



UNIVERSITÉ
DE GENÈVE

FACULTY OF MEDICINE
Department of Pathology
and Immunology

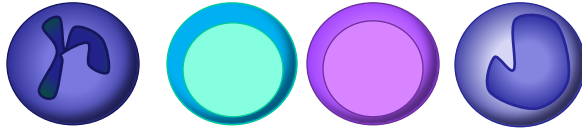
Fonctions des cellules lymphoïdes innées

Université de Genève,
13.03.2026

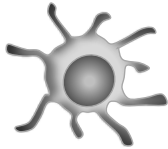
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2 branches du système immunitaire

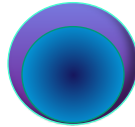
Système immunitaire inné
Précoce, sans spécificité antigénique



Neutrophiles Eosinophiles Basophiles Monocytes

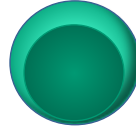


Cellules dendritiques

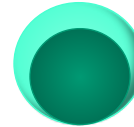


Cellules lymphoïdes innées (NKs, ILCs)

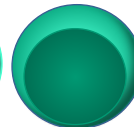
Système immunitaire adaptatif
Tardif, spécifique de l'antigène, mémoire



Lymphocytes



Cellules B



Cellules T



Lymphocytes innés

Cellules natural killer (NKs)

Découvertes en 1975, comme des cellules ayant la capacité naturelle de tuer les tumeurs

(Kiessling R., et al., *EJI*, 1975;

Herberman RB., et al., *Int J Canc*, 1975)



European Journal of
Immunology
Basic-Clinical-Translational

Article

„Natural” killer cells in the mouse. II. Cytotoxic cells with specificity for mouse Moloney leukemia cells. Characteristics of the killer cell

R. Kiessling, Eva Klein, H. Pross, H. Wigzell

First published: February 1975 | <https://doi.org/10.1002/eji.1830050209> | Citations: 798

IJC

INTERNATIONAL
JOURNAL of CANCER

UICC

Article | [Full Access](#)

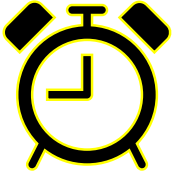
Natural cytotoxic reactivity of mouse lymphoid cells against syngeneic and allogeneic tumors. I. Distribution of reactivity and specificity

Ronald B. Herberman, Myrthel E. Nunn, David H. Lavrin

First published: 15 August 1975 | <https://doi.org/10.1002/ijc.2910160204> | Citations: 968

Lymphocytes innés

Cellules lymphoïdes innées (ILCs)



130 ans après l'identification des cellules lymphoïdes et myéloïdes
> 40 ans après l'identification des lymphocytes B et T

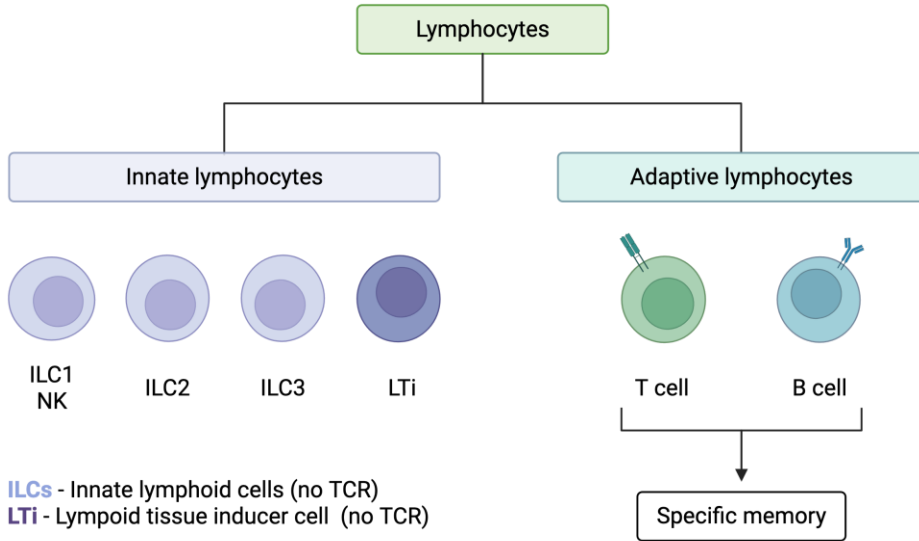
Innate lymphoid cells how did we miss them?

Walker JA., et al. *Nat Rev Immunol*, 2013

Innate lymphoid cells: A new paradigm in immunology

Eberl G., et al. *Science*, 2015

Lymphocytes innés et adaptatifs



Développement

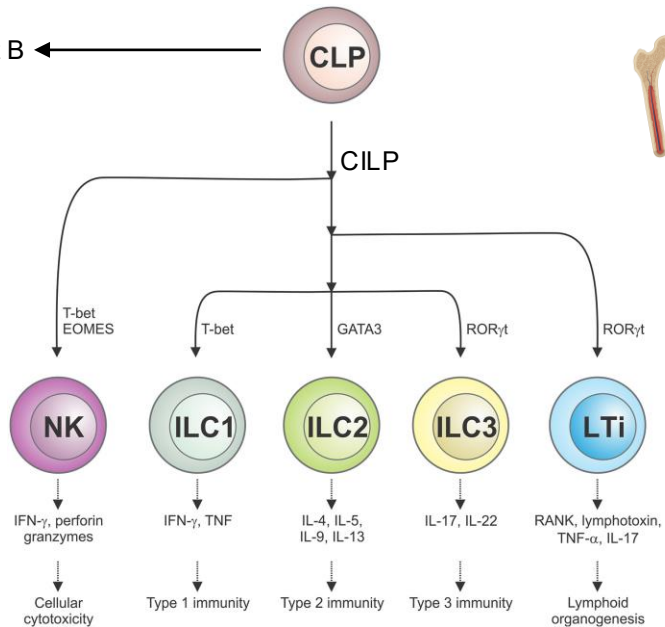


Foie chez le fœtus



Moelle osseuse
chez l'adulte

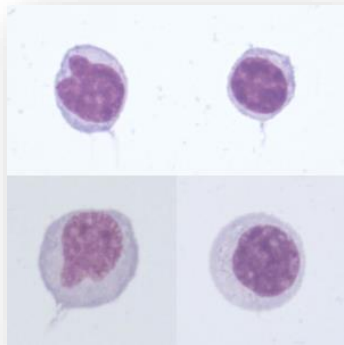
Lymphocytes T et B ←



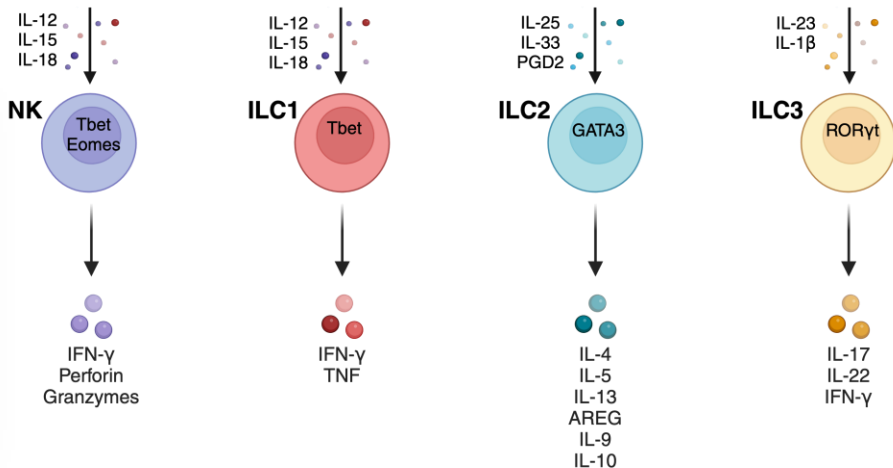
CLP: Common lymphoid progenitor

CILP: Common innate lymphoid progenitor

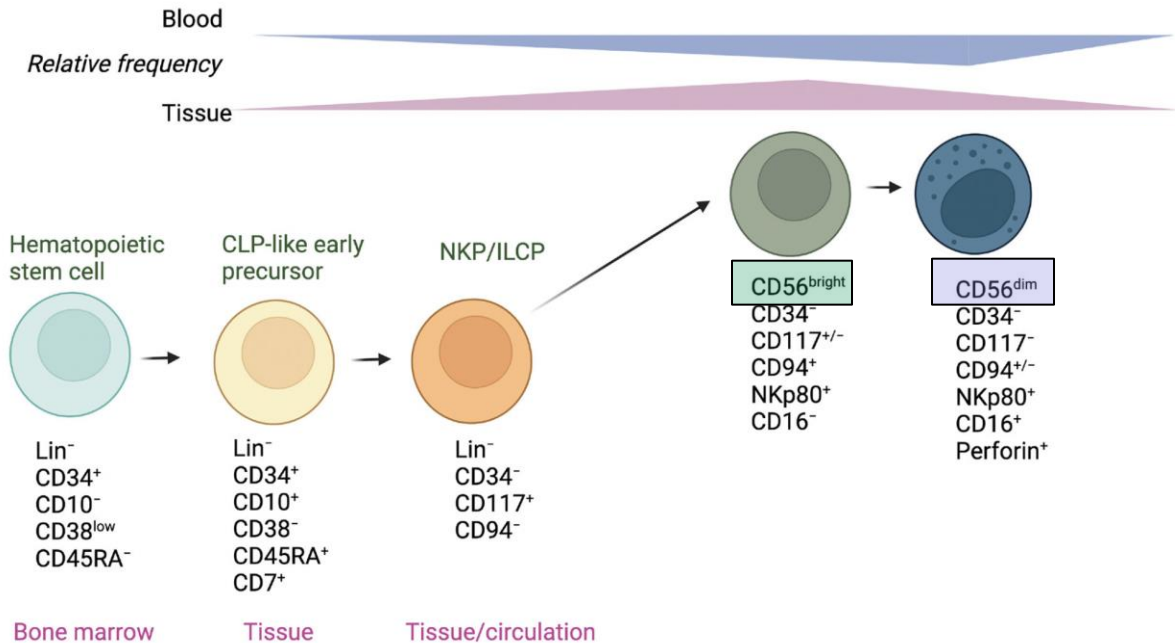
Les lymphocytes innés reflètent les lymphocytes adaptatifs



Hazenberg MD. & Spits H., *Blood*, 2014

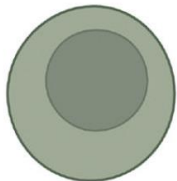


Les cellules NK

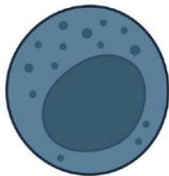


Sous-populations des cellules NK et leurs récepteurs

CD56^{bright}



CD56^{dim}



Localisation Tissue

Cytotoxicité -

Secretion de cytokines ++

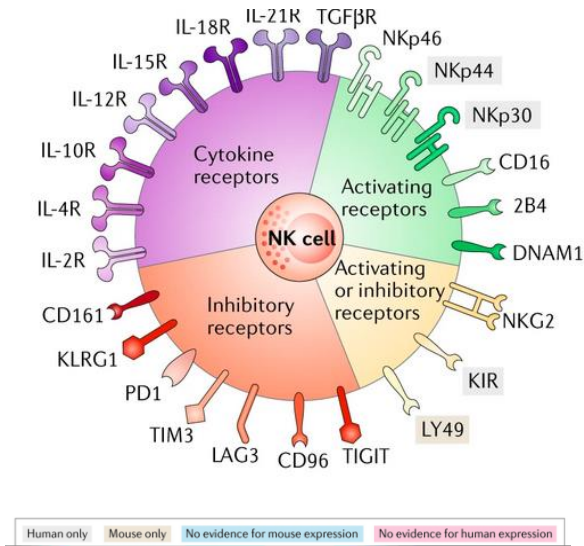
ADCC -

Sang

++

+/-

++

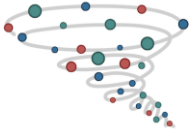


Fonctions effectrices des cellules NK



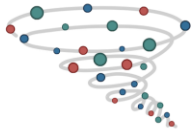
Cytotoxicité

- voie perforine-granzyme
- Récepteurs de mort (TRAIL, Fas)



Production de cytokines

- pro-inflammatoires ($\text{IFN}\gamma$, $\text{TNF}\alpha$, GM-CSF)
- anti-inflammatoires (IL-10)

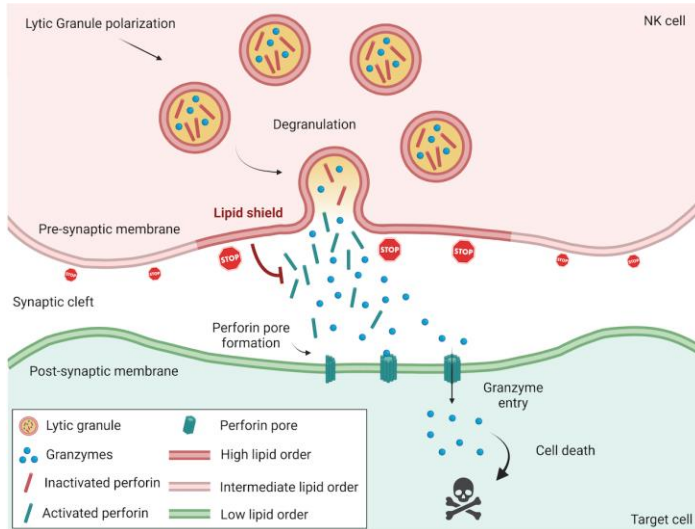


Production de chimiokines

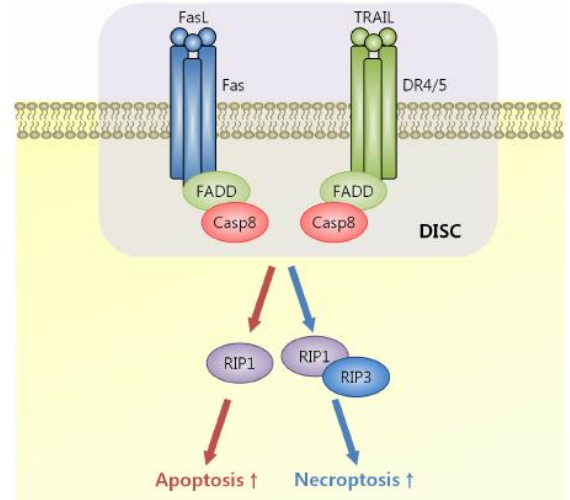
- Macrophage Inflammatory Proteins ($\text{MIP-1}\alpha$ and $\text{MIP-1}\beta$)

La cytotoxicité des cellules NK

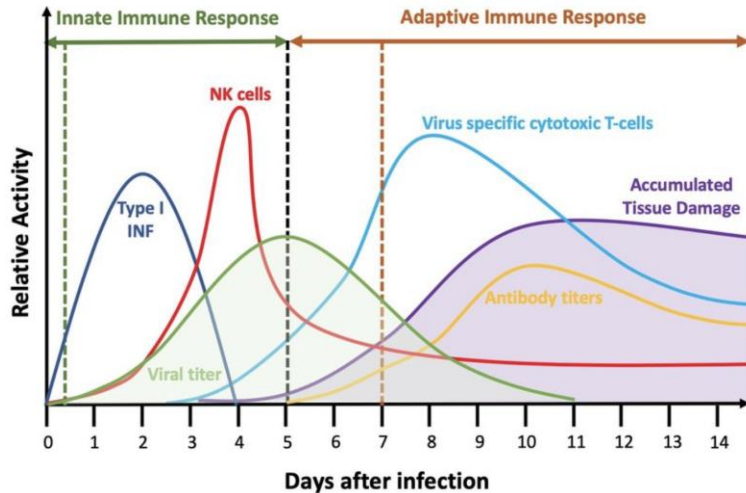
La voie perforine-granzyme



Récepteurs de mort



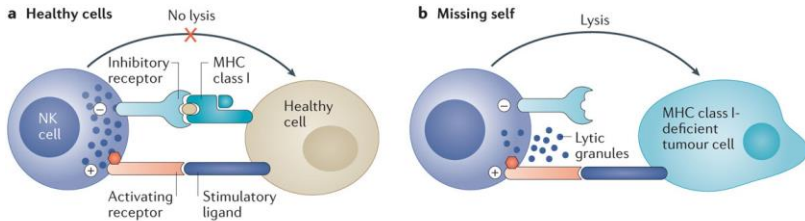
La réponse médiée par les cellules NK



Réponse des cellules NK: missing-self theory (“soi manquant”)

Destruction selon la „missing-self theory” (Klas Kärre, 1981):

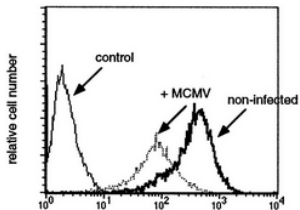
Les cellules privées de molécules du CMH I deviennent susceptibles à la destruction par les cellules NK



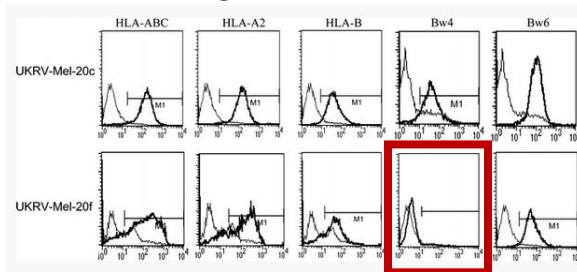
Perte d'expression du CMH-I

- Mutations des gènes du CMH-I
- Perte de $\beta 2$ -microglobuline ($\beta 2m$)
- Mutations dans la machinerie de traitement des antigènes
- Perte de NLRC5 (facteur de transcription)
- Activation d'oncogènes / altération de gènes suppresseurs de tumeurs

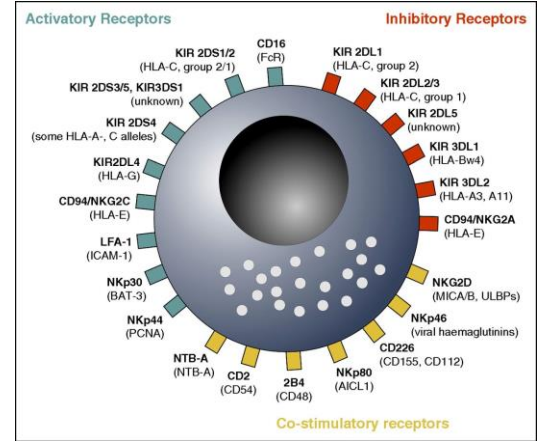
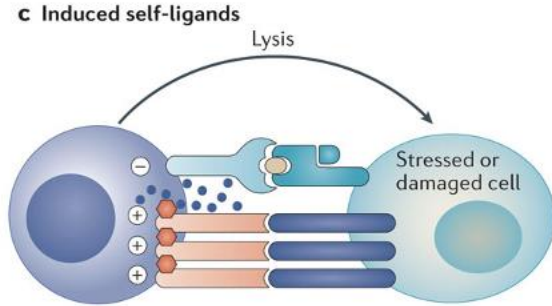
Cellule infectée par virus



Cellule tumorale



Réponse des cellules NK : équilibre entre signaux activateurs et inhibiteurs



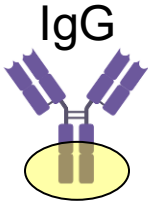
Handgretinger R, et al. *Blood*, 2016

KIR: Immunoglobulin superfamily

CD94-NKG2A/C/E: C-type lectin-related family

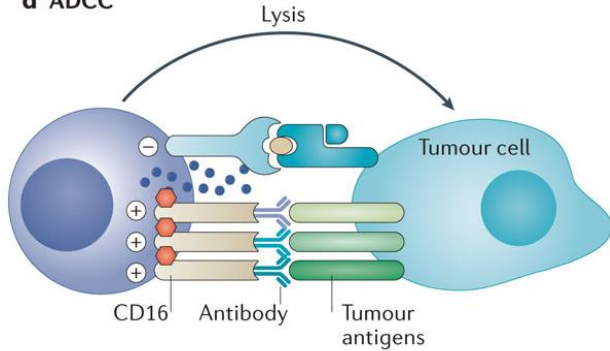
Réponse des cellules NK : ADCC

ADCC: Antibody-Dependent Cellular Cytotoxicity

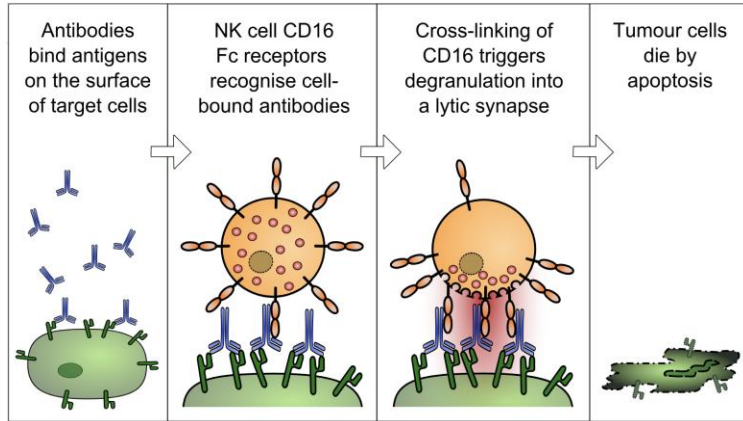


CD16= Récepteur Fc γ

d ADCC

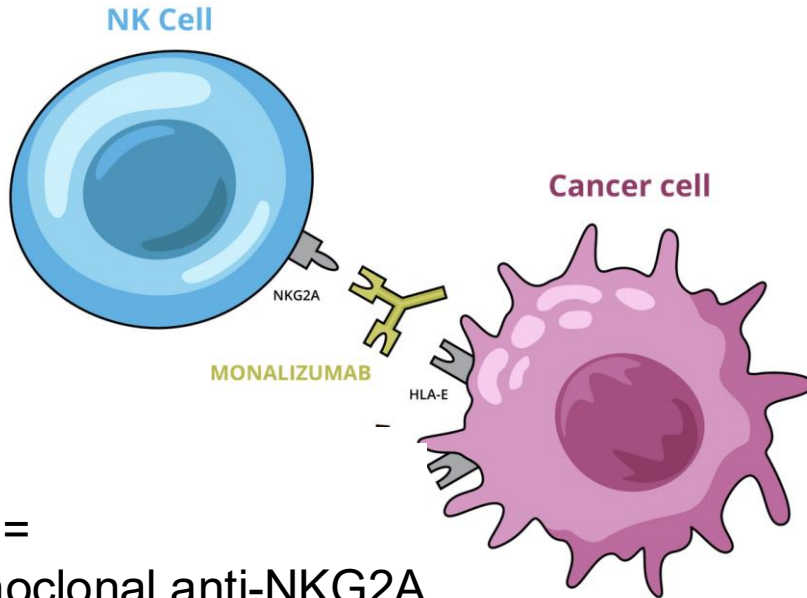


Nature Reviews | Cancer



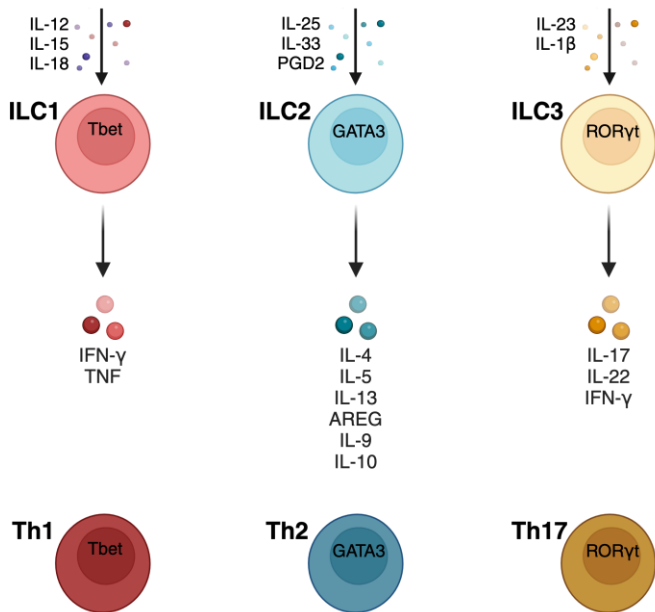
Intervention thérapeutique ciblant les cellules NK

Cibler les récepteurs inhibiteurs sur les cellules NK



Monalizumab =
anticorps monoclonal anti-NKG2A

Les ILC



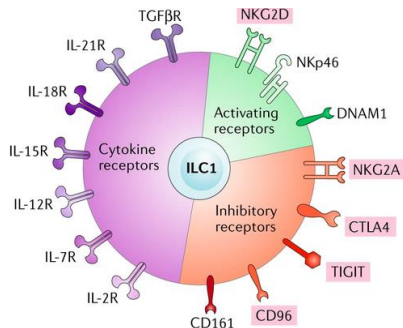
Principalement résidentes dans les tissus

Expriment le marqueur CD127 (IL7R-alpha)

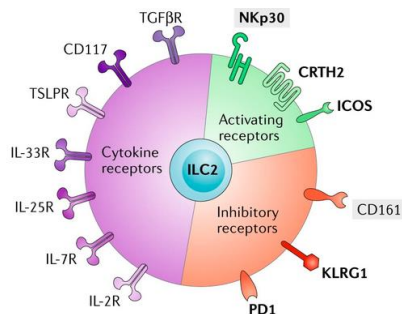
Reflètent les lymphocytes T CD4 auxiliaires

Sous-populations des cellules ILC et leurs récepteurs

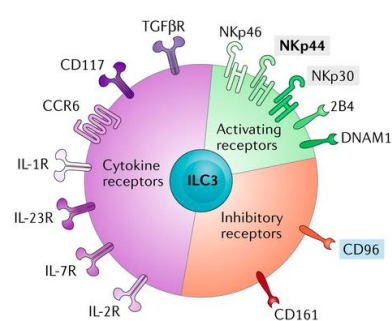
ILC1 (Tbet⁺)



ILC2 (GATA-3⁺)

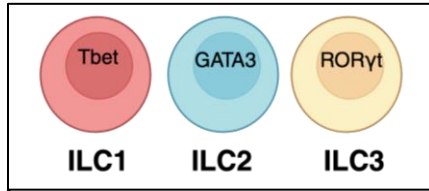


ILC3 (RORγt⁺)

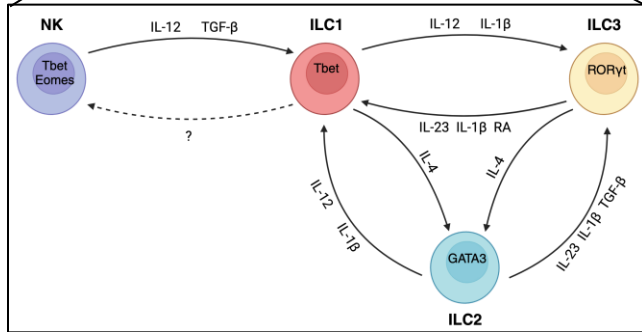


Sous-populations des ILC et leur plasticité

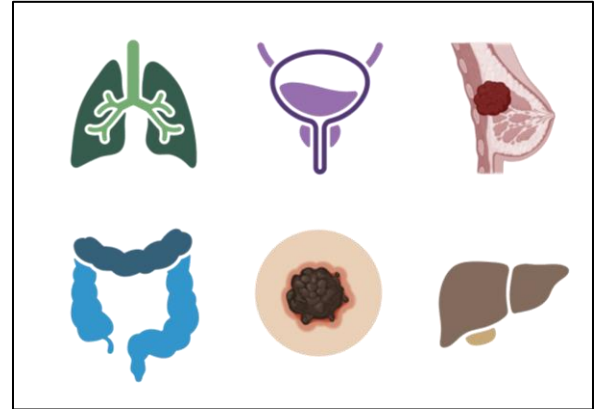
Sous-populations



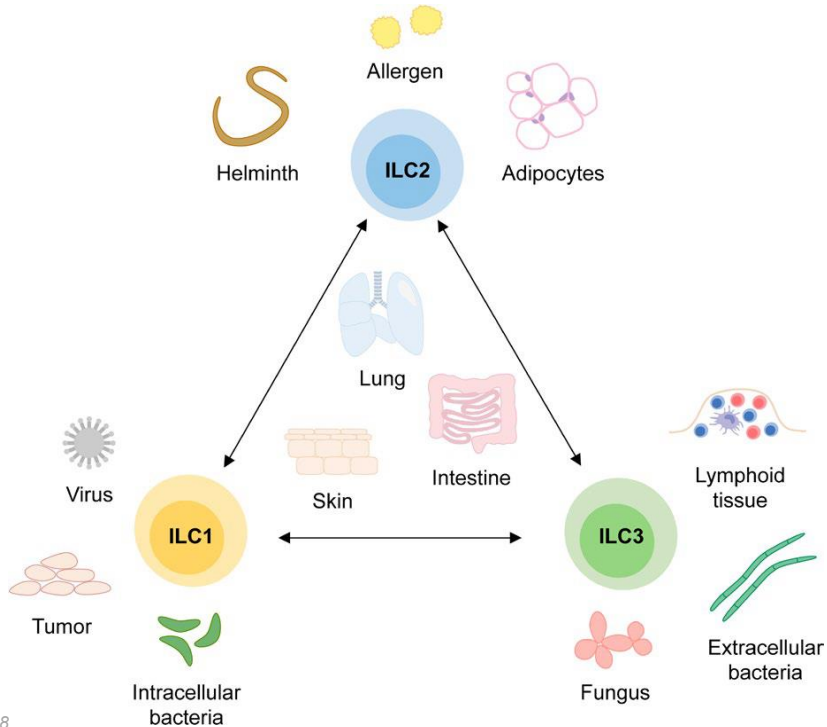
...and plasticity



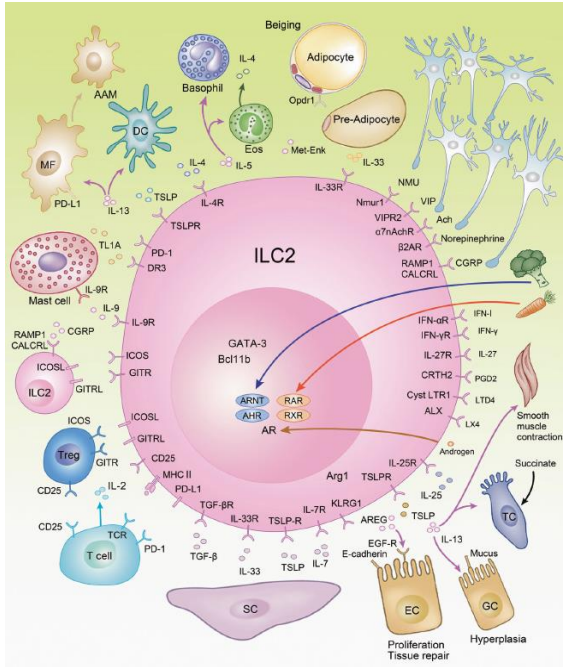
Organ



Les fonctions des ILC



Les fonctions des ILC2



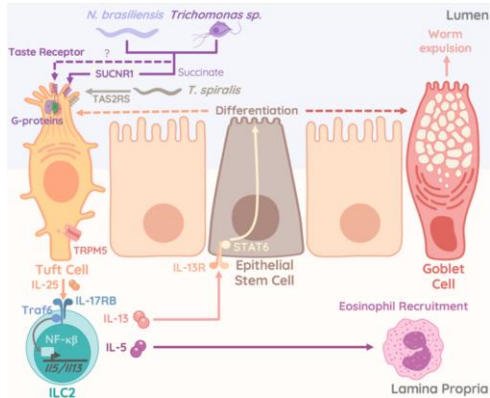
Detection de l'environnement:

- Alarmines (IL-33, IL-25, TSLP)
- Lipides
- Vitamines
- Facteurs d'origine neuronale
- Hormones
- Cytokines
- ...

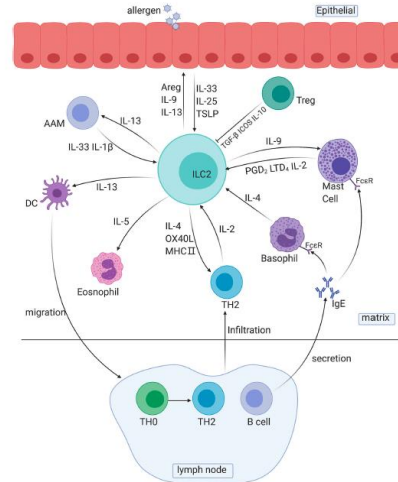
Les fonctions des ILC2

Physiologie:

Réponse anti-protozoaire:
Trichomonas, *N. brasiliensis*
Cellules en touffe, Cellules caliciformes,
eosinophiles



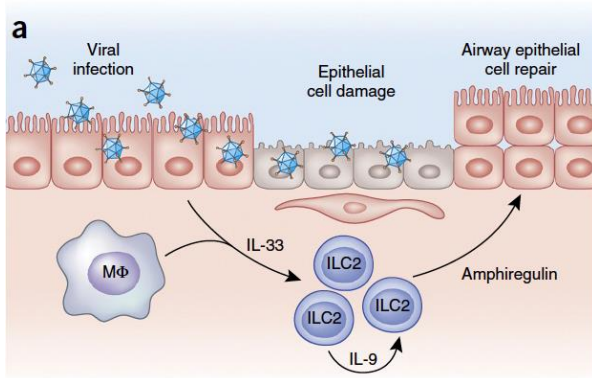
Réponse anti-allergénique:
Eosinophiles, macrophages M2,
Basophiles, Mastocytes, CD4 Th2



Les fonctions des ILC2

Physiologie:

Résolution de l'inflammation



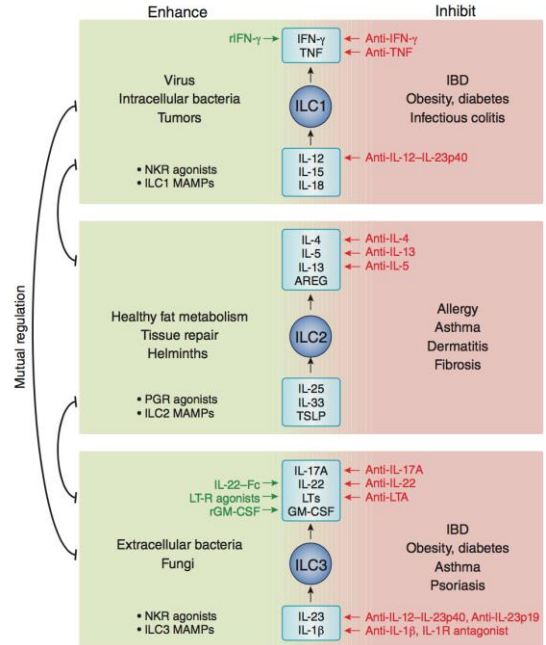
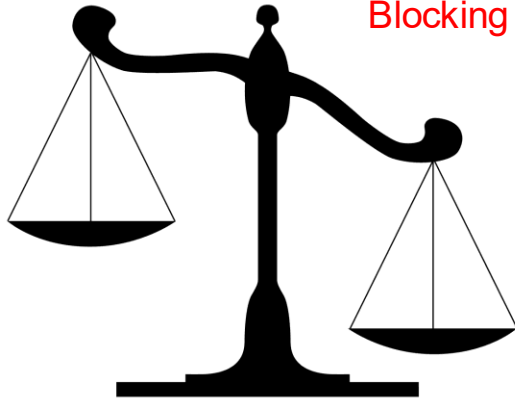
Pathologie:

Maladie atopique:
Dermatite atopique
Allergie
Asthme allergique

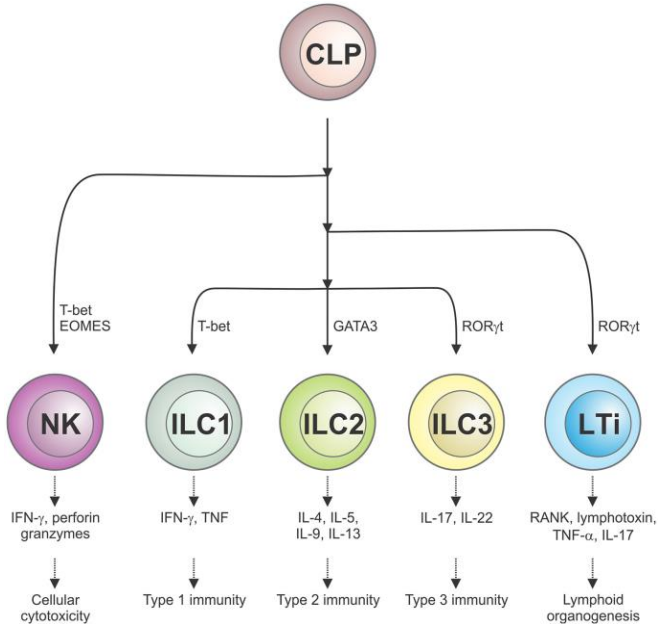
Fibrose

Intervention thérapeutique ciblant les ILC

Unleashing

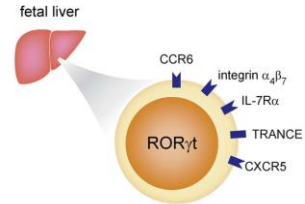


Lymphoid Tissue inducer cells (LTi)



LTi: un membre divergent de la famille des ILC

Essentiel à la formation des organes lymphoïdes secondaires tels que les ganglions lymphatiques et les plaques de Peyer



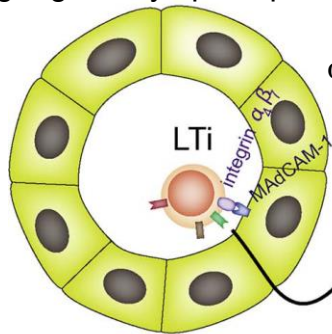
Absence de conversion vers les autres sous-populations de ILC

Les fonctions des LTI

Physiologie:

Formation des organes lymphoïdes secondaires

Ebauche de ganglions lymphatiques



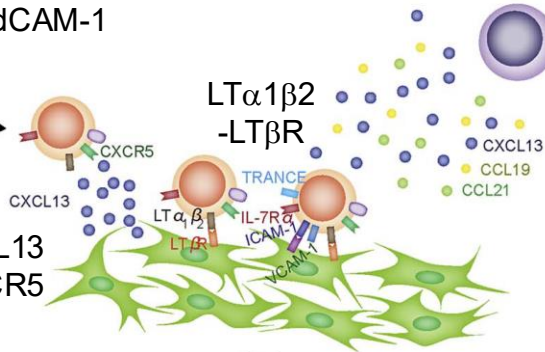
$\alpha_4\beta_7$ -MadCAM-1

HEV

High endothelial venules

$\alpha_4\beta_7$ -MadCAM-1

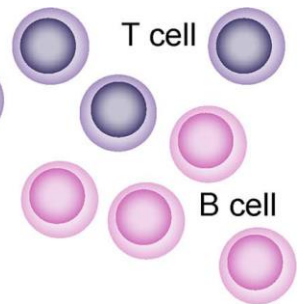
CXCL13
-CXCR5



$LT\alpha\beta$
- $LT\beta R$

LTo

Lymphoid tissue organizer =
cellules stromales spécialisées



T cell

B cell

Recrutement
d'autres lymphocytes

Les fonctions des LTI

Physiologie: Modulation de la réponse immunitaire adaptative

