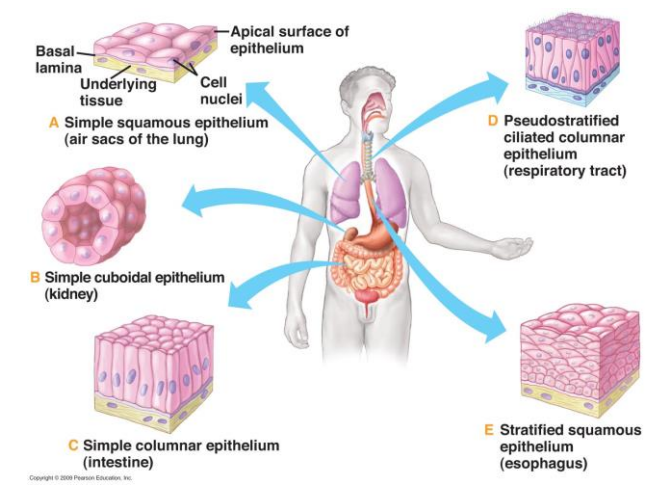
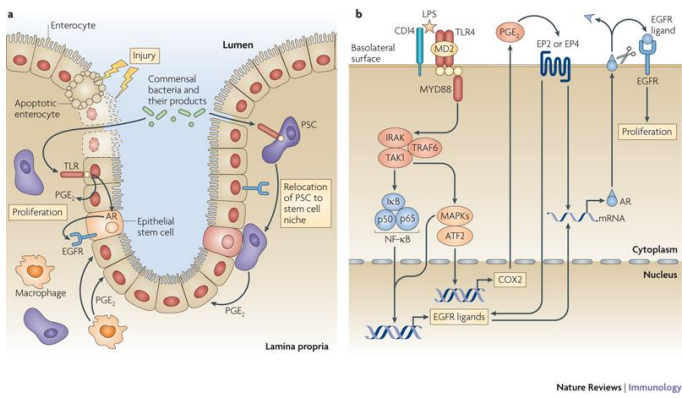




# Épimmunome

SSMG 10/12/2016



# NIH Public Access

## Author Manuscript

*Nat Immunol.* Author manuscript; available in PMC 2011 August 1.

Published in final edited form as:

*Nat Immunol.* 2010 August ; 11(8): 656–665. doi:10.1038/ni.1905.

## Epithelial decision-makers : in search of the “epimmunome”

**Mahima Swamy<sup>1</sup>, Colin Jamora<sup>2</sup>, Wendy Havran<sup>3,4</sup>, and Adrian Hayday<sup>1,4</sup>**

<sup>1</sup> London Research Institute, CRUK, and Peter Gorer Dept of Immunobiology, King's College London at Guy's Hospital, London, UK

<sup>2</sup> Section of Cell and Developmental Biology, Division of Biological Sciences, Natural Science Building, Room 6311, 9500 Gilman Drive, MC 0380, La Jolla, California 92093, USA

<sup>3</sup> Department of Immunology and Microbial Science, The Scripps Research Institute, La Jolla, CA 92037, USA



# NIH Public Access

## Author Manuscript

*Nat Immunol.* Author manuscript; available in PMC 2011 August 1.

Published in final edited form as:

*Nat Immunol.* 2010 August ; 11(8): 656–665. doi:10.1038/ni.1905.

## Epithelial decision-makers : in search of the “epimmunome”

### Abstract

Frequent microbial and non-microbial challenges to epithelial cells trigger discrete pathways, promoting molecular changes, such as the secretion of specific cytokines and chemokines, and alterations to molecules displayed at the epithelial cell surface. In combination, these molecules impose major decisions on innate and adaptive immune cells. Depending on context, those decisions can be as diverse as those imposed by professional antigen presenting cells, benefitting the host by balancing immune competence with the avoidance of immunopathology. Nonetheless, this potency of epithelial cells is also consistent with the causal contribution of epithelial dysregulation to myriad inflammatory diseases. This pathogenic axis provides an attractive target for tissue-specific clinical manipulation. In this context, a research goal should be to identify all molecules used by epithelial cells to instruct immune cells. We term this the epimmunome.

Quand le microbiote parle aux  
épithélia

Quand les épithélia parlent au  
système immunitaire

Épimmunome

Quand microbiote et épithélia  
orientent la réponse immunitaire

Les épithélia aux commandes

C'est

Un bel

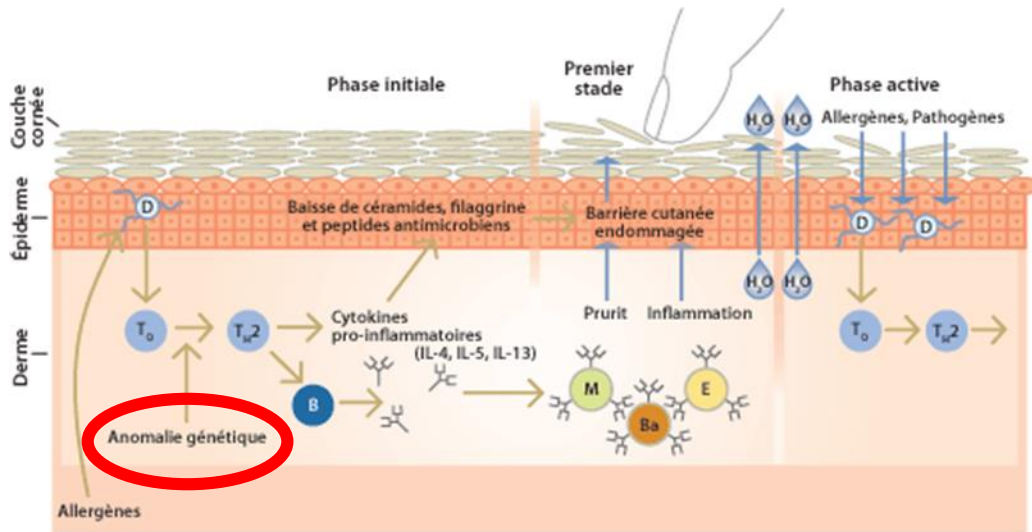
Épimmunome

Outil de

Communication

# Evolution des paradigme

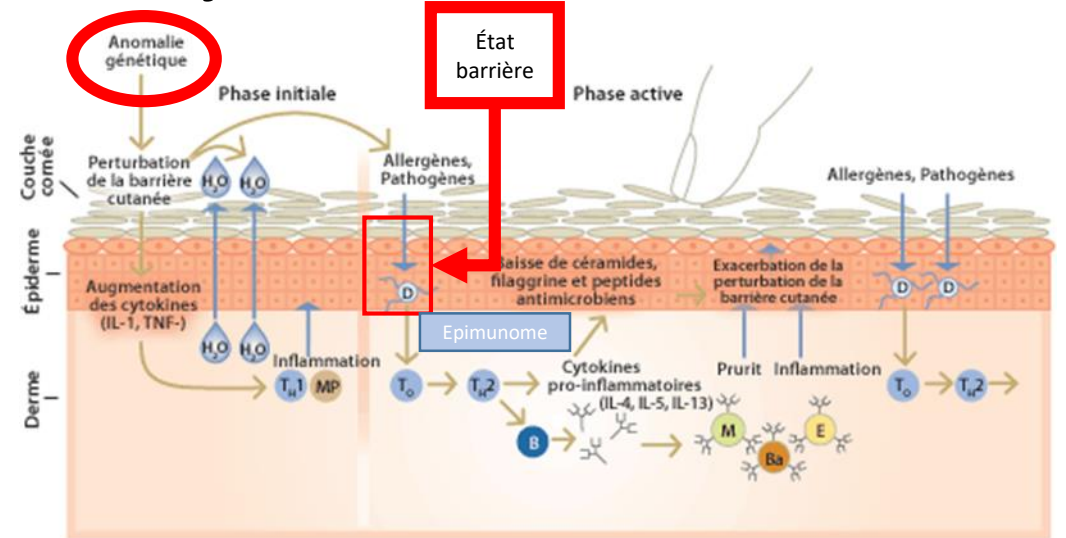
Avant : « Inside ➔ out »



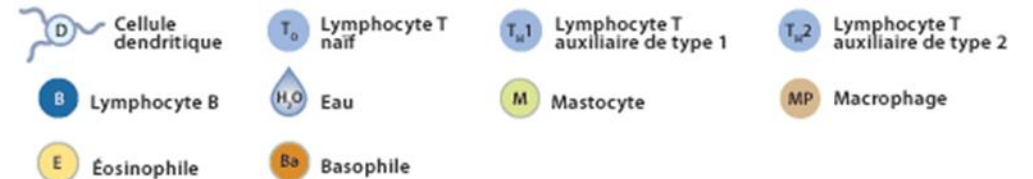
Légende :



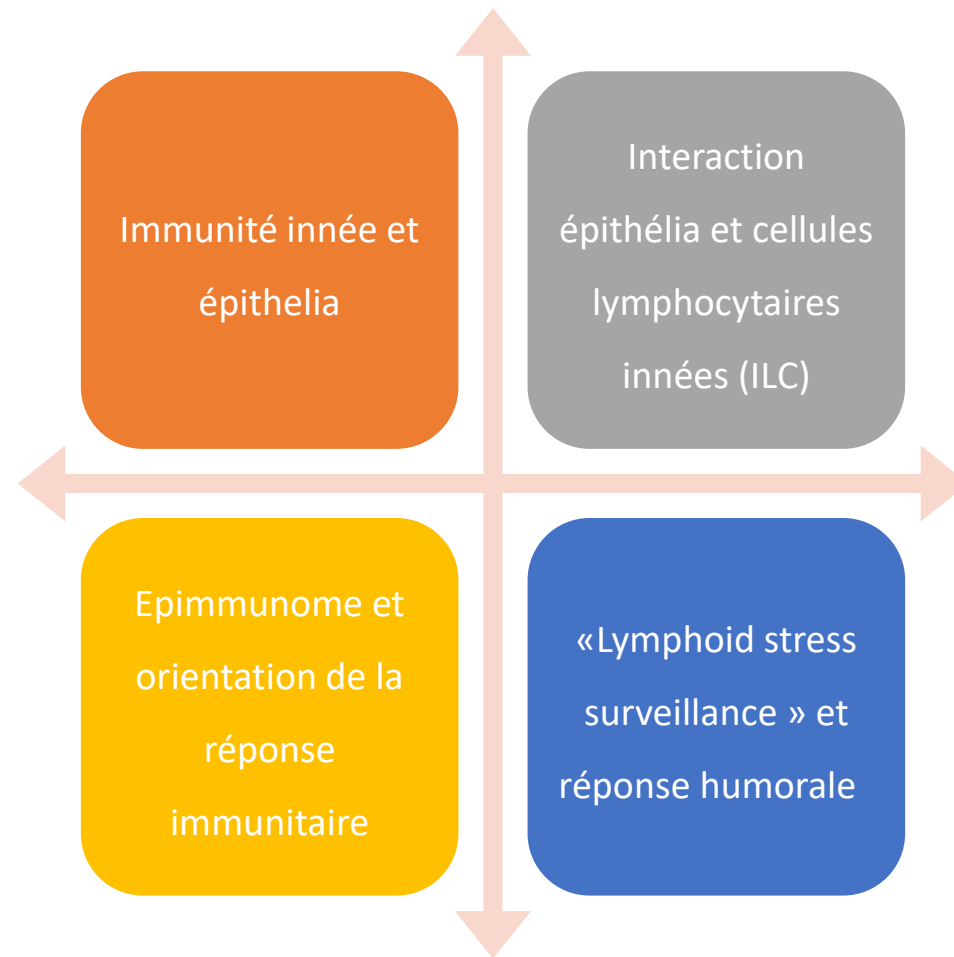
Aujourd'hui : « Outside ➔ in »



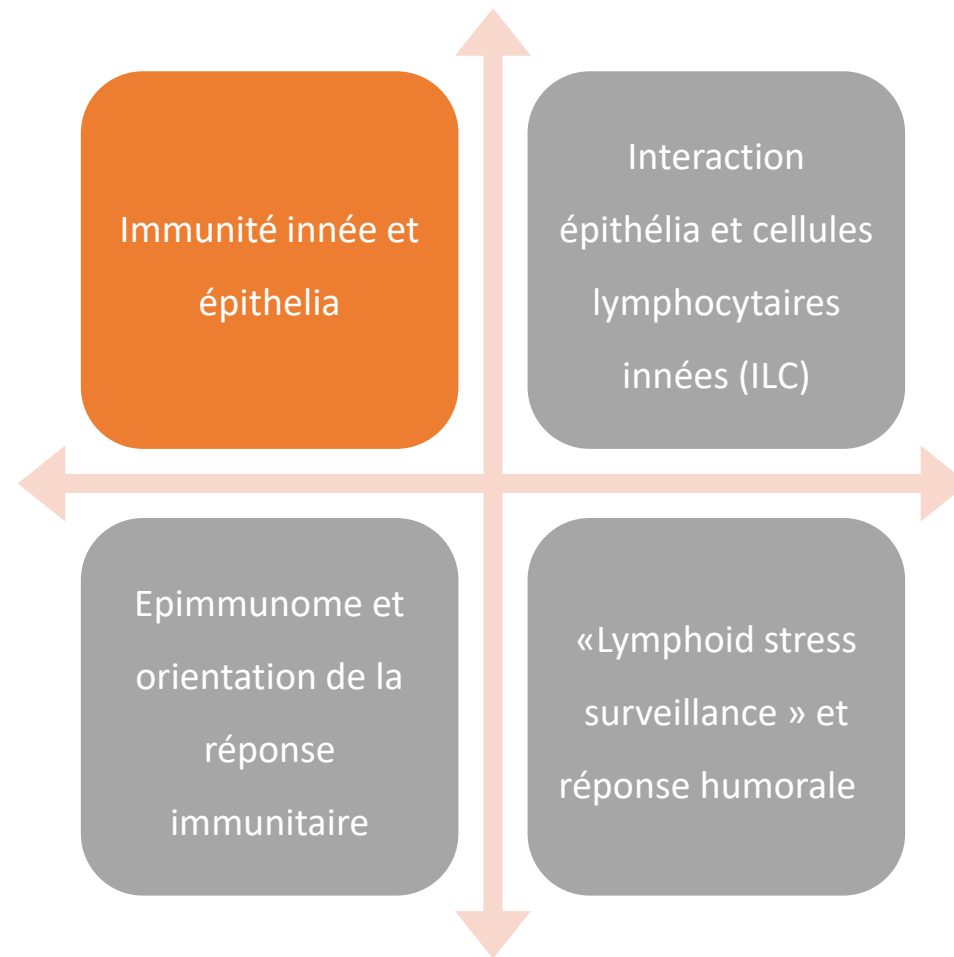
Légende :



# Épimmunome?

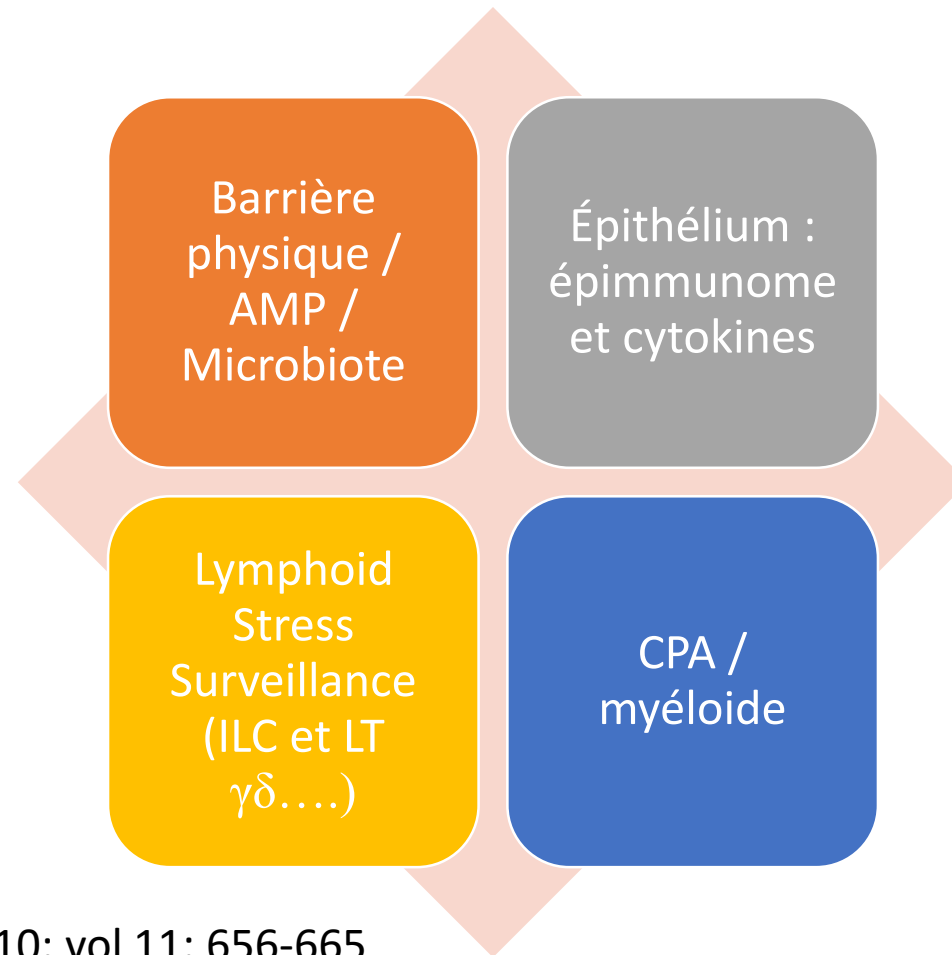


# Épimmunome?



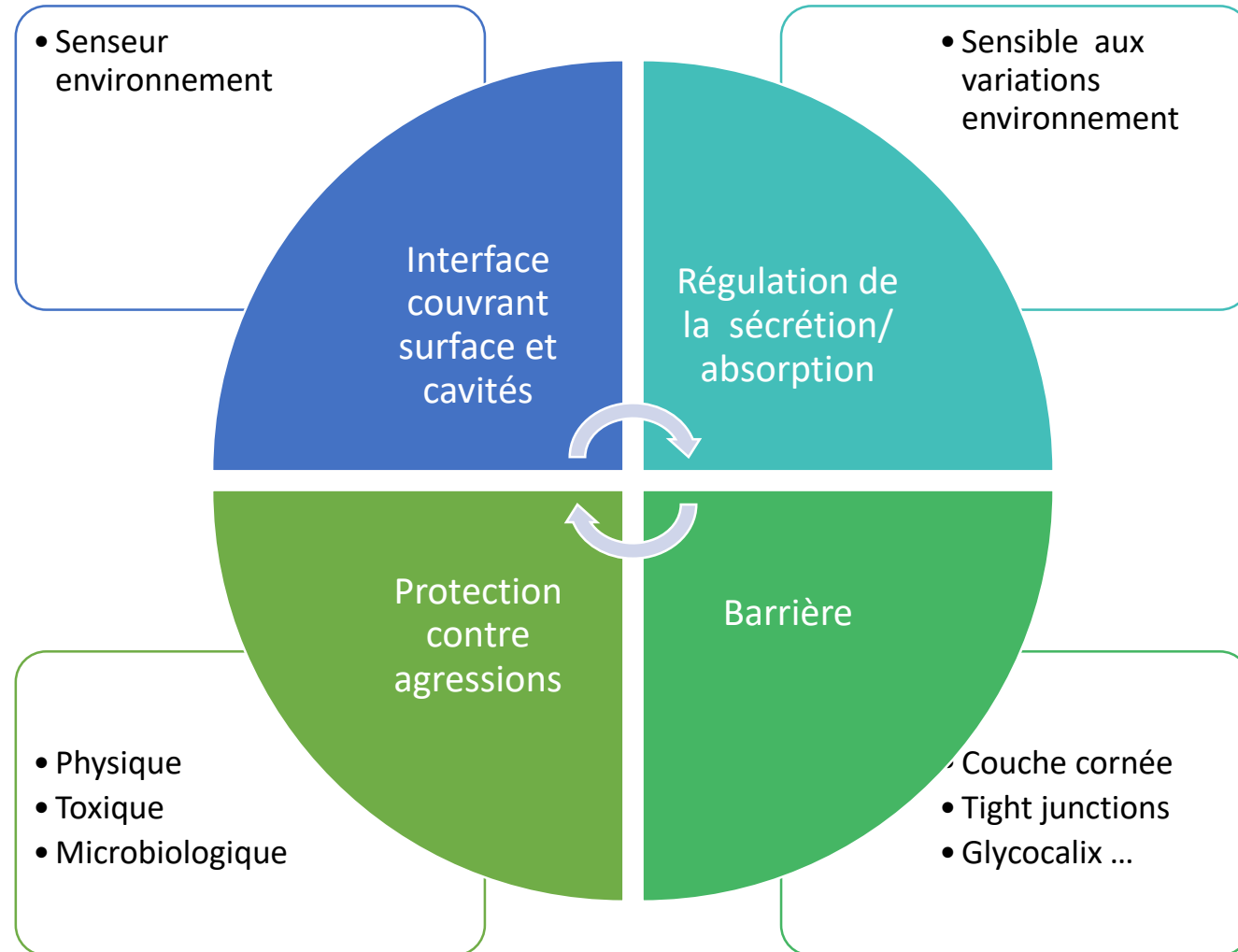
# Immunité innée et épithélia

AMP : **A**nti **M**icrobial **P**roteins : defensine et cathélicidine

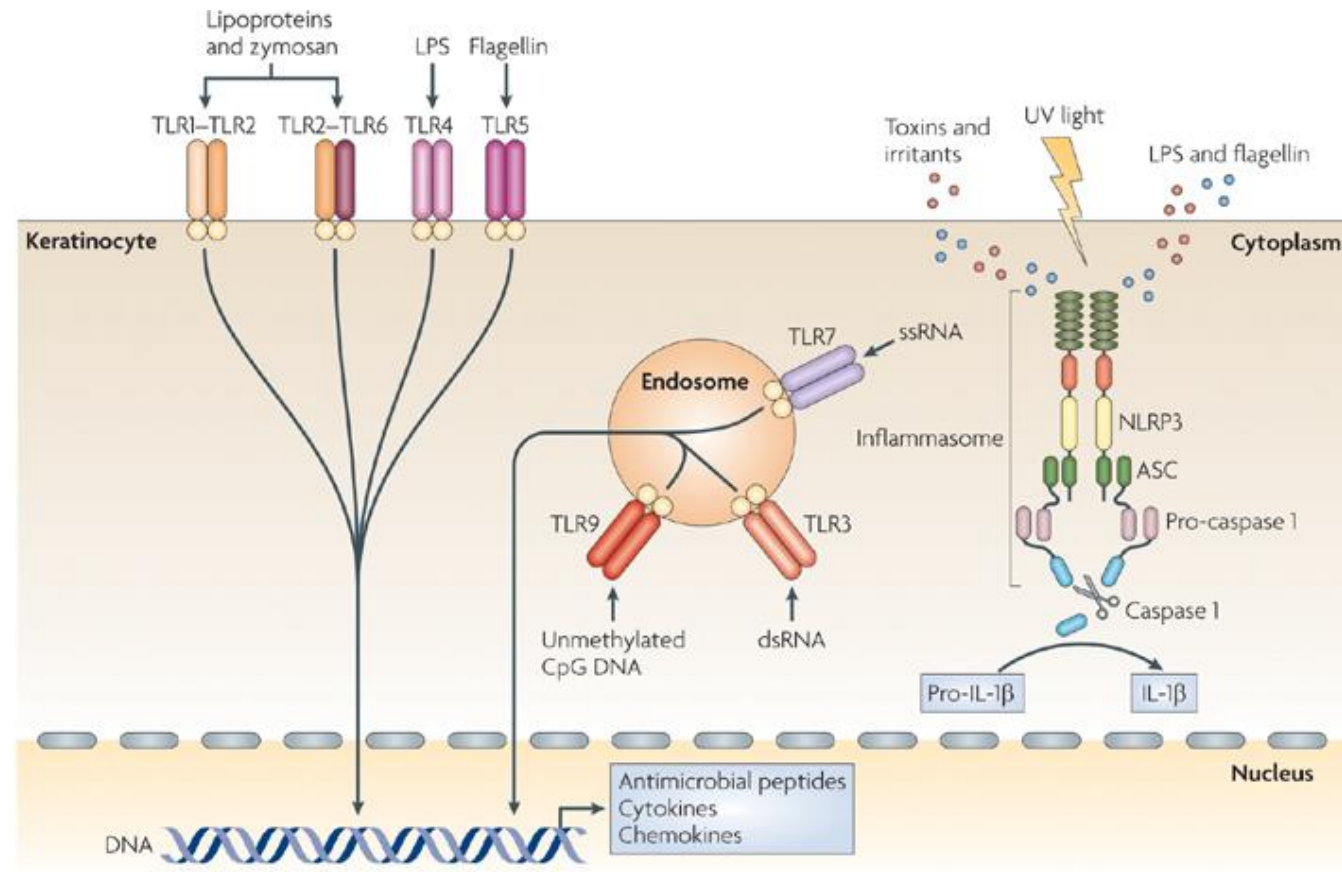


Nature Rev Immunol 2010; vol 11: 656-665

# Cellules épithéliales



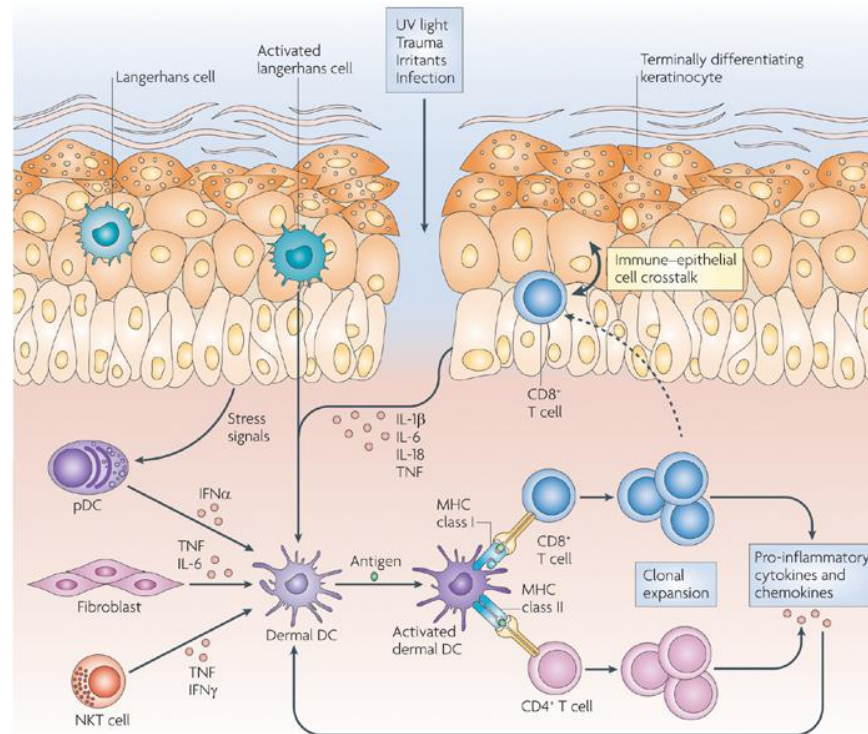
# Cellules épithéliales : senseurs du danger



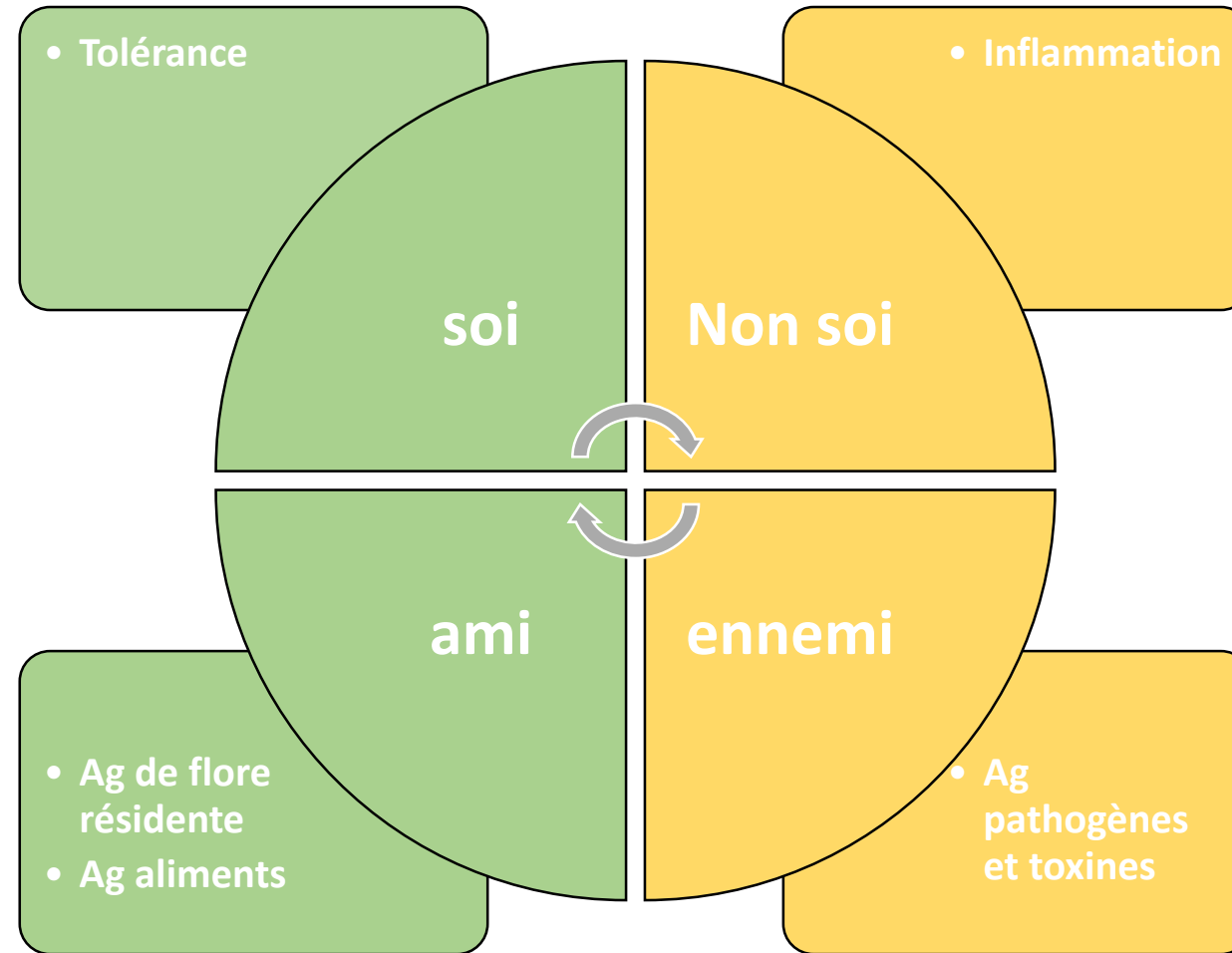
Nature Reviews | Immunology

# Kératinocytes

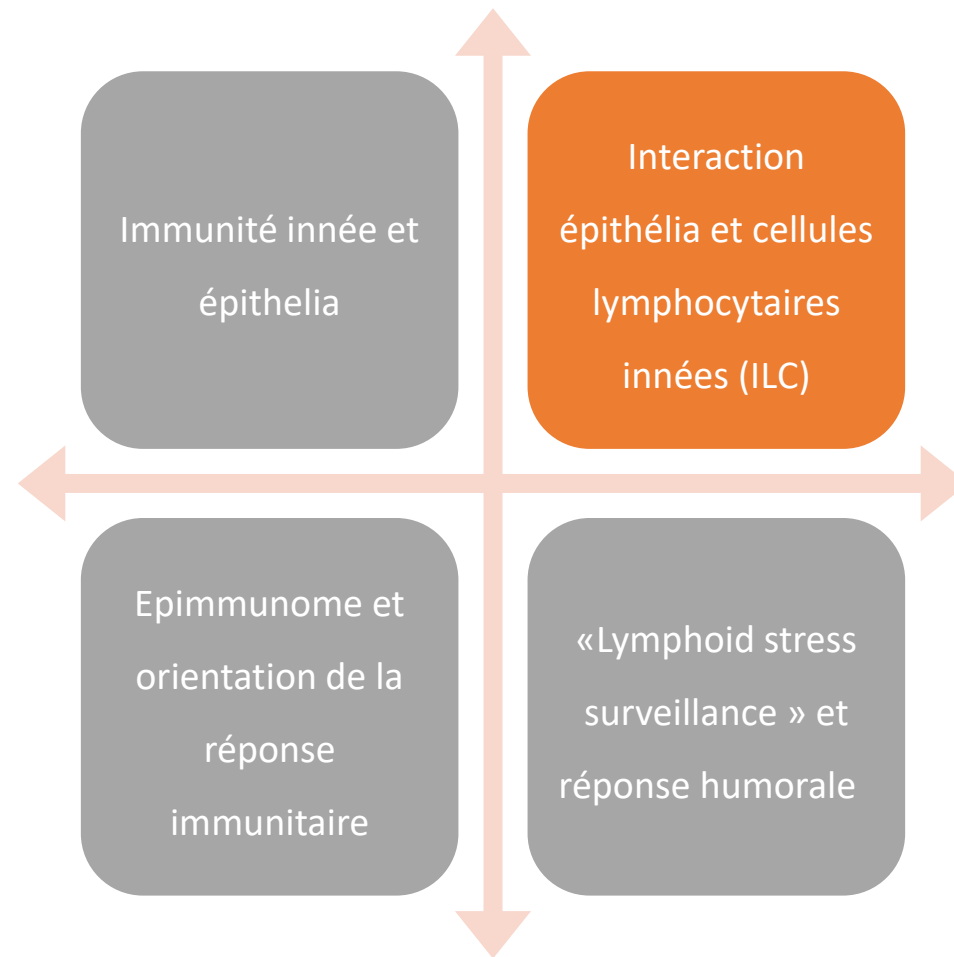
## Véritables sentinelles immunitaires cutanées



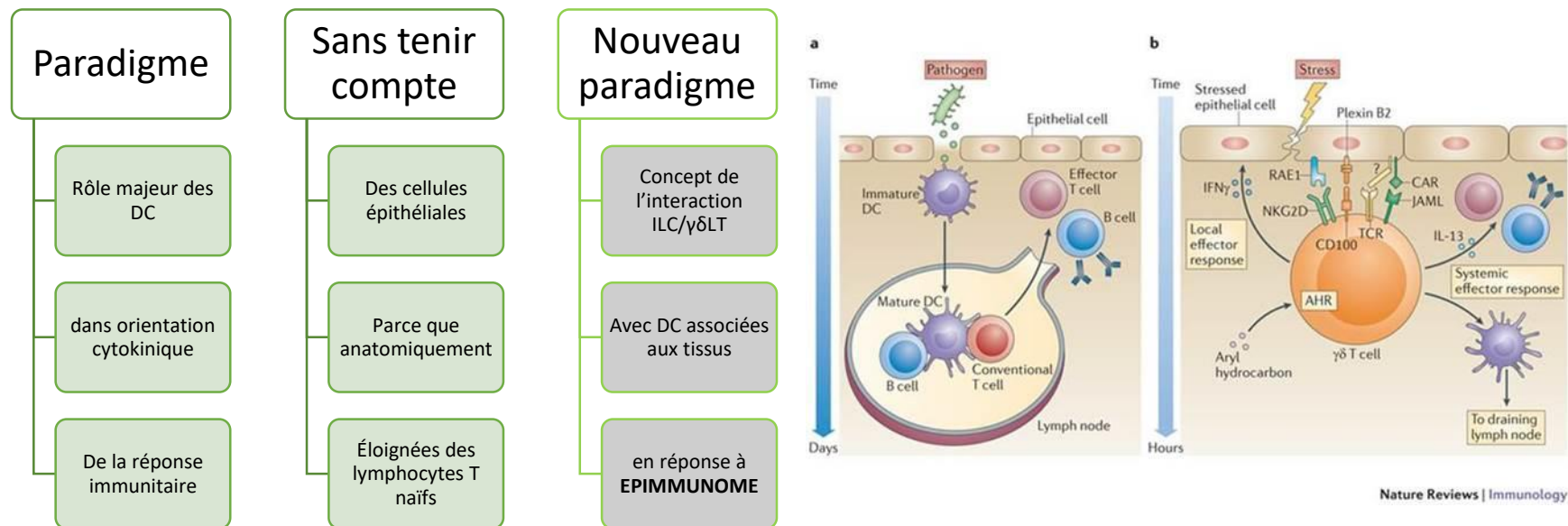
# Défis du système immunitaire



# Épimmunome?



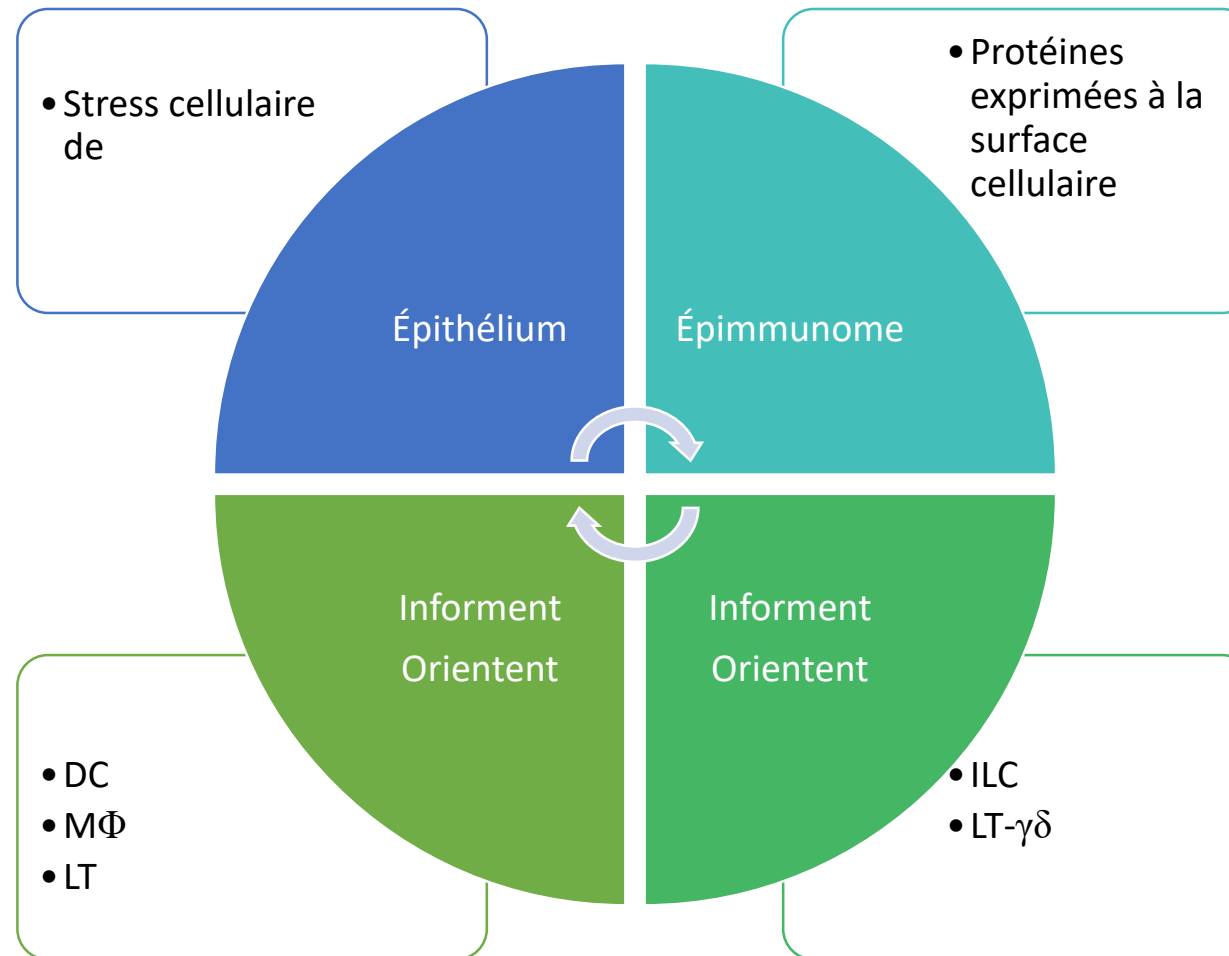
# Interaction épithélium / DC / cellules lymphocytaires



Nature Rev Immunol feb 2013; vol 13: 88-99

Nature Rev Immunol 2010; vol 11: 656-665

# « Body-surface specific » inflammatory pathways



Nature Rev Immunol feb 2013; vol 13: 88-99

Nature Rev Immunol 2010; vol 11: 656-665

# Réponse immunitaire précoce

## Innate lymphocytes

Où

Surveillance de

Rôles dans

Sites  
d'interaction  
avec micro  
organismes

État de la  
barrière

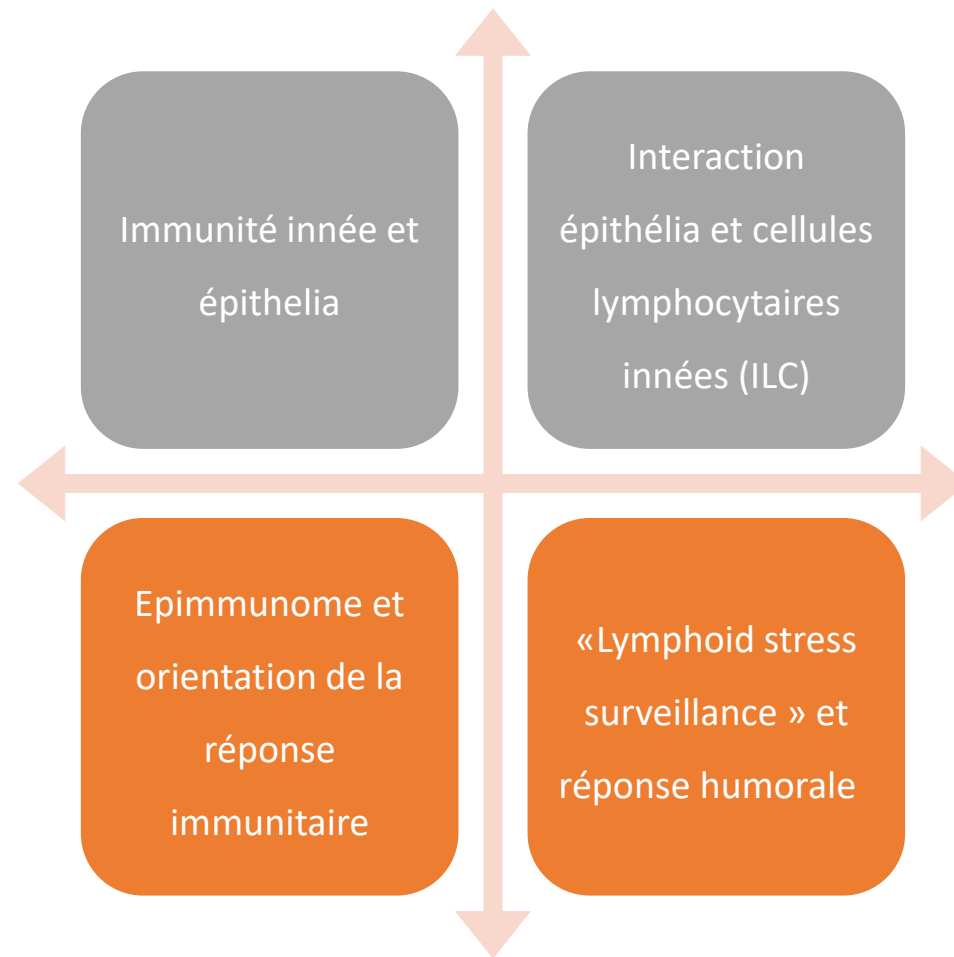
Intégrité de  
épithélium

Maladies  
inflammatoires

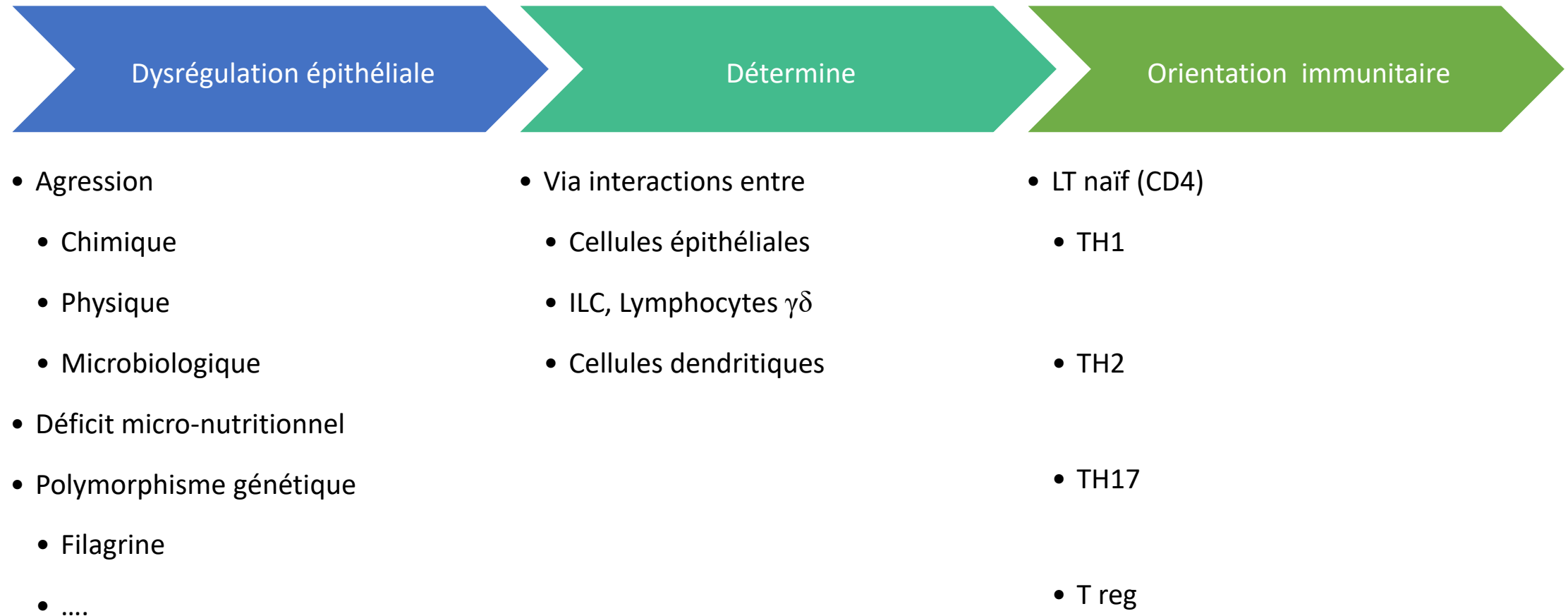
Embryogenèse  
tissulaire

Embryogenèse  
des organes  
lymphoïdes

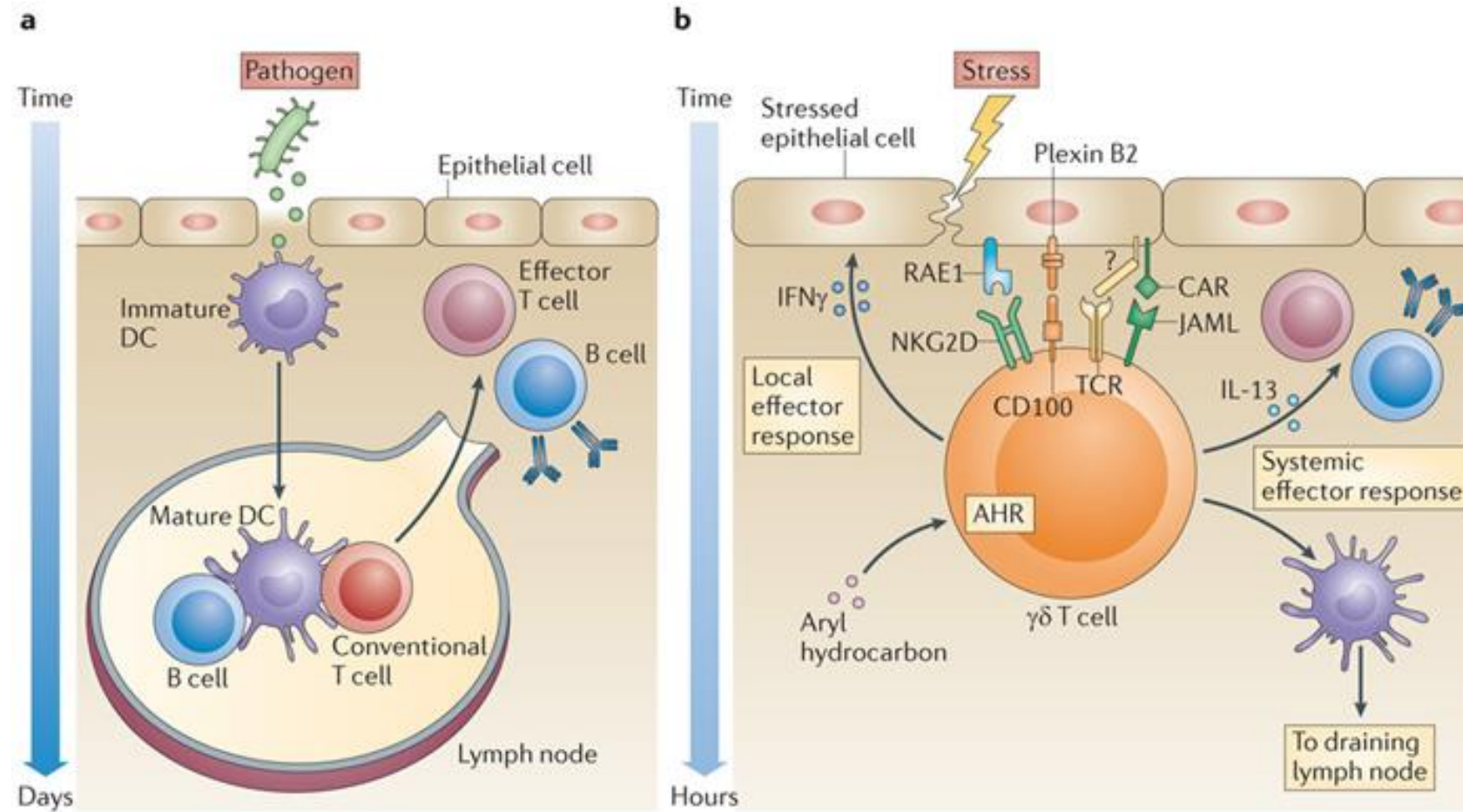
# Épimmunome?



# Le statut épithélial détermine la réponse immunitaire

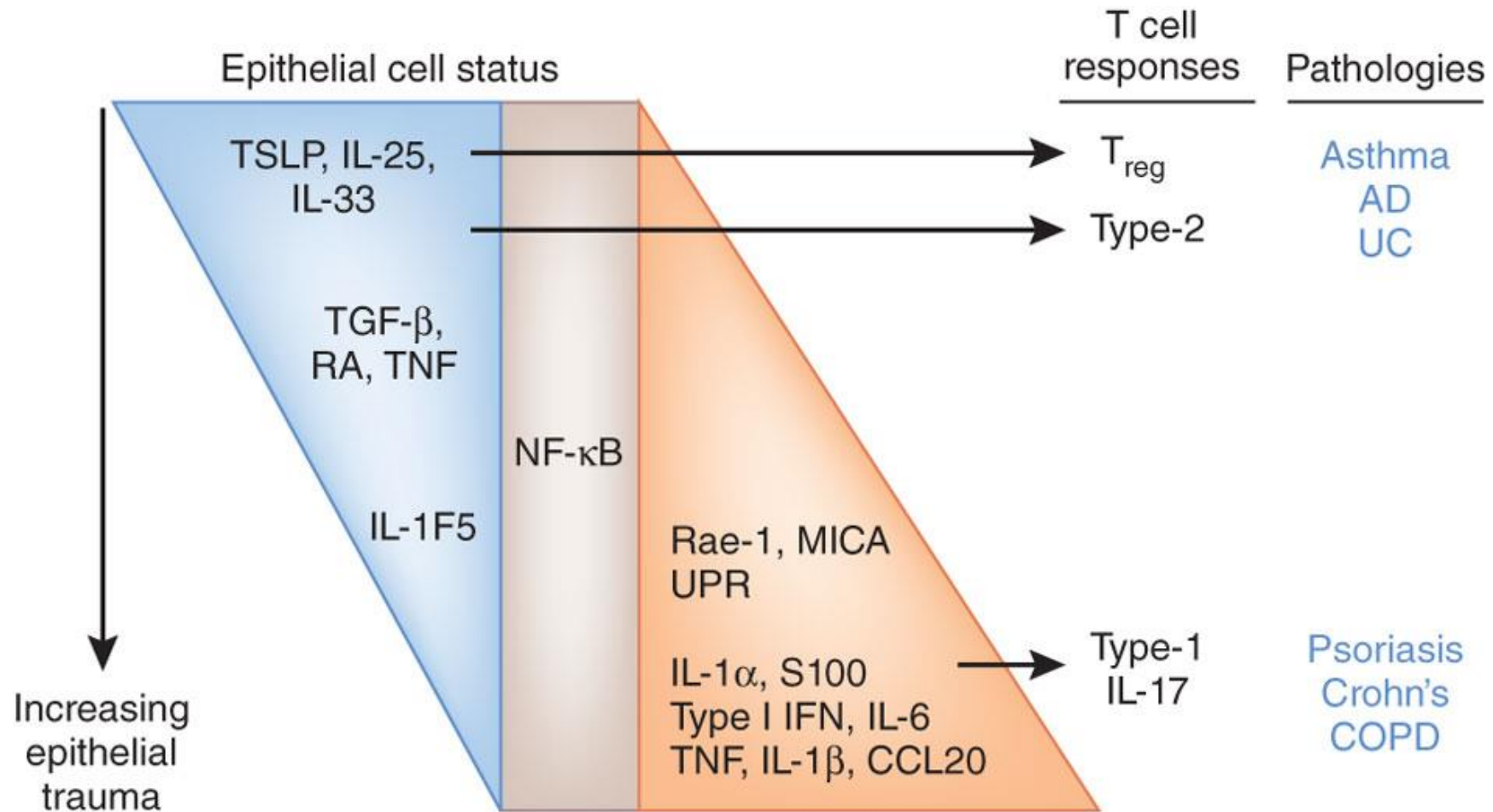


# Epimmunome

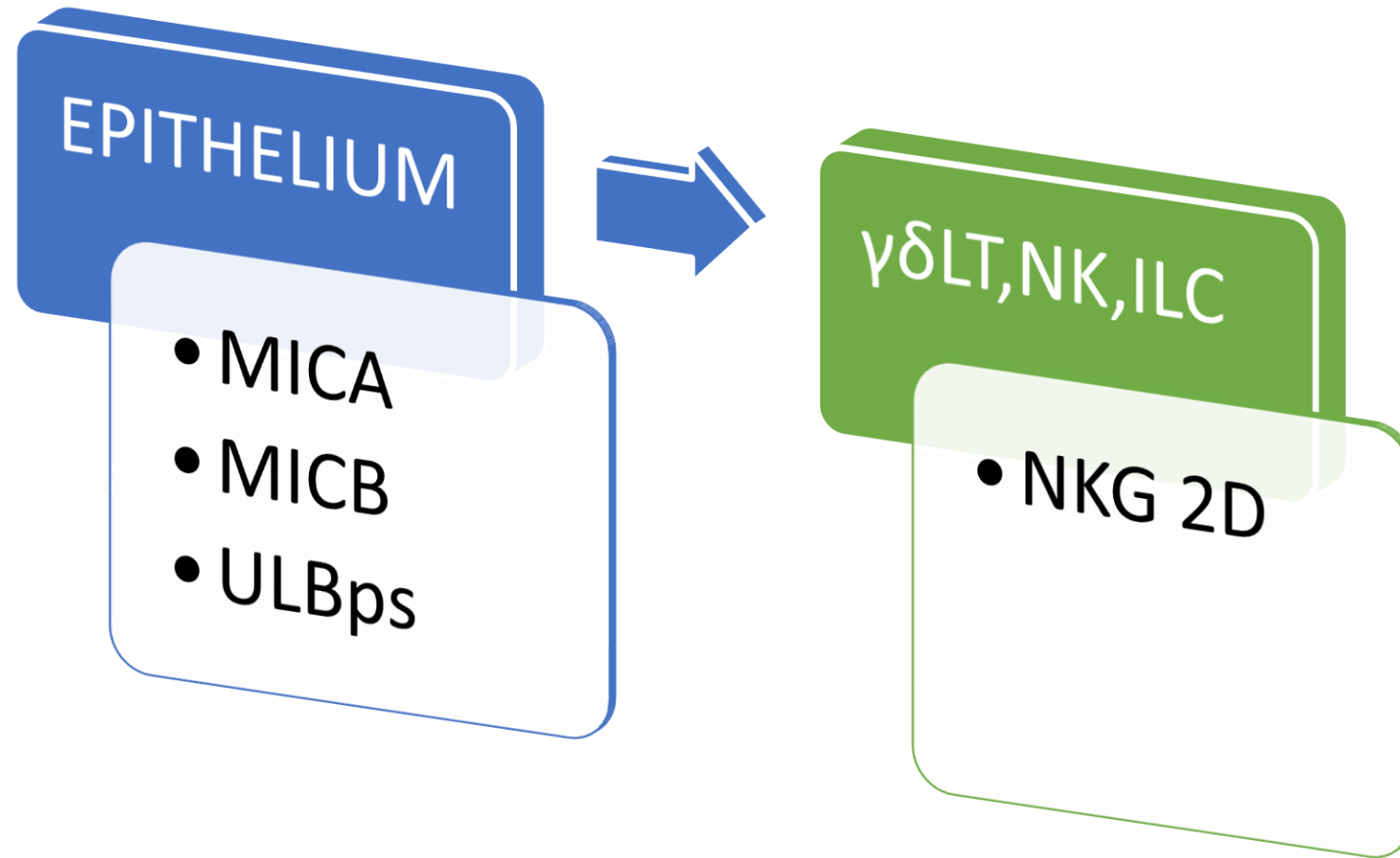


Nature Reviews | Immunology

# Epimmunome: indicateur du niveau de stress

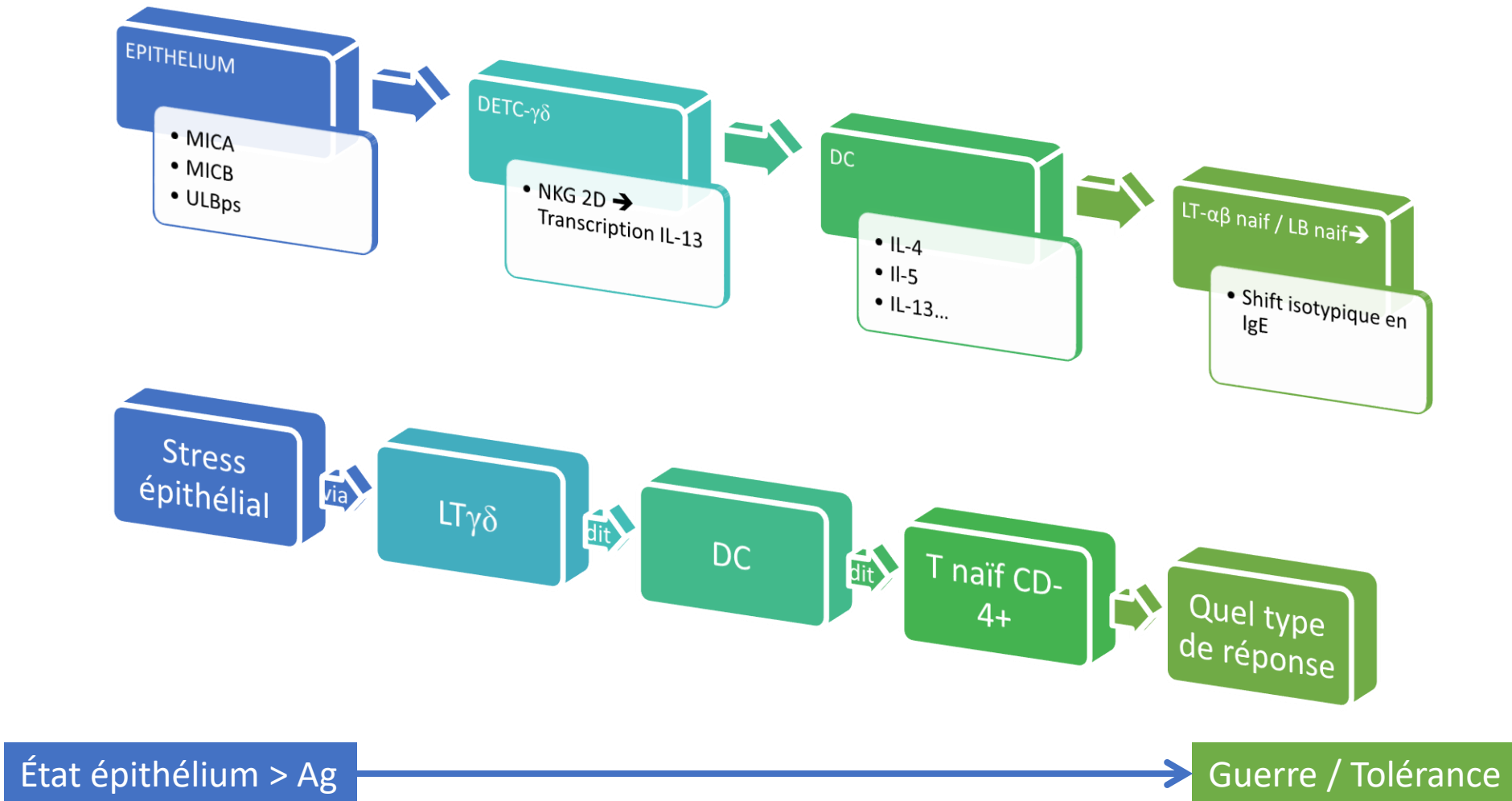


# Palpation des protéines d'alarme épithéliales par les ILC



# Interaction: épithélium /ILC/DC

C'est l'état de l'épithélium qui orientera vers la tolérance ou la guerre

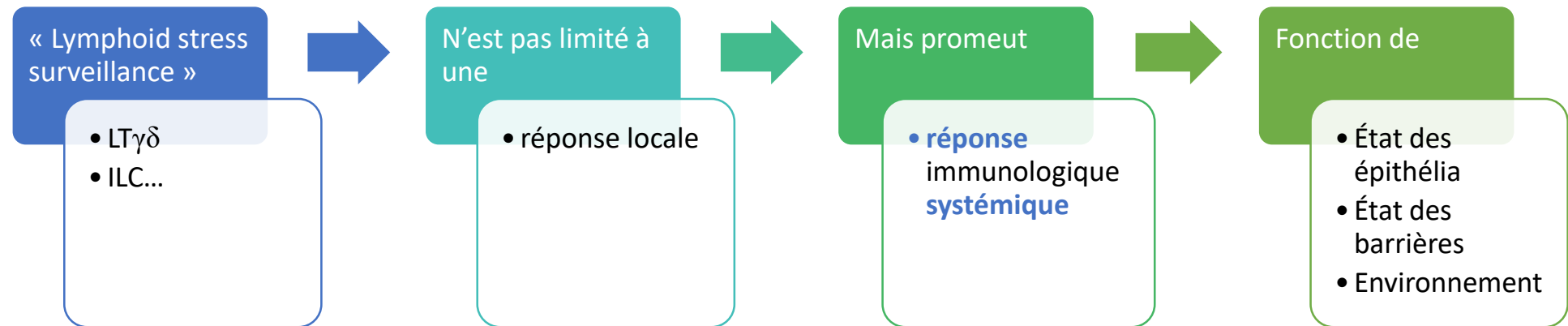


Nature Rev Immunol feb 2013; vol 13: 88-99

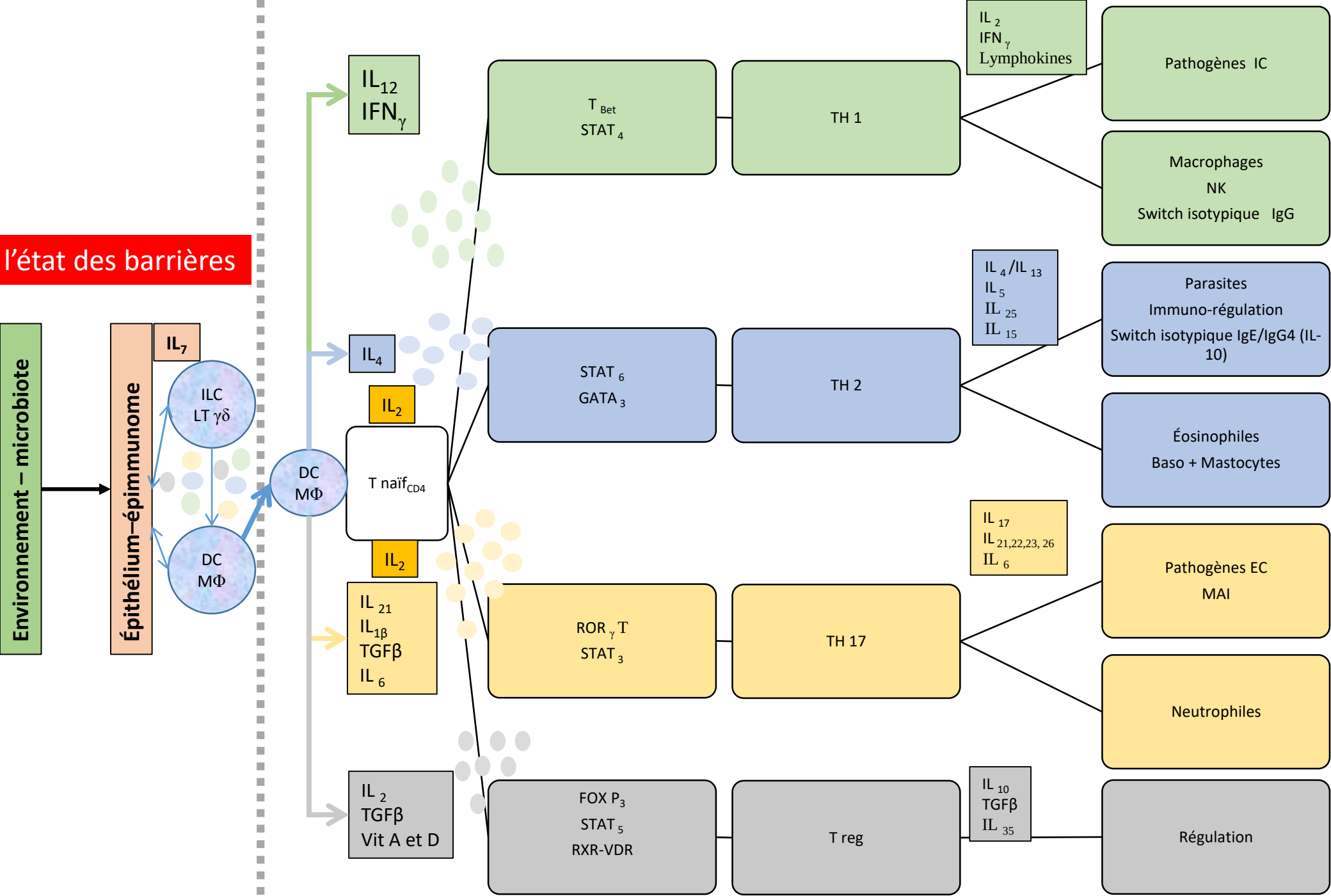
Nature Rev Immunol 2010; vol 11: 656-665

DETC : Dermal T Cell

# Epimmunome en expansion



Selon l'état des barrières



[Display Settings:](#) ☒ Abstract[Send to:](#) ☒

*Immunology*. 2014 Mar 26. doi: 10.1111/imm.12289. [Epub ahead of print]

## 1 $\alpha$ ,25-dihydroxyvitaminD3 in combination with TGF $\beta$ increases the frequency of Foxp3+ Tregs through preferential expansion and usage of IL-2.

Chambers ES<sup>1</sup>, Suwannasaen D, Mann EH, Urry Z, Richards DF, Lertmemongkolchai G, Hawrylowicz CM.

### [+ Author information](#)

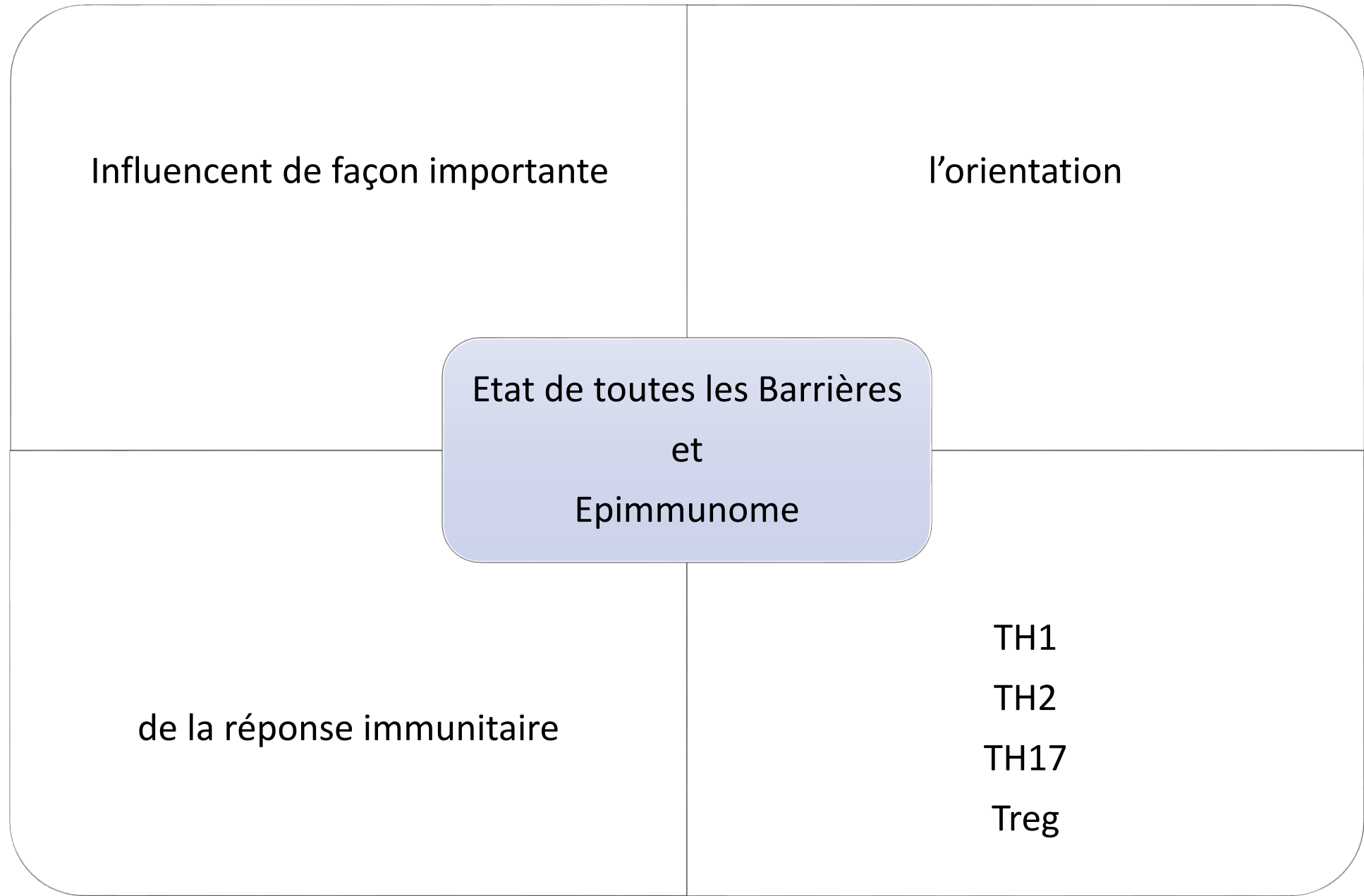
#### Abstract

A high prevalence of vitamin D insufficiency and deficiency exists worldwide, which is associated with an increased incidence and severity of a range of immune-mediated diseases. This has resulted in considerable interest in the immunodulatory functions of vitamin D. The active form of vitamin D, 1 $\alpha$ ,25-dihydroxyvitamin D3 (1,25(OH)<sub>2</sub> D3), has been shown to increase the frequency of Foxp3+ CD4+ T regulatory cells (Tregs) when present at high concentrations or under strong T cell stimulation in culture. Supporting evidence exists in vivo for a positive association between serum 25(OH)D and Foxp3+Treg numbers in humans. The aim of this work was to identify the cytokine milieu required in vitro to promote Foxp3+ Tregs in cultures containing 1,25(OH)<sub>2</sub> D3 at more moderate concentrations (10<sup>-7</sup> M). Stimulation of human CD4+ T cells with a combination of 1,25(OH)<sub>2</sub> D3 and TGF $\beta$  greatly increased the frequency of Foxp3+ Tregs, which is proposed to result from the preferential expansion of Foxp3<sup>+</sup> Tregs, as compared to the Foxp3- Teffector cells, in culture. The differential effect on proliferation may result from enhanced availability and usage of IL-2 by the Foxp3+ Tregs as compared to Foxp3- Teffector cells. In summary, modulation of the cytokine environment to one high in TGF $\beta$  in the presence of 1,25(OH)<sub>2</sub> D3 (10<sup>-7</sup> M) significantly increased Foxp3+ Treg frequency. This data provides additional evidence for the important immunomodulatory properties of 1,25(OH)<sub>2</sub> D3 that exist and may help to control inflammatory diseases. This article is protected by copyright. All rights reserved.

This article is protected by copyright. All rights reserved.

**KEYWORDS:** 1 $\alpha$ , 25-dihydroxyvitamin D3, Foxp3+ Tregs, IL-2 and TGFbeta

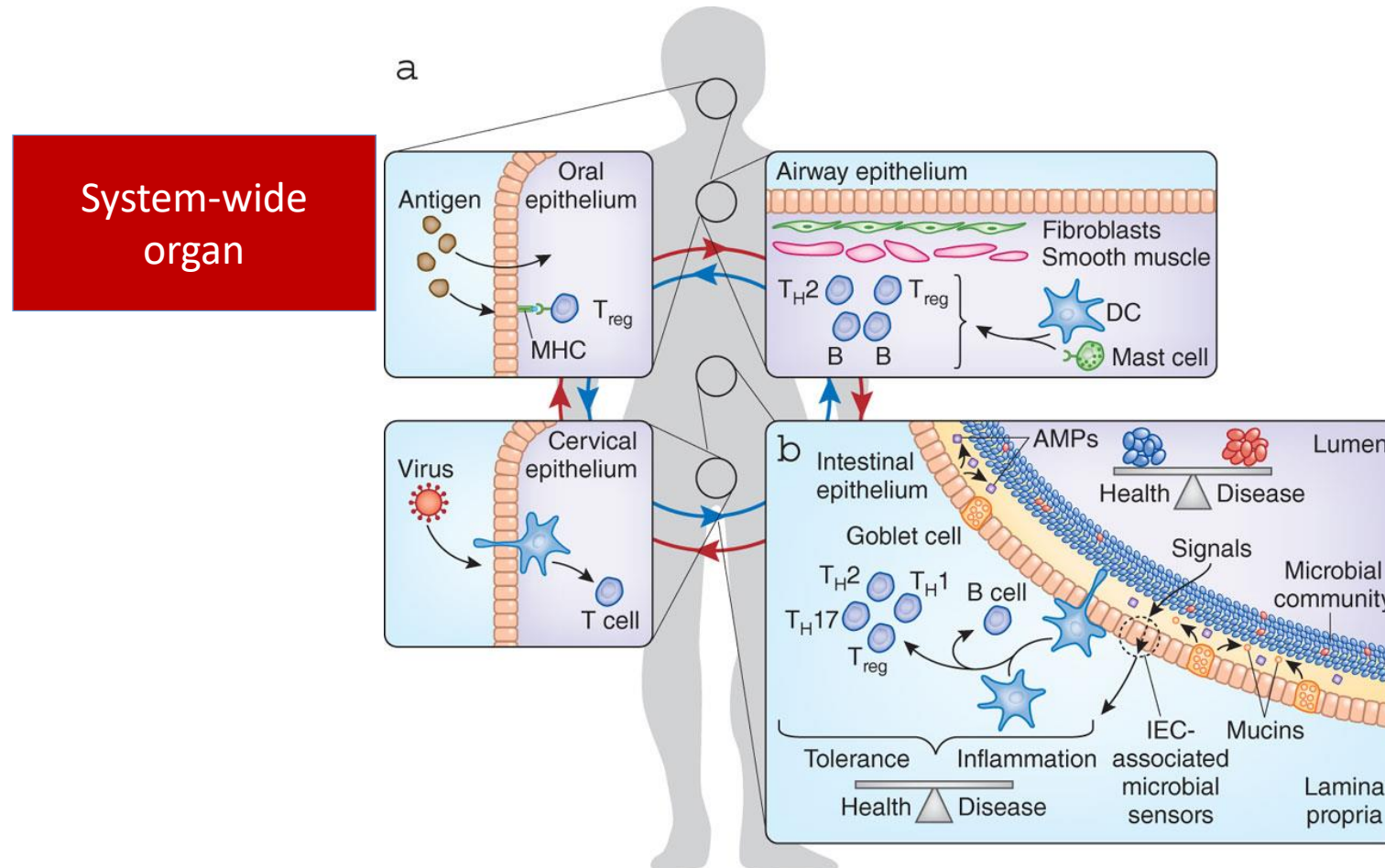
# Conclusions



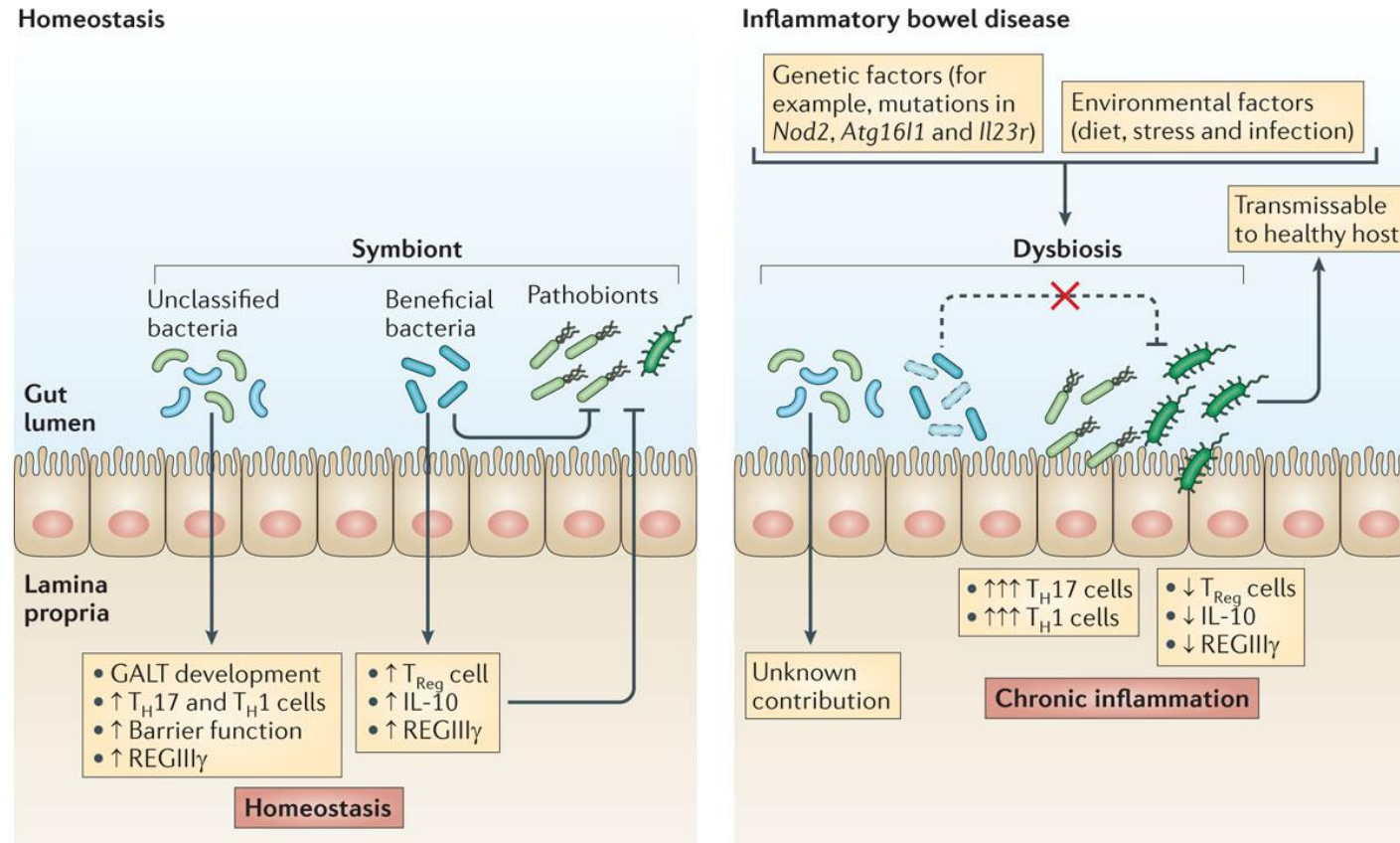
# Le système immunitaire des muqueuses et de la peau

UN SYSTÈME INTEGRE

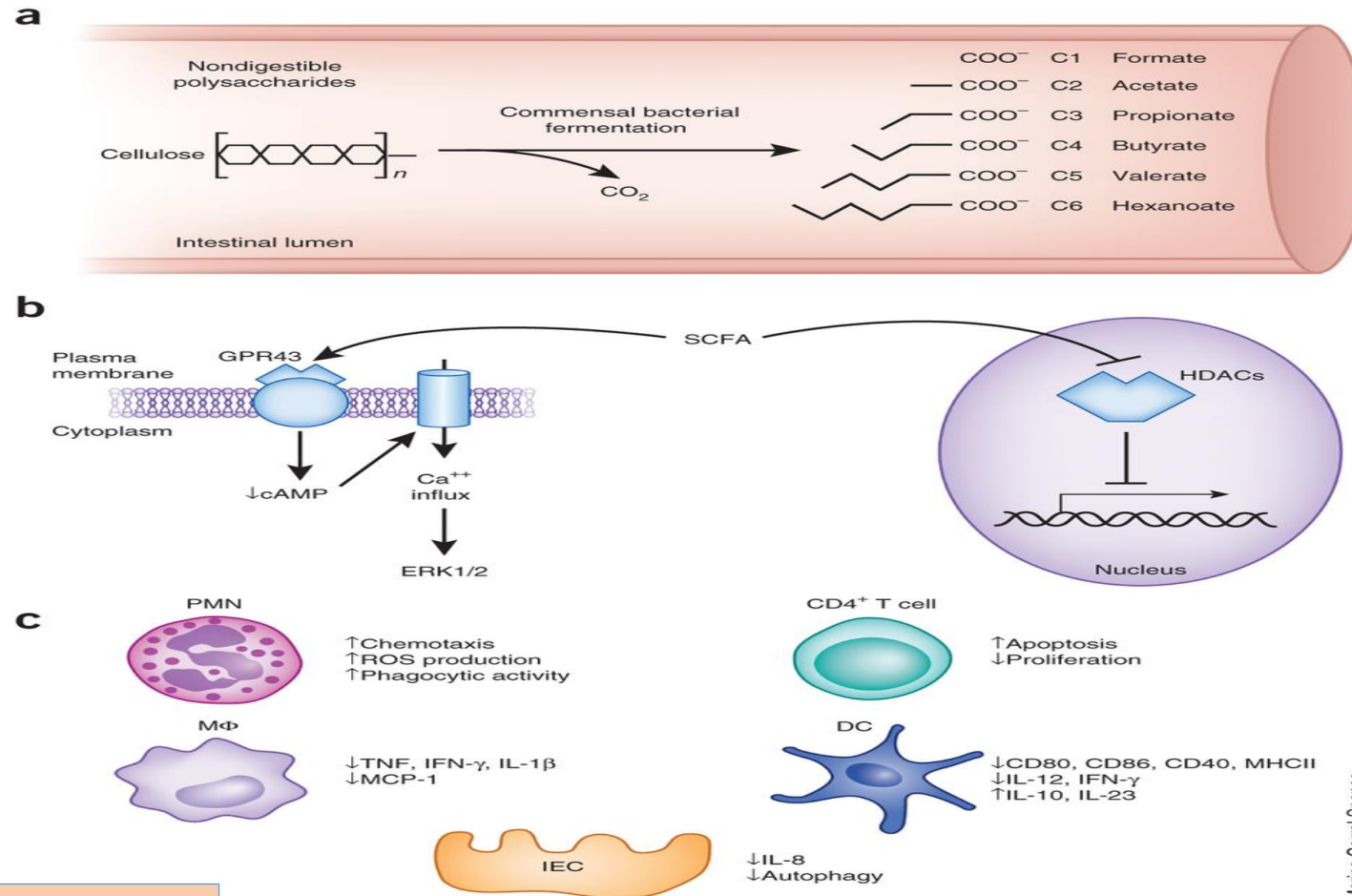
# Le système immunitaire des muqueuses et de la peau: un système intégré



# Protection ou pathogénie de la microflore

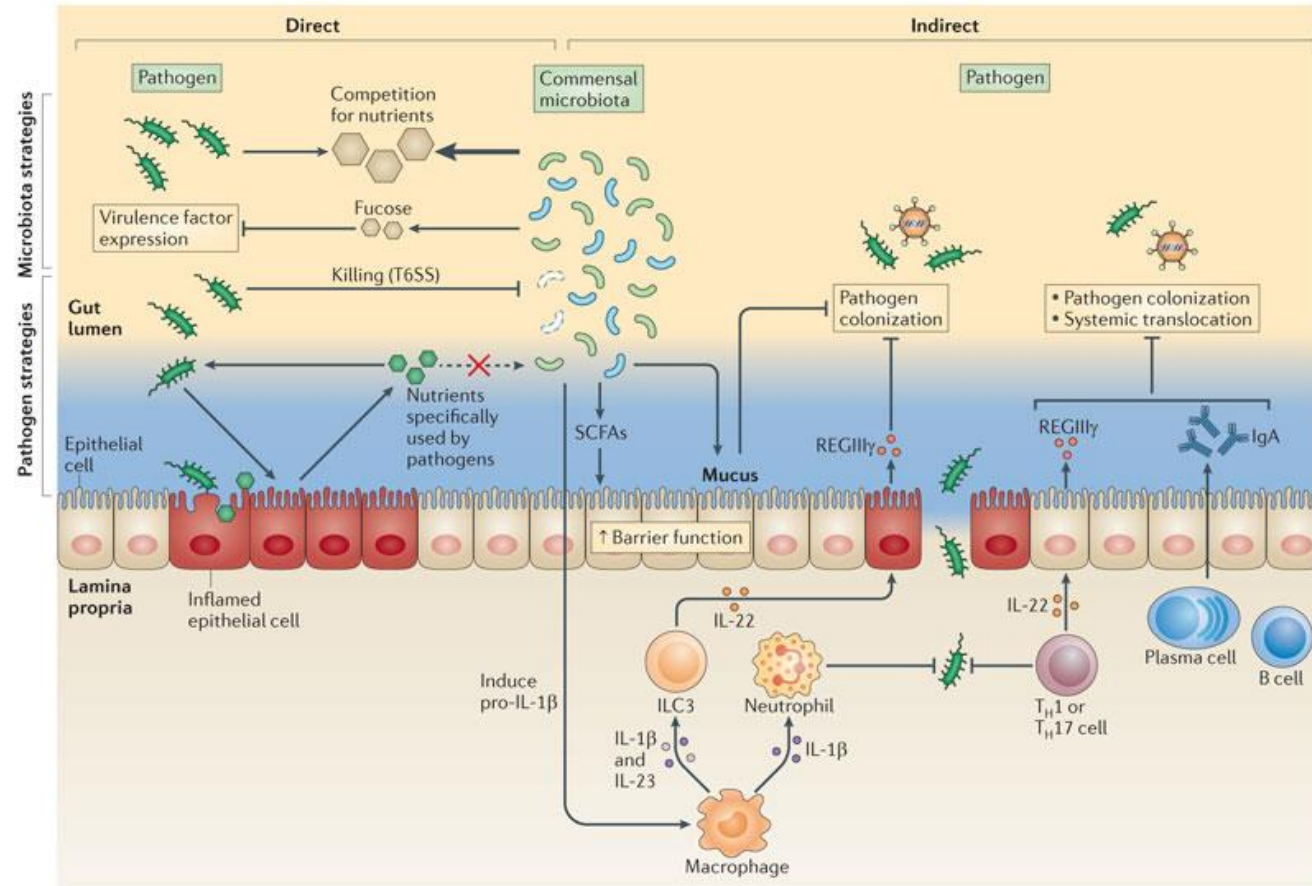


# Commensaux et immunité: SCFA's



SCFA= Short Chain Fatty Acids

# Protection de l'hôte par le microbiote

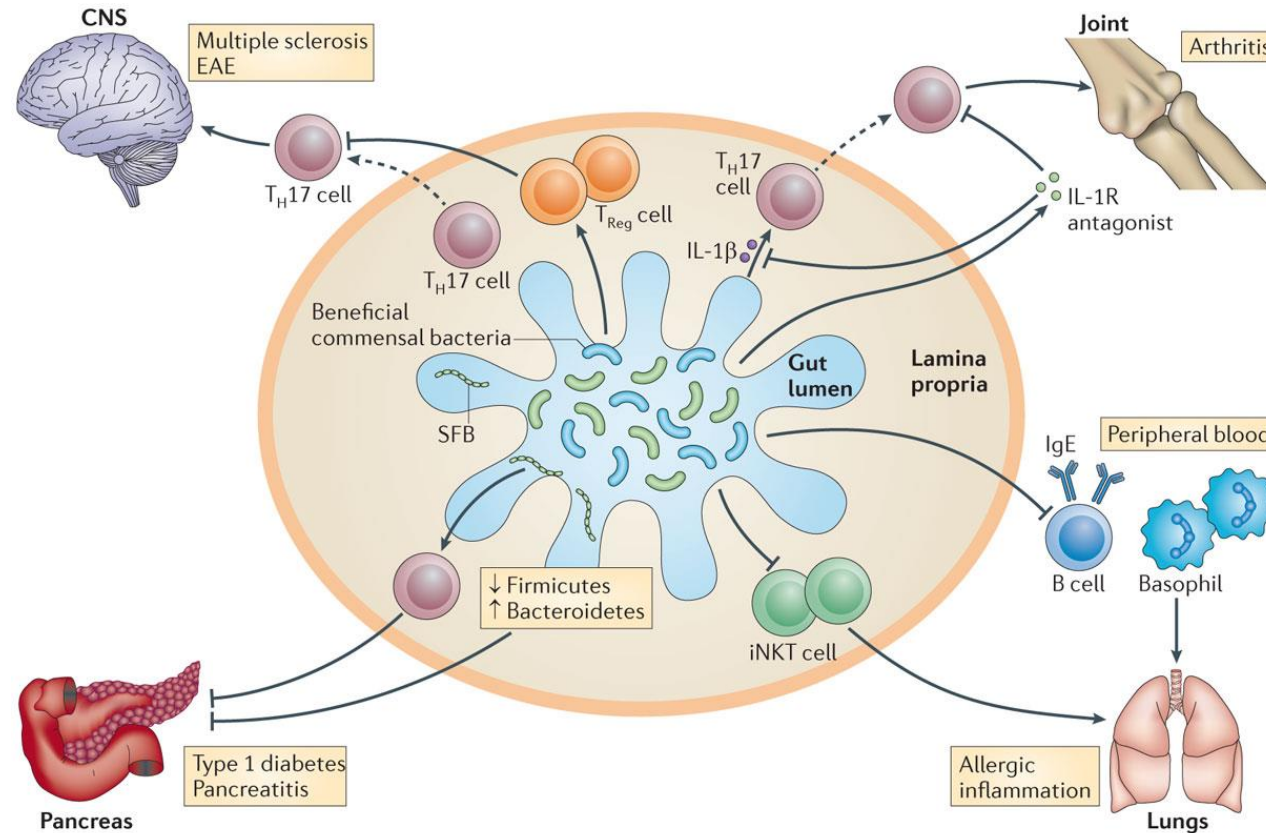


Nature Reviews | Immunology

Mai 2013

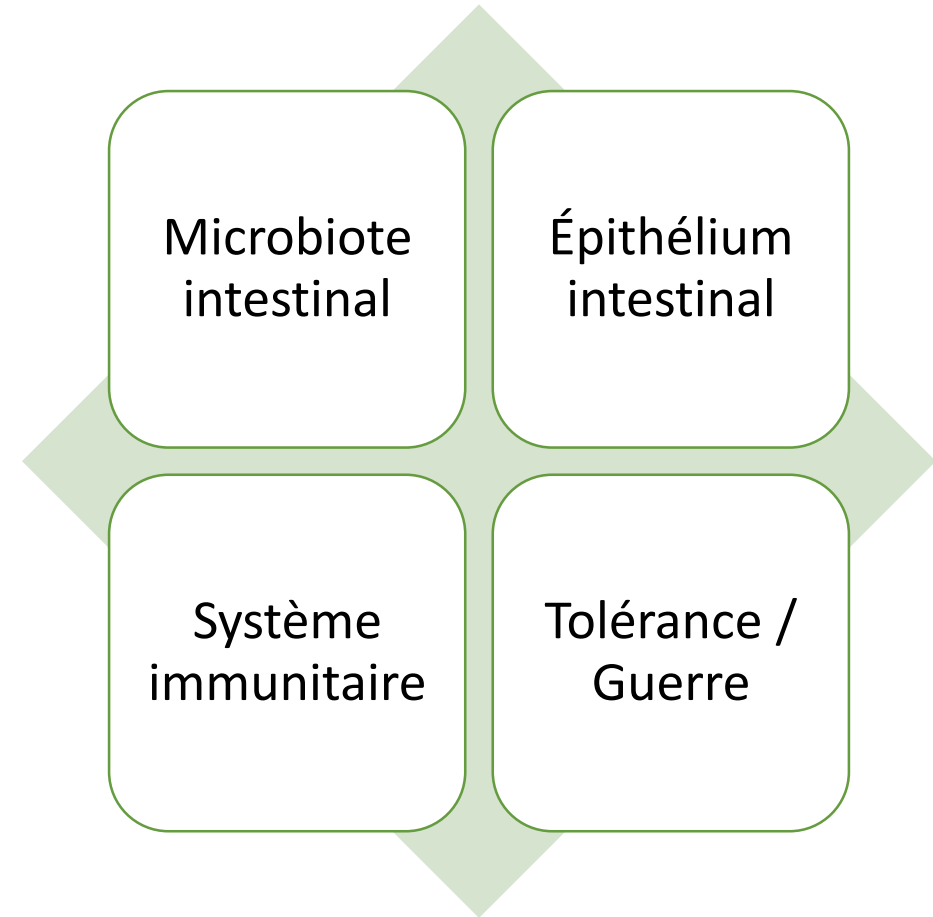
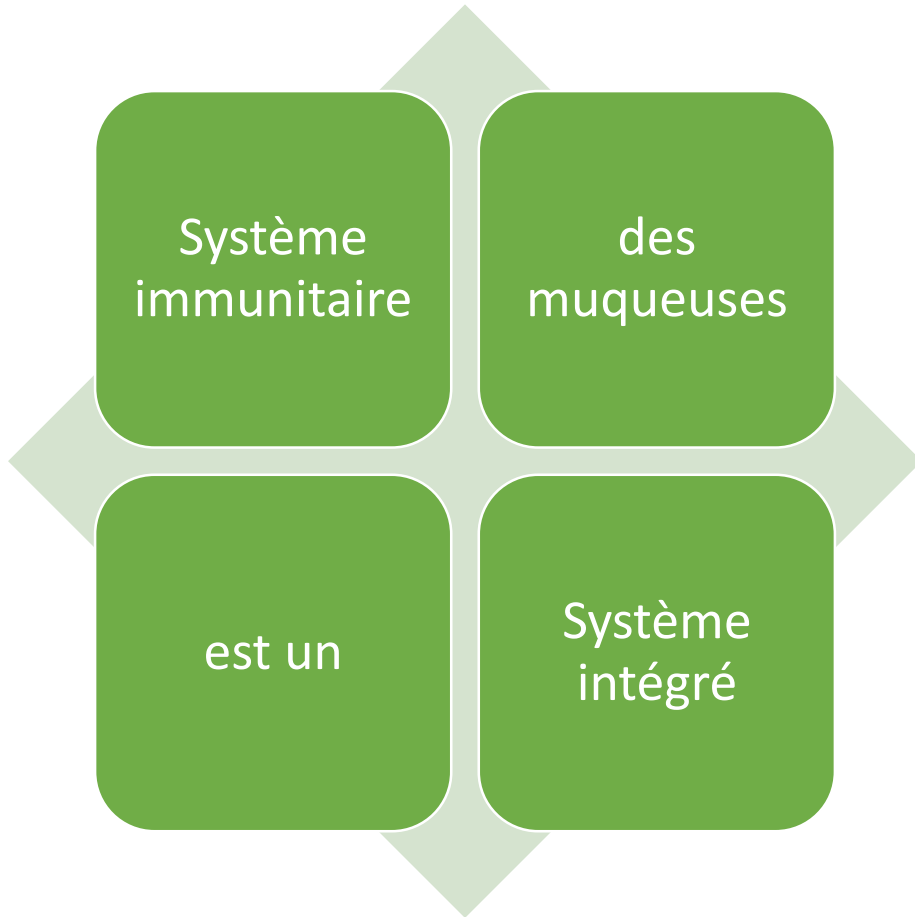
ID

# Microbiome intestinal et maladies auto-immunes extra-intestinales



Nature Reviews | Immunology

# Conclusions



# Messages

Intégrité = état des épithélia (barrières)

- Est contrôlée par des facteurs
  - Microbiologiques
  - Nutritionnels

Les états (de stress) des épithélia

- Orientent la réponse immunitaire vers
  - Tolérance
  - Allergie
  - Auto-immunité

Penser aux choses les plus simples pour le retour à équilibre

- Alimentation
- Médicaments
- Stress