

**Théo ACCOGLI**

**Directeurs: Dr Frédérique Végran**

**Pr François Ghiringhelli**

# **Identification des fonctions non-canoniques de NLRP3 dans les Th17 – Intérêts thérapeutiques pour promouvoir la réponse immunitaire anti- tumorale**

T. Accogli, C. Hibos, J. Melin, E. Humblin, R. Mary, A. Bernard, F. Chalmin, M. Bruchard, C. Richard, S. Macedo, L. Clerc, S. Chevrier, B. Ryffel, L. Apetoh, R. Boidot, F. Ghiringhelli, F. Vegran

**UMR1231 – Equipe CADIR**

**2017 - 2021**

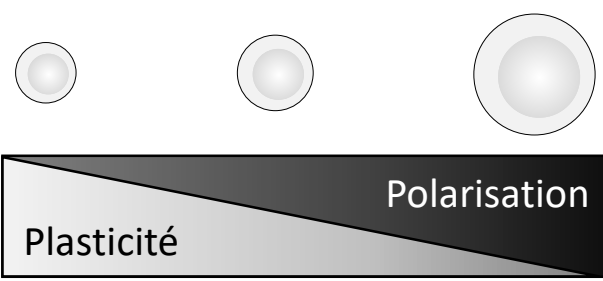
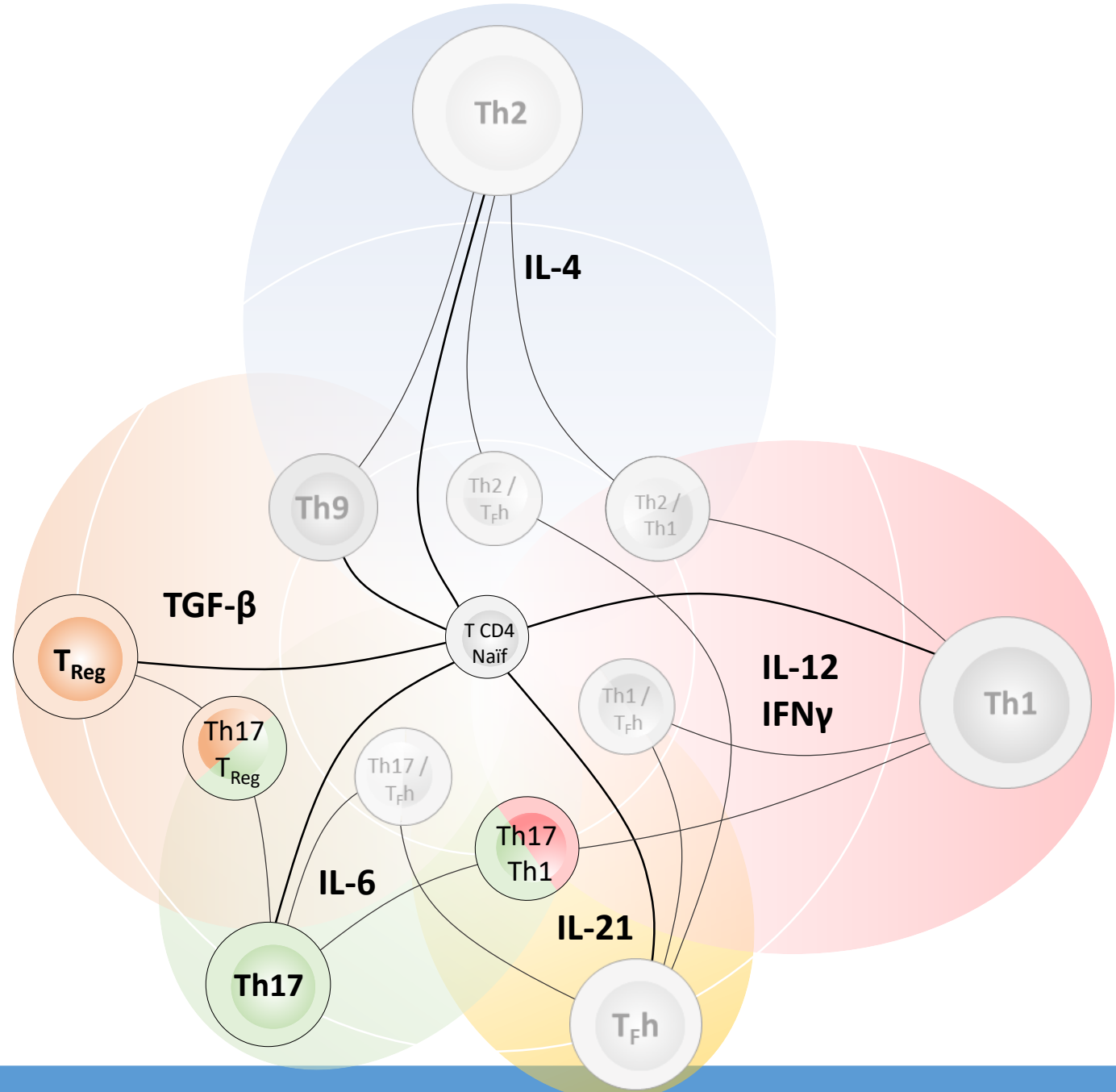


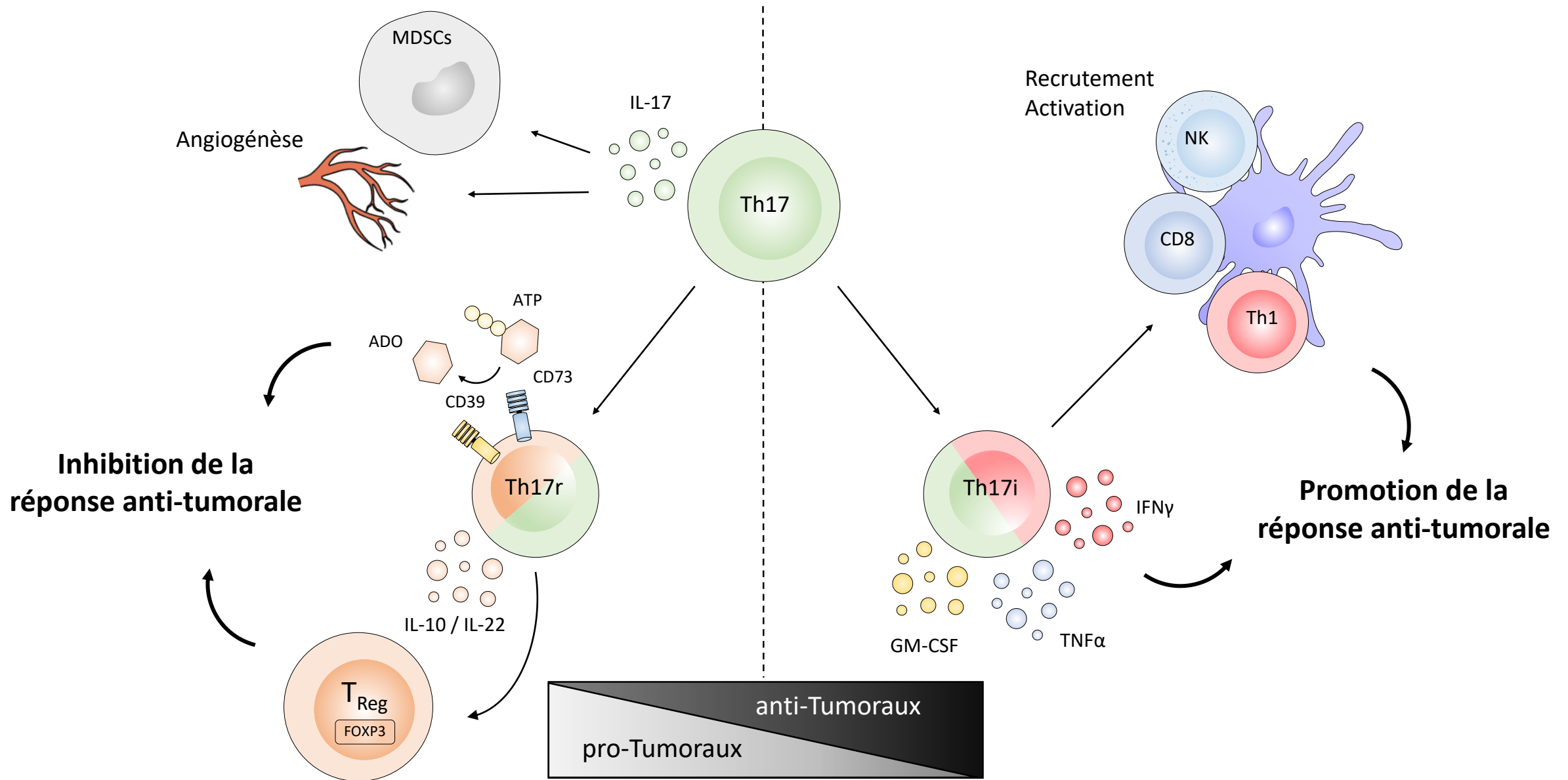
---

# Introduction

---

Partie 1: Les lymphocytes Th17 dans l'immunité anti-tumorale







---

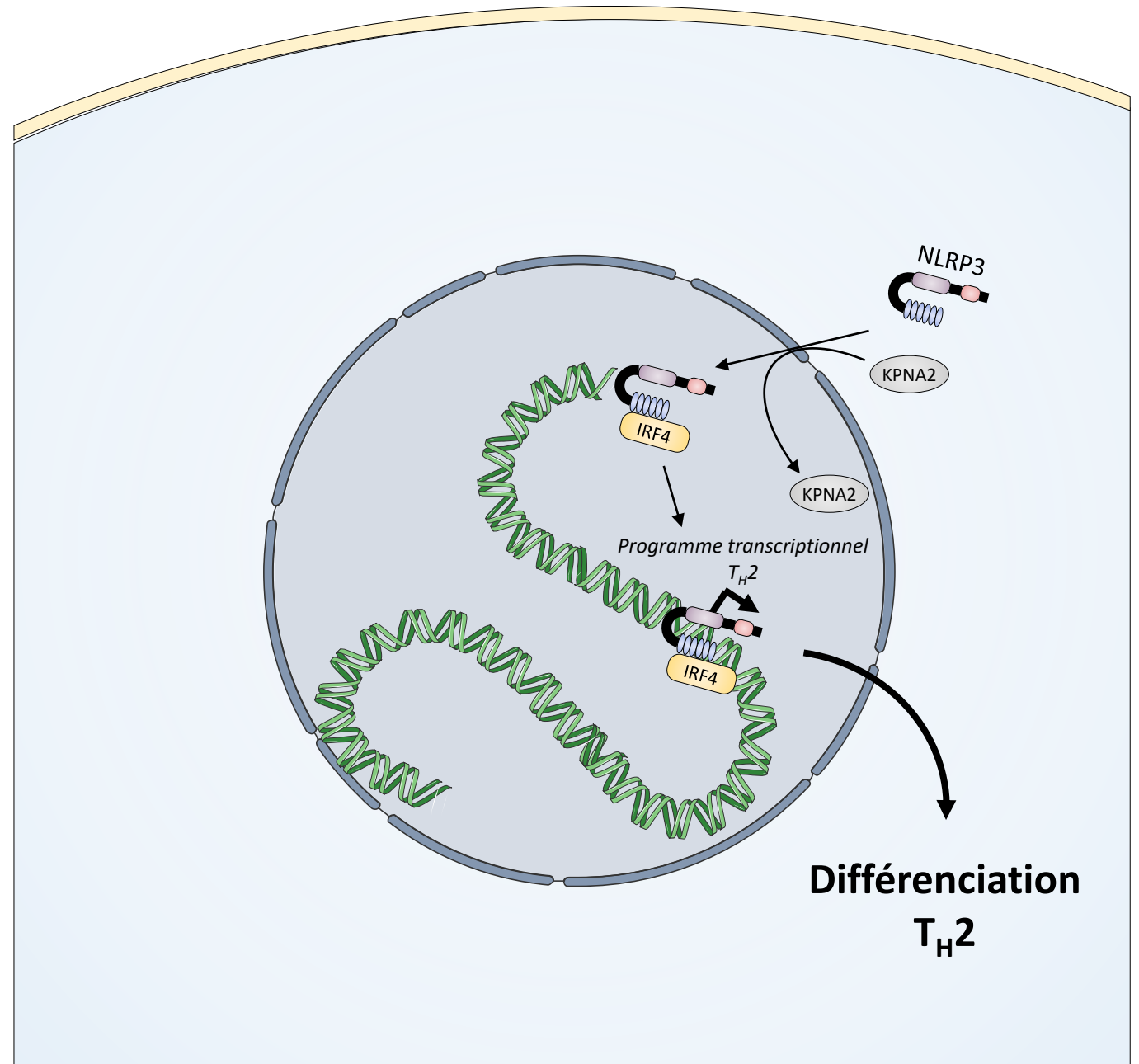
# Introduction

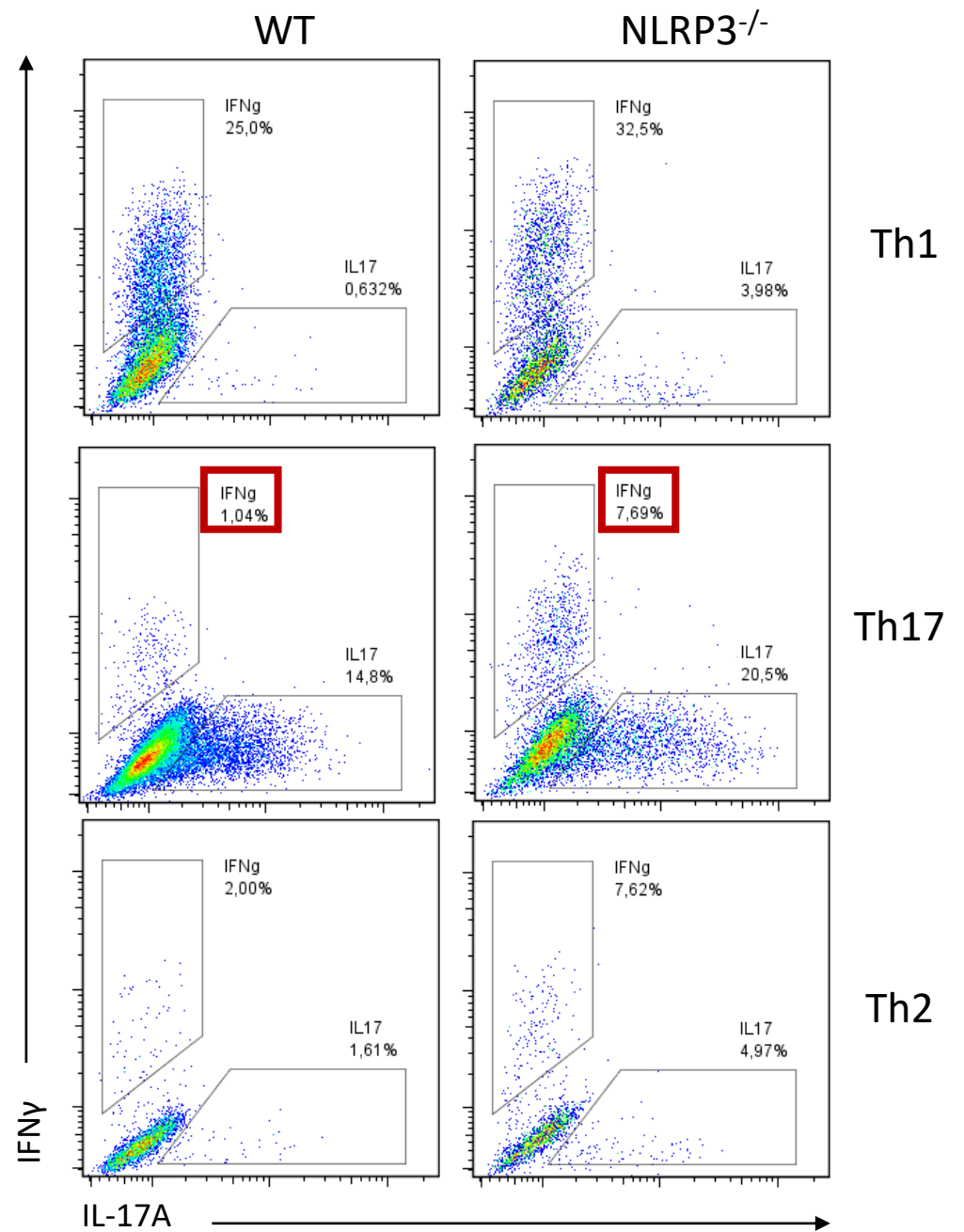
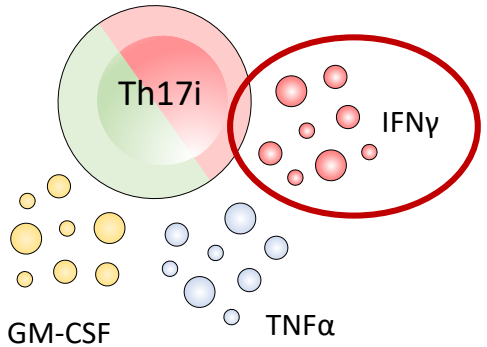
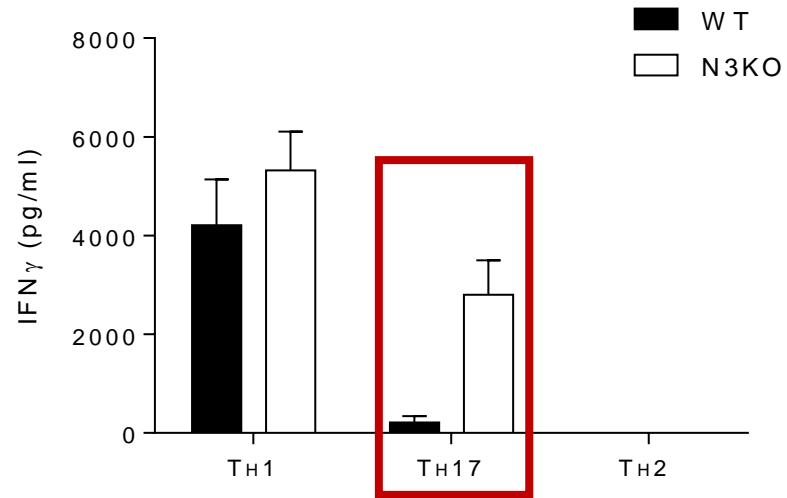
---

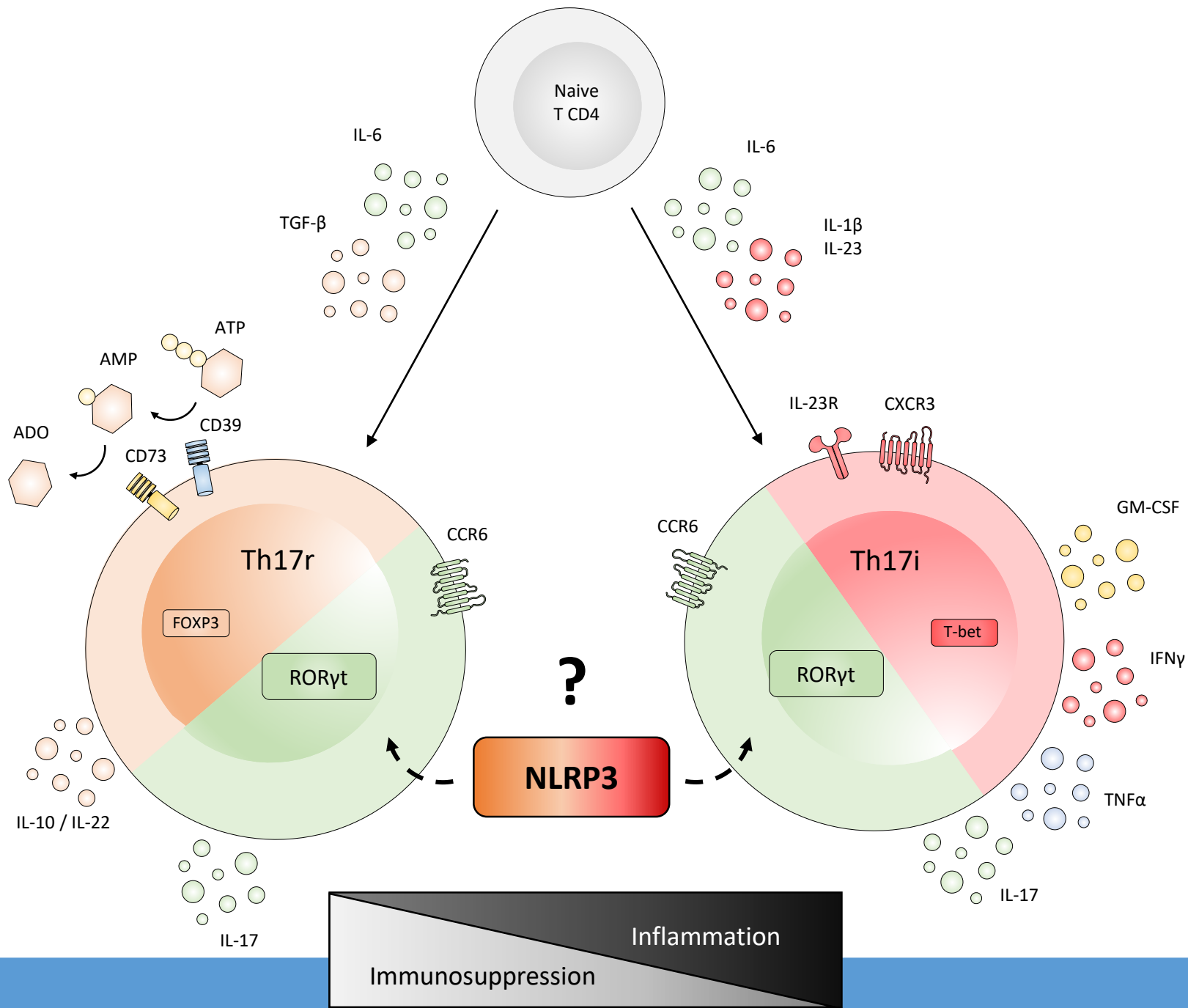
Partie 2: NLRP3, une protéine multifonctionnelle

M. Bruchard *et al.* The receptor NLRP3 is a transcriptional regulator of T<sub>H</sub>2 differentiation. *Nat Immunol* (2015)

- NLRP3: facteur de transcription dans les Th2
- Promeut leur différenciation







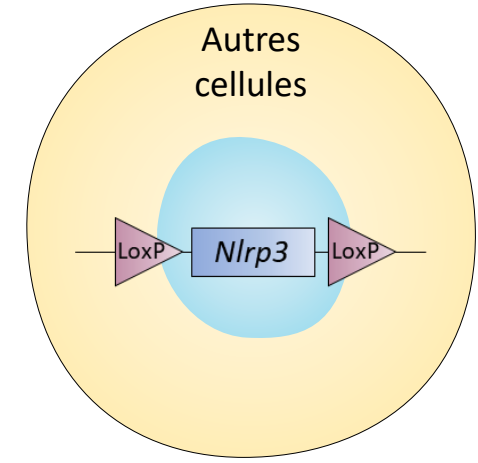
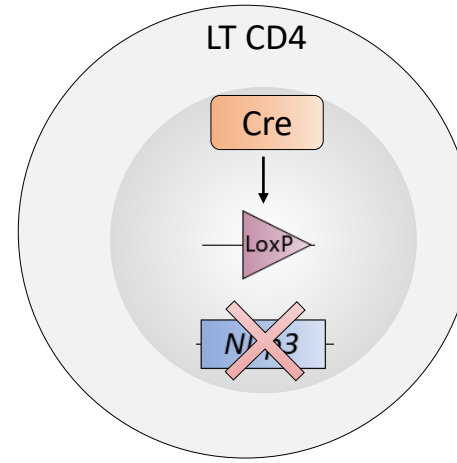
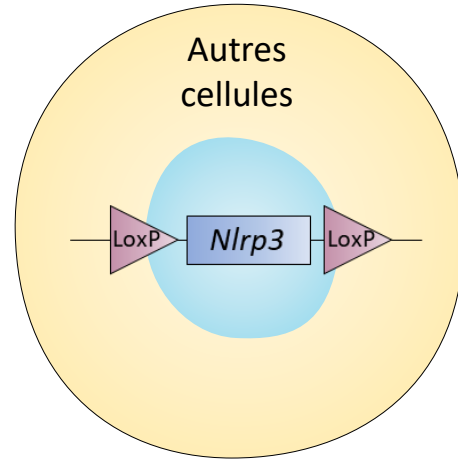
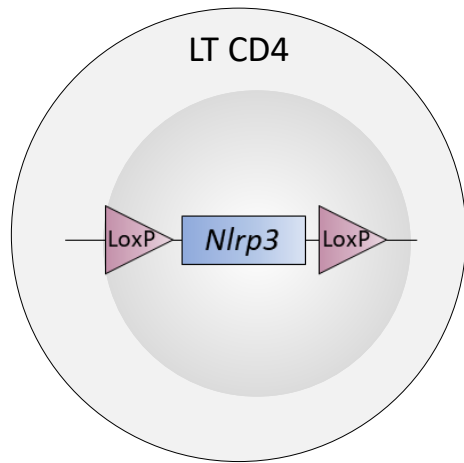
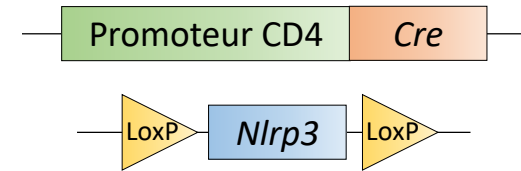
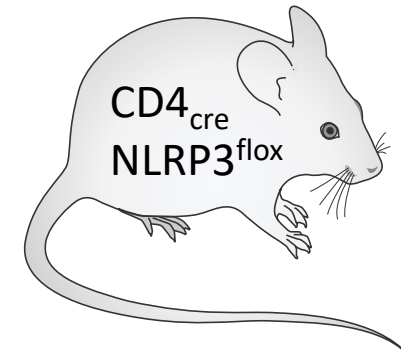
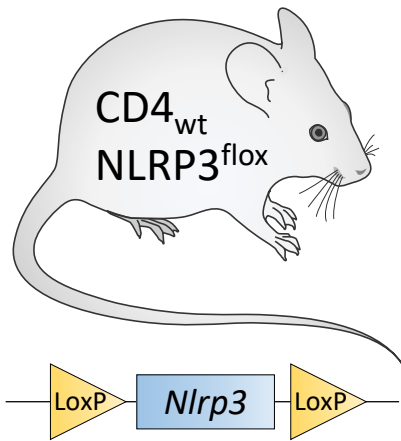


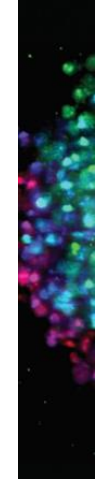


---

# Méthodologie

---



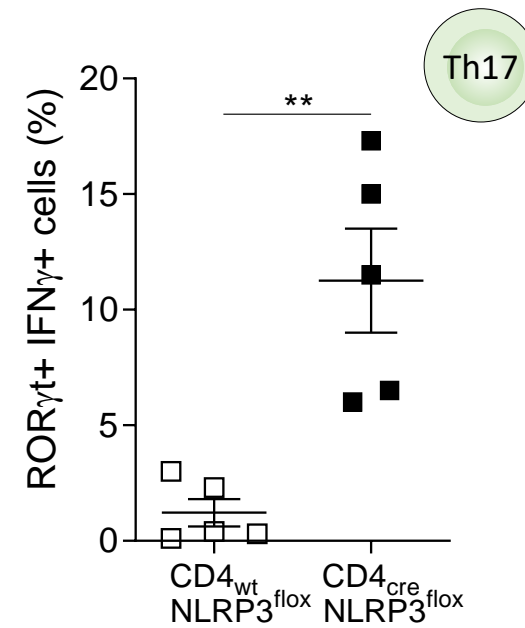
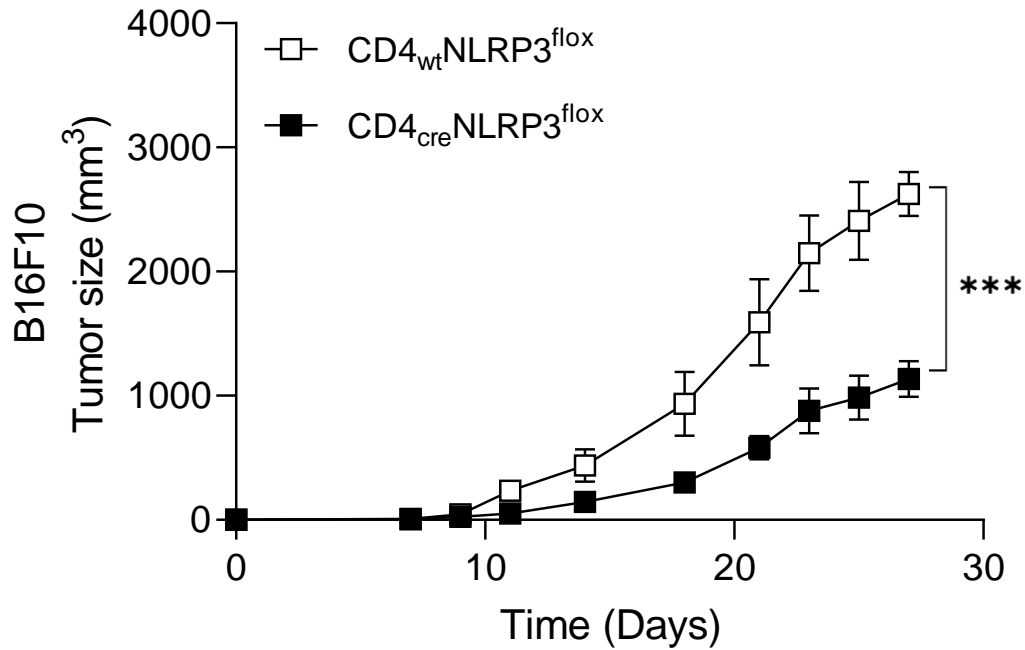
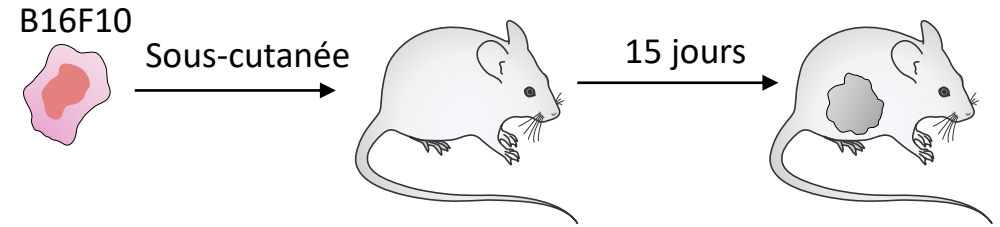


---

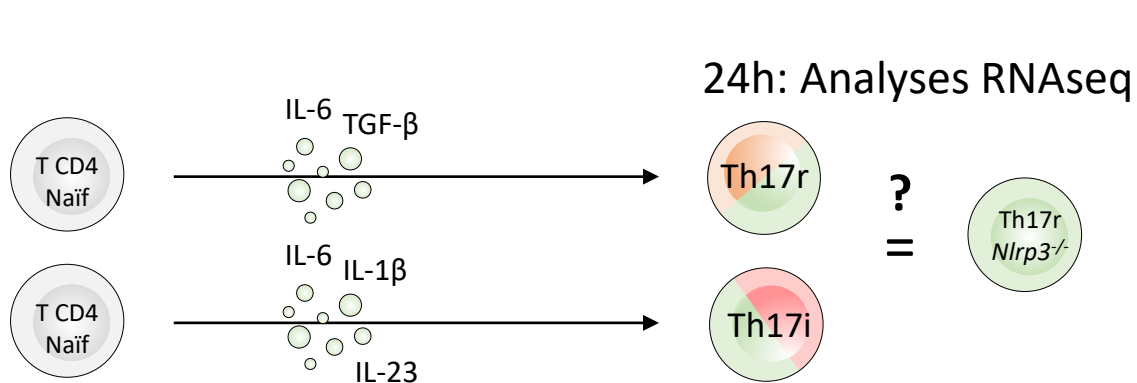
# Résultats

---

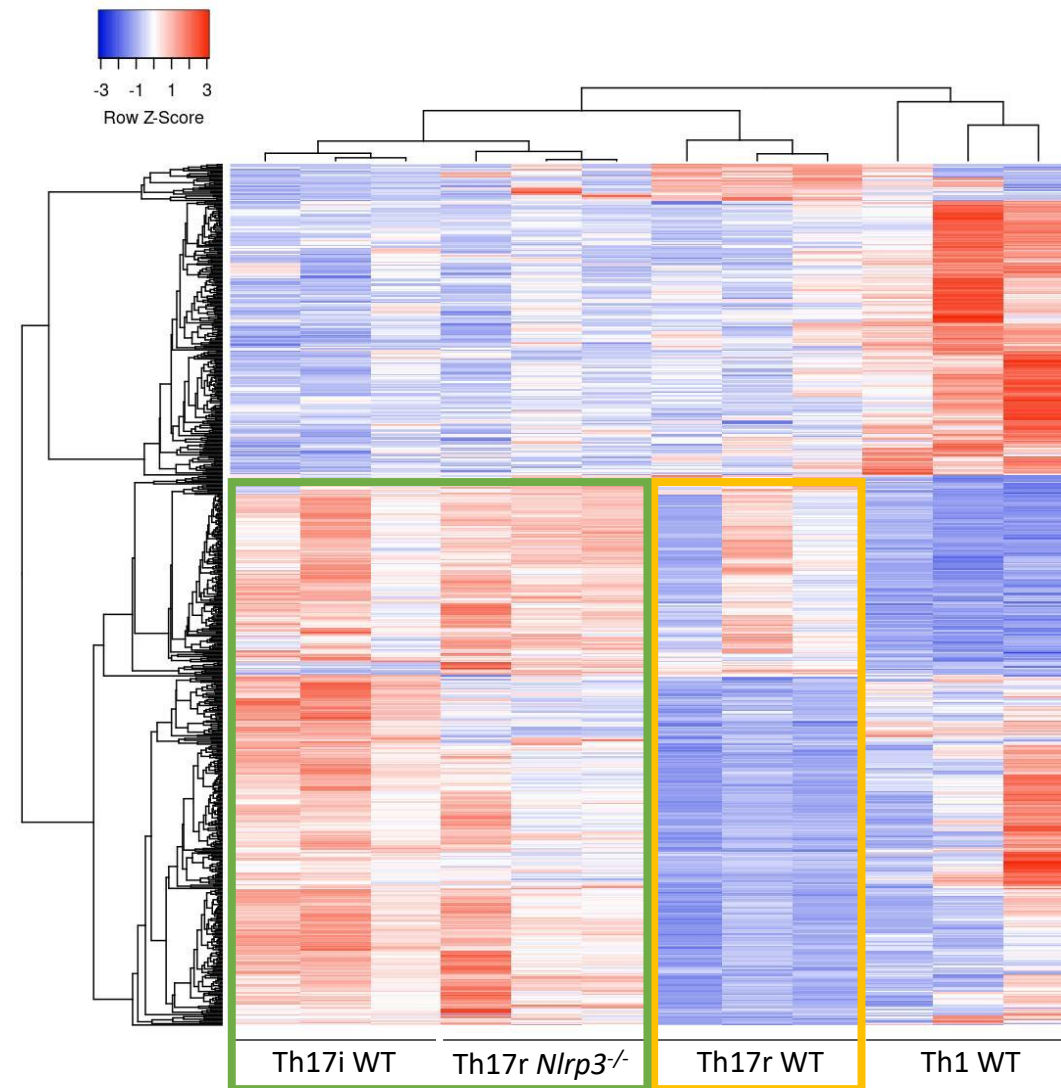
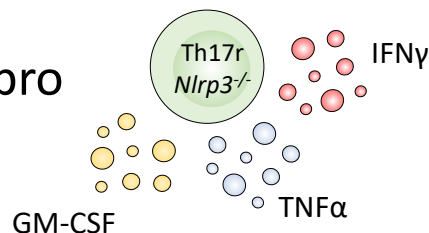
# Les Th17 TILs de souris $CD4_{cre} NLRP3^{flox}$ surexpriment l'IFN $\gamma$



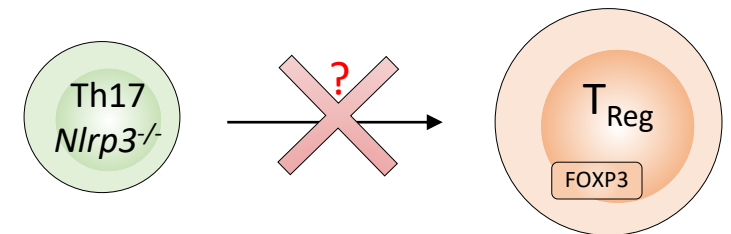
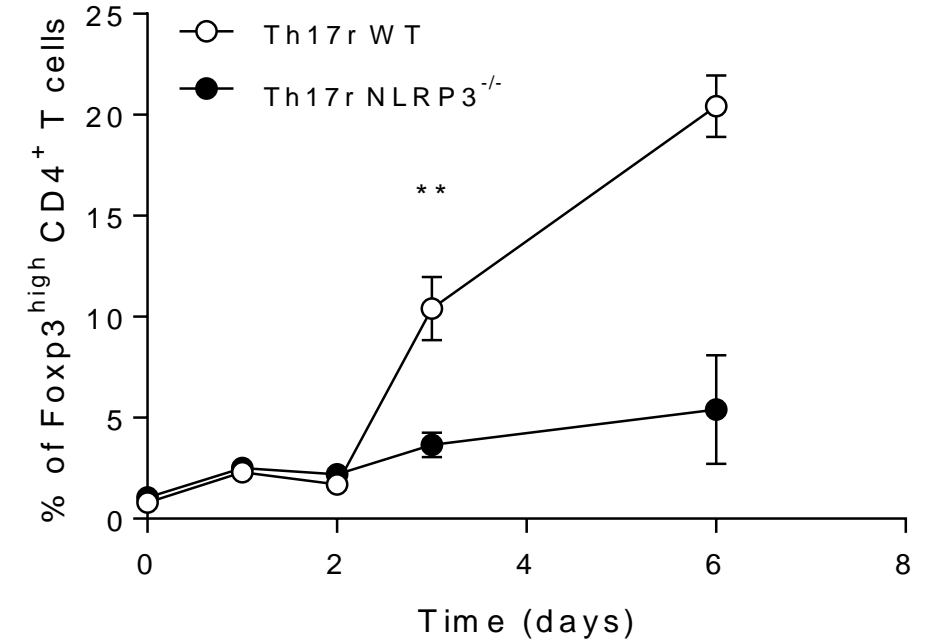
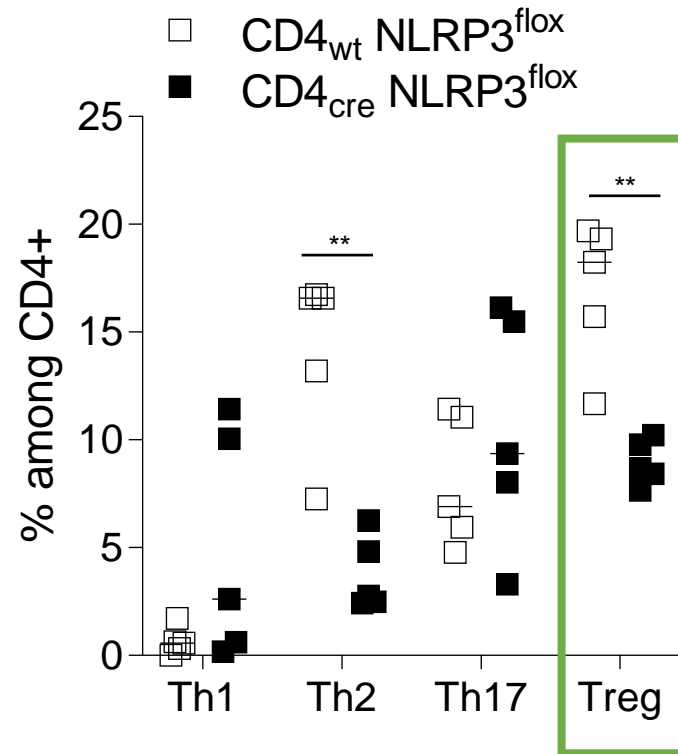
# Les Th17r *NLRP3*<sup>-/-</sup> surexpriment des gènes caractéristiques du profil Th17i



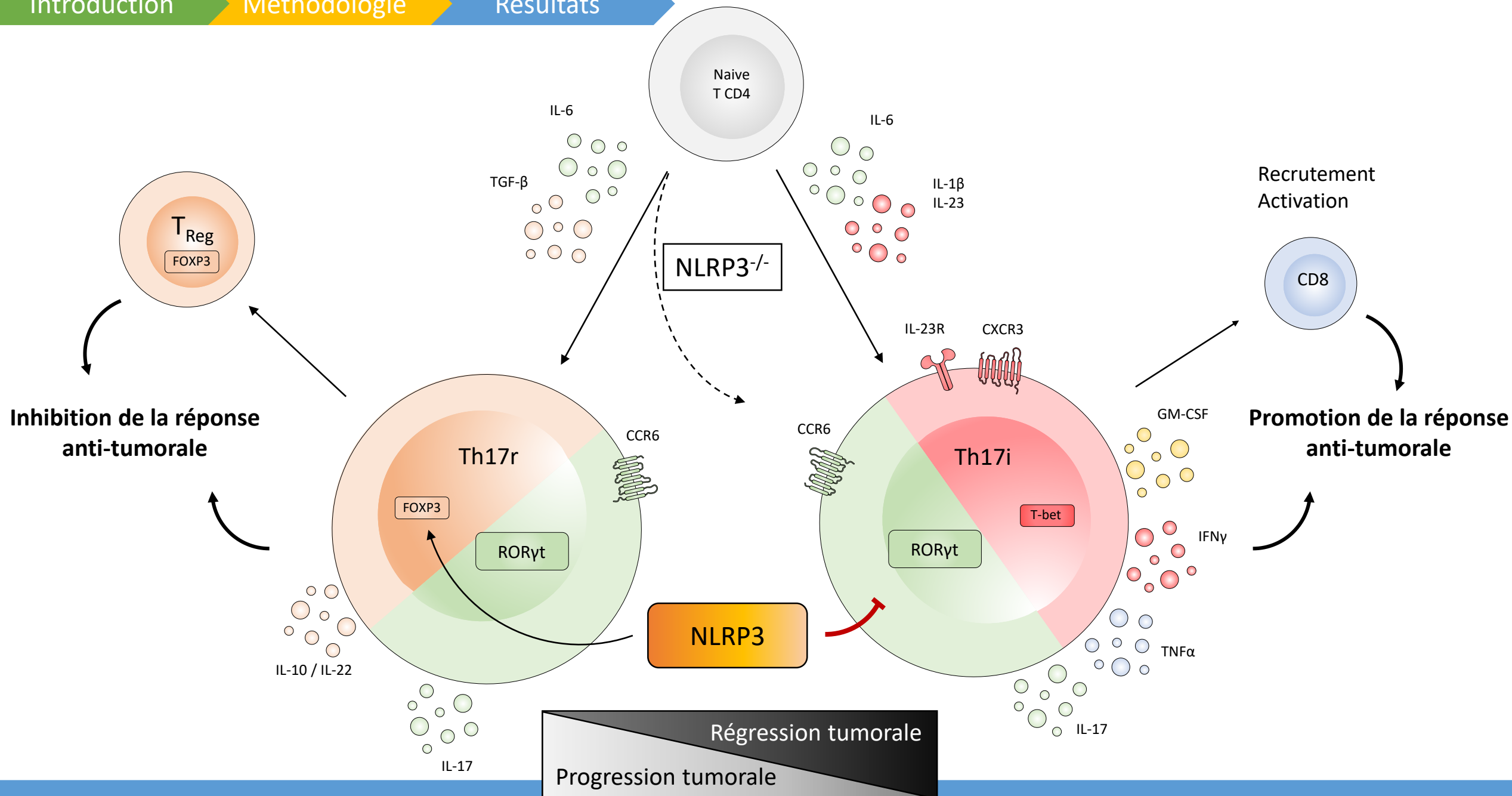
- Les Th17 *Nlrp3*<sup>-/-</sup> ont un profil transcriptionnel proche des Th17i
- Les Th17 *Nlrp3*<sup>-/-</sup> expriment des gènes caractéristiques du profil Th17i
- Traduit par l'expression de cytokines pro inflammatoires



Les Th17 *Nlrp3*<sup>-/-</sup> ne se transdiffèrent plus en T<sub>Reg</sub>

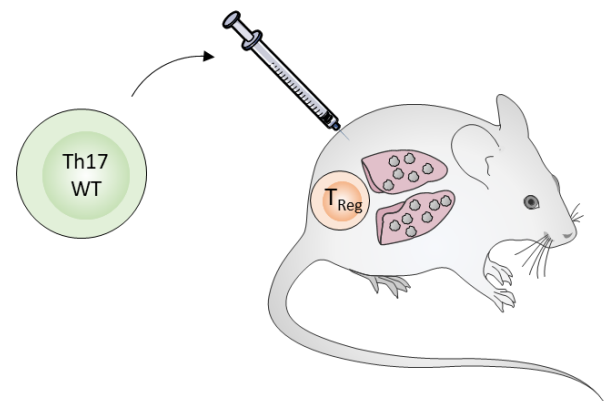


- Les T<sub>Reg</sub> ne sont pas impactés par la déficience en NLRP3
- La déficience en NLRP3 empêche les Th17 d'alimenter le pool de T<sub>Reg</sub>

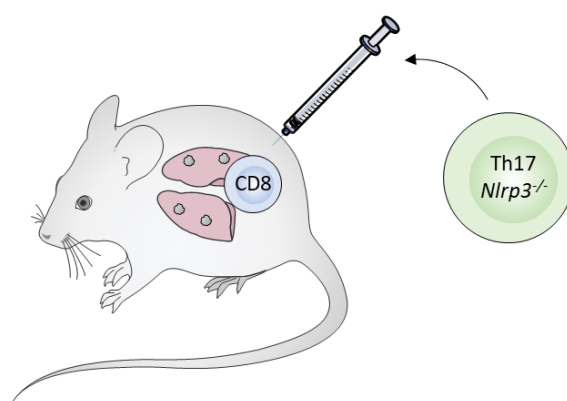


# Les Th17 *Nlrp3*<sup>-/-</sup> sont efficaces en thérapie cellulaire

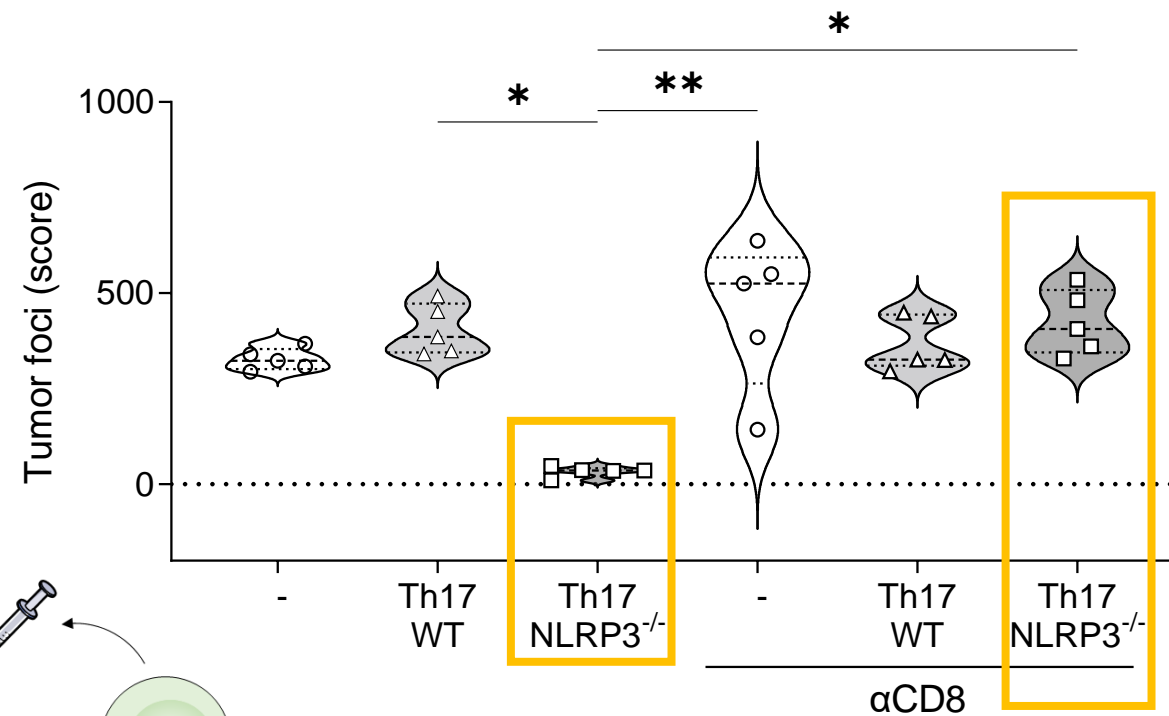
- Les Th17 *Nlrp3*<sup>-/-</sup> ont un effet anti-tumoral dépendant des LT CD8<sup>+</sup>



Pas d'effet sur la croissance tumorale



Diminution de la croissance tumorale



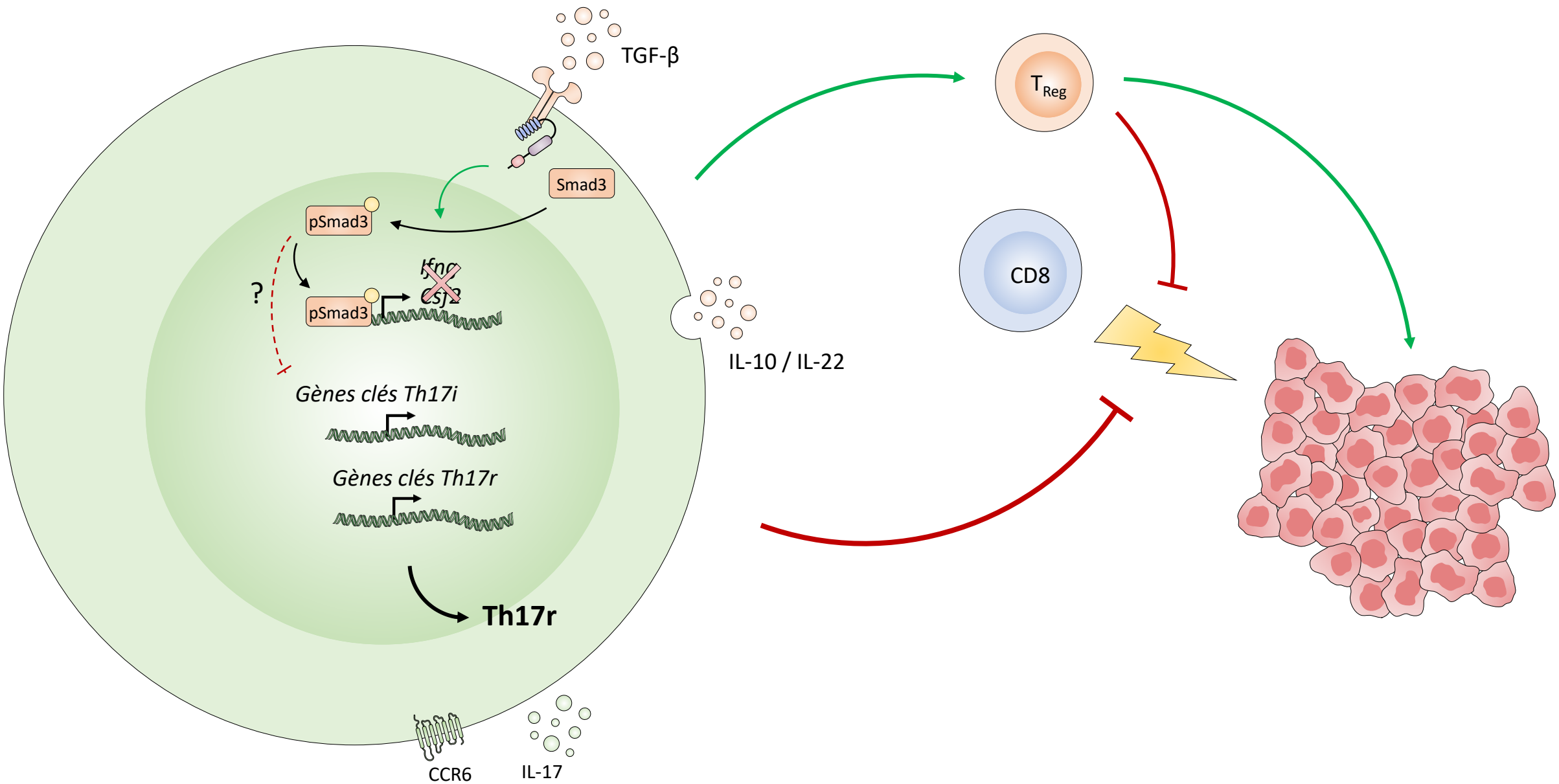


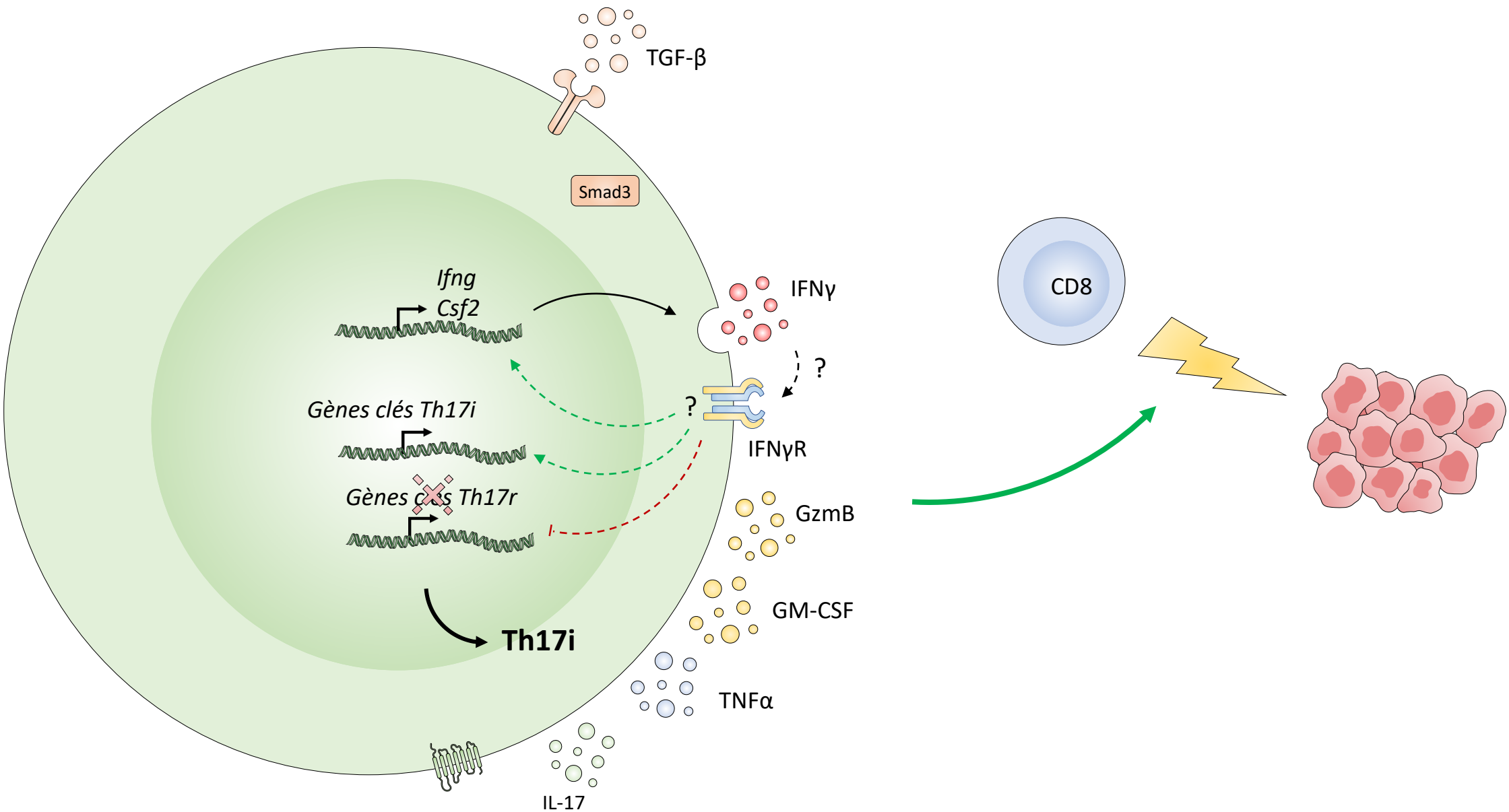


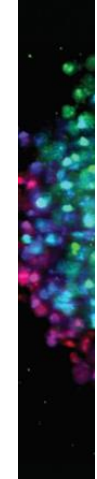
---

# Discussion

---







---

# Conclusion

---



NLRP3 inhibe le phénotype  
Th17i



NLRP3 est nécessaire pour la  
transdifférenciation  
Th17/T<sub>Reg</sub>



Les Th17 *Nlrp3*<sup>-/-</sup> favorisent  
la réponse anti-tumorale  
dépendante des LT CD8

# Remerciements

## Equipe CADIR

Pr. François Ghiringhelli

Dr. Frédérique Végran

Dr. Romain Boidot

Dr. Fanny Chalmin

Dr. Mélanie Bruchard

Dr. Etienne Humblin

Dr. Antoine Bernard

Dr. Romain Mary

Dr. Pierre Martine

Christophe Hibos

Joséphine Melin

Pierre Chaudron

Mannon Geindreau

Clarisse Cornebise



## Equipe CD4DNA

Dr. Lionel Apetoh

Dr. Alvaro Baeza Garcia

Dr. Elise Jacquin

Dr. Isis Benoît-Lison

Daria Vinokurova

A l'ensemble du 3<sup>ème</sup> étage de  
l'UFR SVTE et au laboratoire LNC



Dr. Anabelle Sequeira-Le Grand

Serge Monier

Nicolas Pernet

## Centre de Zootechnie de Dijon

Valérie Saint-Giorgio

## CNRS TAAM



I-SITE BFC

