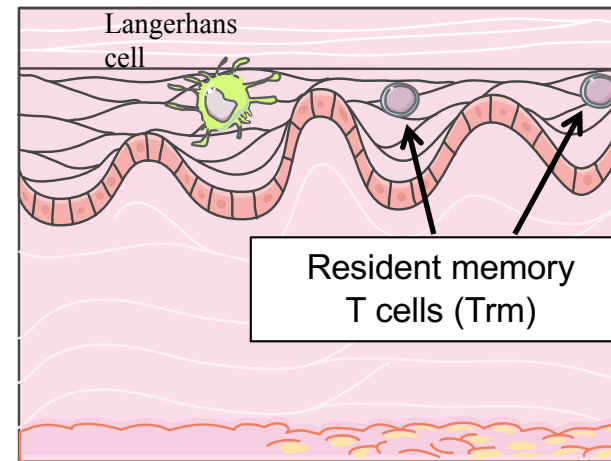
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Innate immunity/ T cell priming

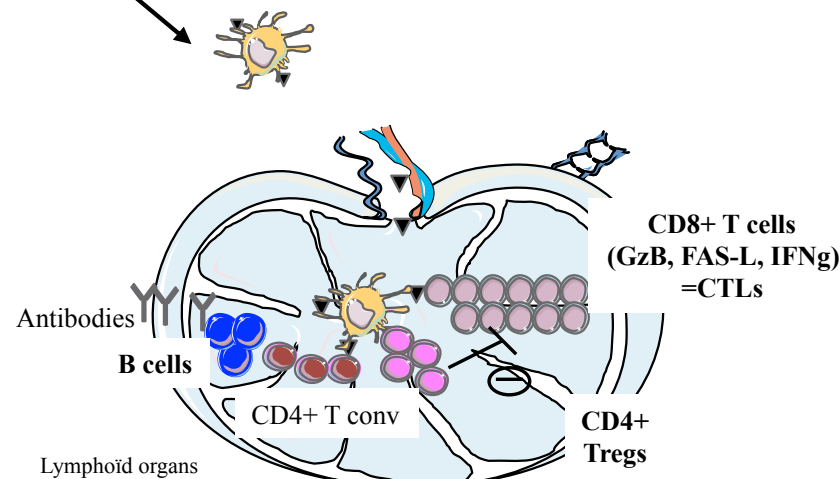


3- Resolution of skin inflammation

Healed lesion/ Persistence of skin T_{RM}

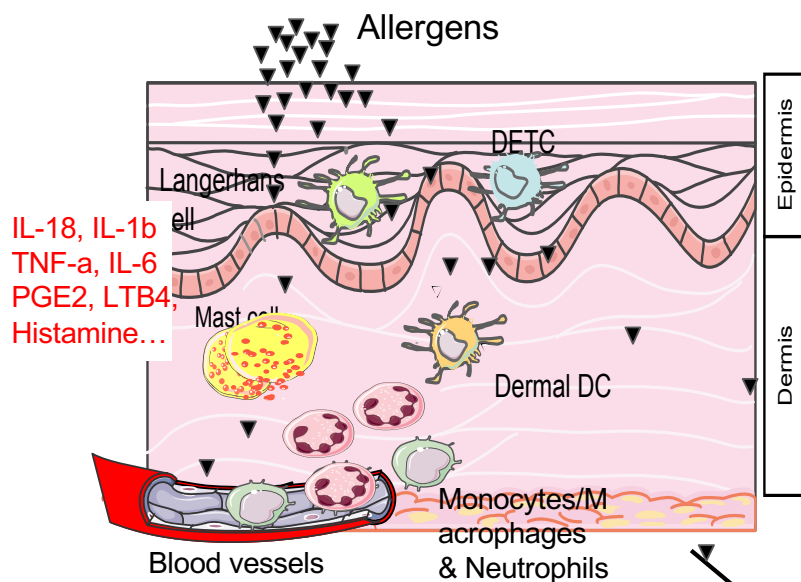


BOUR et al. *Eur J Immunol*, 1995
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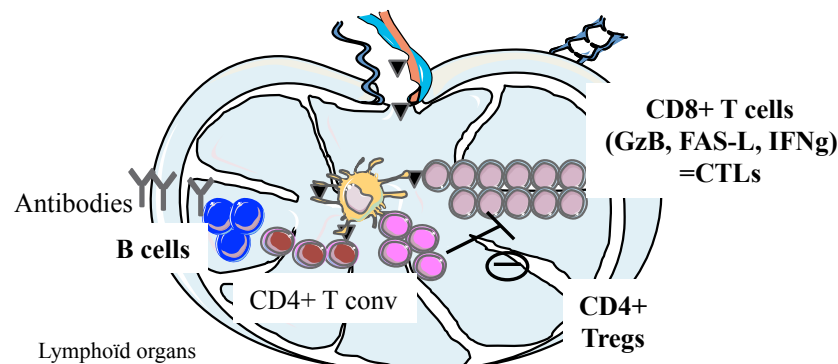
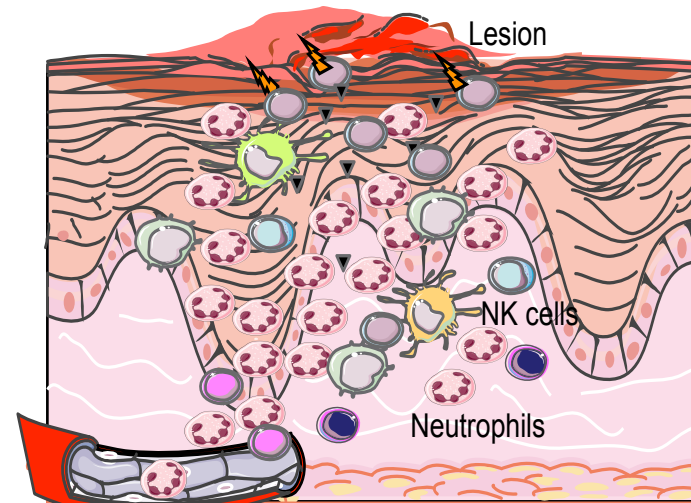
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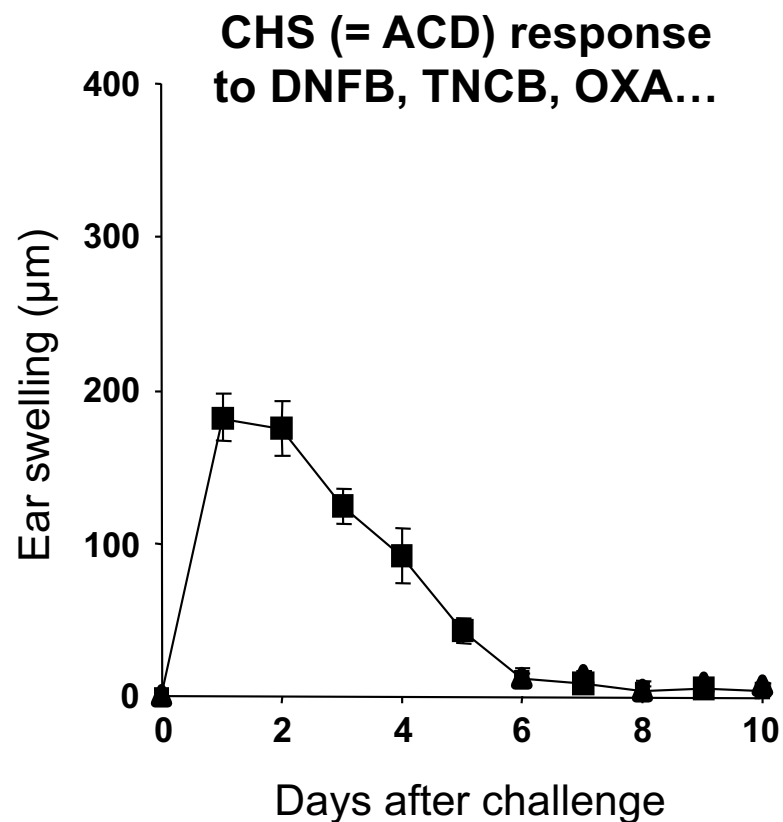
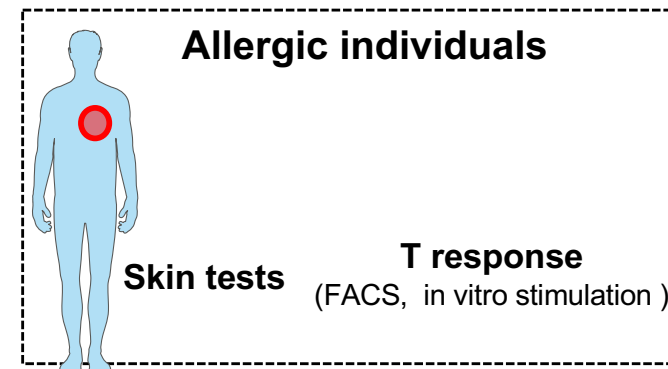
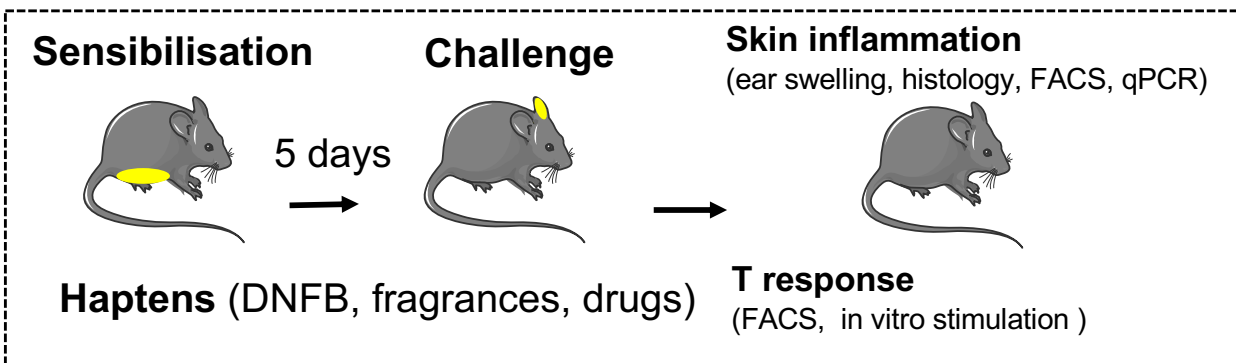
4- Recurrence / Severity / Chronicity

New exposure / Flares



BOUR et al. *Eur J Immunol*, 1995
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 KEHREN et al. *J Exp Med*, 1999
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 SAINT-MEZARD et al. *J Immunol*, 2003
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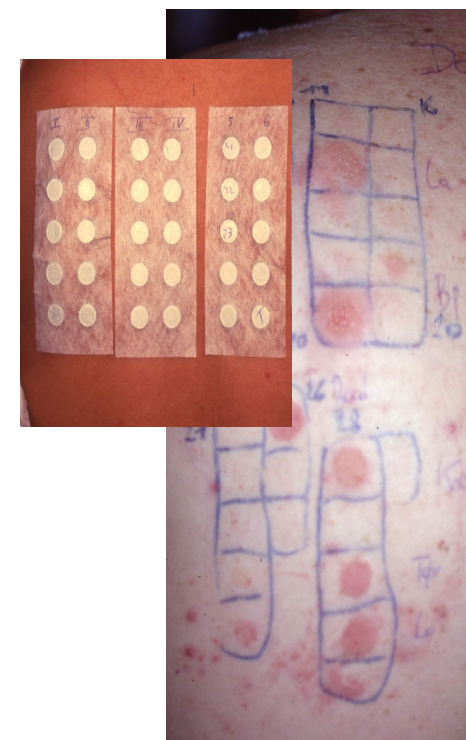
Experimental models of ACD in mouse, in human



ACD lesions



Positive patch-tests to reference allergens



Permeation of haptens into the skin

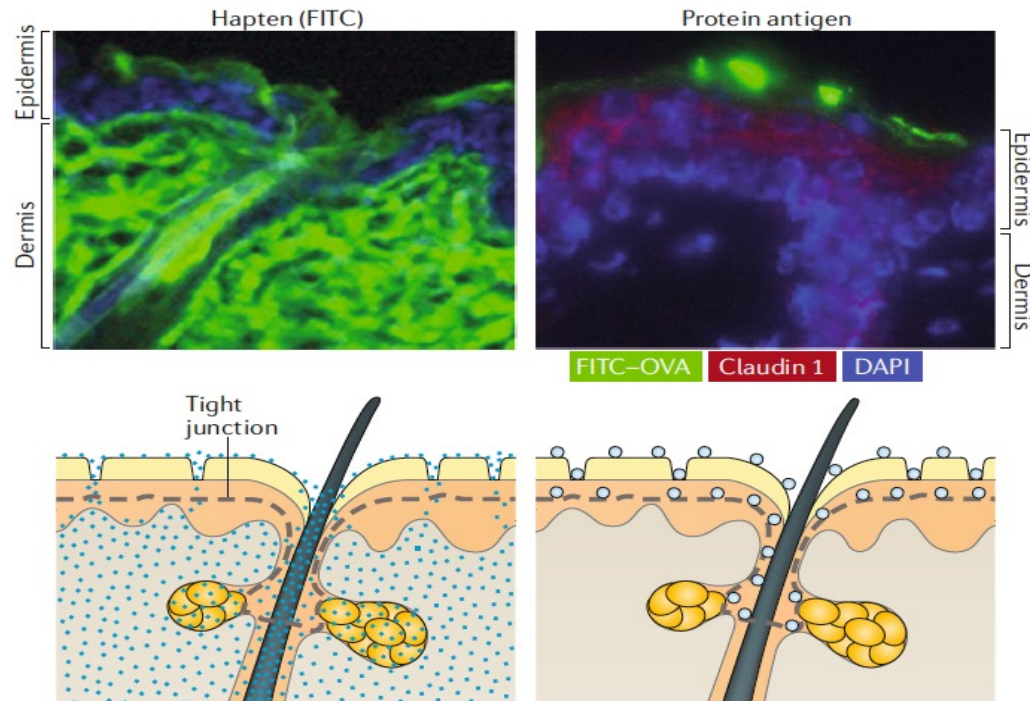
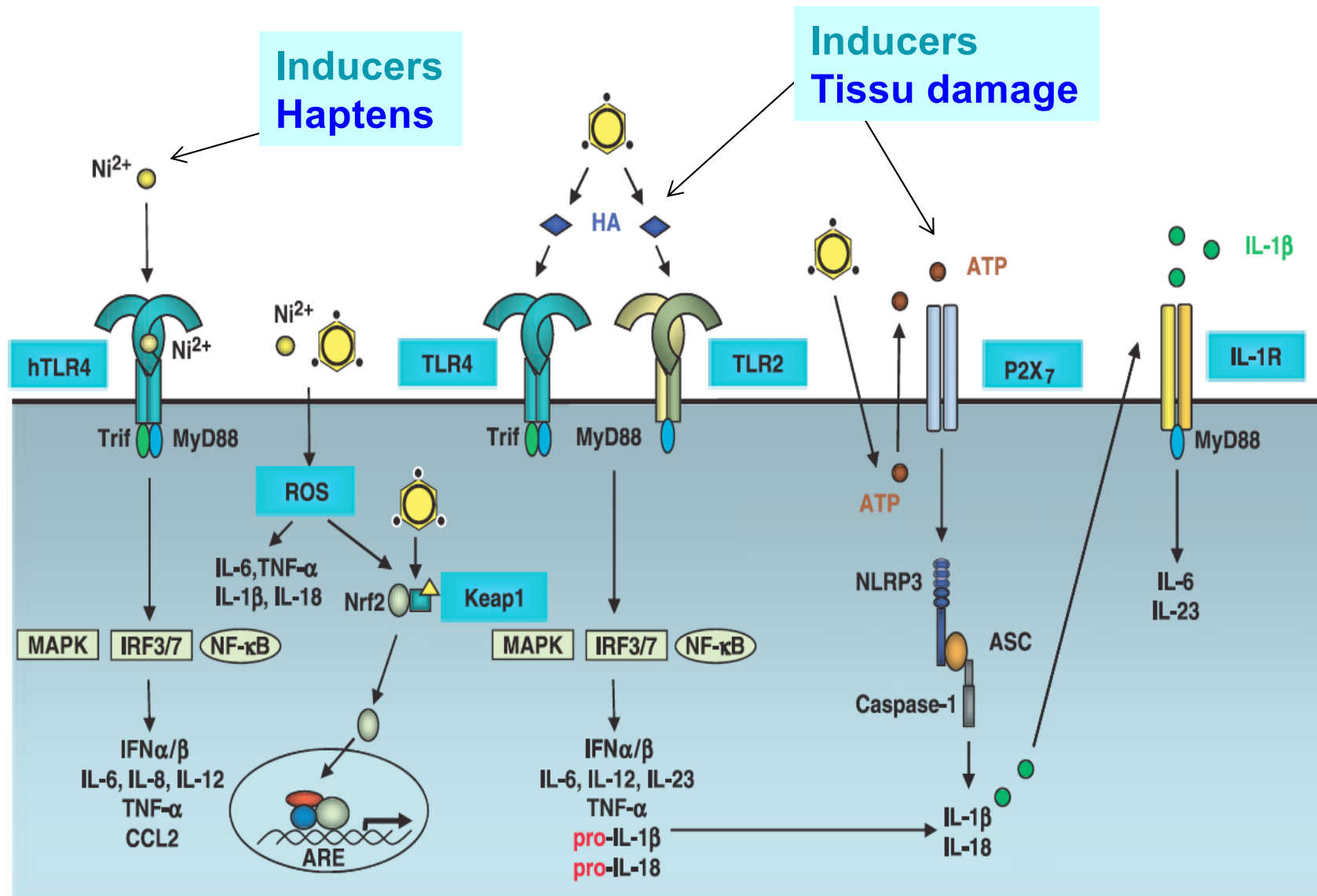


Fig. 4 | Penetration of hapten and proteins into the skin. A hapten (fluorescein isothiocyanate (FITC); molecular mass = 389; left) or FITC-conjugated ovalbumin (FITC-

- Les haptènes sont pour la plus part des substances hydrophobes
- Pénétration dépend de l'hydrophobicité (LogP), mais aussi de la présence de groupes chargés, la taille (poids moléculaire < 1000 Daltons), la forme moléculaire et du véhicule.
- Les peaux altérées (blessures physiques, chimiques ou anomalie génétique) favorisent l'apparition d'un eczéma de contact

How haptens activate innate immunity?



Les diverses étapes de la sensibilisation : activation de l'immunité innée

- Rôle crucial de la structure du TLR4 humain sur le développement de la réponse d'EAC

Conserved histidines on human TLR4 as potential binding sites for nickel

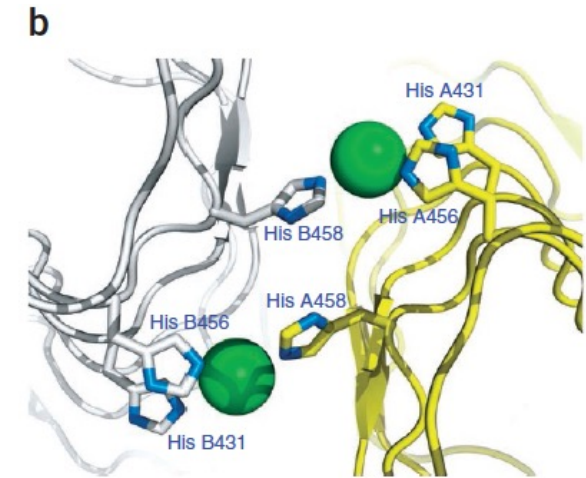
nature
immunology

Crucial role for human Toll-like receptor 4 in the development of contact allergy to nickel

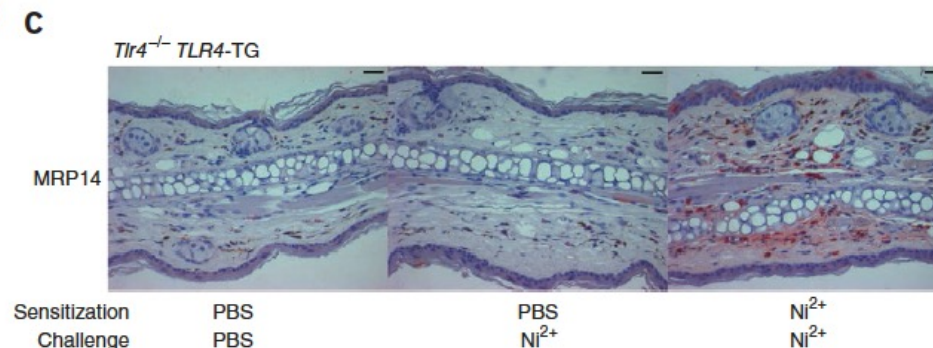
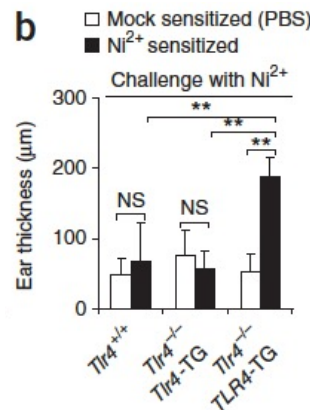
Marc Schmidt^{1,2}, Badrinarayanan Raghavan^{1,2}, Verena Müller^{1,2}, Thomas Vogl³, György Fejer⁴, Sandrine Tchapchet⁴, Simone Keck⁴, Christoph Kalis⁴, Peter J Nielsen⁴, Chris Galanos⁴, Johannes Roth³, Arne Skerra⁵, Stefan F Martin⁶, Marina A Freudenberg⁴ & Matthias Goebeler^{1,2}

a

hTLR4	LRR14	DLPSEFLDLSRNLGSLFKGCCSQSDF	396
mTLR4	LRR14	ALPFLSYLDLSRNALSFSGCCSYSDL	394
hTLR4	LRR15	GTTSILKYLDFNGVITMSSNFL	419
mTLR4	LRR15	GTNSLRHLDFNGAIIIMSANFM	417
hTLR4	LRR16	GLEQLQLHLDFOH ⁴³¹ SNLQKQMFSEFVFL	444
mTLR4	LRR16	GLEELQLHLDFOH ⁴³¹ STLKRKRVTEFSAPL	442
hTLR4	LRR17	SLRNLIYLDIS ⁴⁵⁸ TH ⁴⁵⁸ TRVAFNGIFN	468
mTLR4	LRR17	SLEKLLYLDIS ⁴⁵⁸ YTN ⁴⁵⁸ TKIDFDGIFL	466
hTLR4	LRR18	GLSSLEVLKMGNSFOENFLPDIET	493
mTLR4	LRR18	GLTSLNLTLMAGNSFKDNTLSNVFA	491
hTLR4	LRR19	ELRNLTFLDLSQCQLQLSPTAFN	517
mTLR4	LRR19	NTNLTFLDLSKQCLEQISWGVFD	515
hTLR4	LRR20	SLSSLQVLNMS ⁵³⁹ HN ⁵³⁹ FFSLDTFPYK	541
mTLR4	LRR20	TLHRLQLLNMS ⁵³⁹ HN ⁵³⁹ LFLDSSHYN	539
hTLR4	LRR21	CLNSLQVLDYSLN ⁵⁶⁶ IM ⁵⁶⁶ TSKKQELQ ⁵⁶⁶ H	566
mTLR4	LRR21	QLYSLS ⁵⁶⁶ TLDCSPN ⁵⁶⁶ LET ⁵⁶⁶ SRGI-LQ ⁵⁶⁶ H	563
hTLR4	LRR22	FPSSLAFNLNTQNDFA	582
mTLR4	LRR22	FPKSLAFFNLTNNSVA	579
hTLR4	LRRCT	CTCE ⁶⁰⁷ H ⁶⁰⁷ QSF ⁶⁰⁷ LQWIKD ⁶⁰⁷ QRQLLVEVERM	607
mTLR4	LRRCT	CICE ⁶⁰⁷ H ⁶⁰⁷ KFLQWVKEQKQFLVNVEQM	604

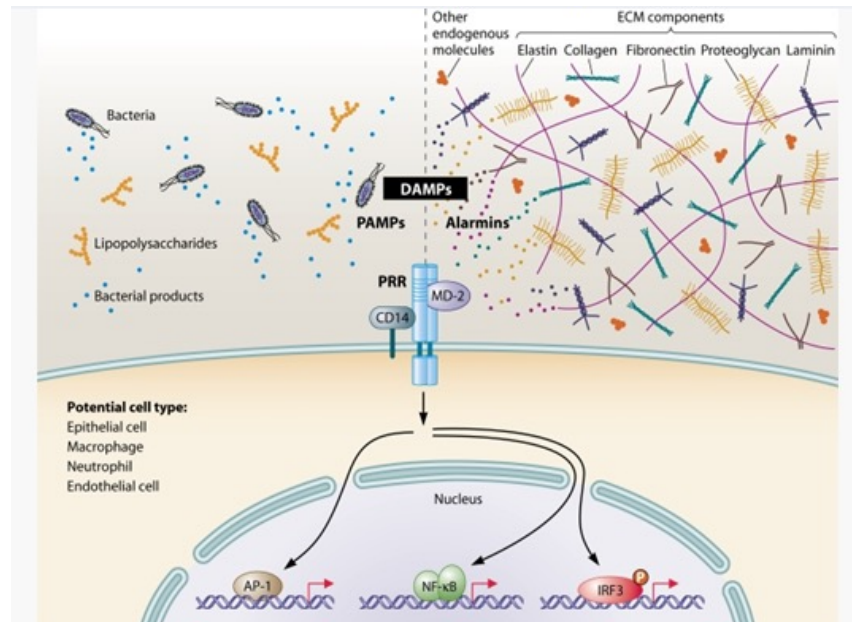


Transgenic expression of human TLR4 in mice confers reactivity toward nickel

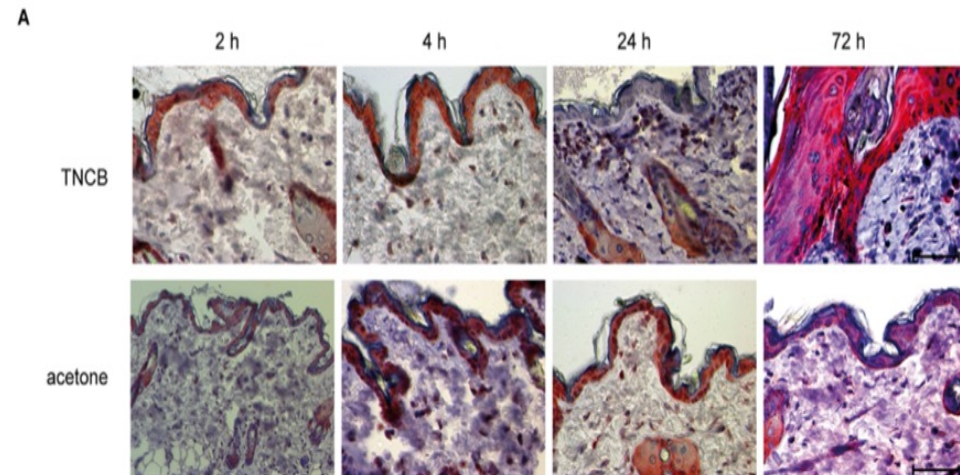


Les diverses étapes de la sensibilisation : activation de l'immunité innée

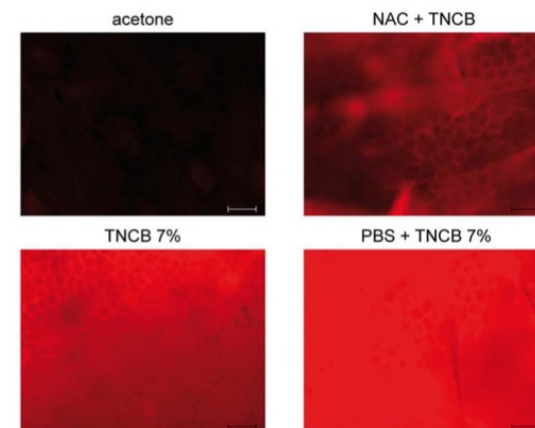
- Impact des médiateurs reconnus par les TLRs sur le développement de la réponse d'EAC



Dégradation Acide Hyaluronique ht PW, 24h après application

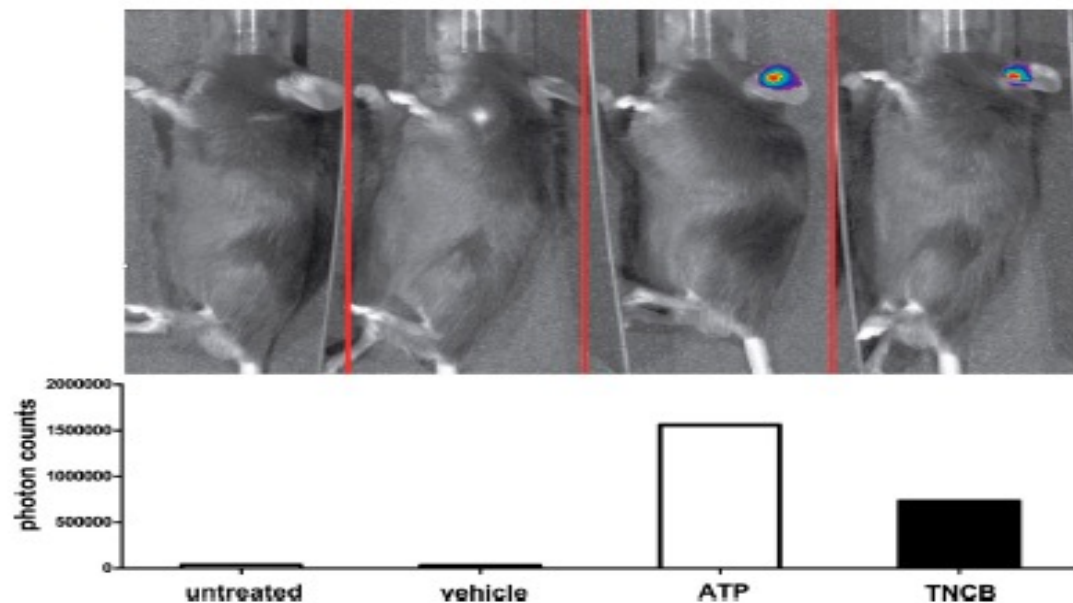


Production ROS, peau challengée

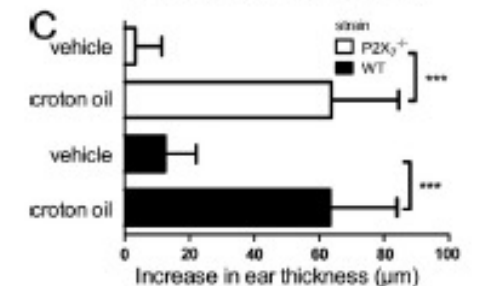
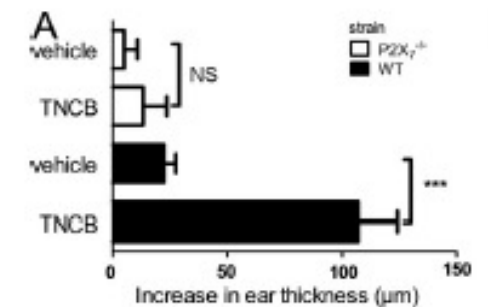


Les diverses étapes de la sensibilisation : activation de l'immunité innée

- Impact des médiateurs reconnus par les NLRs sur le développement de la réponse d'EAC



Relargage ATP, peau challengée

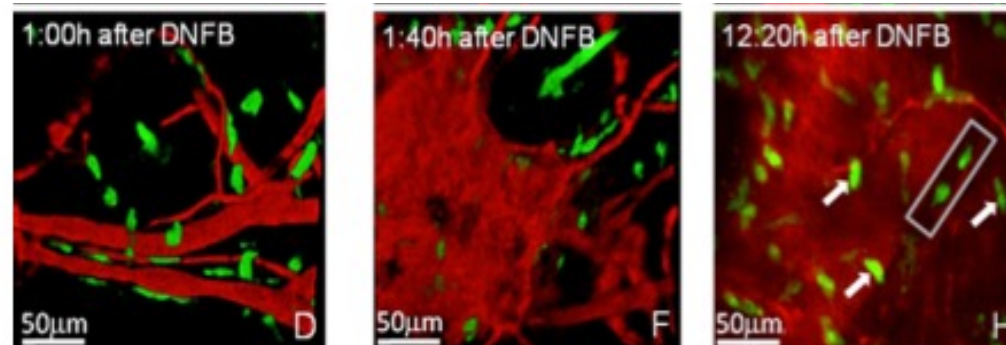


Ear skin mast cells and blood vessels respond to hapten

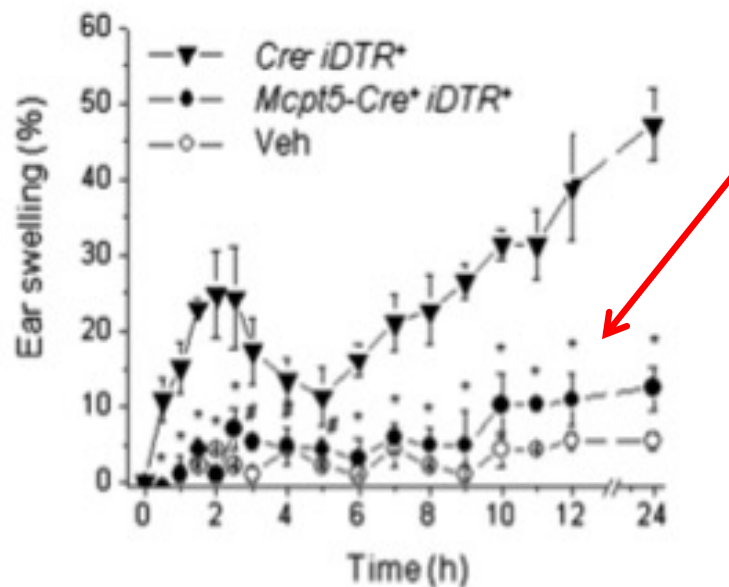
Immunity
Article

Mast Cells Are Key Promoters of Contact Allergy that Mediate the Adjuvant Effects of Haptens

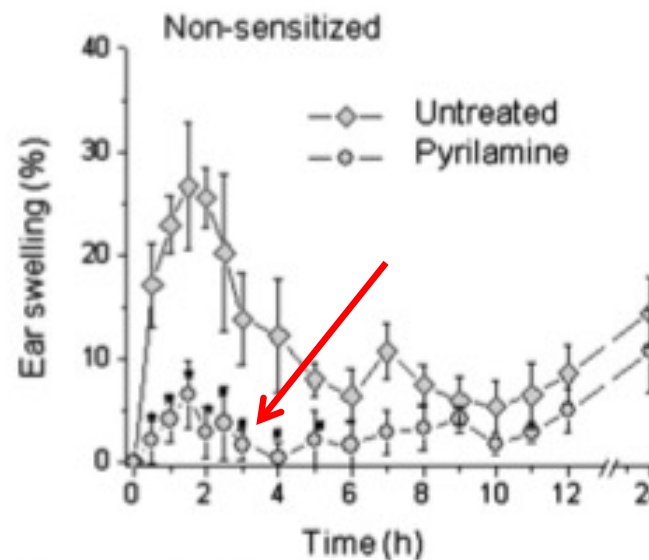
Anne Dudeck,^{1,8} Jan Dudeck,^{1,8} Julia Scholten,^{2,8} Anke Petzold,¹ Sangeetha Surianarayanan,¹ Anja Köhler,³ Katrin Peschke,¹ David Vöhringer,⁴ Claudia Waskow,⁵ Thomas Krieg,² Werner Müller,⁶ Ari Waisman,⁷ Karin Hartman, Matthias Gunzer,^{3,8,*} and Axel Roers^{1,8,*}



Dramatic decrease of ACD response in animals conditionally depleted in mast cells



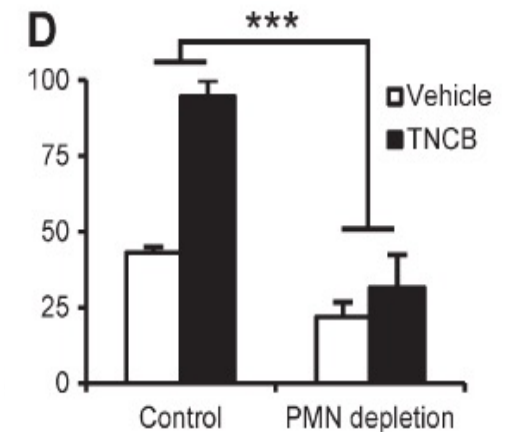
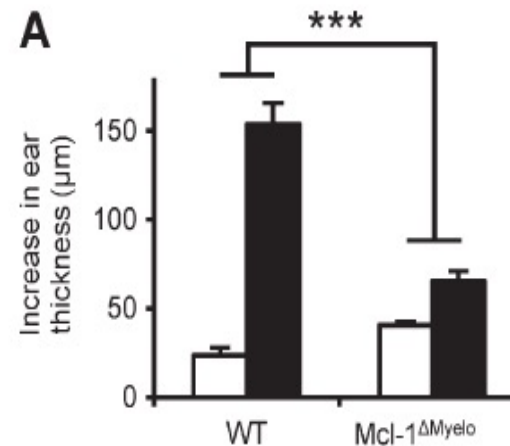
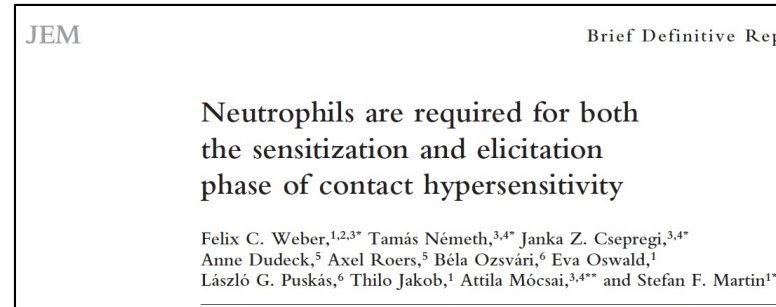
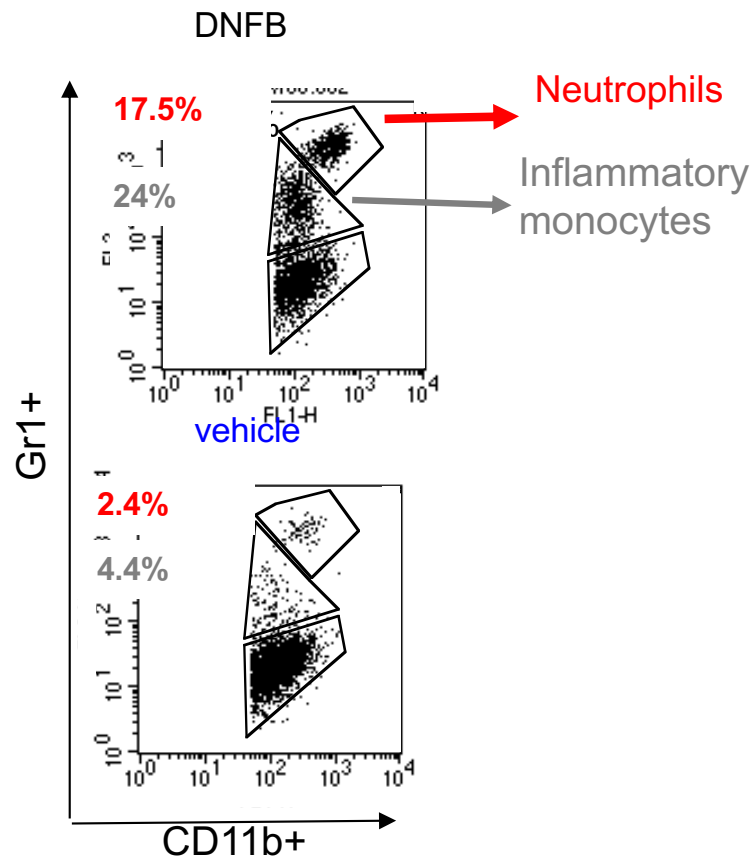
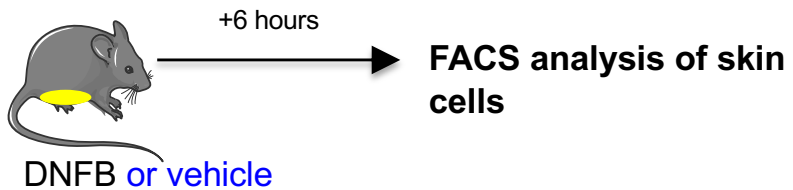
Skin inflammation is histamine-dependent



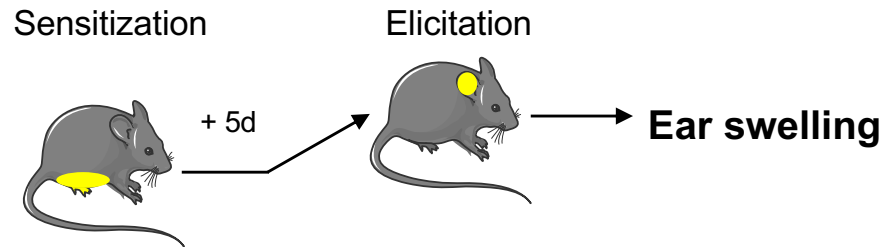
Contribution of innate cells? Neutrophils

Large infiltration of neutrophils
in the hours following hapten application

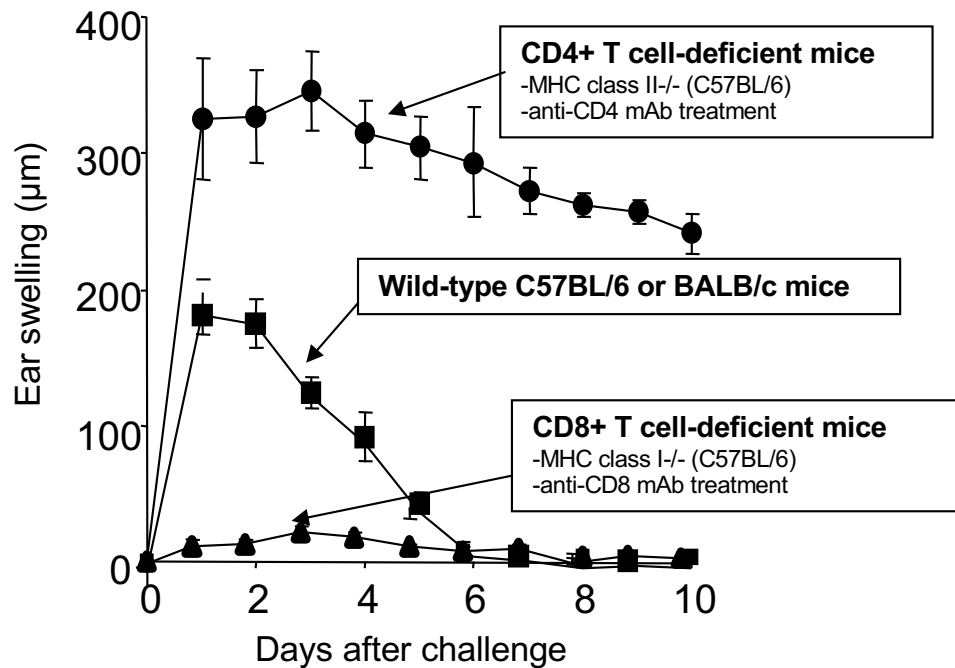
Lack of neutrophils (depletion, transgenic animals)
prevents T cell priming and development of skin inflammation



Main effectors? CD8+ CTLs

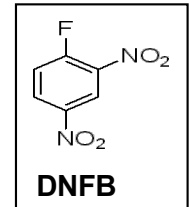
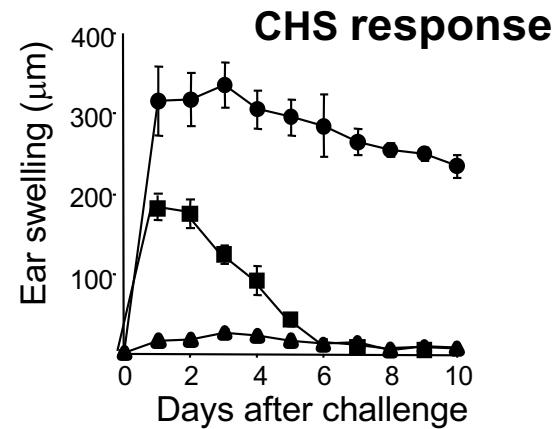
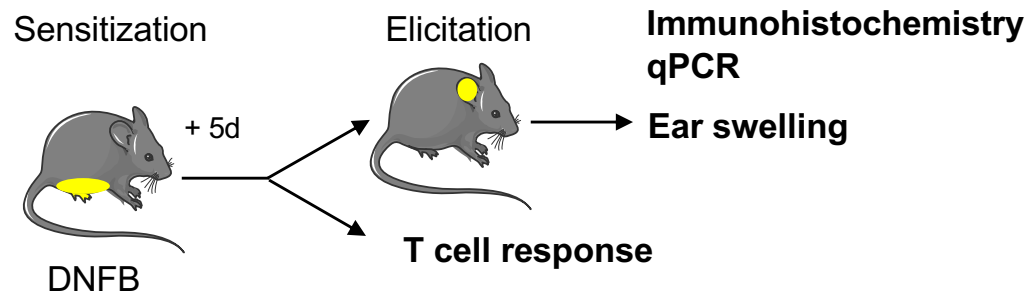


Strong haptens: DNFB, TNCB, OXAZOLONE...



- CD8+ T cells are effector cells
- CD4+ T cells comprise regulatory T cells

Main effectors? CD8+ CTLs



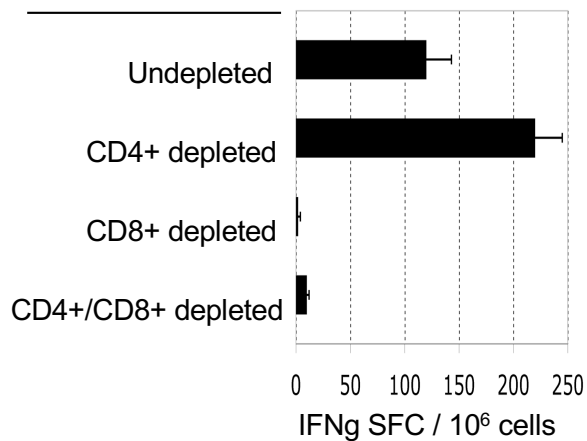
Priming of

IFN γ -producing CD8+ T cells

T cell response
(draining lymph nodes)

Elispot assay

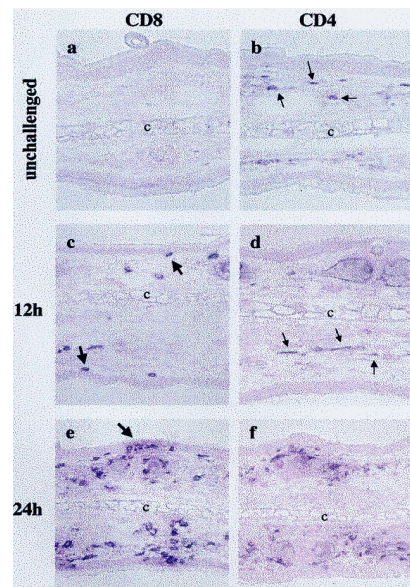
mAb Treatment



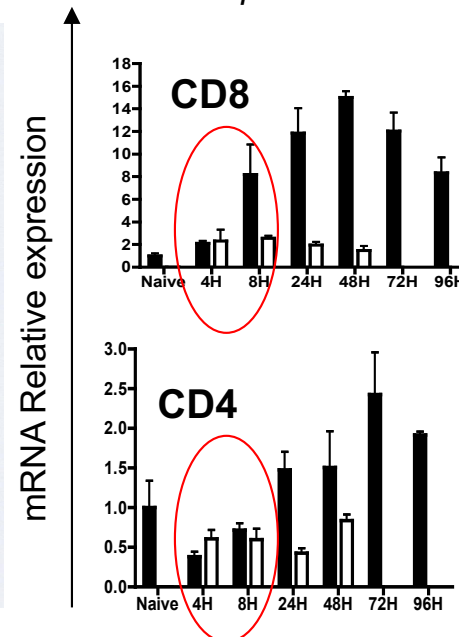
Early recruitment of CD8+ T cells initiates eczema

T cells recruitment
(challenged ears)

Immunostaining

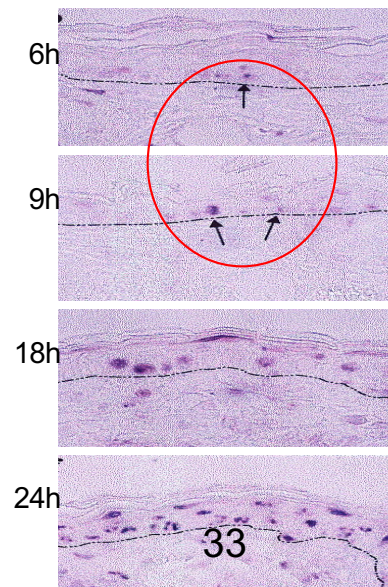


qRT-PCR



Keratinocytes:
target of CTLs

TUNEL



33

Main effectors? CD8+ CTLs

Recurrence, chronicity

Inhibitory checkpoint receptors control CD8⁺ resident memory T cells to prevent skin allergy

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2019

Pia Gamradt, PhD,^{a,b,c,d,e,*} Léo Laoubi, MSc,^{a,b,c,d,e,*} Audrey Nosbaum, MD, PhD,^{a,b,c,d,e} Virginie Mutez, MSc,^{a,b,c,d,e}
Vanina Lenief, MSc,^{a,b,c,d,e} Sophie Grande, MD,^f Daniel Redouès, PhD,^g Anne-Marie Schmitt, MD, PhD,^h
Jean-François Nicolas, MD, PhD,^{a,b,c,d,e,f} and Marc Vocanson, PhD^{a,b,c,d,e} Lyon, Pierre-Benite, and Toulouse, France

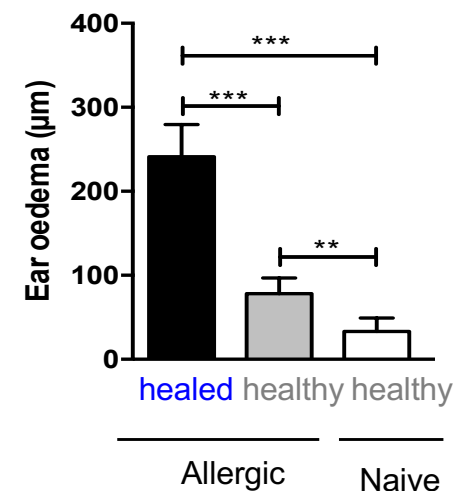
Healthy skin



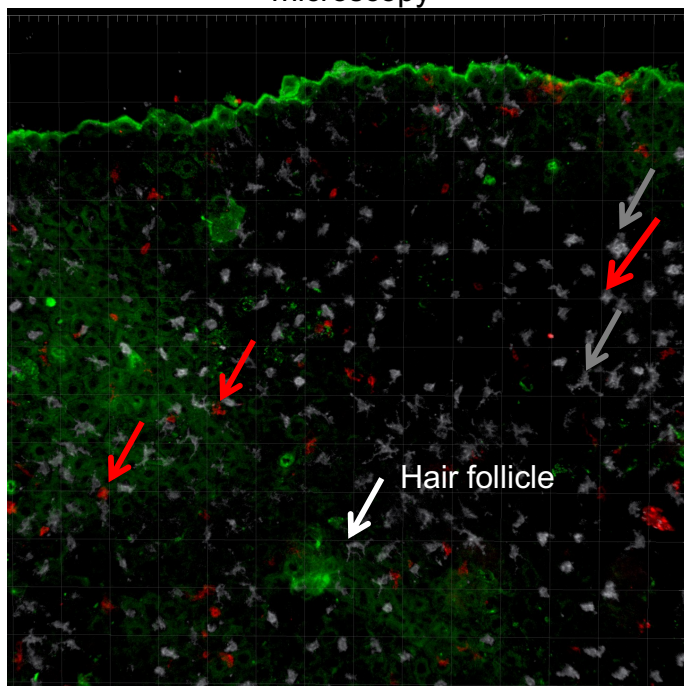
Healed lesion

allergic animal

Flare-up reaction



Epidermal sheet, Confocal microscopy



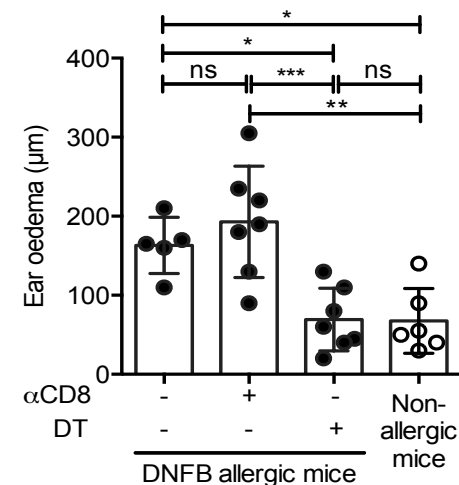
Skin edge

CD8+ T cells

Ag = DNP moities

DETC

Acute depletion of CD8+Trm abrogates flares



Injection of diphteria toxin or anti-CD8+ mAbs
IDTR transgenic animals

Main effectors? NK cells

- NK cells are far less important than CD8+ CTLs for eczema

European Journal of Immunology

Natural killer cells and T cells induce different types of skin reactions during recall responses to haptens

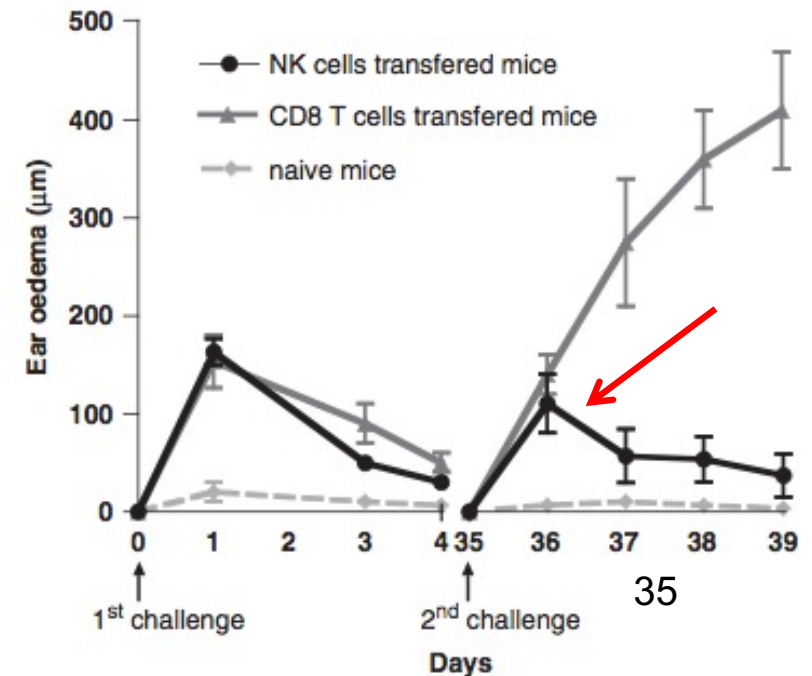
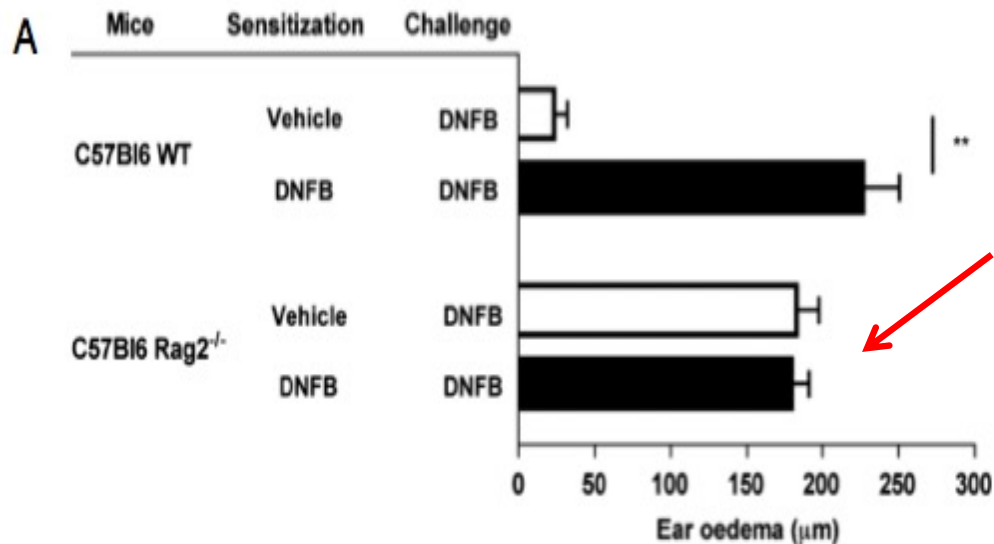
Paul Rouzairé^{1,2,3}, Carmelo Luci⁴, Elisabeth Blasco^{1,2,3}, Jacques Bienvenu^{1,2,3}, Thierry Walzer^{1,2}, Jean-François Nicolas^{1,2,5} and Ana Hennino^{1,2}

Paulst S. Nat Immunol 2011

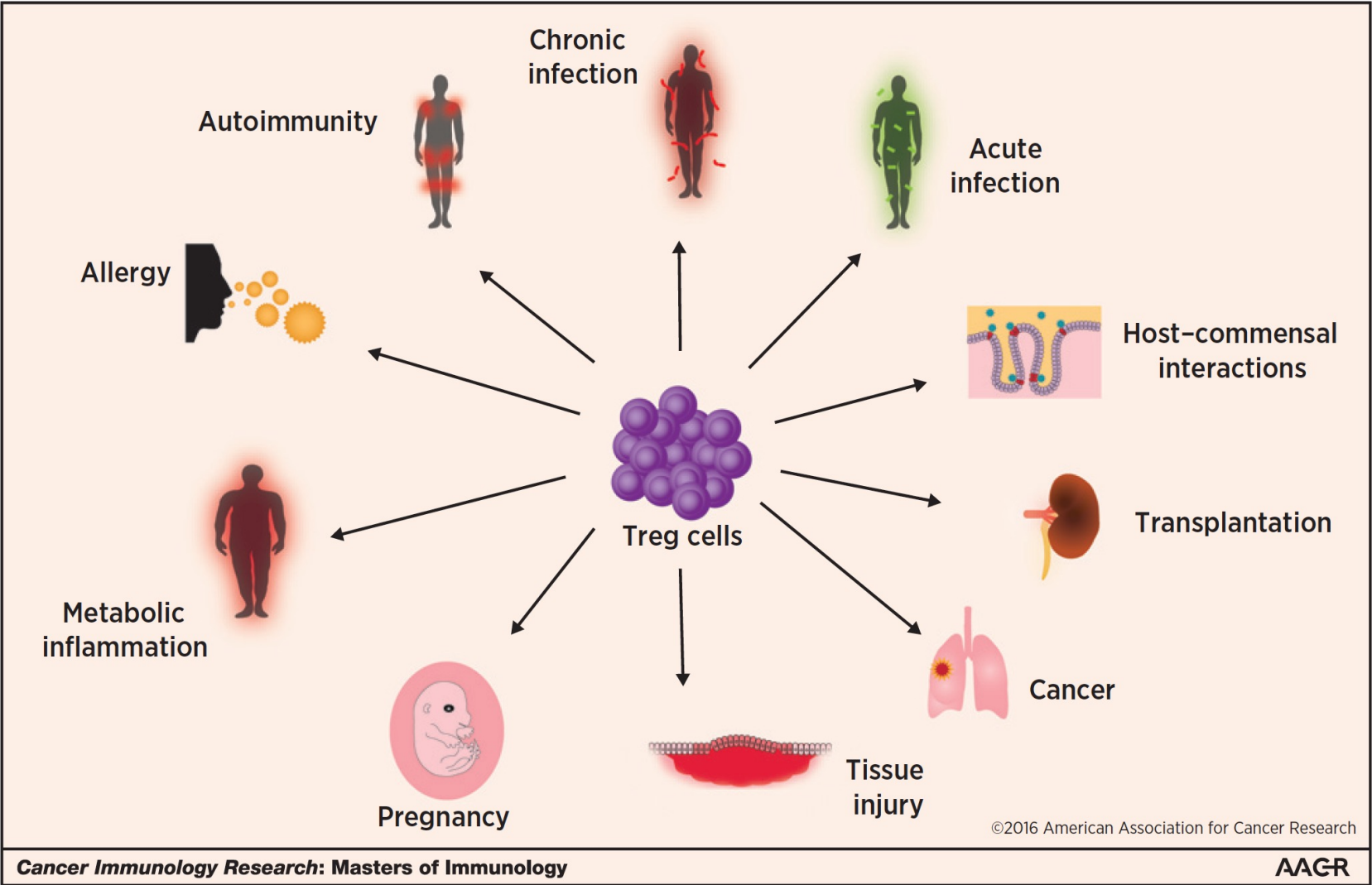
NK cells confer CHS and recall responses, when extracted from liver and transferred into recipient animals

-> NK cell « memory »

No CHS response in T cell-deficient strains

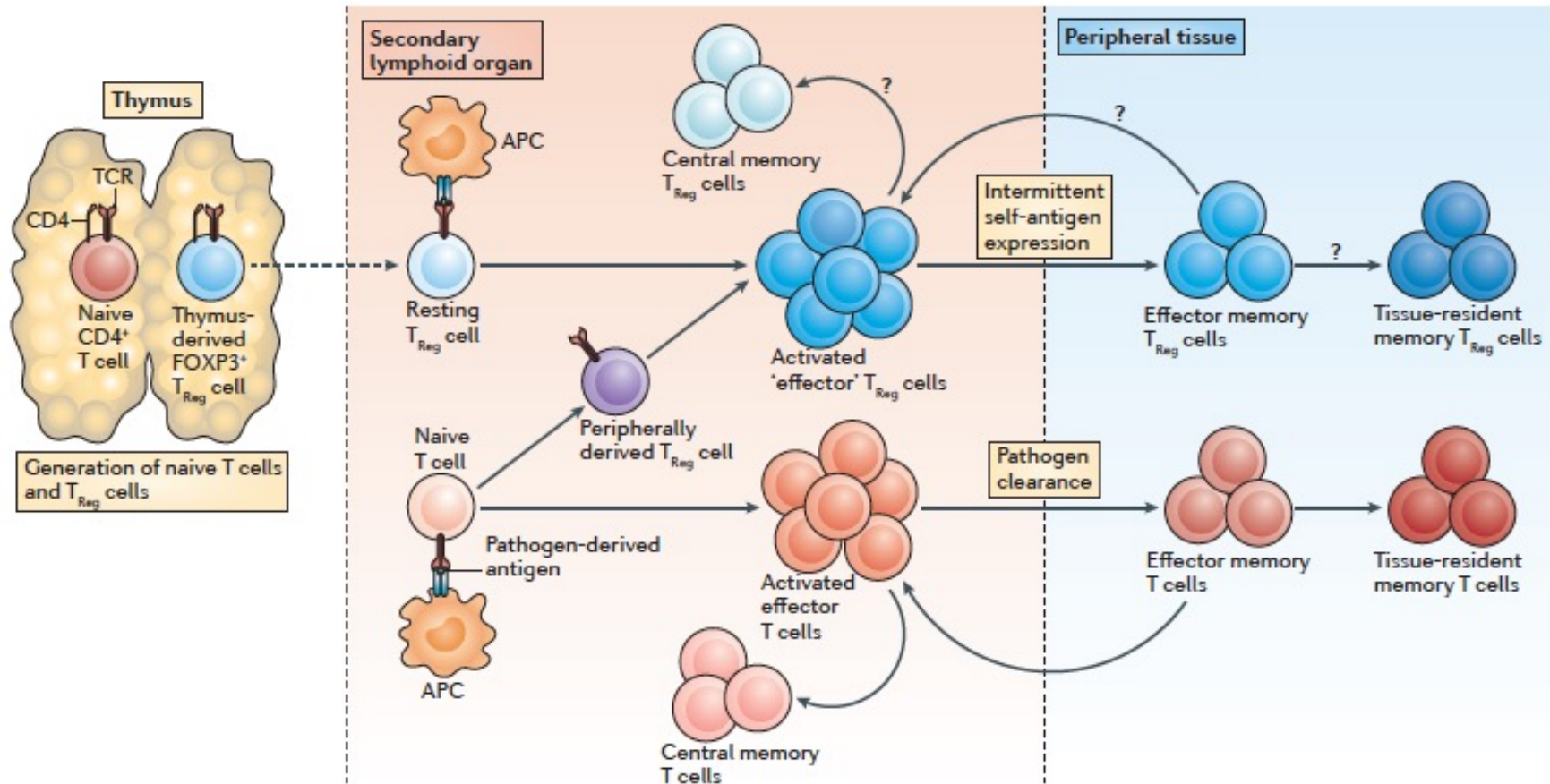


Les lymphocytes T régulateurs FoxP3+



Les lymphocytes T régulateurs FoxP3+

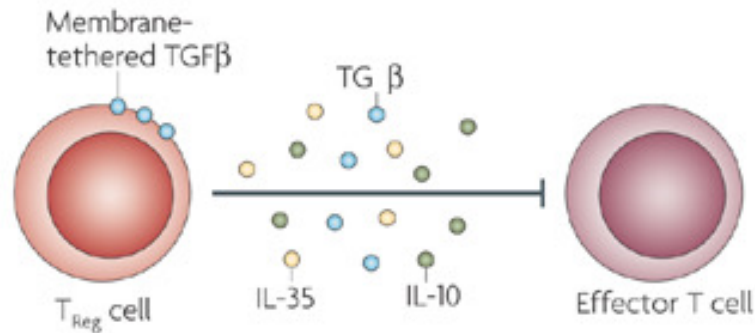
Ontogeny: Life Cycle of Regulatory and Conventional T cells



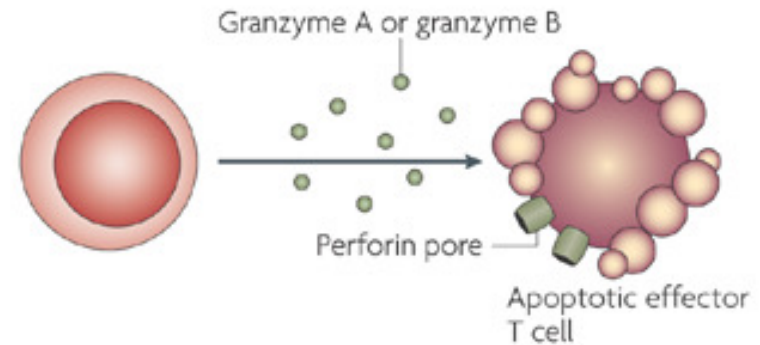
Les lymphocytes T régulateurs FoxP3+

Suppressive mechanisms used by Tregs

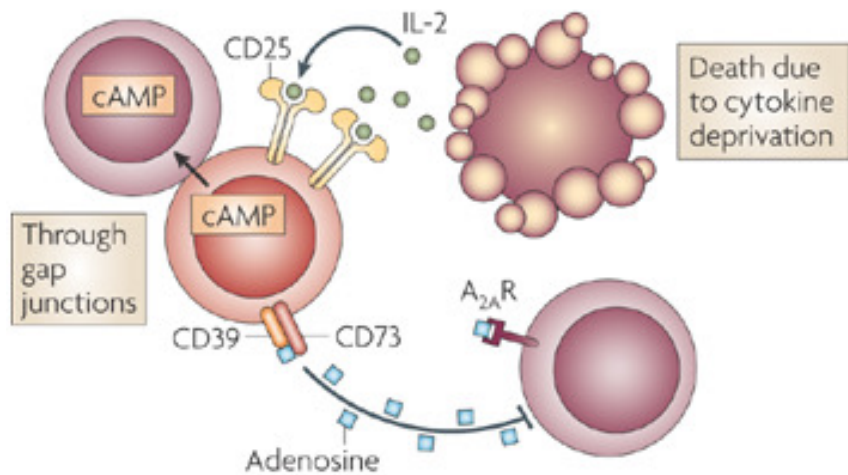
a Inhibitory cytokines



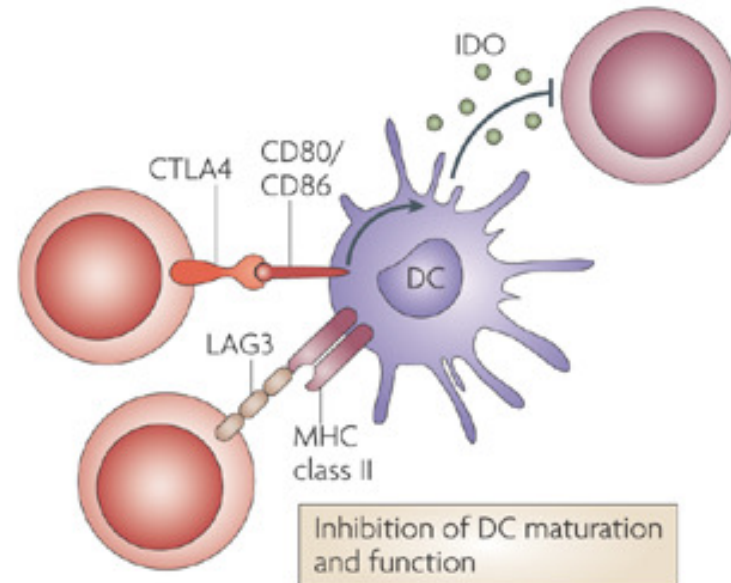
b Cytolysis



c Metabolic disruption



d Targeting dendritic cells



Main regulatory cells? FoxP3+Tregs

- Multifunctional FoxP3+ICOS+ regulatory T cells control CTL-induced skin inflammation

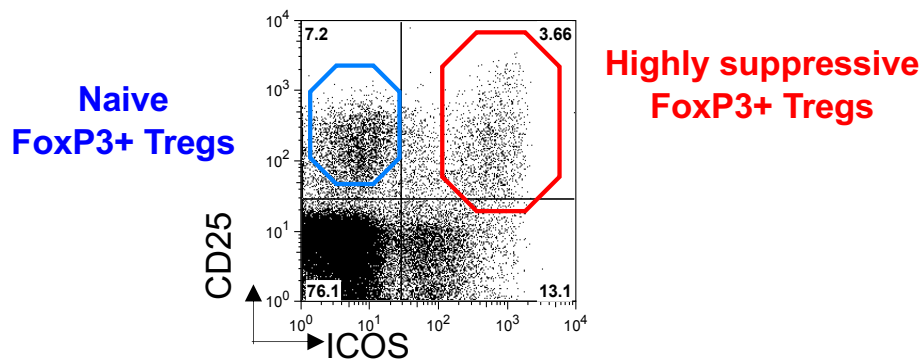
Inducible costimulator (ICOS) is a marker for highly suppressive antigen-specific T cells sharing features of T_H17/T_H1 and regulatory T cells

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VOLUME 126, NUMBER 2

Marc Vocanson, PhD,^{a,b,c} Aurore Rozieres, PhD,^{a,b,c} Anca Hennino, PhD,^{b,c} Gaelle Poyet, MSc,^{a,b,c}
Vincent Gaillard, BSc,^{a,b,c} Sarah Renaudineau, MSc,^{b,c} Amine Achachi, PhD,^{b,c} Josette Benetiere, BSc,^{a,b,c}
Dominique Kaiserlian, PhD,^{b,c} Bertrand Dubois, PhD,^{b,c} and Jean-François Nicolas, MD, PhD^{a,b,c,d} *Lyon, France*

Activation of CD4+CD25+FoxP3+ICOS+ Tregs
in the draining lymph nodes of hapten-sensitized mice

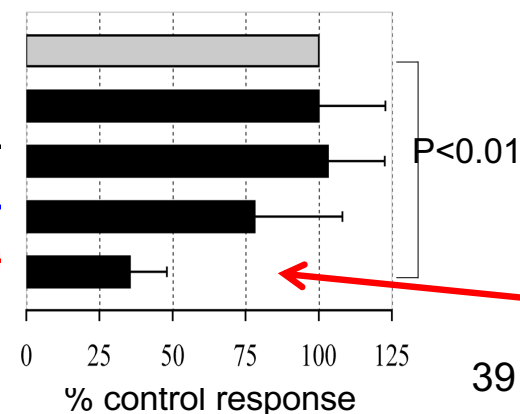
Transfer of FoxP3+ICOS+ Tregs prevents the priming of CD8+ CTLs
and the development of skin inflammation in an antigen-dependant
manner



Transferred cells

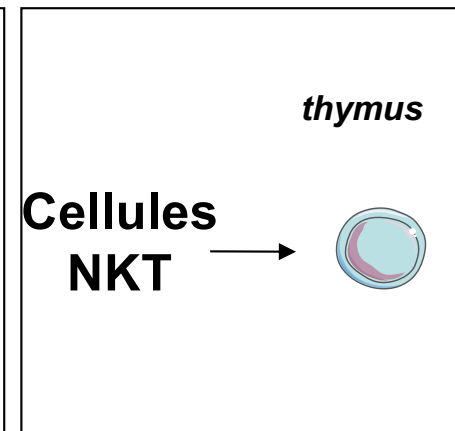
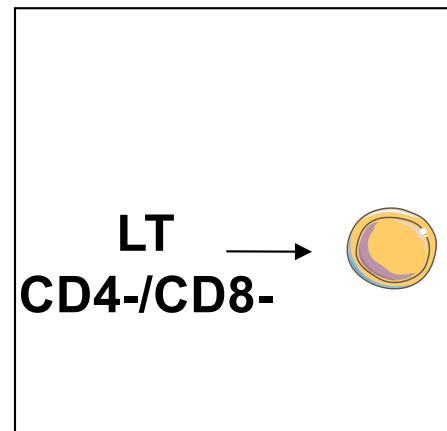
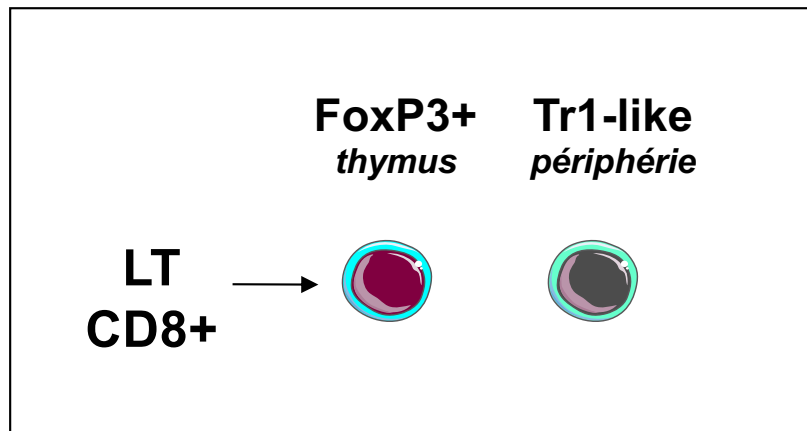
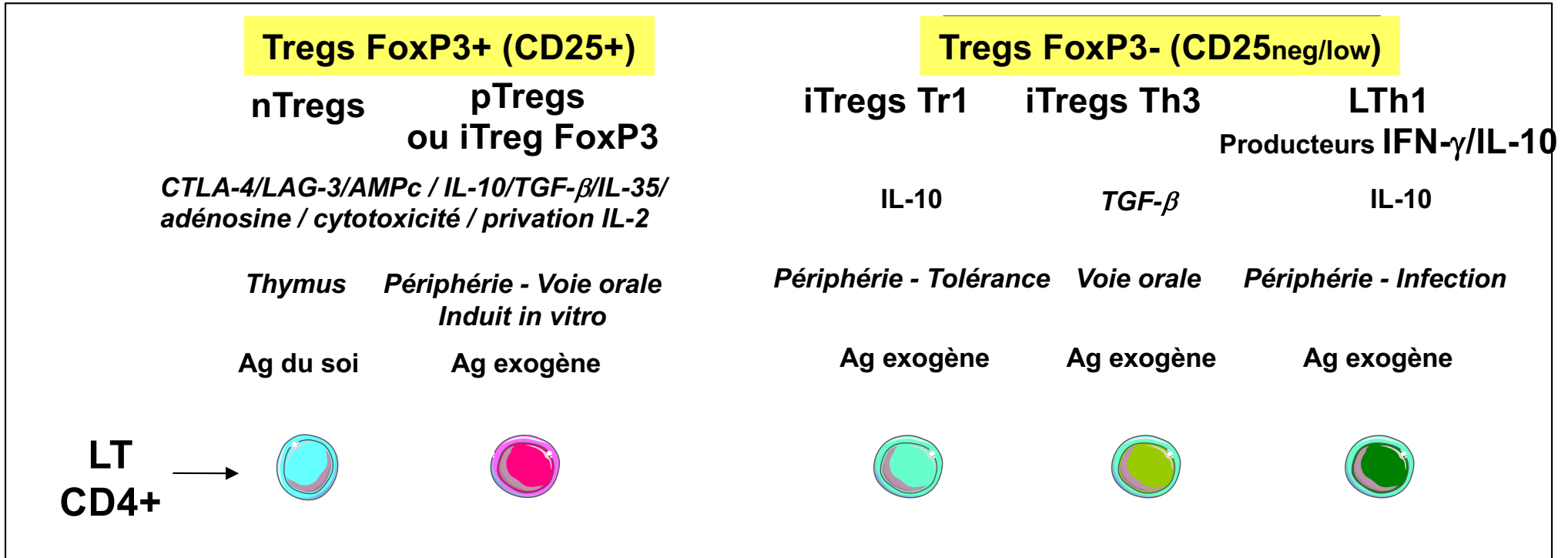
CHS response 48h

PBS
CD4+CD25-ICOS-
CD4+CD25-ICOS+
CD4+CD25+ICOS-
CD4+CD25+ICOS+



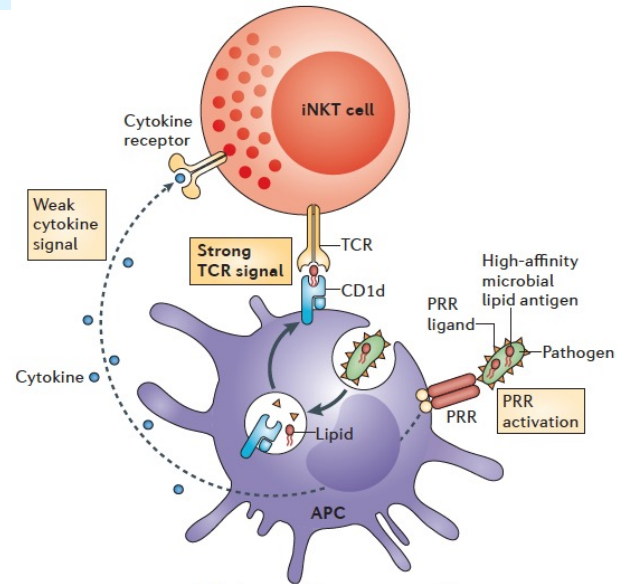
39

De nombreux lymphocytes régulateurs

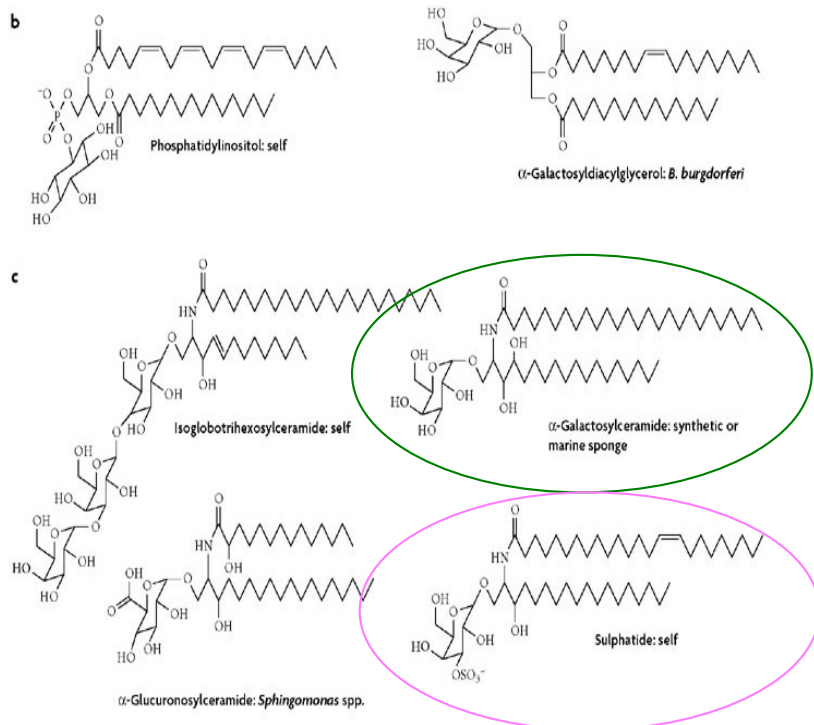


Les lymphocytes non conventionnels : les cellules NKTs

TCR-driven activation



Main recognized lipids



Main features

- 2 groups of NKT cells:
 - ✓ invariant NKT cells (iNKT cells) = TCR $V\alpha 24J\alpha 18$ and mainly $V\beta 11$
 - ✓ non-invariant NKT cells (oligoclonal)
- iNKT predominant in mice, few in humans
- NKT cells promote immunity against cancers and microbes but suppress autoimmunity
- Functional versatility \rightarrow different subsets (NKT1, NKT2, NK17, NKT_{FH}...)
- iNKT cells respond to self and microbial lipids similar to the glycosphingolipid α -GalCer
- Non-invariant NKT cells respond to lipids similar to sulfatide
- CD1d-restriction

Other regulatory cells? iNKT cells

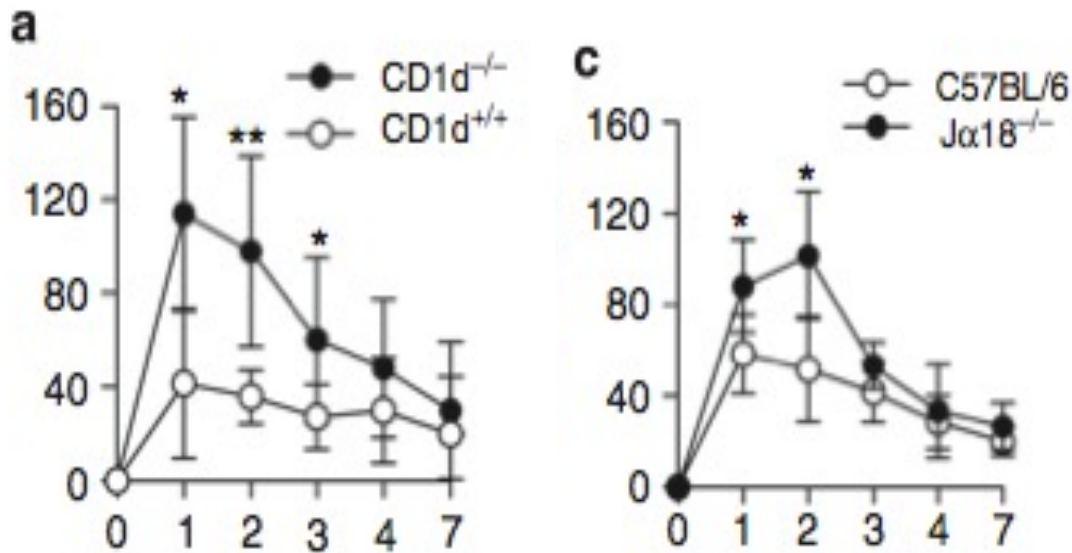
- iNKT cells are non-redundant downregulators of CTL-mediated CHS responses

Invariant NKT Cells Suppress CD8⁺ T-Cell-Mediated Allergic Contact Dermatitis Independently of Regulatory CD4⁺ T Cells

Anne Goubier^{1,2,3,6}, Marc Vocanson^{1,2,3,6}, Claire Macari^{1,2,3}, Gaëlle Poyet^{1,2,3}, André Herbelin^{4,5}, Jean-François Nicolas^{1,2,3}, Bertrand Dubois^{1,2,3,6} and Dominique Kaiserlian^{1,2,3,6}

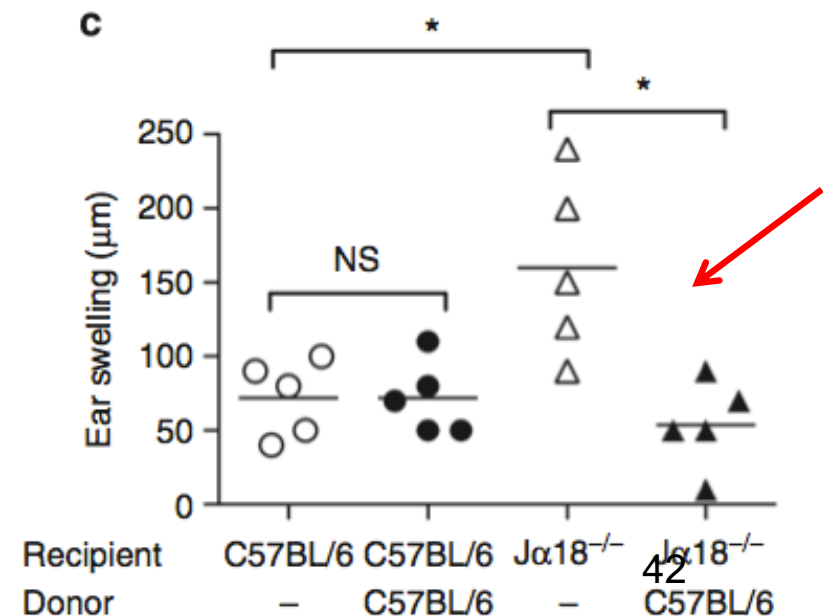
Journal of Investigative Dermatology (2013) 133, 980–987; doi:10.1038/jid.2012.404; published online 29 November 2012

Decreased CHS to DNFB response in NKT deficient mice (B6)




Other studies argue against the regulatory functions of iNKT cells and suggest stimulatory functions

Adoptive transfer of iNKT in Ja18^{-/-} mice normalises CHS response



Other regulatory cells? B cell subsets

- Other regulatory cells (peritoneal B-1a cells) participate to the resolution of skin inflammation

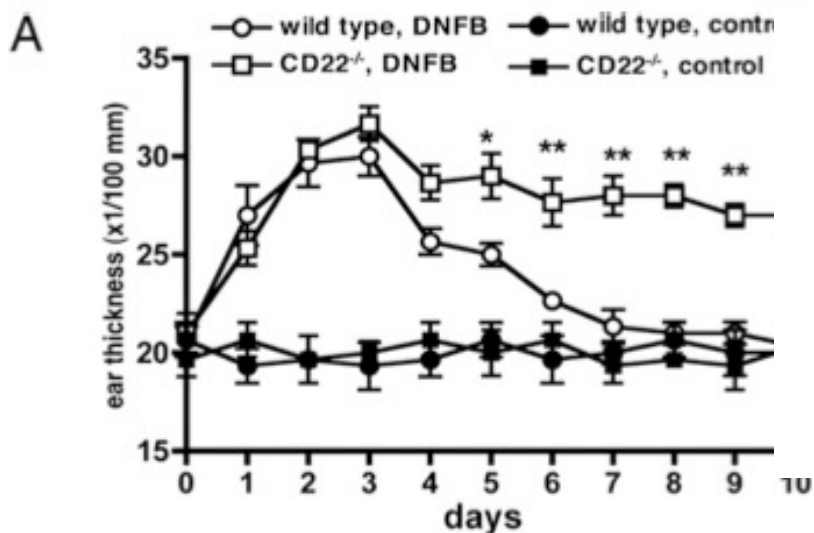
 **CD22 Expression Mediates the Regulatory Functions of Peritoneal B-1a Cells during the Remission Phase of Contact Hypersensitivity Reactions**

This information is current as of June 24, 2014.

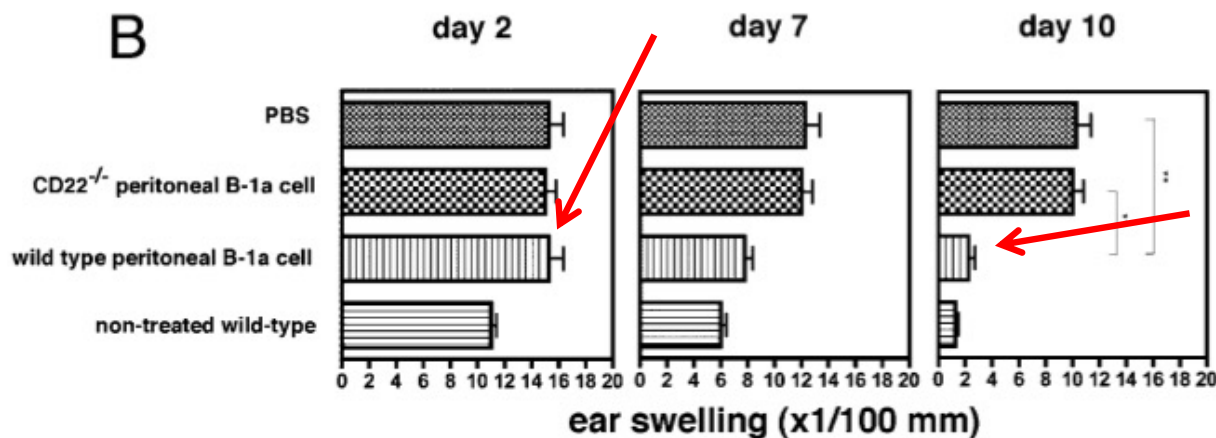
Hiroko Nakashima, Yasuhito Hamaguchi, Rei Watanabe, Nobuko Ishiura, Yoshihiro Kuwano, Hitoshi Okochi, Yoshimasa Takahashi, Kunihiko Tamaki, Shinichi Sato, Thomas F. Tedder and Manabu Fujimoto

J Immunol 2010; 184:4637-4645; Prepublished online 24 March 2010;
doi: 10.4049/jimmunol.0901719
<http://www.jimmunol.org/content/184/9/4637>

Absence of CHS resolution in CD22^{-/-} animals

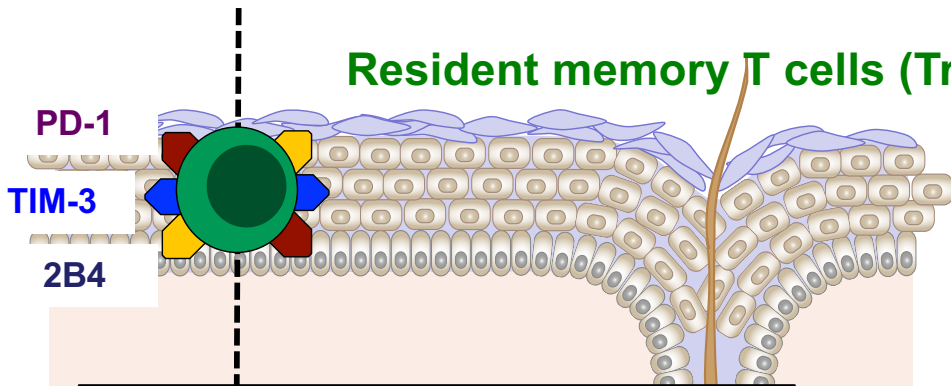


Adoptive transfer of B1-a cell promotes the resolution of skin inflammation in CD22^{-/-} animals

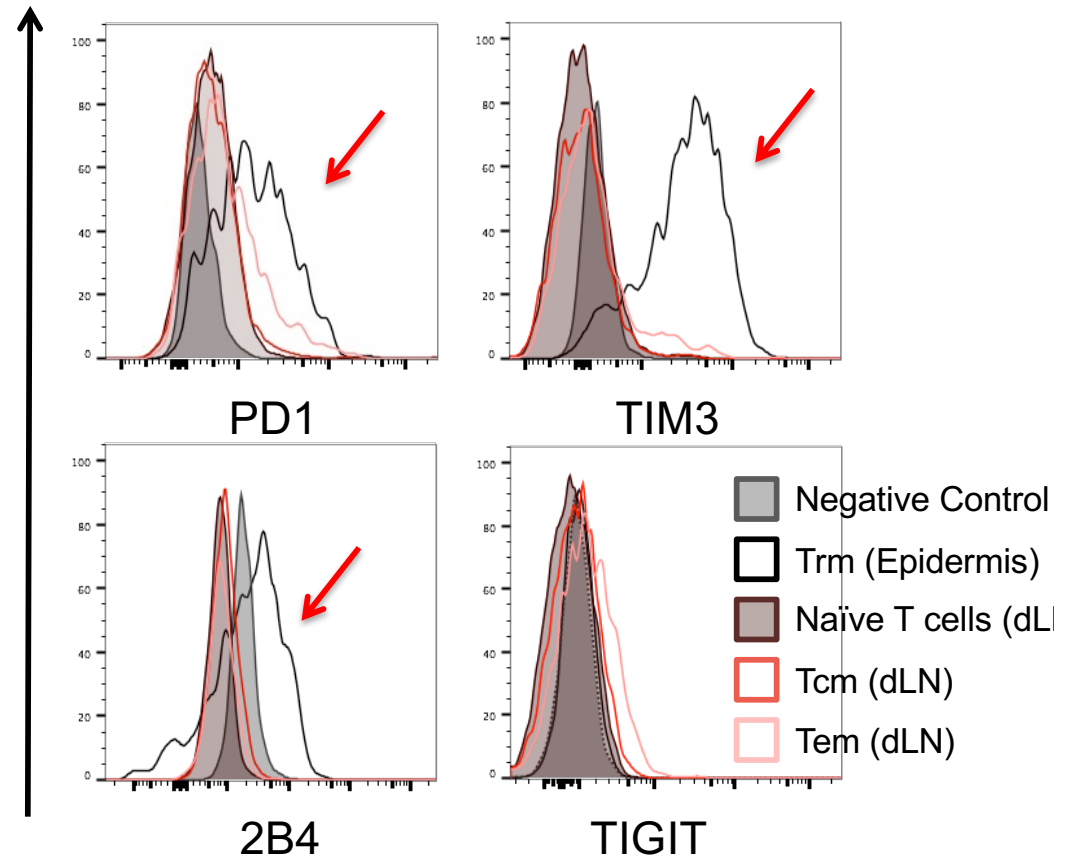
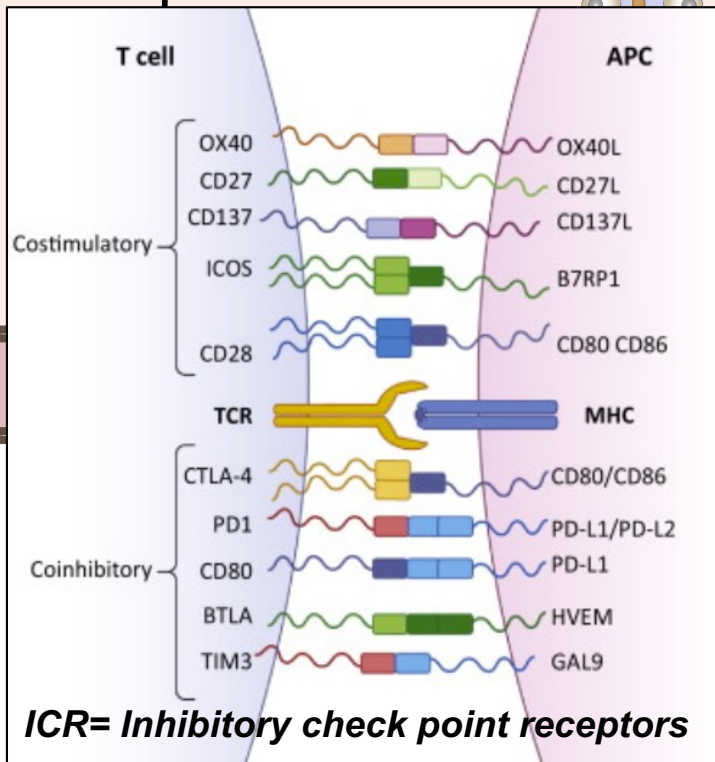


Les mécanismes de régulation intrinsèques: Les récepteurs inhibiteurs

DNFB allergic mice  **Healed**
→ FACS

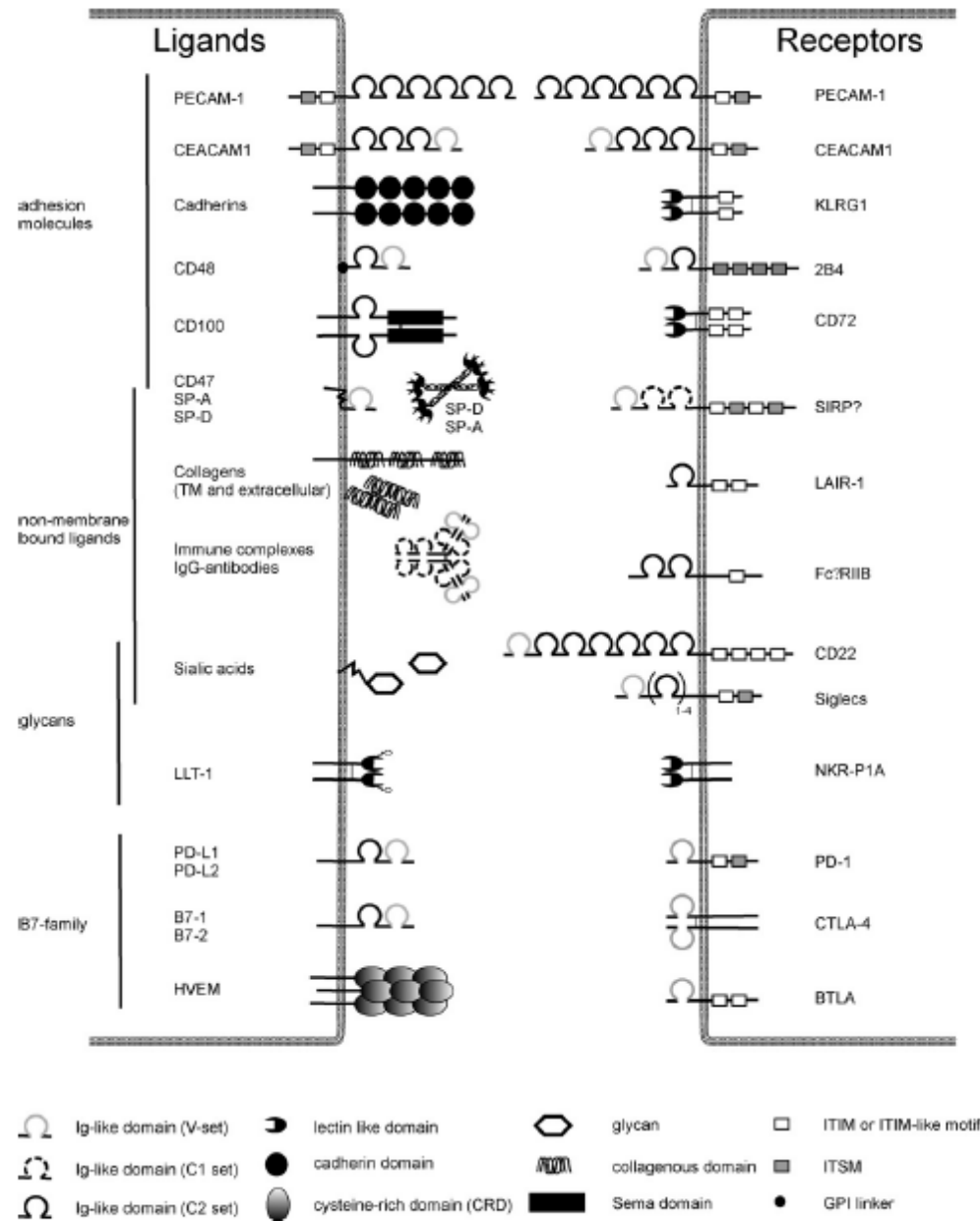


Expression of ICRs on skin CD8+ Trm



- Certain ICRs are expressed on skin CD8+ Trm but not on circulating memory T cells → they limited recurrences & exacerbations

D'autres mécanismes de régulation par le tissu?

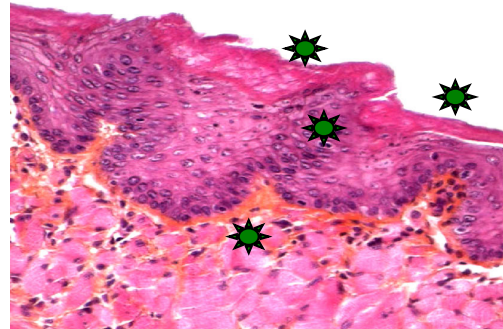


Eczéma allergique de contact : les facteurs de risques

Ignorance?



Tolérance



**Sensibilisation
Eczéma**

- > la nature de l'antigène = "le danger"
- > les conditions d'exposition (dose, fréquence, durée, route)
- > le polymorphisme génétique (barrière cutanée, enzymes de détoxification...),
âge, sexe
- > l'environnement (maladie sous-jacente, stress, pollution...)

Les facteurs génétiques

5. Studies on probably functionally relevant polymorphisms in contact allergic patients from our study, from more recent studies (columns I–IV, rows 1, 5, 6, and 9), and replication studies (column V)

	II	III	
	Polymorphisms	Results	
	Filaggrin null mutations (combined)	Results inconclusive	contact dermatitis vs controls: no
Table 3.	Difference in sensitization rates between children of sensitized and non-sensitized parents. 'The potent allergen DNCB is probably overpowering genetic influences'; Walker et al. (21)		contact dermatitis sensitization to nickel
	Percentage of children sensitized		nickel
Status of parents	DNCB	NDMA	sensitizers'
Sensitized	65	51	increased;
Not sensitized	52	29	decreased.
	$p < 0.10$	$p < 0.01$	VAT2*4
			in patients
			finds as
			group allergic
			acid – 9
			reference
			gene pairs in intrac
			ally increased
Cytokines: <i>ILB</i> – 511, <i>ILB</i> +3953, <i>ILRA</i> , <i>IL6</i> – 174, <i>TNFA</i> – 238, <i>TNFA</i> – 308		<i>TNFA</i> – 308 (G → A): increased (in polysensitized individuals) <i>TNFA</i> – 308 G/G and <i>ILRA</i> polymorphism (77) increased in Turkish patients ($n = 50$)	
Cytokine: <i>IL-16</i>		<i>IL16</i> – 295 (T → C) increased (in polysensitized individuals)	
Cytokine <i>IL-4</i>		No difference between chromate allergics and controls with regard to <i>IL4</i> – 590 polymorphism	

Le pouvoir sensibilisant des haptènes varient en fonction de la nature des molécules

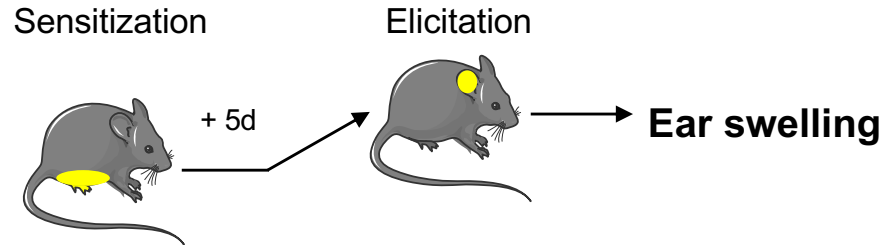
Chimique	Secteur	Pouvoir sensibilisant
Oxazolone	Chimie	Extrême
2,4-Dinitrofluorobenzene	Chimie	Extrême
2,4-Dinitrochlorobenzene	Chimie	Extrême
Glutaraldehyde	Conservateur, antiseptique	Fort
Formaldehyde	Cosmétique, Colorant	Fort
Cinnamaldehyde	Parfum, arôme	Modéré
Hexyl cinnamaldehyde	Cosmétique, Parfum	Modéré/Faible
Eugenol	Cosmétique, Parfum	Faible
Hydroxycitronellal	Cosmétique, Parfum	Faible
Linalool	Cosmétique	Faible
Citral	Parfum, arôme	Faible
Vanillin	Parfum, arôme	Faible
2,4-Dinitrocyano benzene	Chimie	Faible
Amoxicilline, cyanamide, ceftrimide	Médicament	Faible

Main effectors? CD8+ CTLs

Journal of Investigative Dermatology (2006) 126, 815-820. doi:10.1038/sj.jid.5700174; published online 2 February 2006

CD8+ T Cells Are Effector Cells of Contact Dermatitis to Common Skin Allergens in Mice

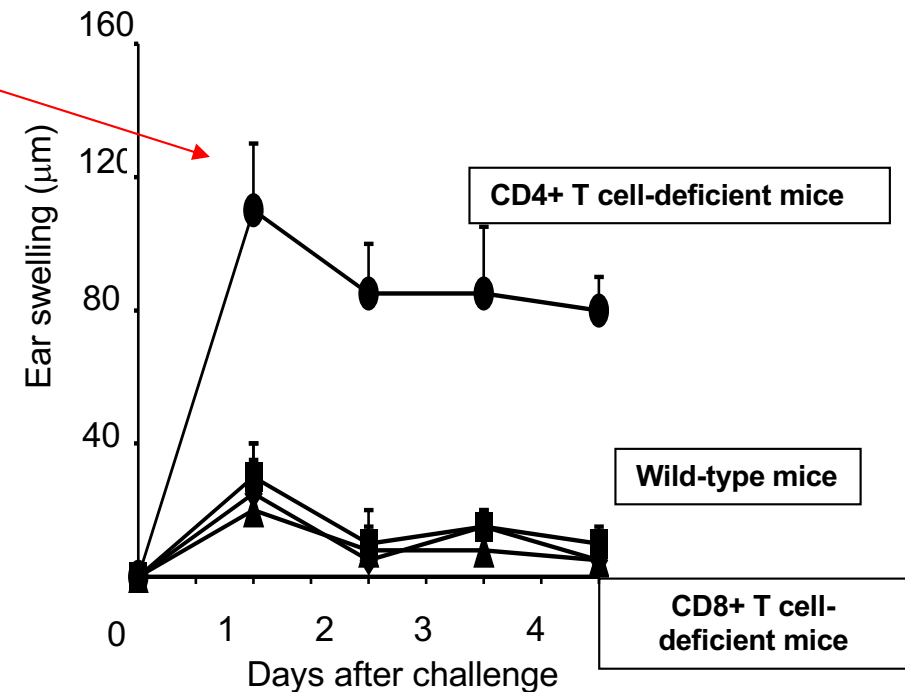
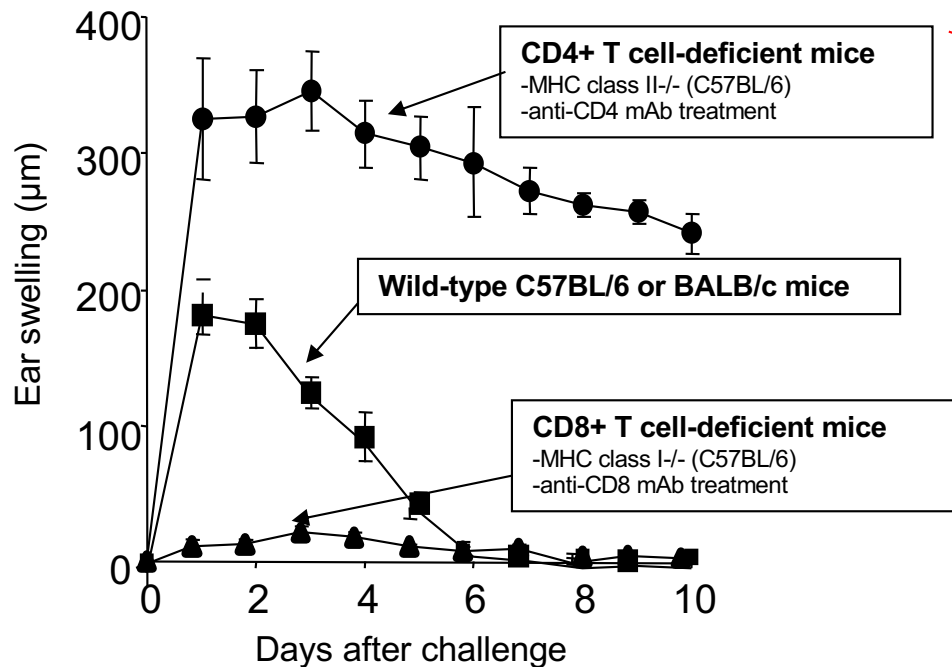
Marc Vocanson¹, Anca Hennino¹, Magalie Cluzel-Tailhardat¹, Pierre Saint-Mezard¹, Josette Benetiere¹, Cyril Chavagnac¹, Frederic Berard^{1,2}, Dominique Kaiserlian³ and Jean-François Nicolas^{1,2}



Strong haptens: DNFB, TNCB, OXAZOLONE...

Weak haptens

- Fragrances (Hexylcinnamaldehyde, Hydroxycitronellal, Eugenol, Dihydrocoumarin, Isoeugenol),
- Dye (paraphenylenediamine)
- Drugs (Amoxicillin, Rosephin, Phenytoin, Sulfasalazin)



- CD8+ T cells are effector cells
- CD4+ T cells comprise regulatory T cells

Département d'Immuno-Allergologie



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Institut national
de la santé et de la recherche médicale



Hôpitaux de Lyon