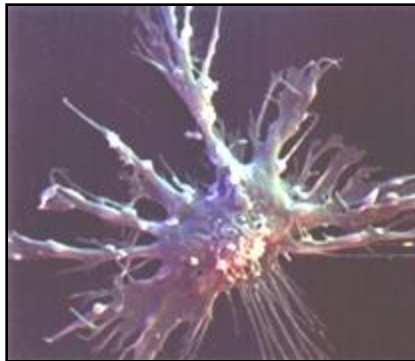
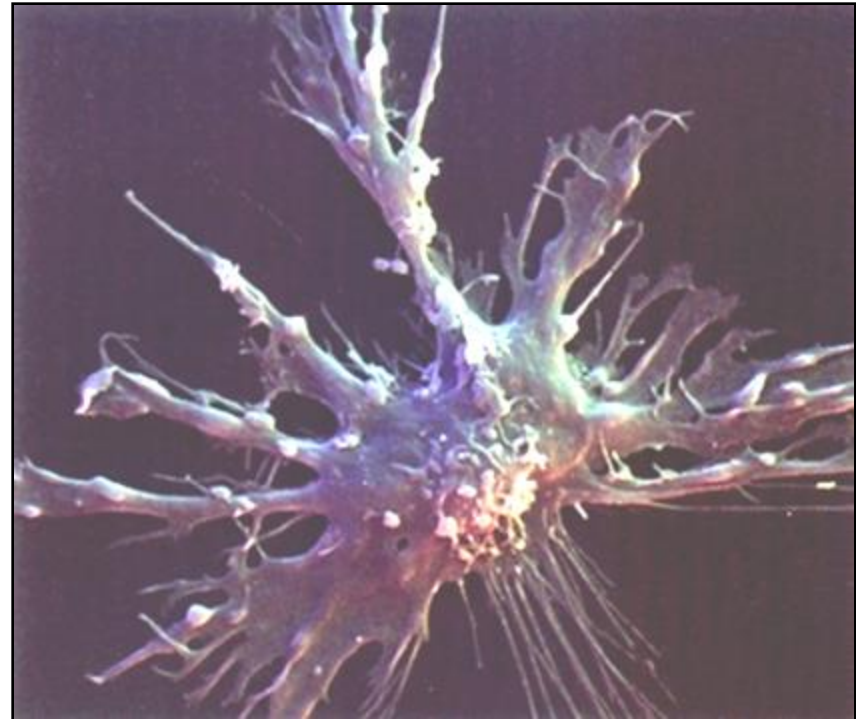


Cellules présentatrices d'antigène et Lymphocytes T



Cellules présentatrices d'antigènes et allergie : phénotype, propriétés, fonctions

- ✓ Antigen Presenting Cell = APC en Anglais
- ✓ Présentation de l'antigène aux Lymphocytes T



Cellules présentatrices d'antigènes et allergie : phénotype, propriétés, fonctions

POPULATION HÉTÉROGÈNE

- ✓ **Fonction commune:** Présenter les peptides étrangers (Antigènes ou allergènes)
 - ✓ Avec le complexe majeur d'histocompatibilité (CMH-I et CMH-II)
 - ✓ Aux lymphocytes T
- ✓ Reconnaissance d'un antigène étranger (Glycoprotéines, Lipides,..) = Détection du "danger"
- ✓ Phagocytose
- ✓ Maintien du signal d'alarme de la réponse immune primaire

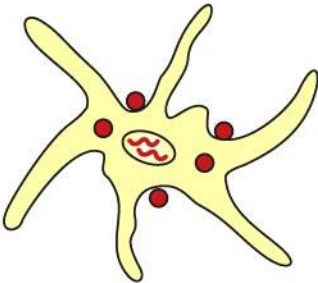
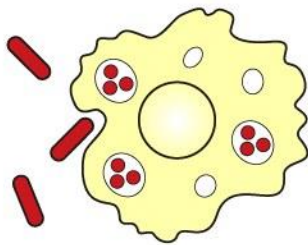
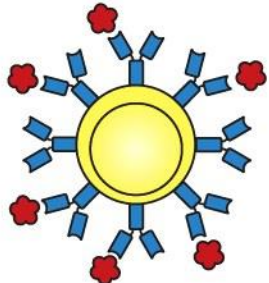
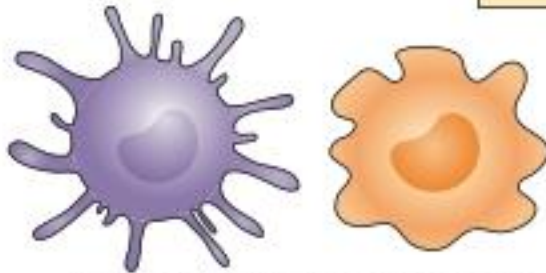
	Dendritic cells	Macrophages	B cells
			
Antigen uptake	+++ Macropinocytosis and phagocytosis by tissue dendritic cells	+++ Macropinocytosis +++ Phagocytosis	Antigen-specific receptor (Ig) ++++
MHC expression	Low on immature dendritic cells High on dendritic cells in lymphoid tissues	Inducible by bacteria and cytokines - to +++	Constitutive Increases on activation +++ to ++++
Co-stimulation delivery	Constitutive by mature, nonphagocytic lymphoid dendritic cells ++++	Inducible - to +++	Inducible - to +++
Location	Ubiquitous throughout the body	Lymphoid tissue Connective tissue Body cavities	Lymphoid tissue Peripheral blood
Effect	Results in activation of naive T cells	Results in activation of macrophages	Results in delivery of help to B cell

Figure 9.16 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Professional APCs



DCs and macrophages



B cells

Key features

- Phagocytic
- Express receptors for apoptotic cells, DAMPs and PAMPs
- Localize to tissues
- Localize to T cell zone of lymph nodes following activation (DCs)
- Constitutively express high levels of MHC class II molecules and antigen processing machinery
- Express co-stimulatory molecules following activation

Key features

- Internalize antigens via BCRs
- Constitutively express MHC class II molecules and antigen processing machinery
- Express co-stimulatory molecules following activation

La Cellule Dendritique est un lien essentiel entre Immunité Innée et Immunité Adaptative

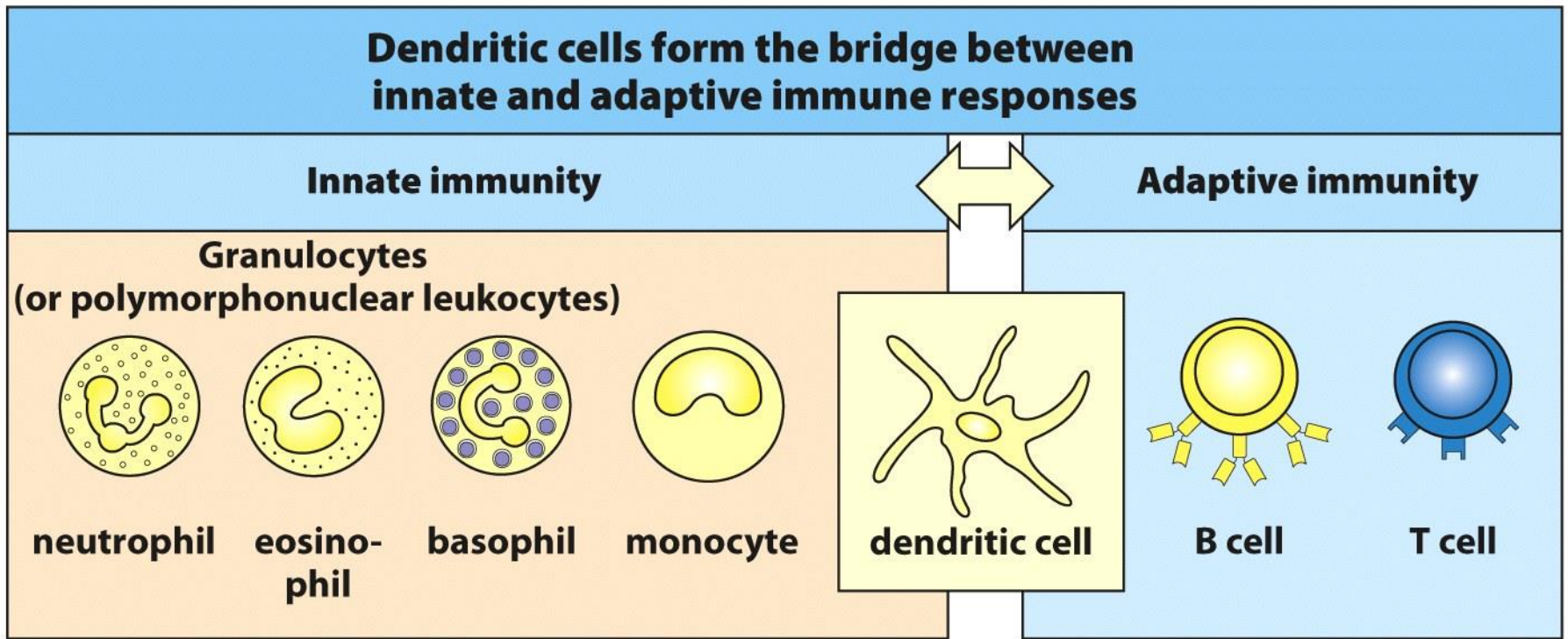
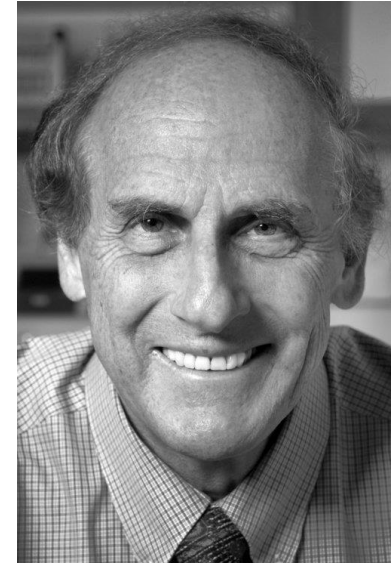
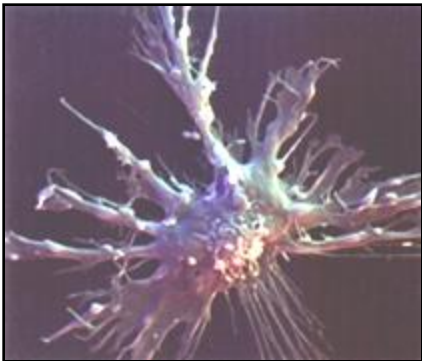


Figure 1.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Caractéristiques des cellules dendritiques conventionnelles (cDCs)

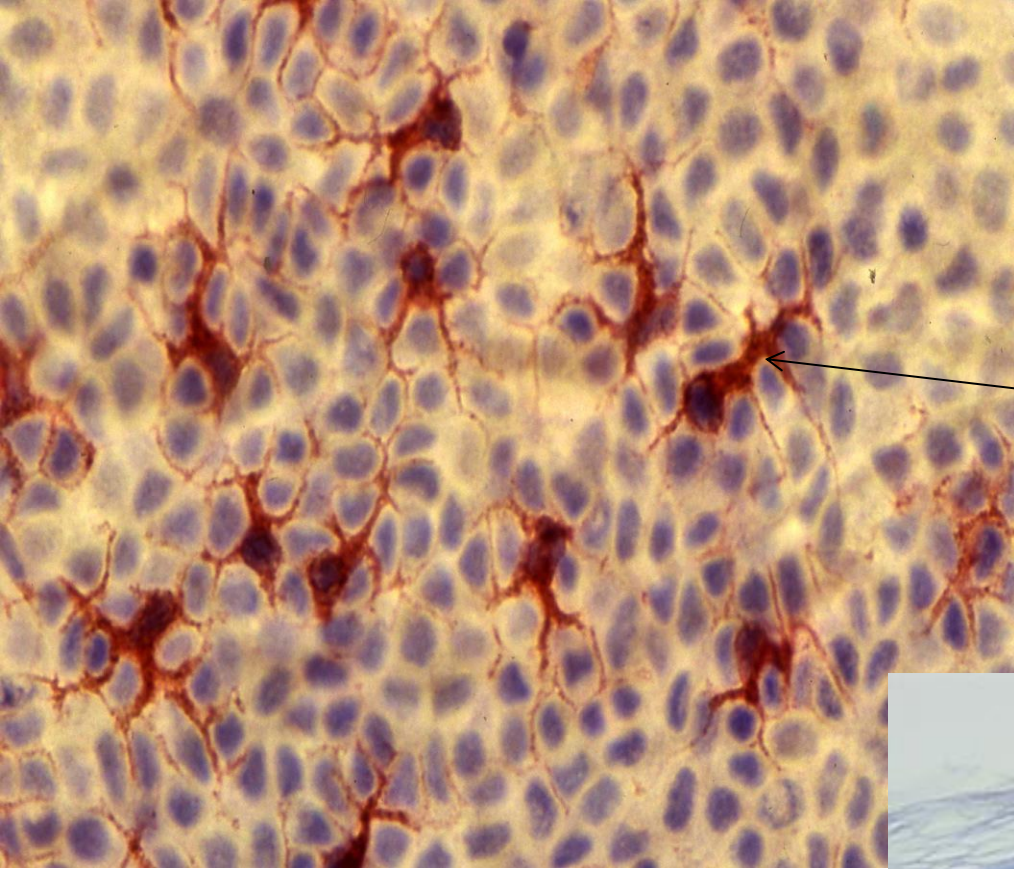
- ✓ Identifiée par R. Steinman
- ✓ Morphologie spécifique avec la présence de dendrites
- ✓ Expression du CMH classe II
- ✓ Capacité à activer les lymphocytes T naïfs



Nobel Prize in Physiology or
Medicine 2011

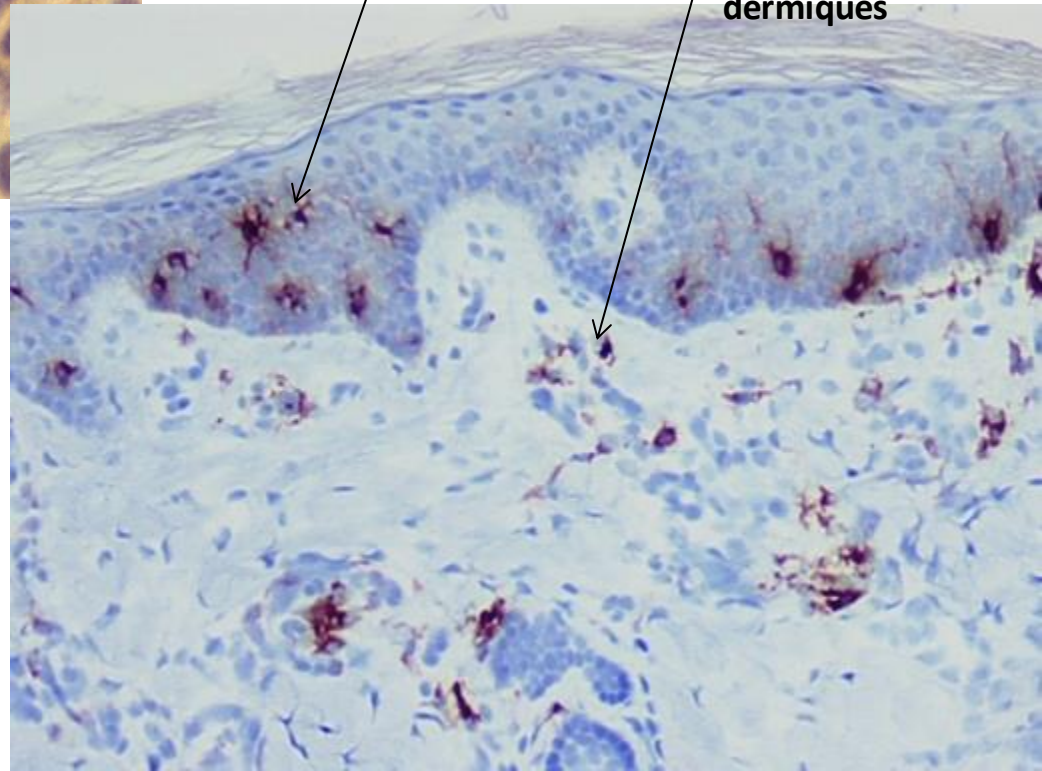
- Présentes dans les tissus à l'état basal = cellules sentinelles
- Population hétérogène

Cellules dendritiques cutanées



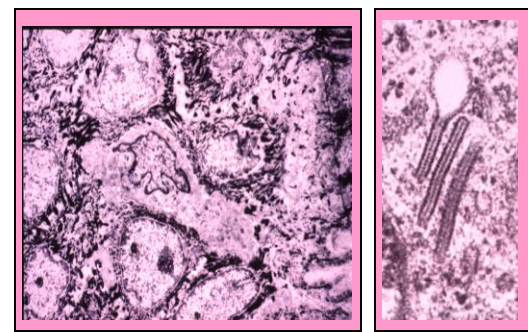
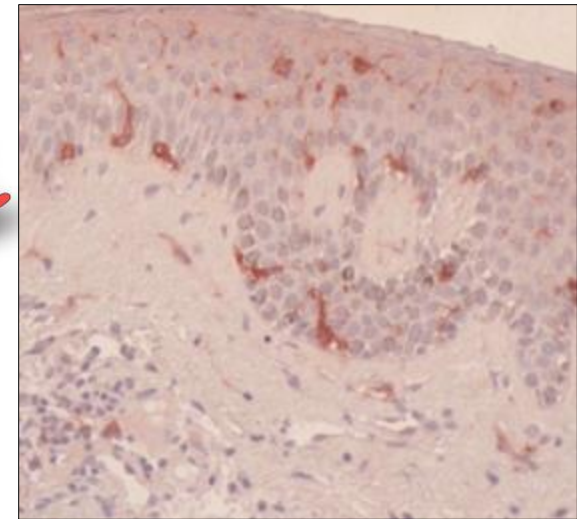
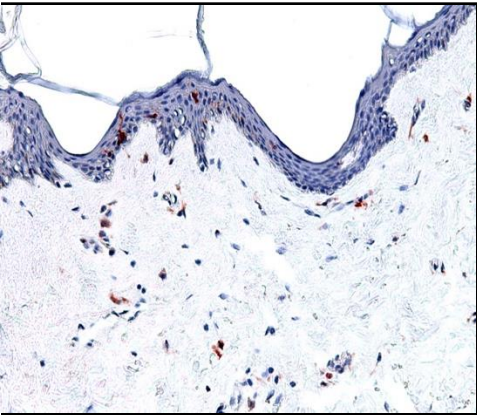
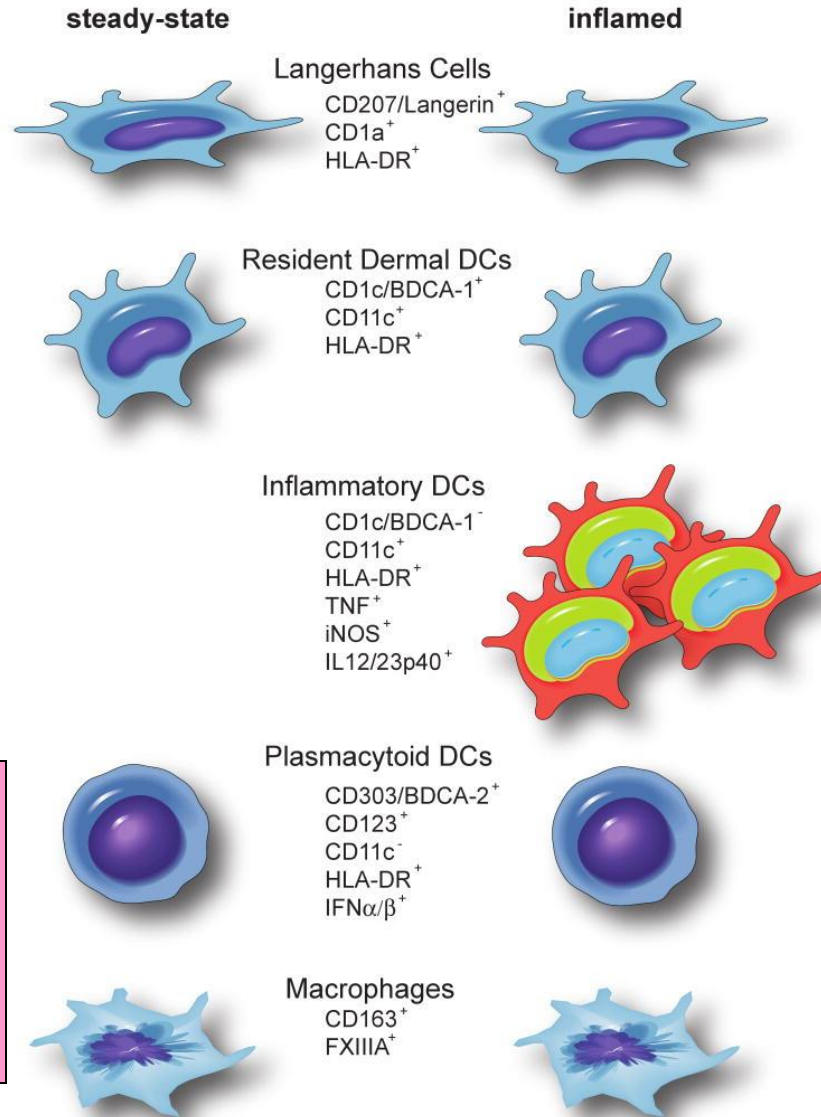
cellules de Langerhans

Cellules dendritiques dermiques



Cellules présentatrices d'antigènes et allergie :

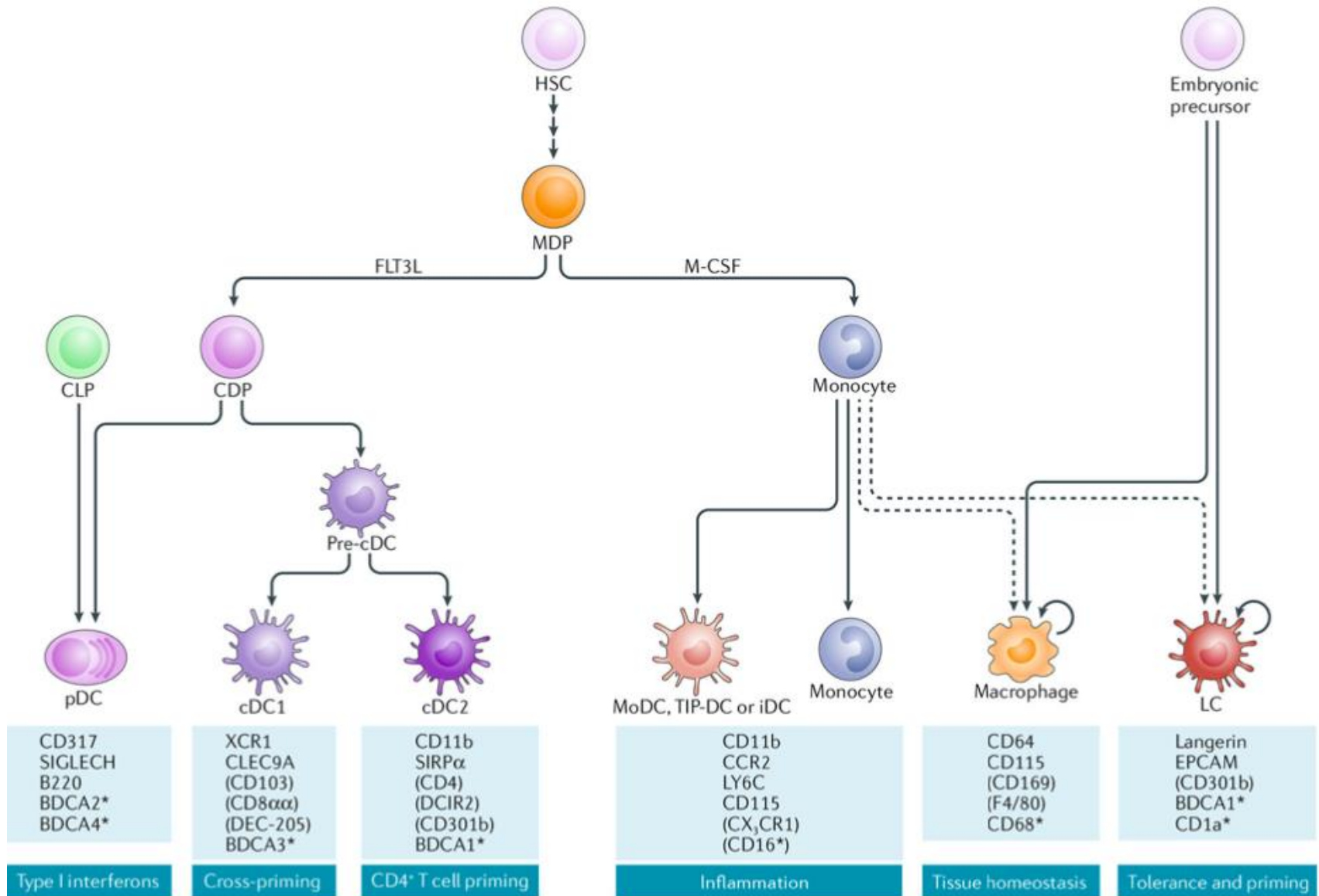
phénotype, propriétés, fonctions



Cellules de Langerhans / Granules de Birbeck

Klechevsky et al, Immunity, 2008
 Haniffa et al. J Exp Med, 2009
 Zaba et al, J Invest Dermatol. 2009

Origine(s) des différentes sous-populations de cellules dendritiques



Cellules dendritiques : fonctions

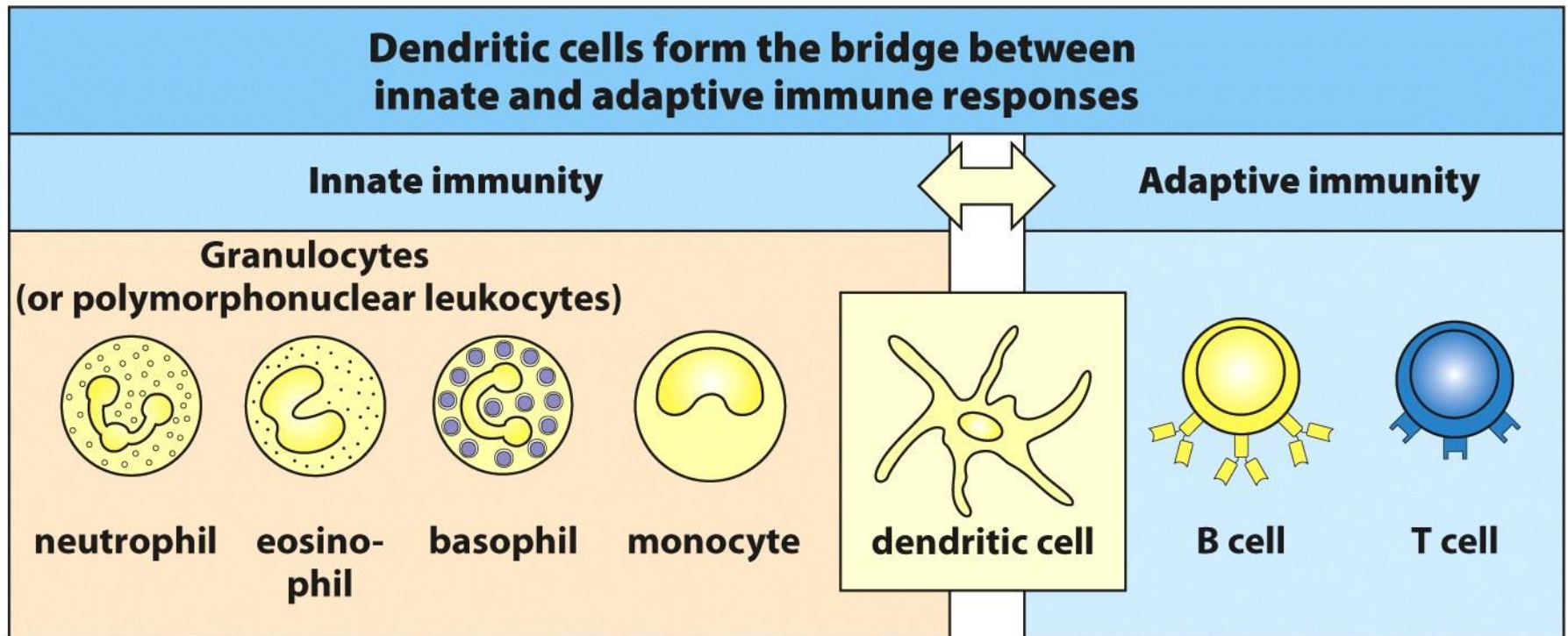
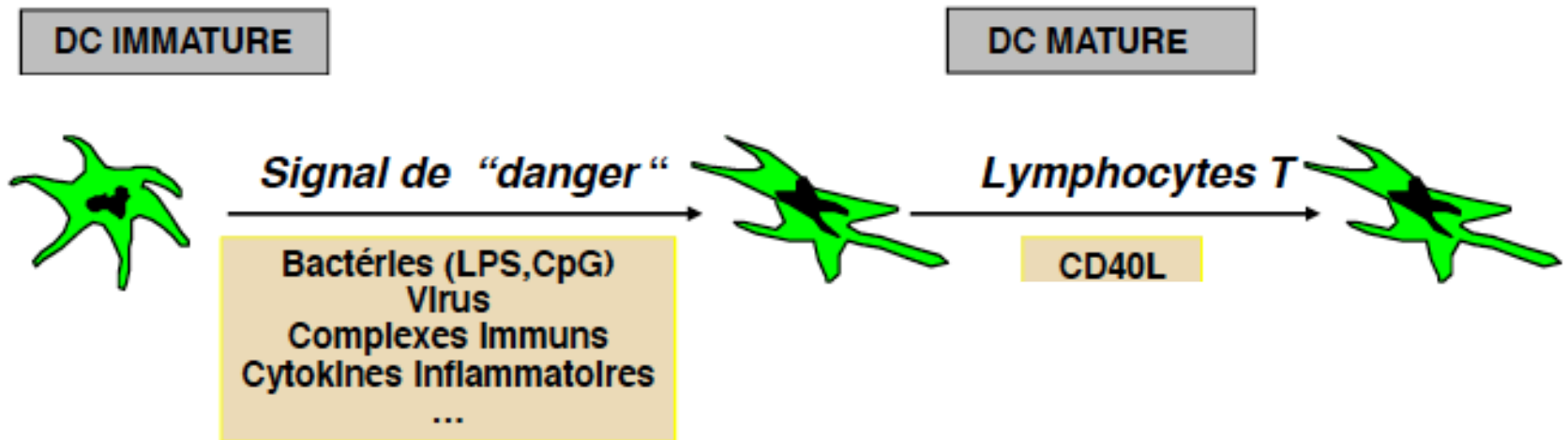


Figure 1.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Immature dendritic cell → Mature dendritic cell

Cellules dendritiques : maturation

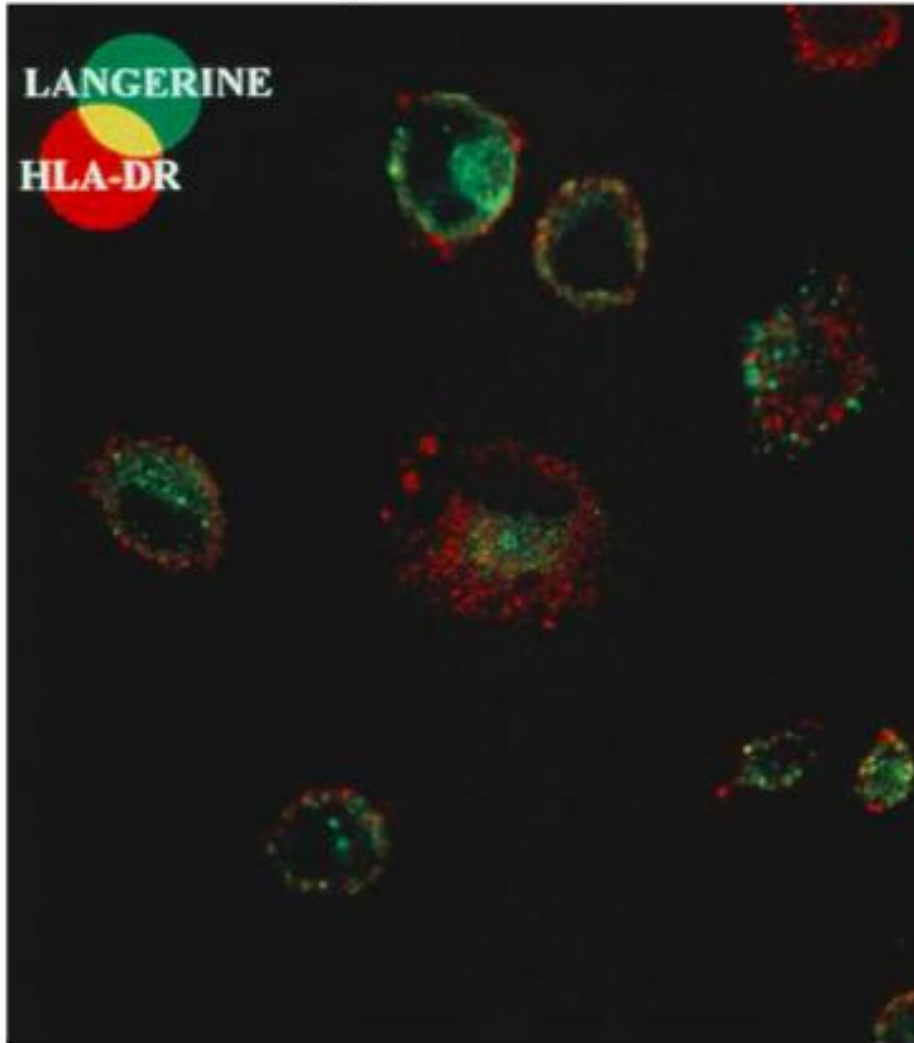


Faible costimulation des LT
CMH de classe II Intracellulaire

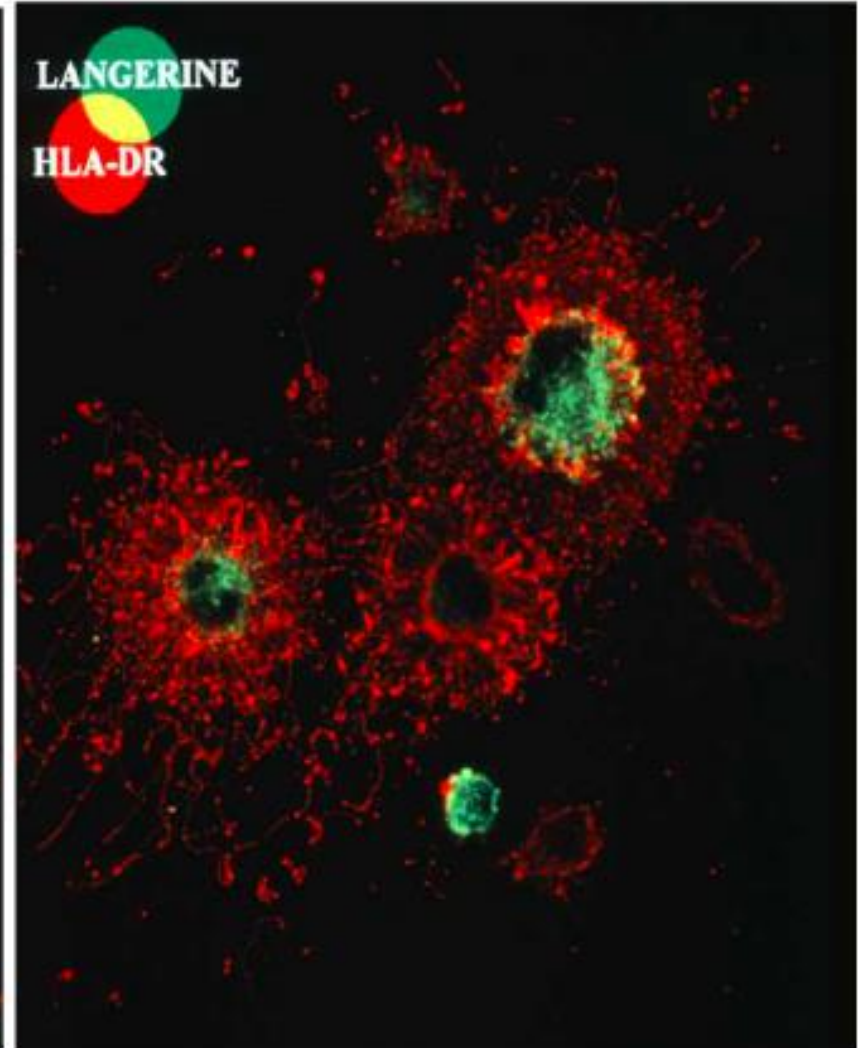
FORTE costimulation des lymphocytes T
CMH de classe II en surface

Cellules dendritiques : maturation

Cellules de Langerhans immatures



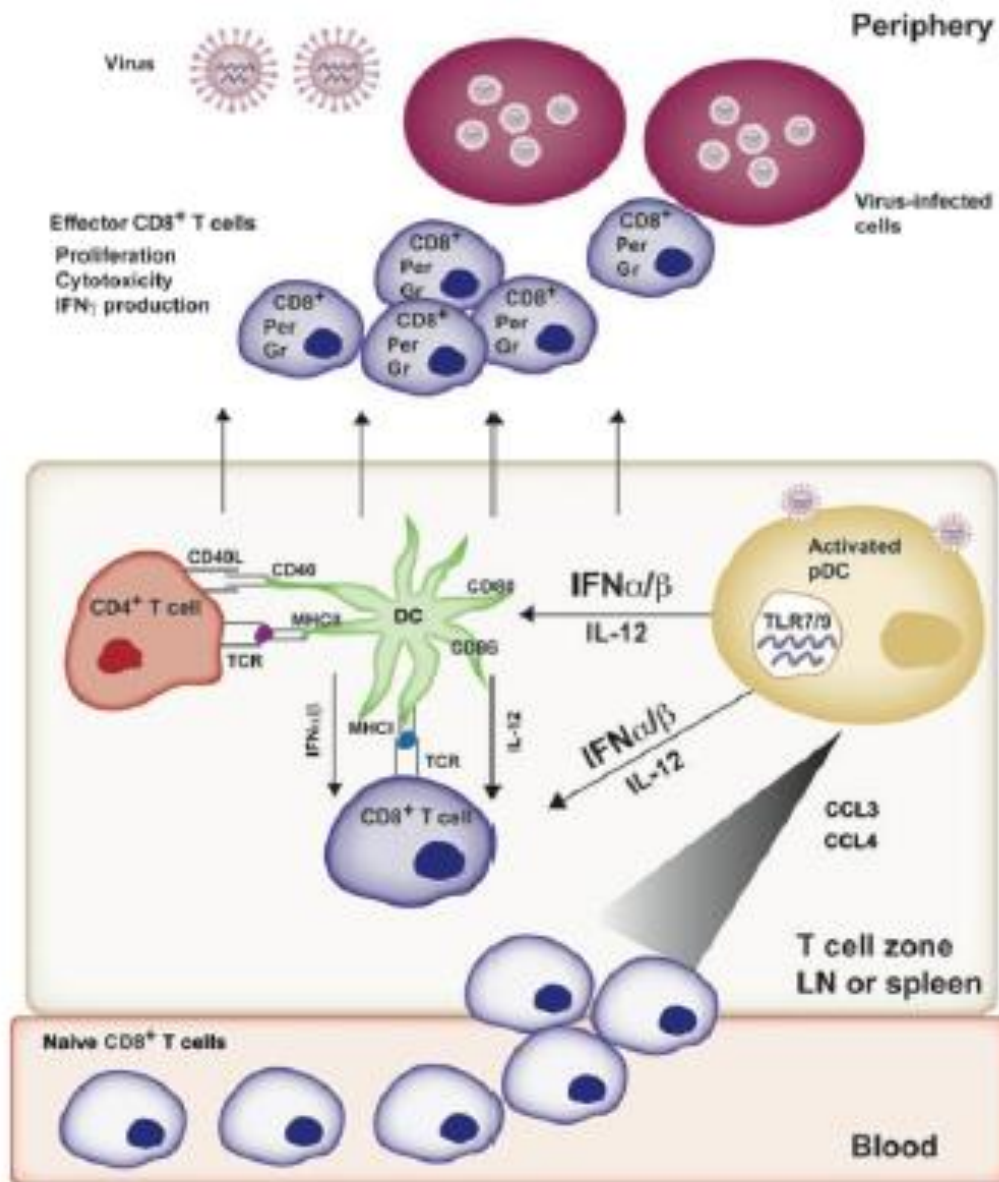
Cellules de Langerhans matures



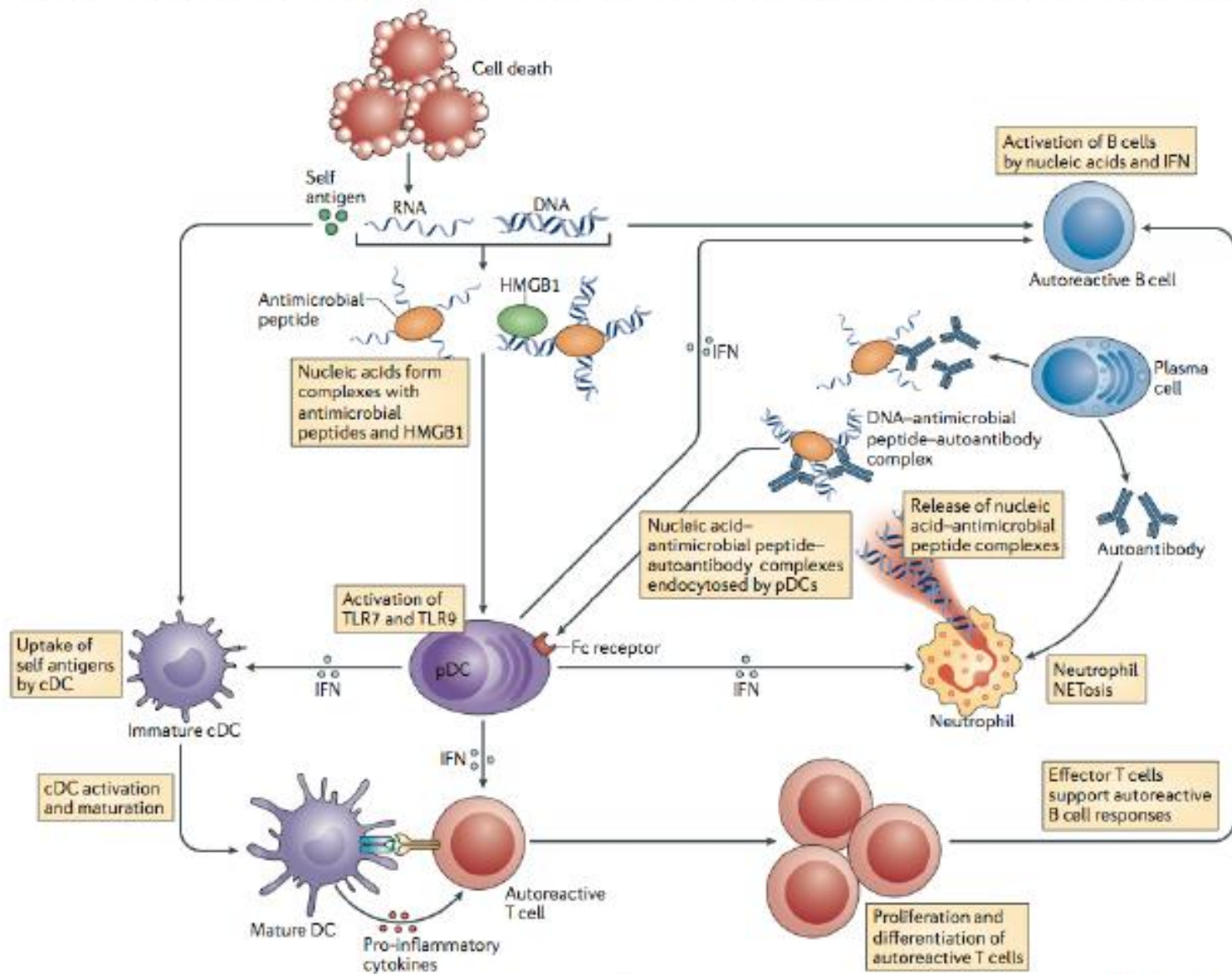
Cellules dendritiques plasmacytoïdes

- ✓ Identifiée en 1999 comme des cellules sécrétrices d'IFN de type 1 (IFN α/β)
- ✓ Morphologie de cellules plasmacytoïdes
- ✓ Faible niveau d'expression du CMH II
- ✓ Sécrète du TNF α et IL-12

pDC viral infection



pDC autoimmunity



La Cellule Dendritique est un lien essentiel entre Immunité Innée et Immunité Adaptative

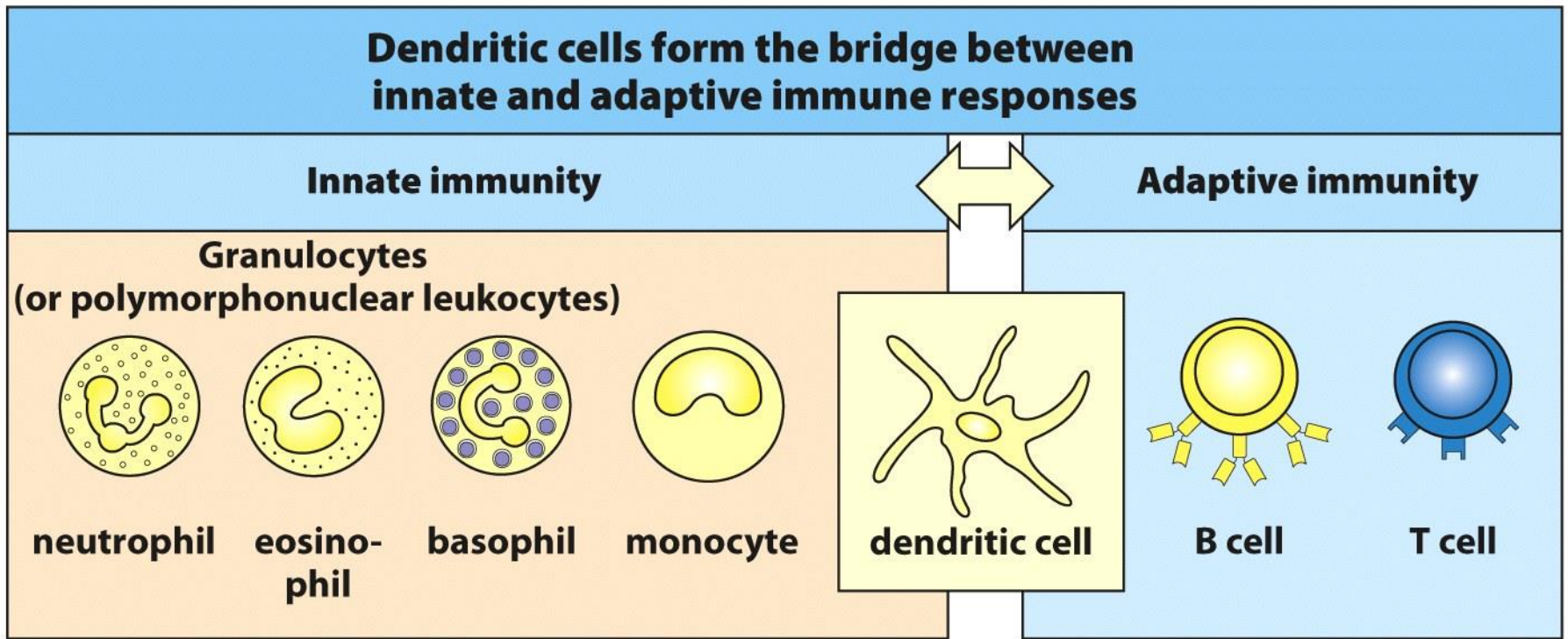
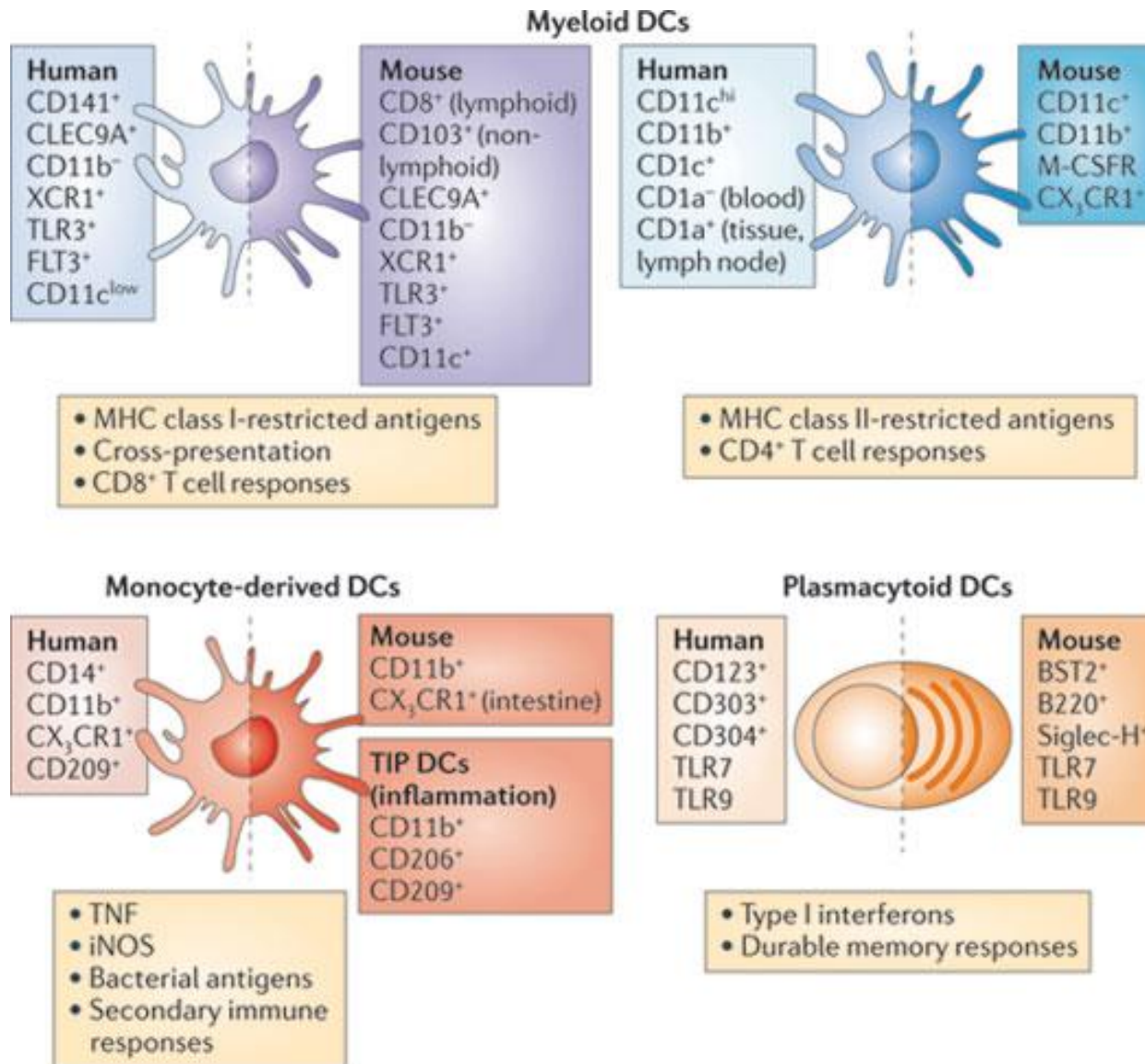


Figure 1.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Immature dendritic cell → Mature dendritic cell

Cellules présentatrices d'antigènes et allergie : phénotype, propriétés, fonctions



Déterminants antigéniques reconnus par les récepteurs de l'immunité innée (PRR)

■ **PRRs**

- Faibles diversités
- Récepteurs reconnaissent des structures moléculaires très conservées présents sur les grands groupes de pathogènes (PAMPs)

■ **PAMPs** présentent 3 caractéristiques communes

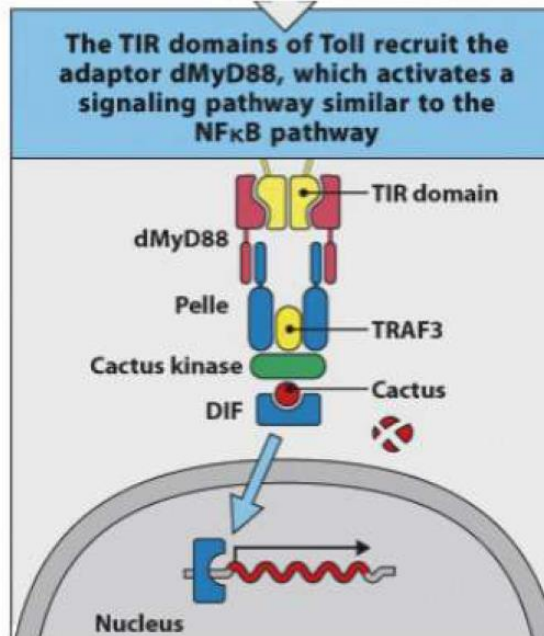
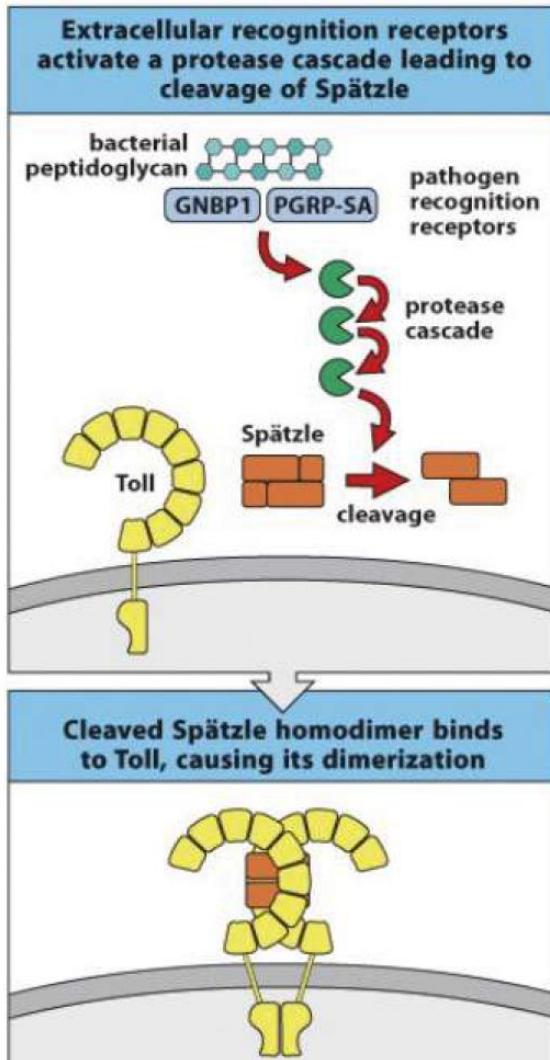
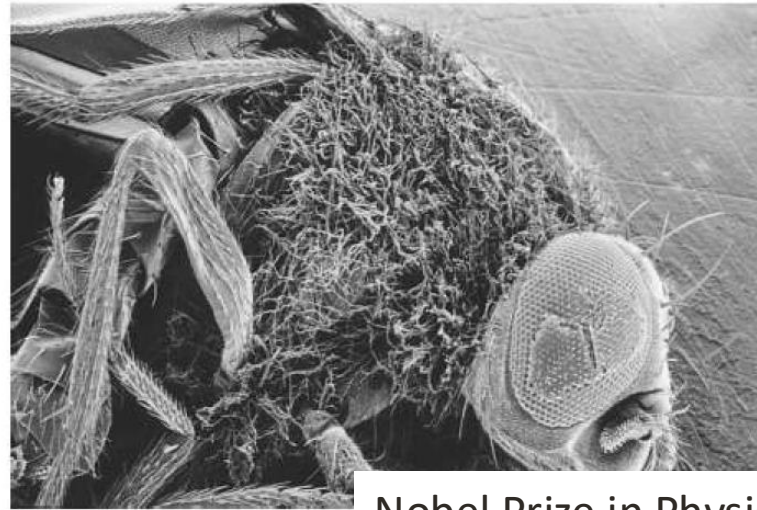
- Sont produits uniquement par les micro-organismes
- Sont invariants entre les microorganismes d'une même classe
- Sont essentiels pour la survie des micro-organismes



SIGNAL DANGER

Découverte des TLR chez les insectes

Récepteur Toll de la drosophile

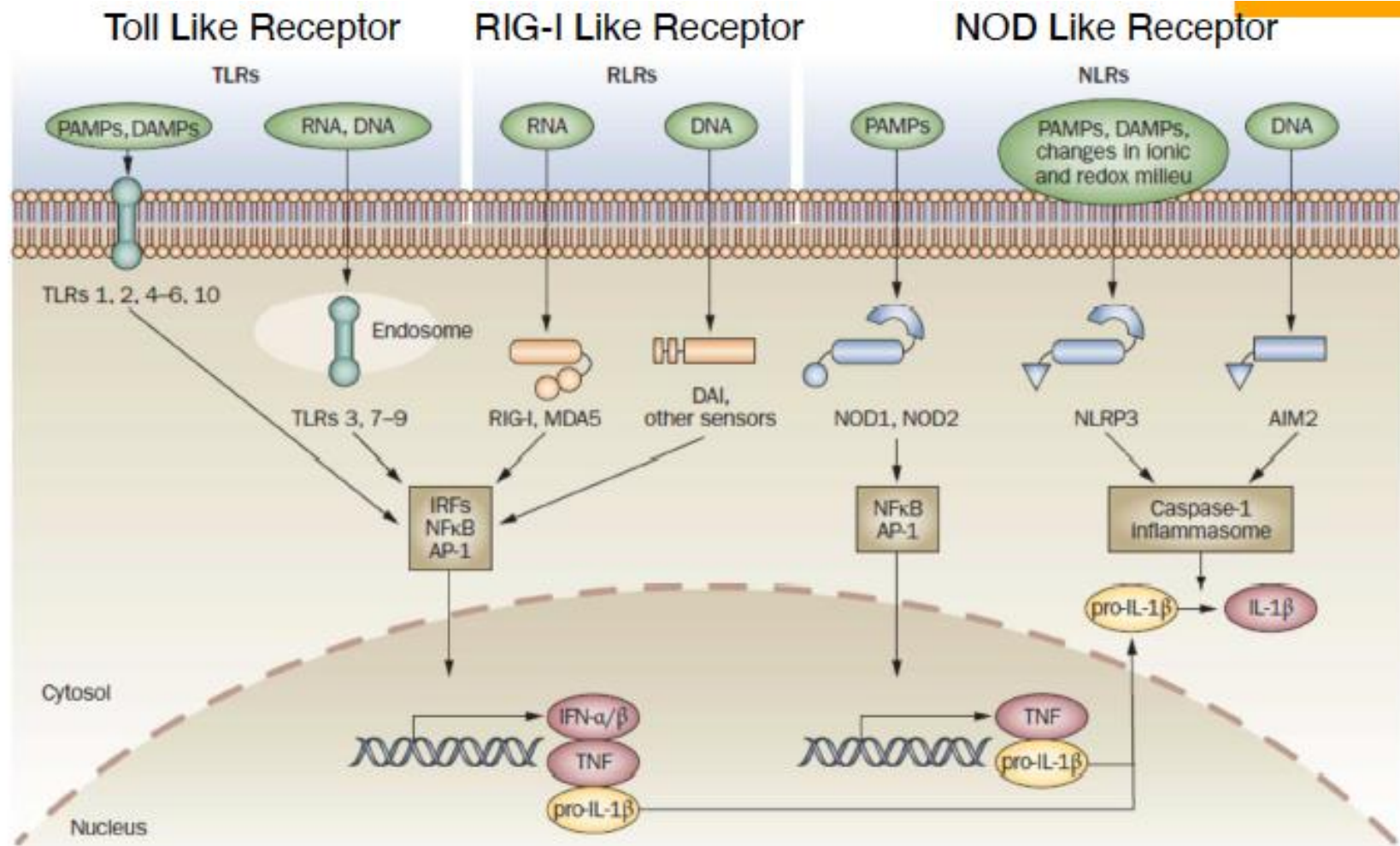


Nobel Prize in Physiology or Medicine 2011

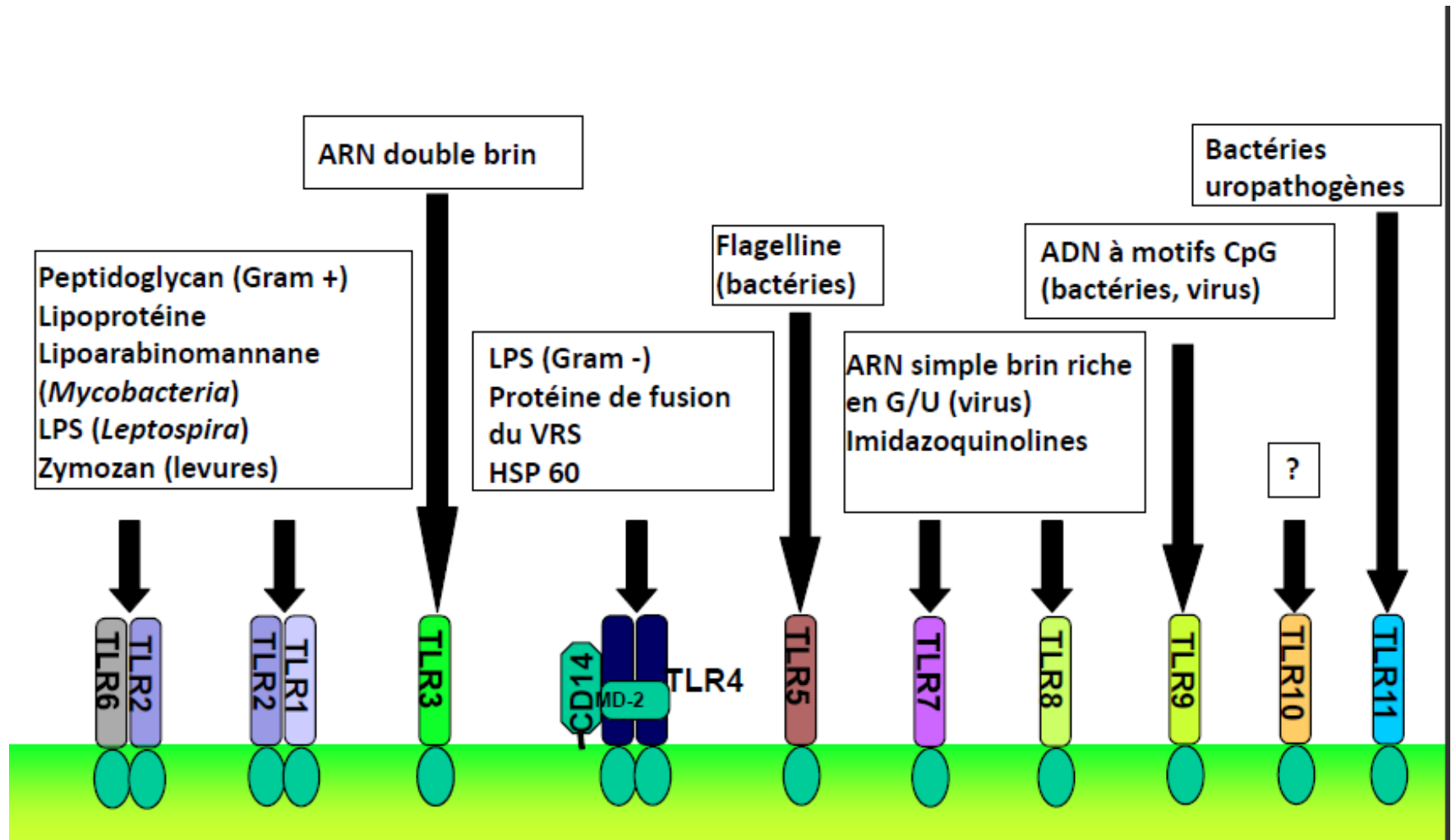


Jules Hoffman

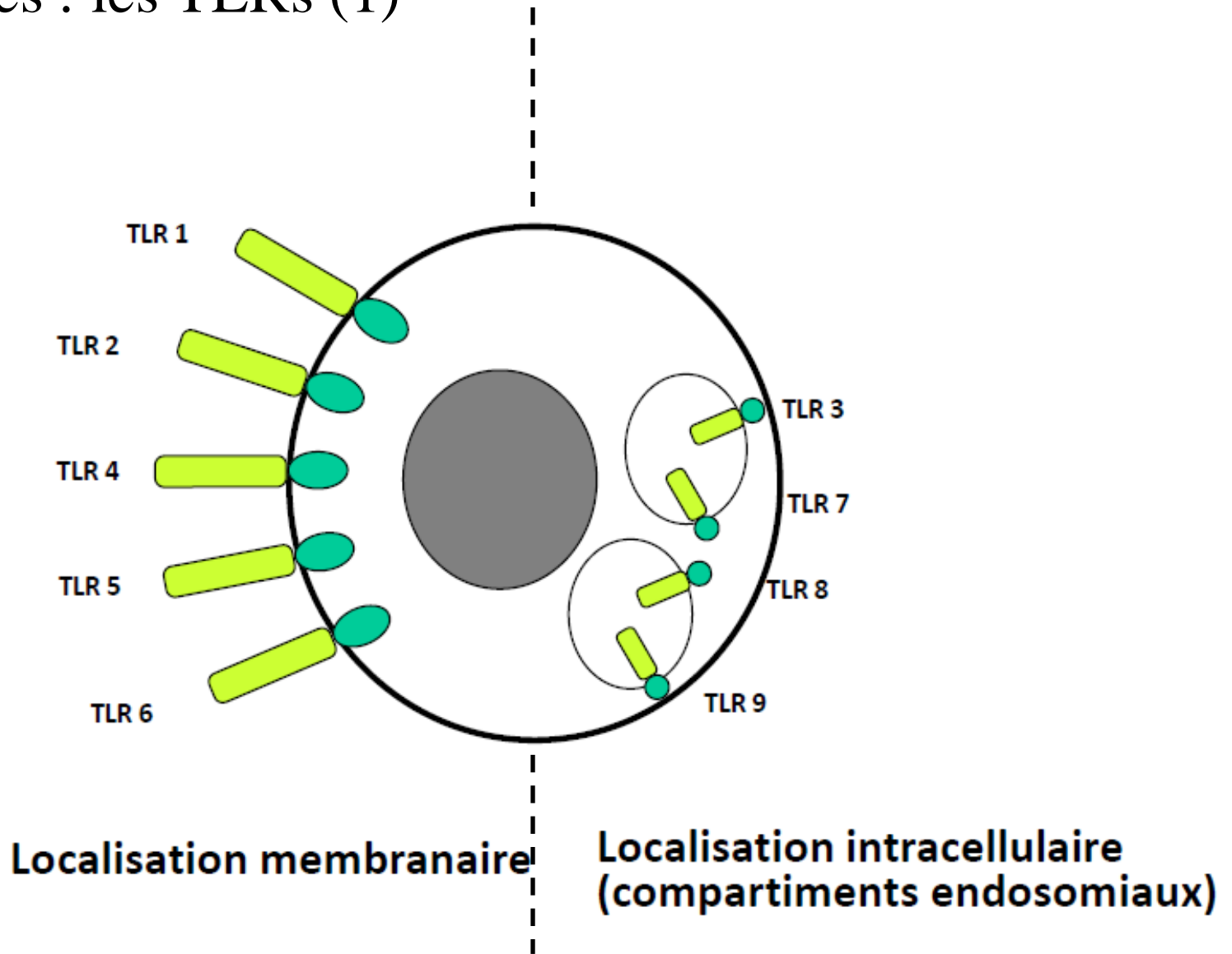
Récepteurs de l'immunité innée (PRR) et cellules dendritiques



Exemples : les TLRs (1)



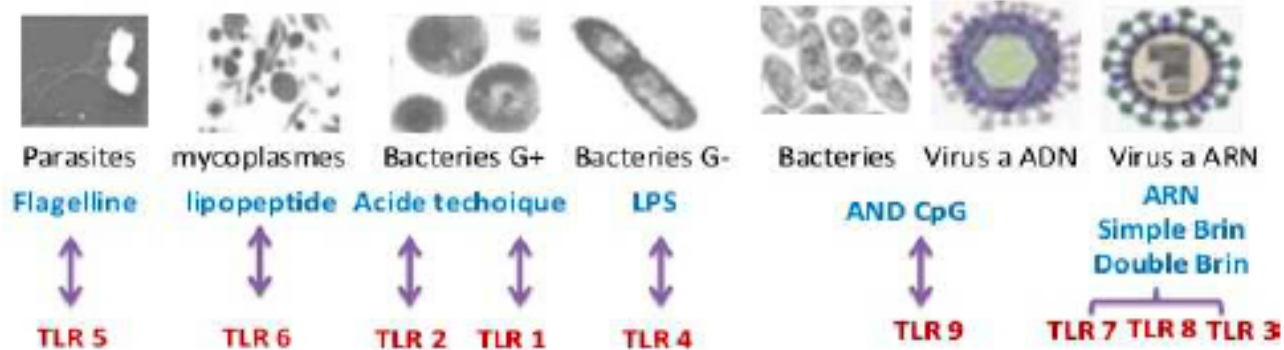
Exemples : les TLRs (1)



Localisation membranaire

Localisation intracellulaire

Récepteurs de l'immunité innée (PRR) et cellules dendritiques



conventionnel DC

Plasmacytoïde DC



cDC1

TLR3
TLR8



cDC2

TLR4
TLR5
TLR1/2
TLR8



**DC
inflammatoire**

TLR4
TLR1/2/6
TLR5
TLR8



**Cellule de
Langerhans**

TLR1/2/6
TLR3
TLR5



TLR7
TLR9

Cellules présentatrices d'antigènes et allergie : phénotype, propriétés, fonctions

PRR= Pathogen Recognition Recepteur

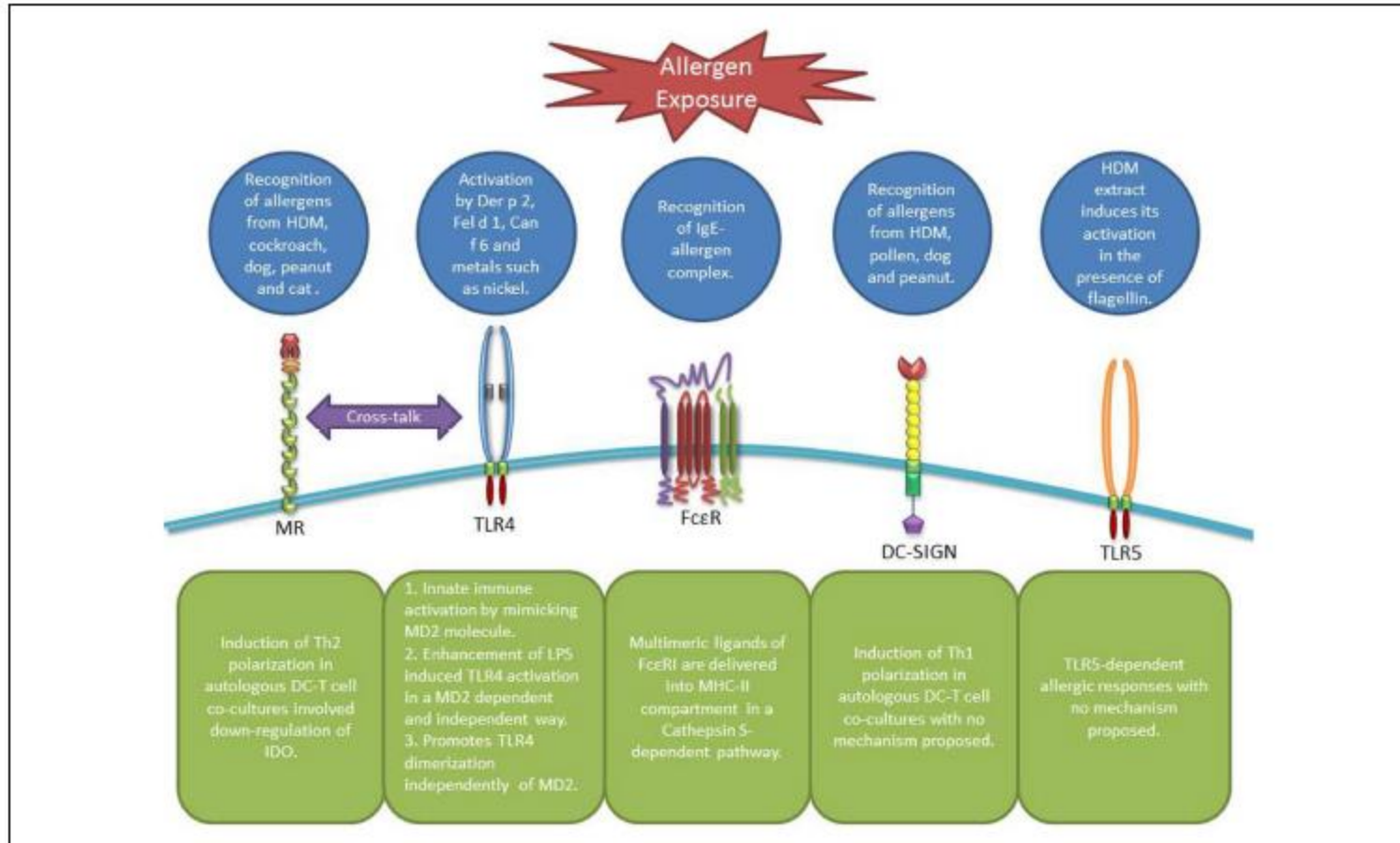
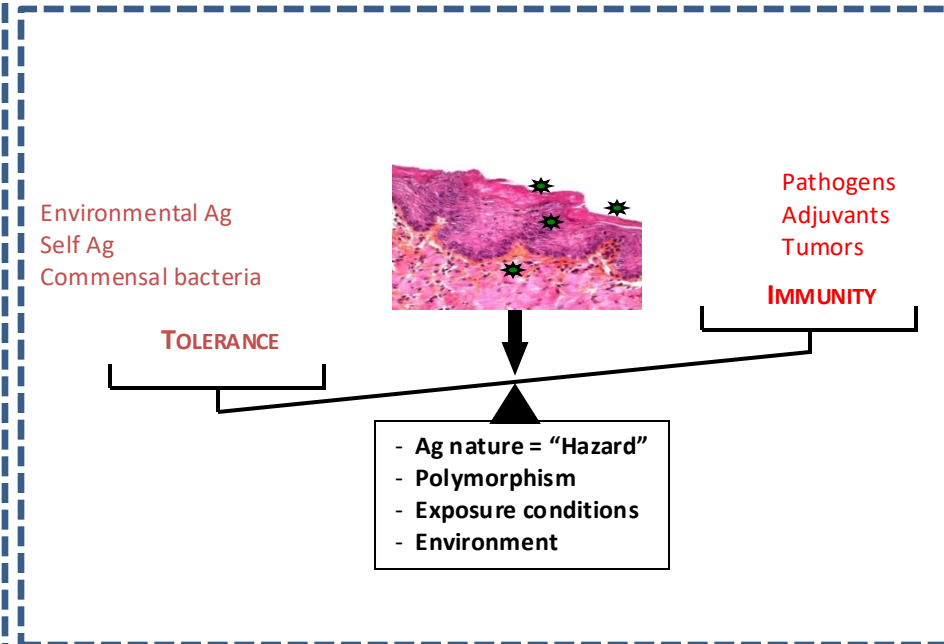
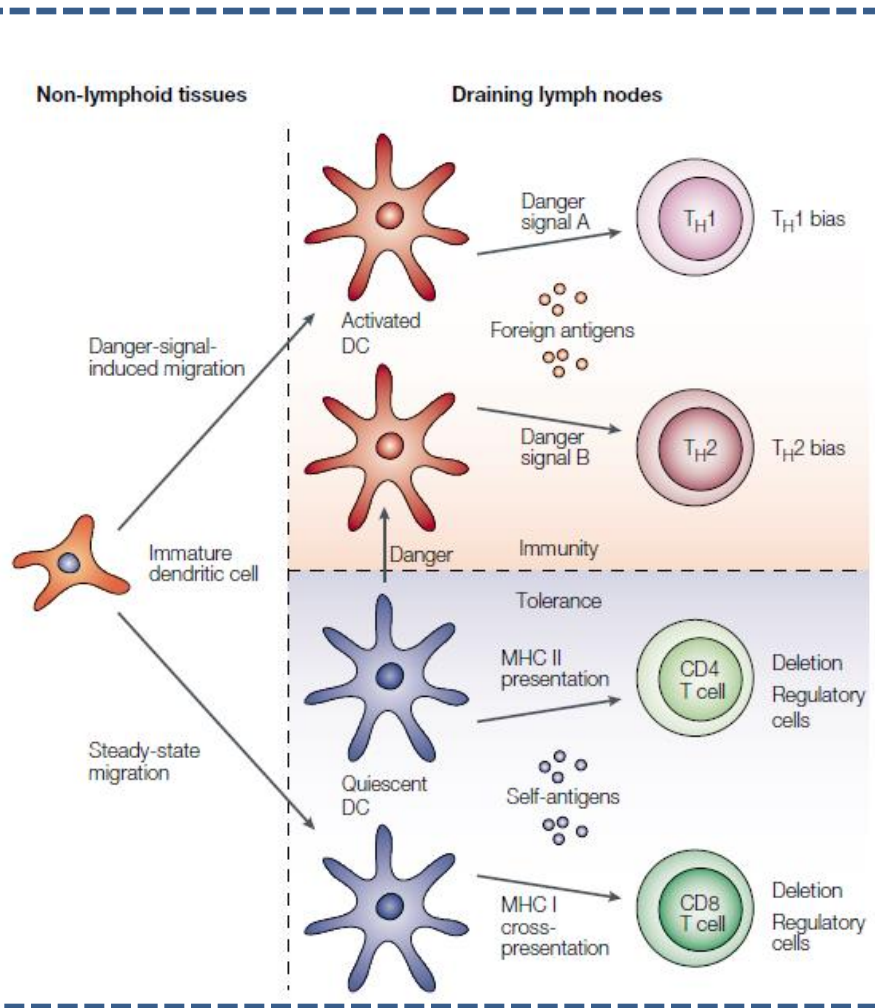


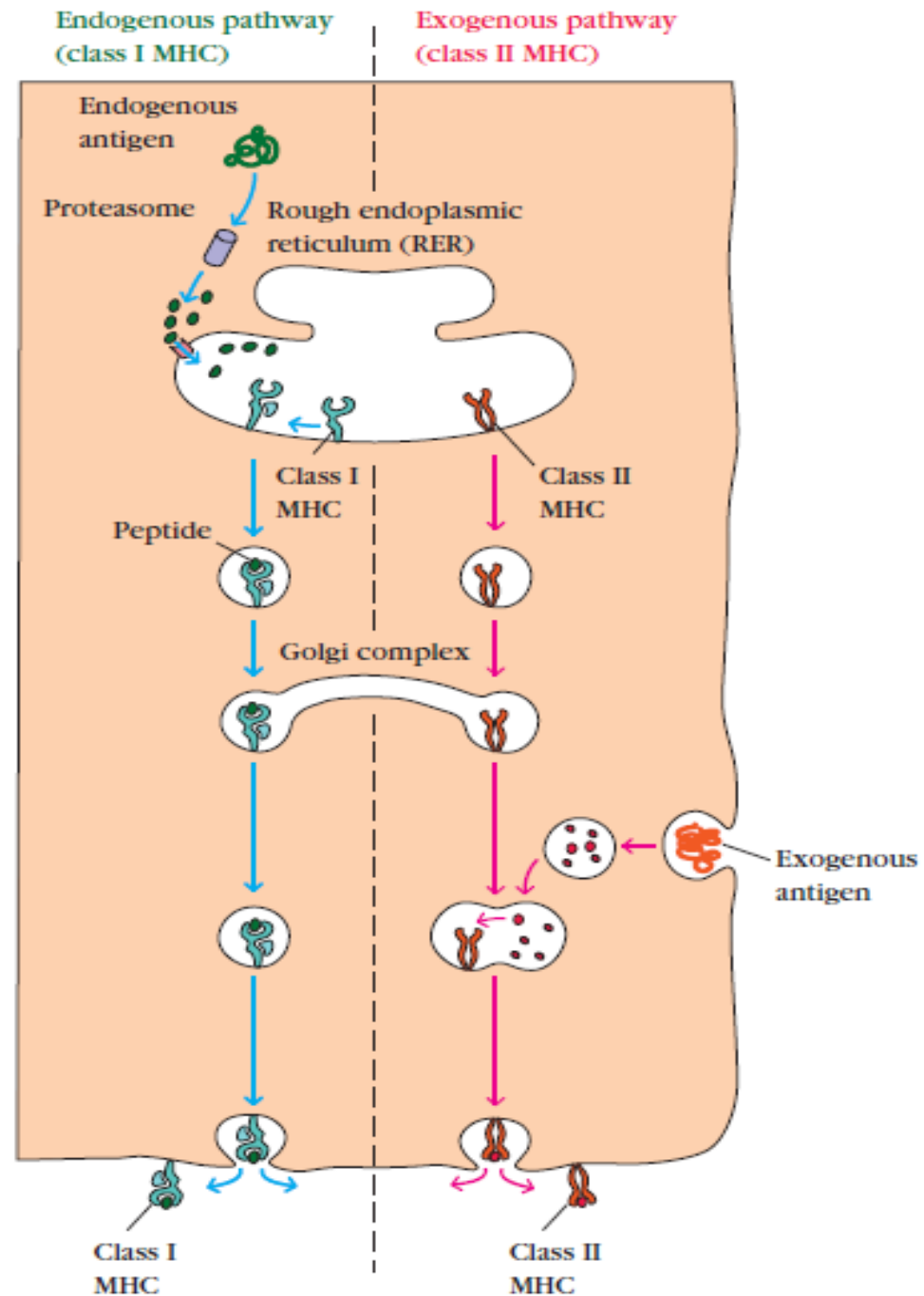
FIGURE 1 | Receptors involved in allergen recognition and uptake by DCs. MR can recognize allergens from diverse sources leading to Th2 polarization and IDO down-regulation in DCs involving a possible cross-talk with TLR4 (19). TLR4 itself can be activated by airborne allergens and diverse metals in an

MD2 dependent or independent way (33, 35–37). FcεR facilitate allergen uptake through the recognition of the IgE-allergen complex (41, 46). DC-SIGN can recognize diverse allergens as well, however, leading to a Th1 polarization. Finally, TLR5 can be activated by HDM extracts containing flagellin (34).

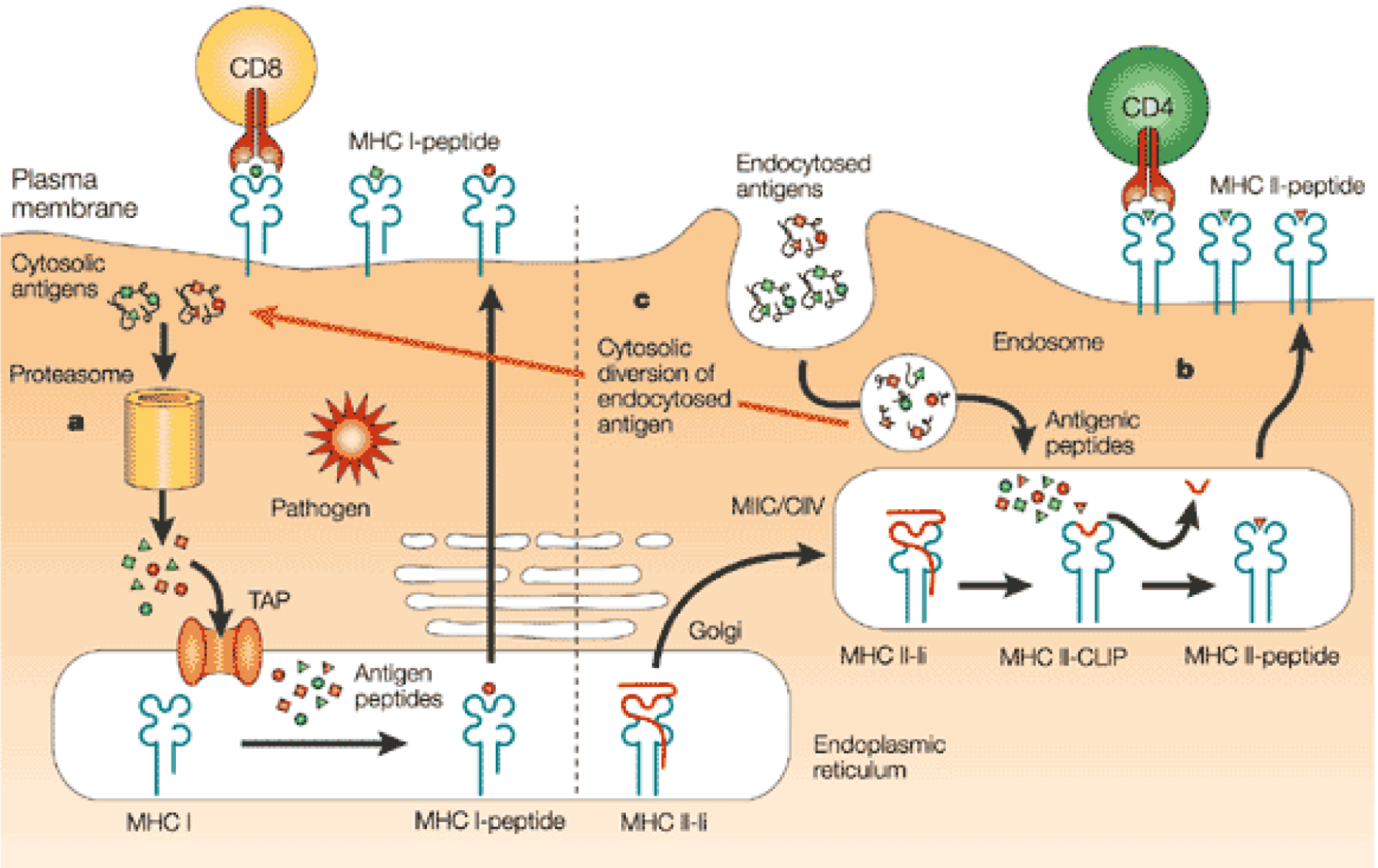
Cellules présentatrices d'antigènes et allergie : phénotype, propriétés, fonctions



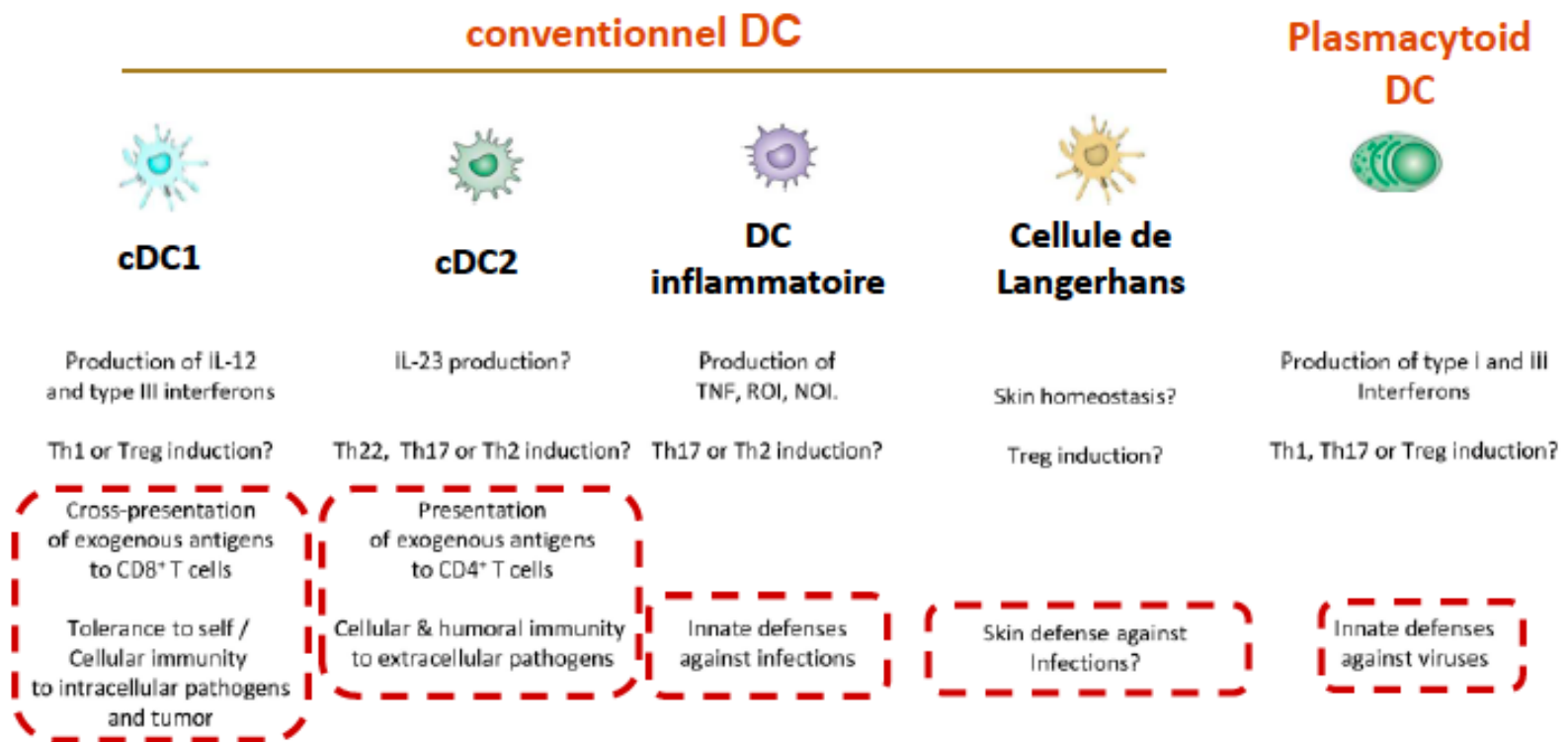
Présentation antigénique et cellules dendritiques

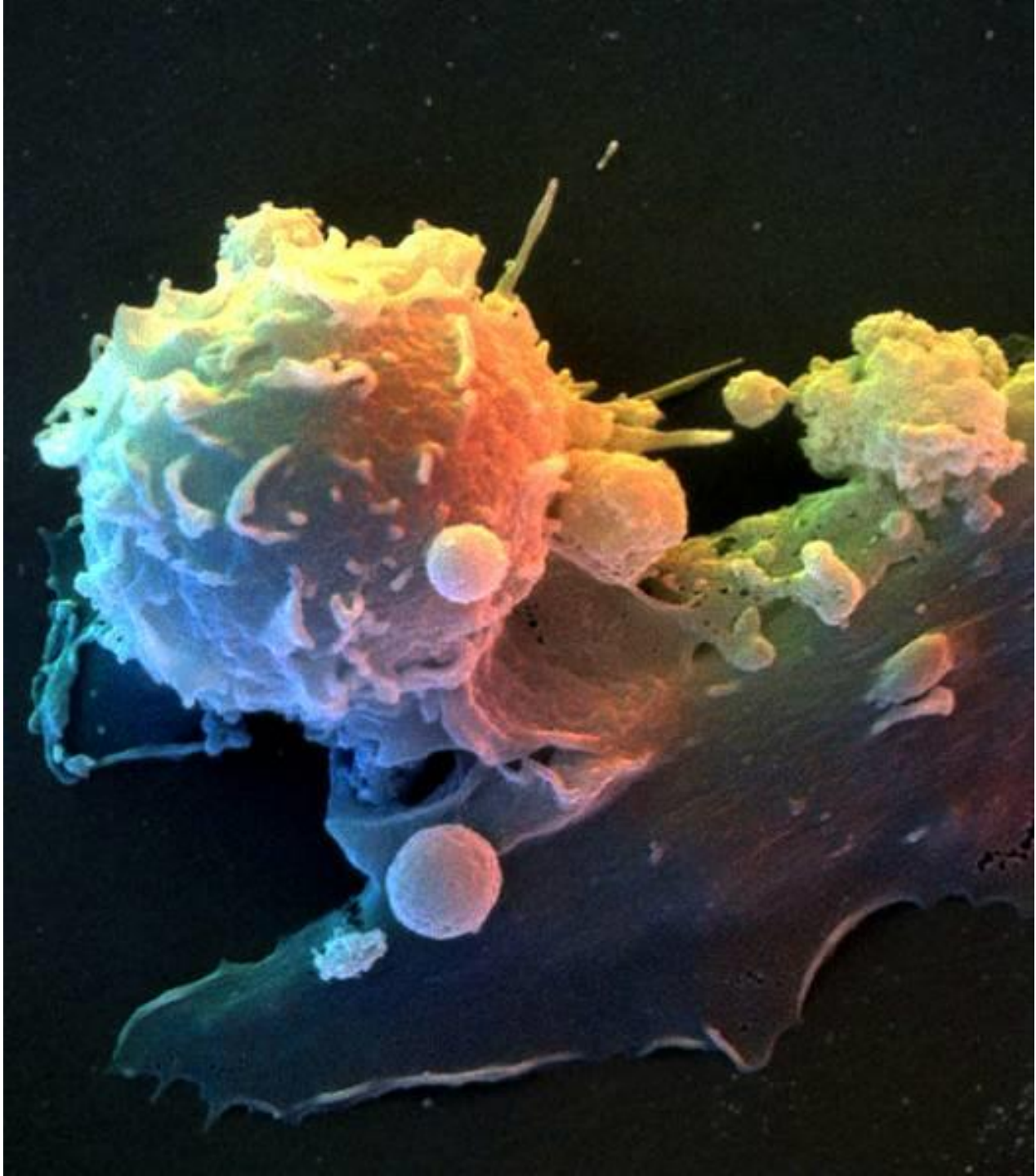


Présentation croisée ou « cross-priming »



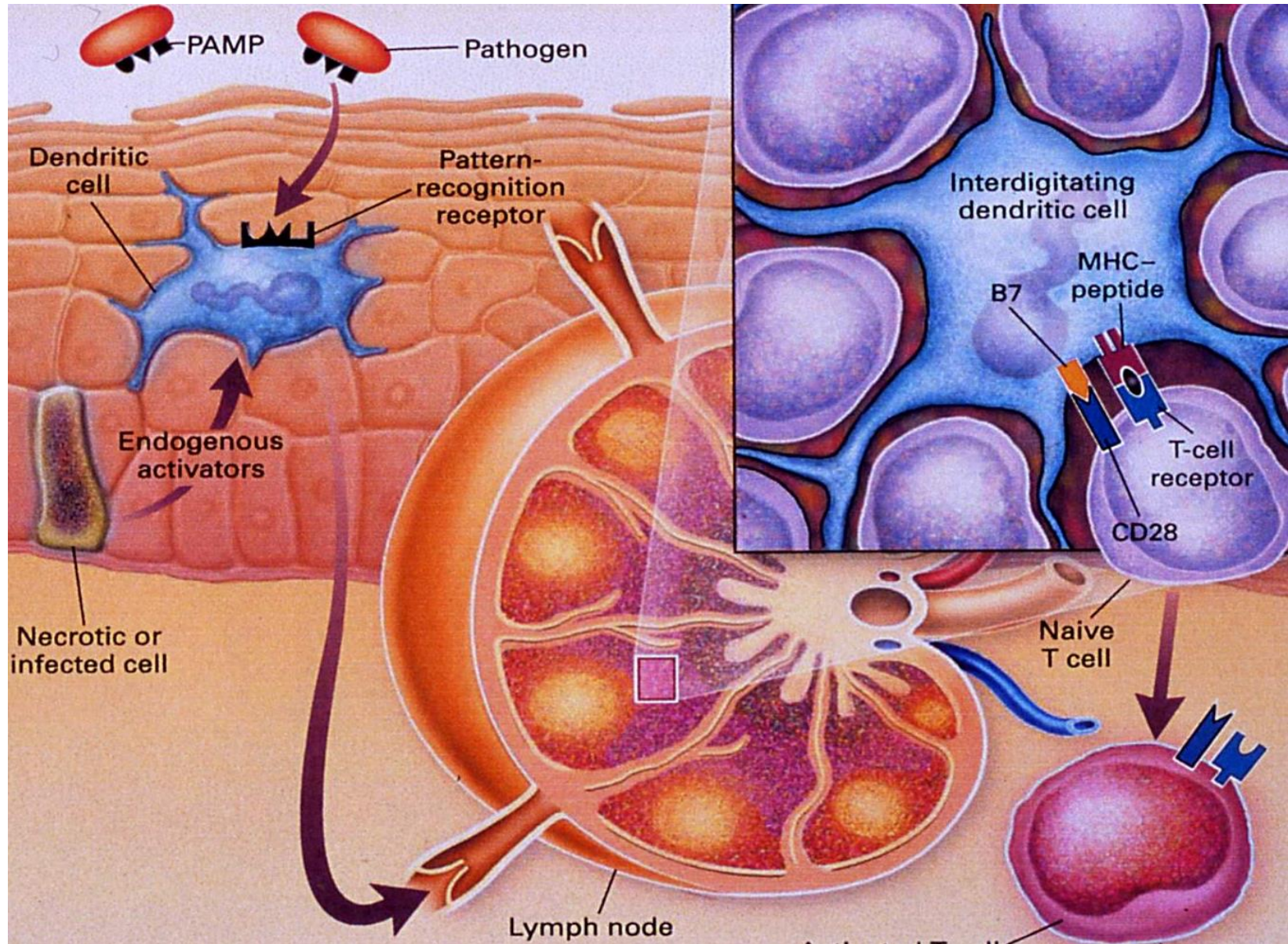
Récepteurs de l'immunité innée (PRR) et cellules dendritiques





Cellules présentatrices d'antigènes et allergie

Présentation de l'antigène



La Cellule Dendritique est un lien essentiel entre Immunité Innée et Immunité Adaptative

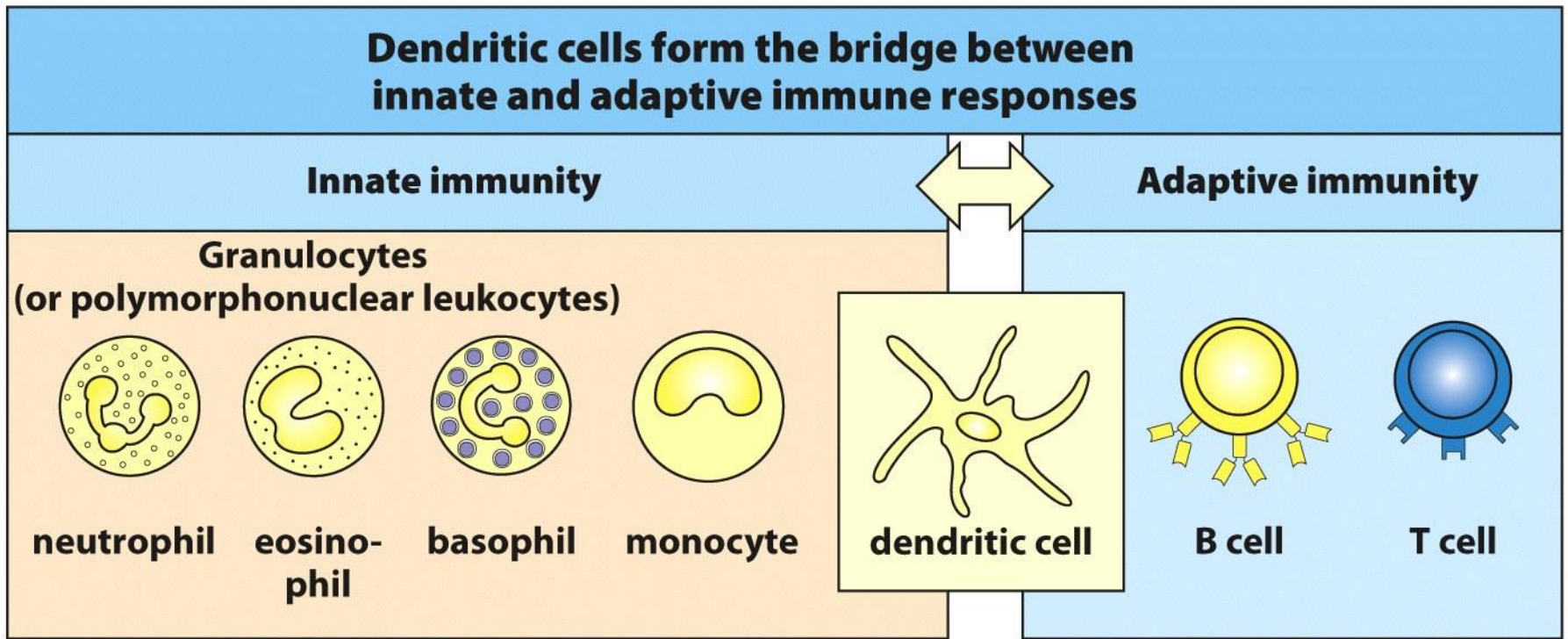
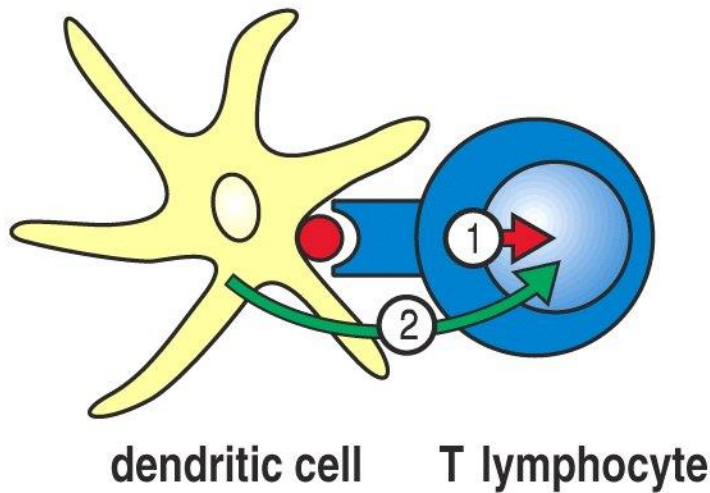


Figure 1.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

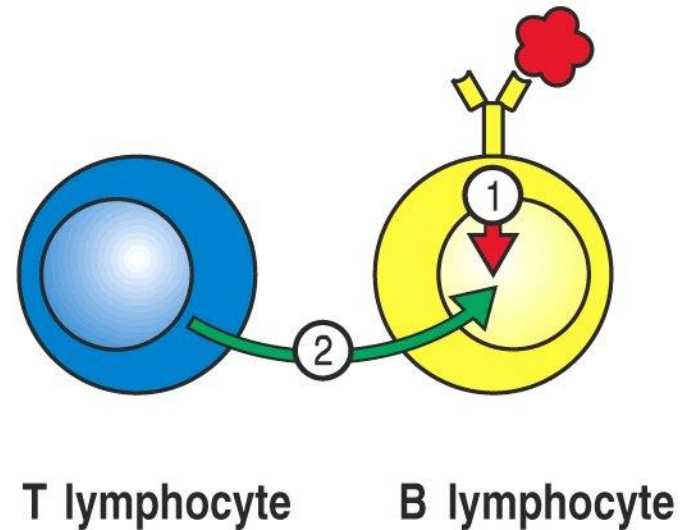
PRESENTATION ANTIGENIQUE

Antigen:receptor binding and co-stimulation of T cell by dendritic cell



Proliferation and differentiation to effector function

Antigen:receptor binding and activation of B cell by T cell



Proliferation and differentiation to effector function

Figure 1-21 Immunobiology, 6/e. (© Garland Science 2005)

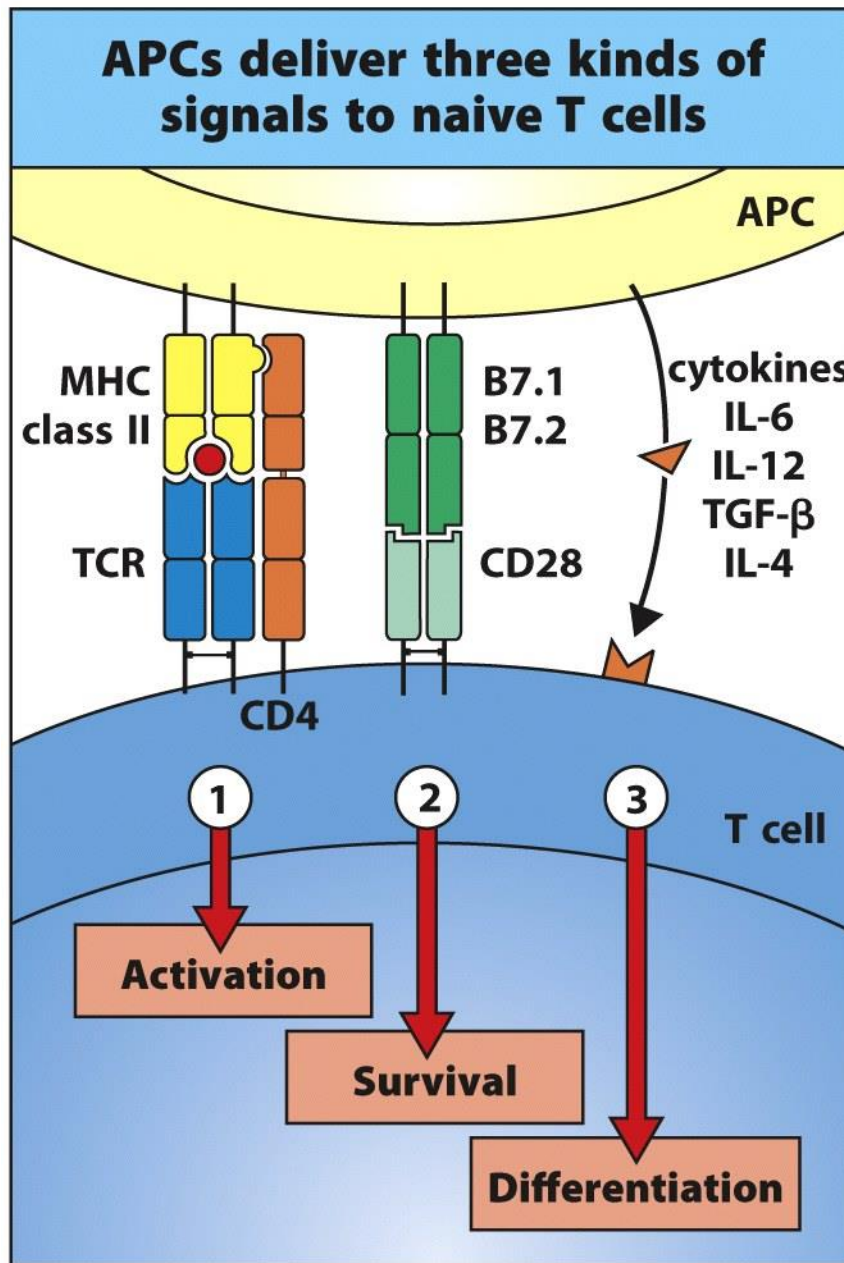
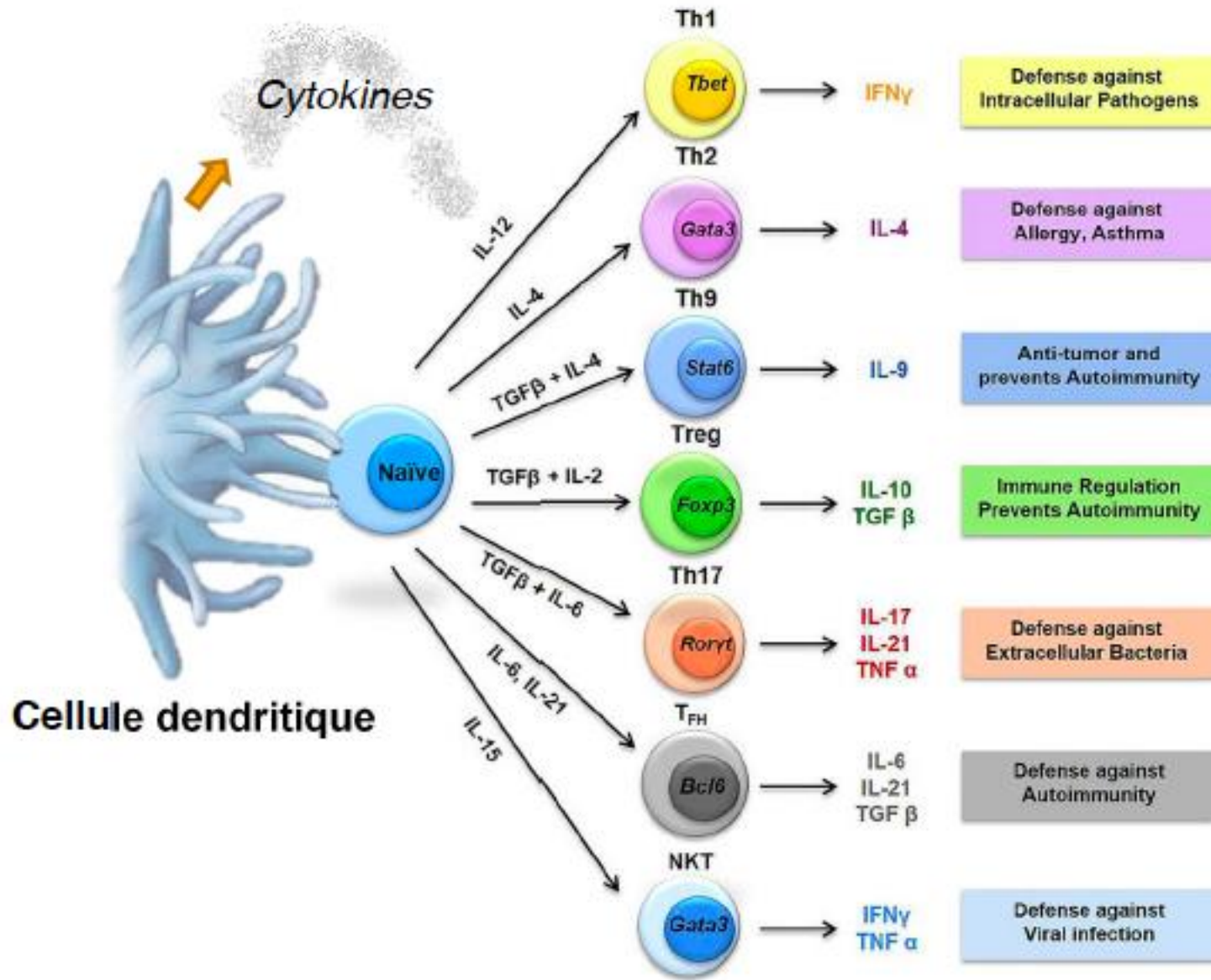


Figure 9.19 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Diversité des cellules dendritiques



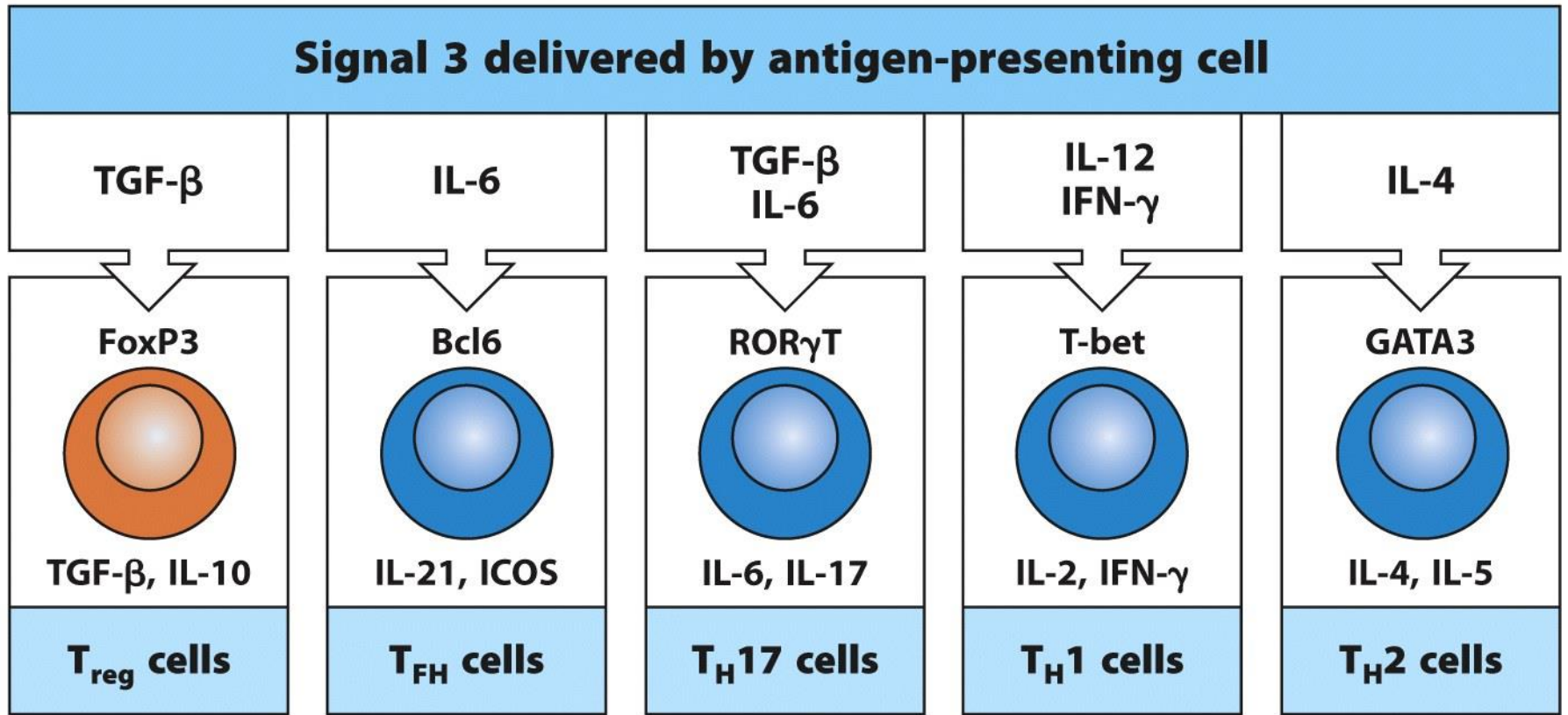


Figure 9.29 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

CD4 T cells: peptide + MHC class II

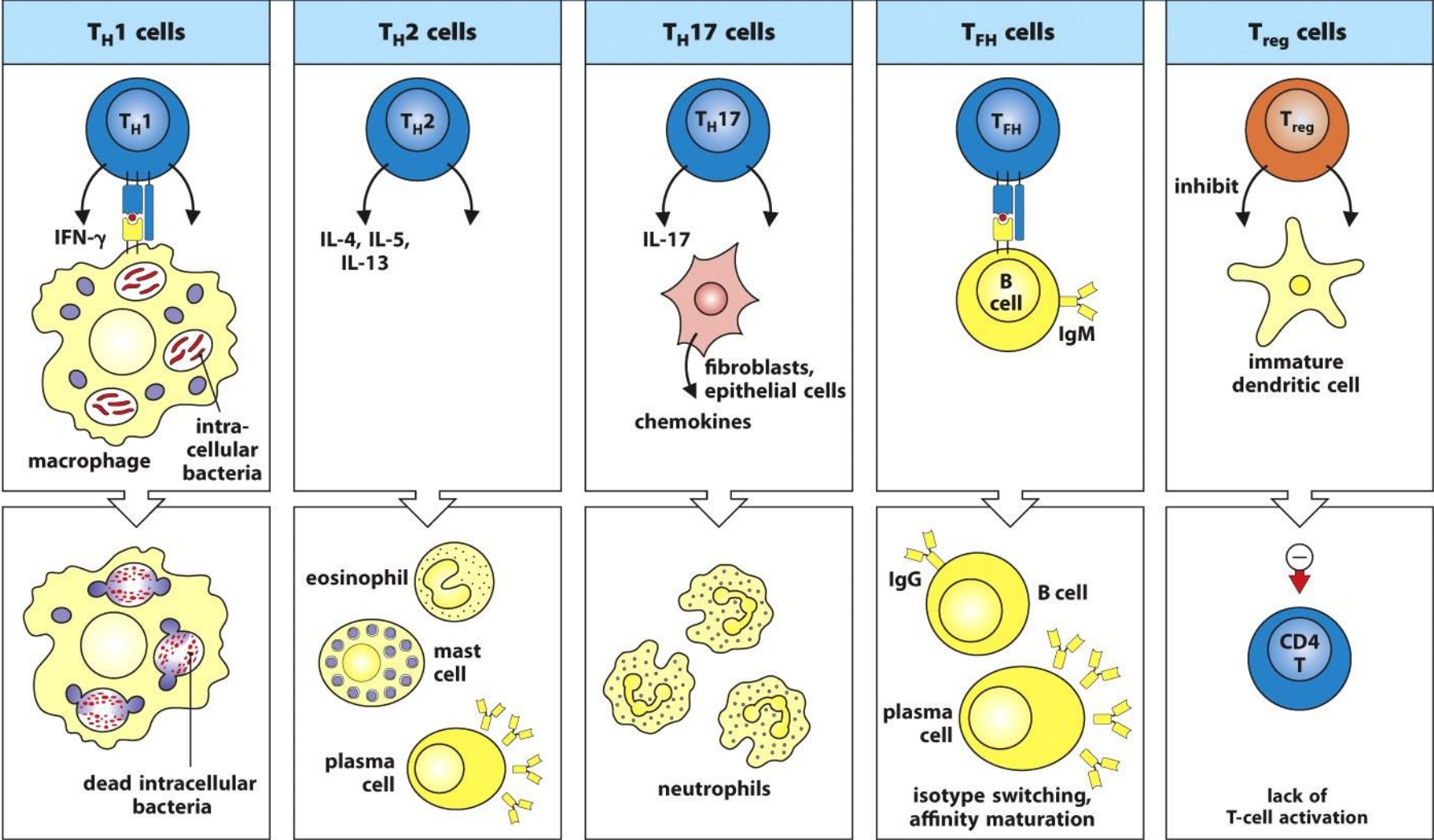


Figure 9.28 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

