



Théo ACCOGLI

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

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UMR1231 – Equipe CADIR

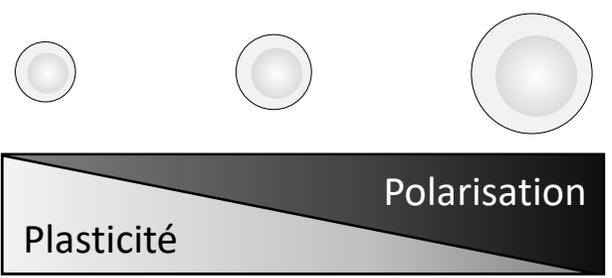
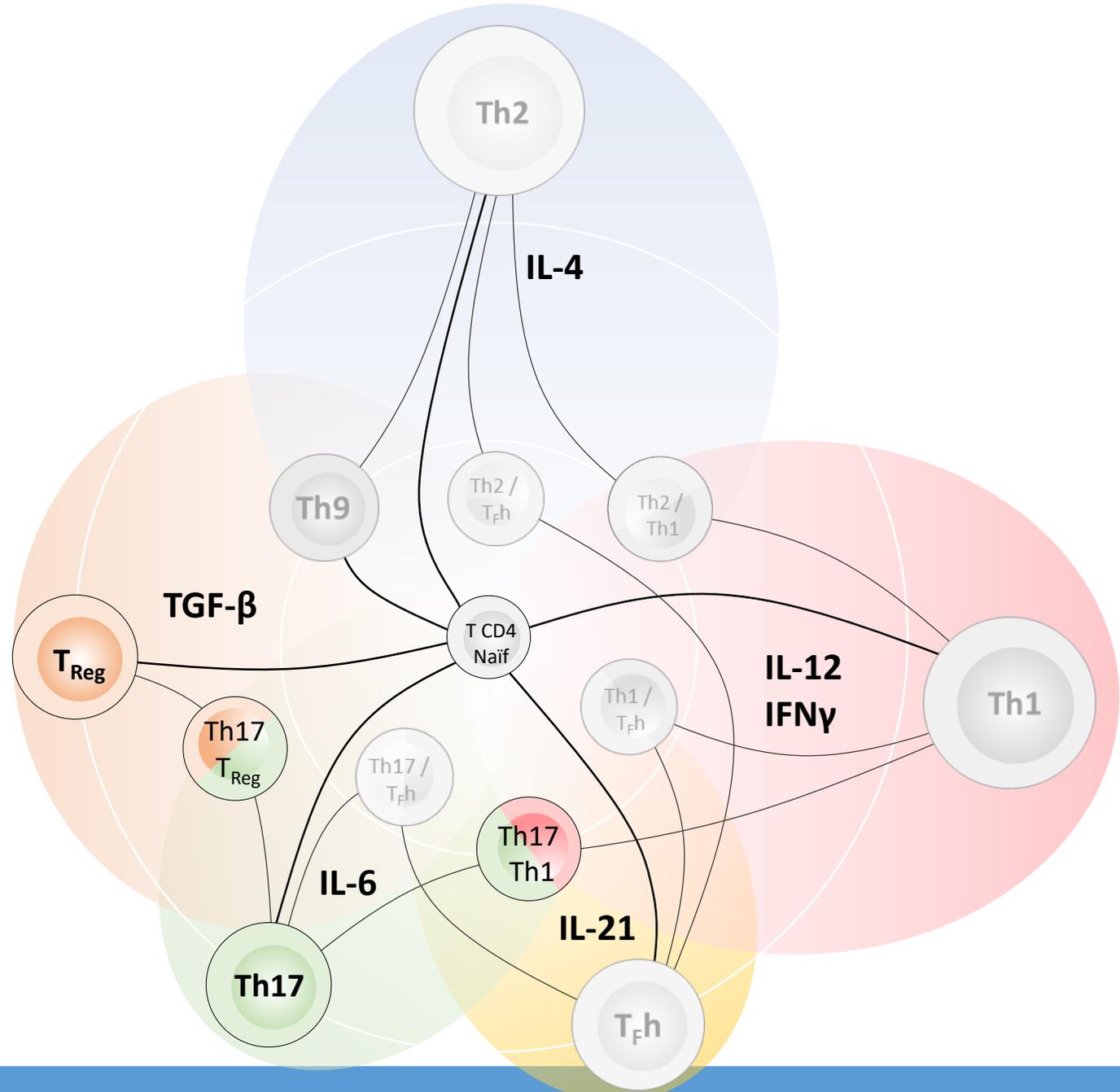
2017 - 2021

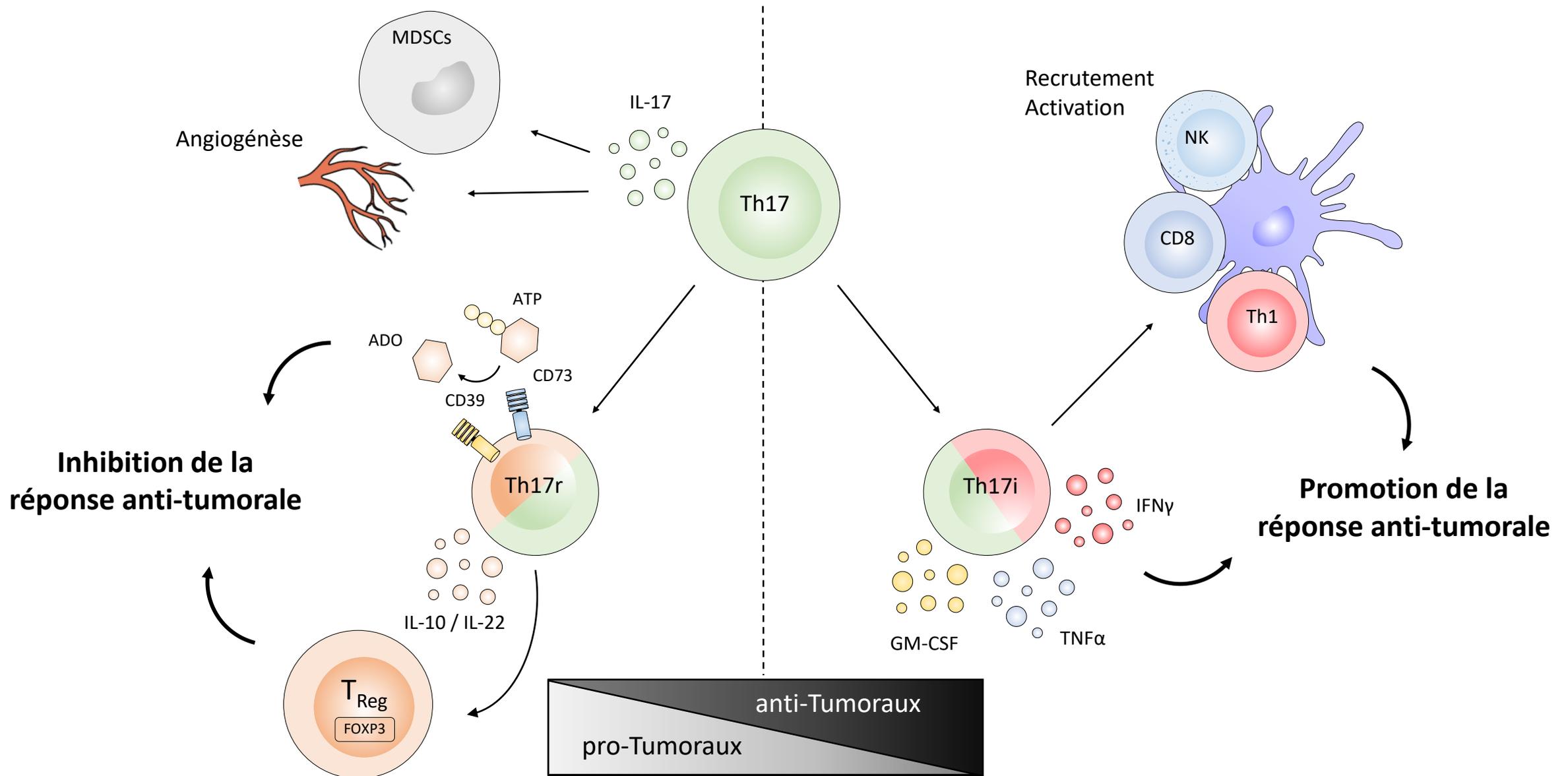




Introduction

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





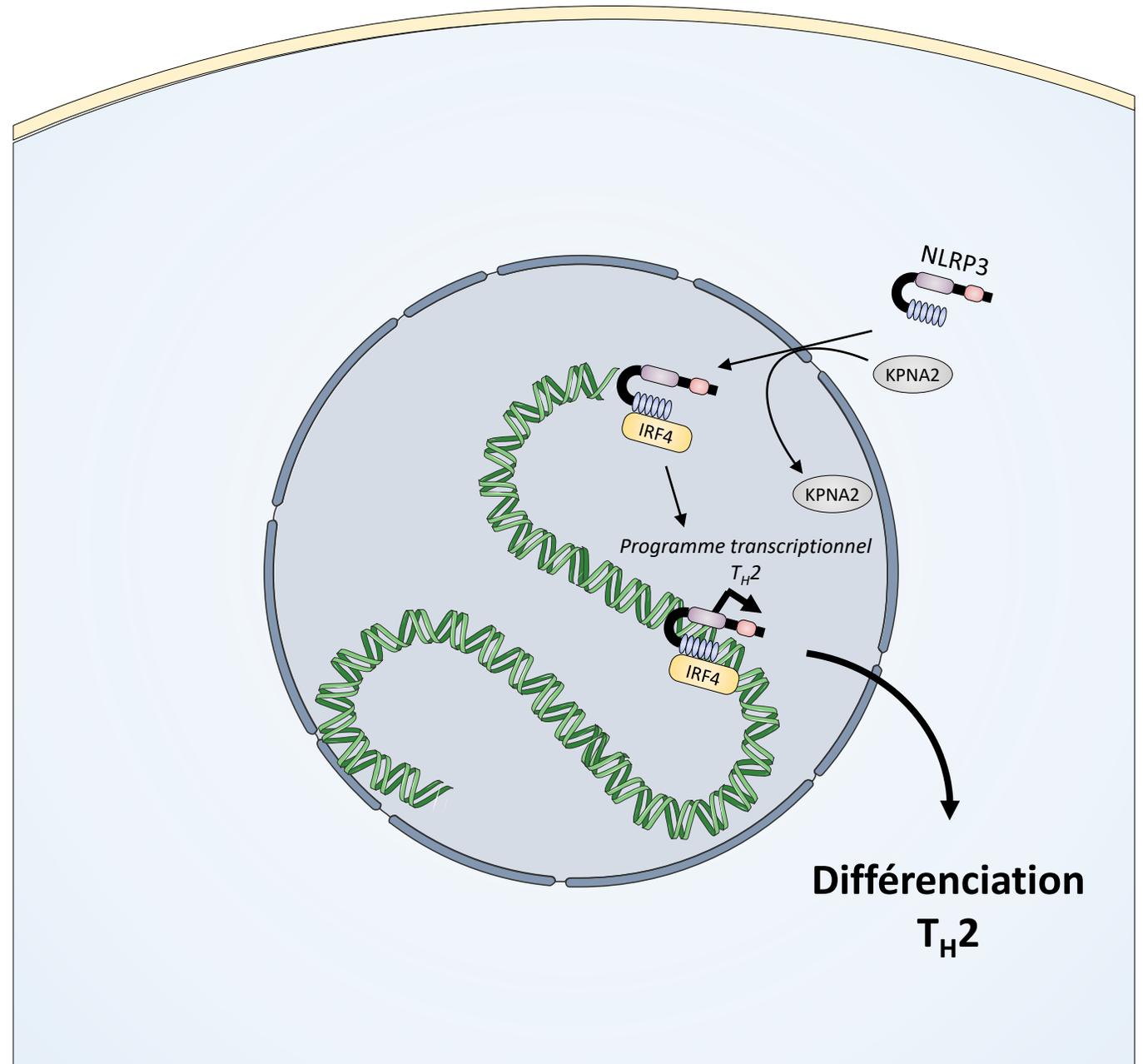


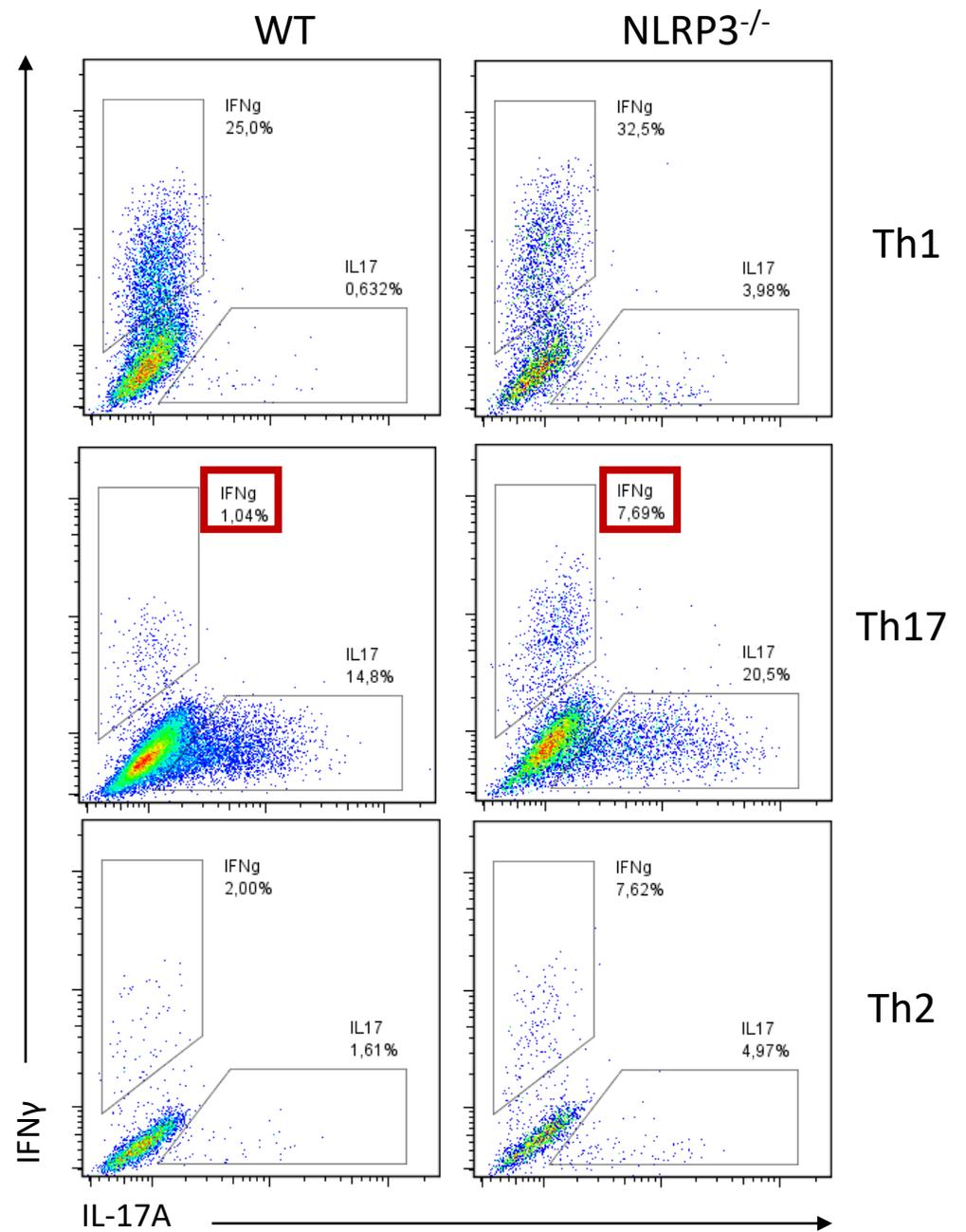
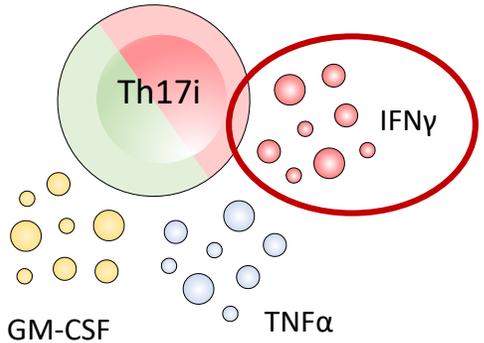
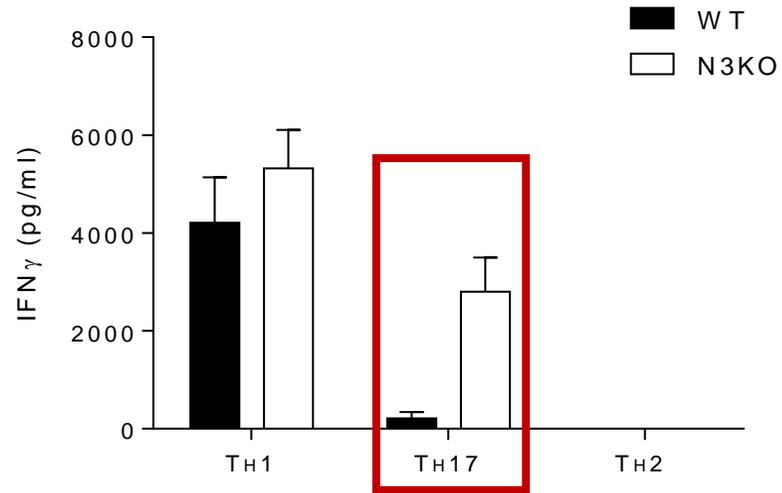
Introduction

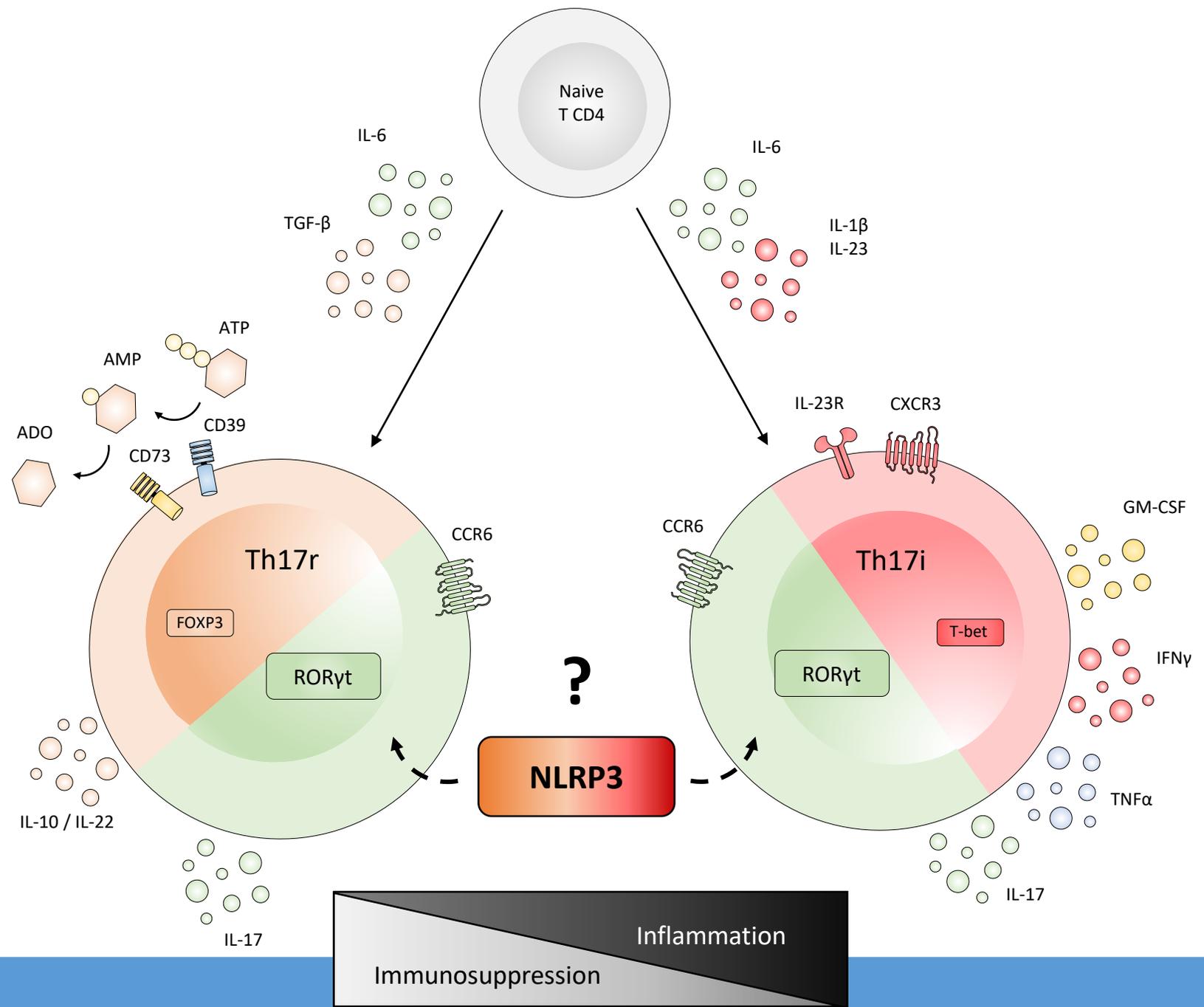
Partie 2: NLRP3, une protéine multifonctionnelle

M. Bruchard *et al.* The receptor NLRP3 is a transcriptional regulator of T_H2 differentiation. *Nat Immunol* (2015)

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

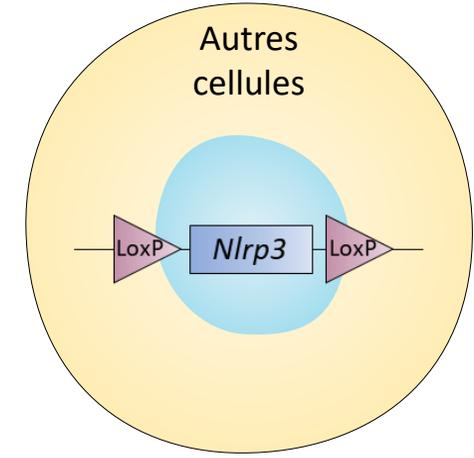
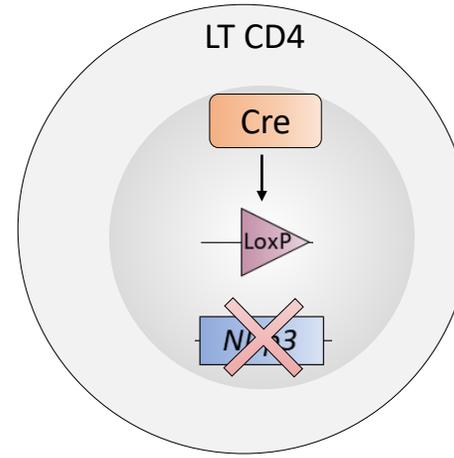
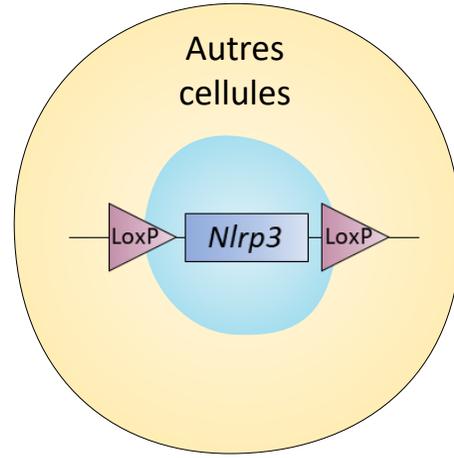
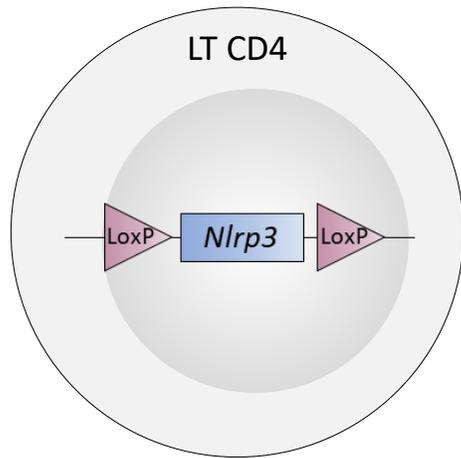
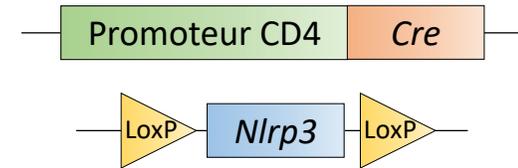
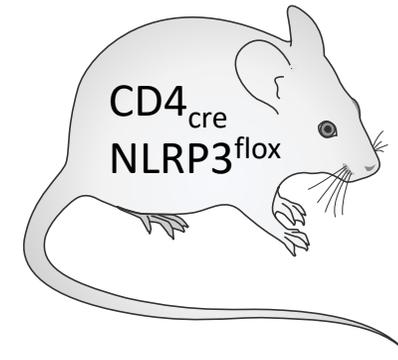
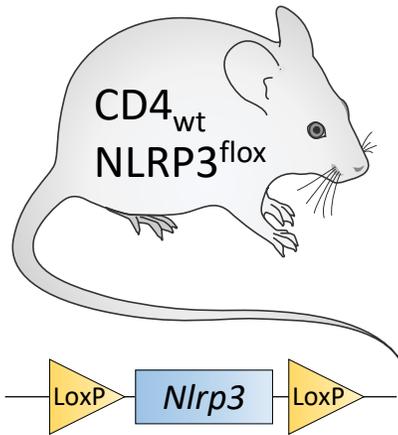








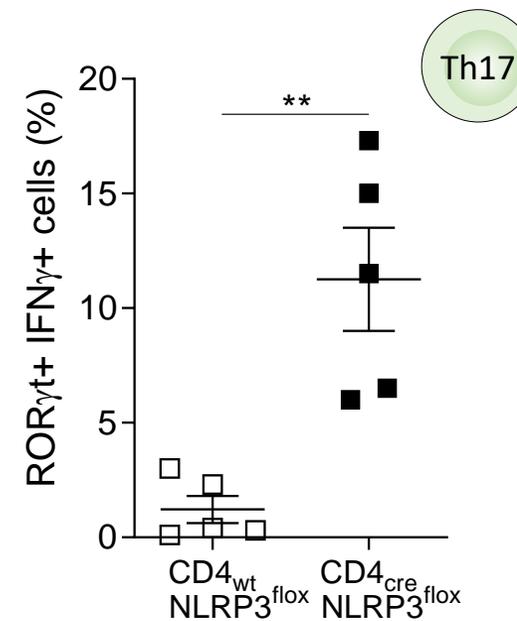
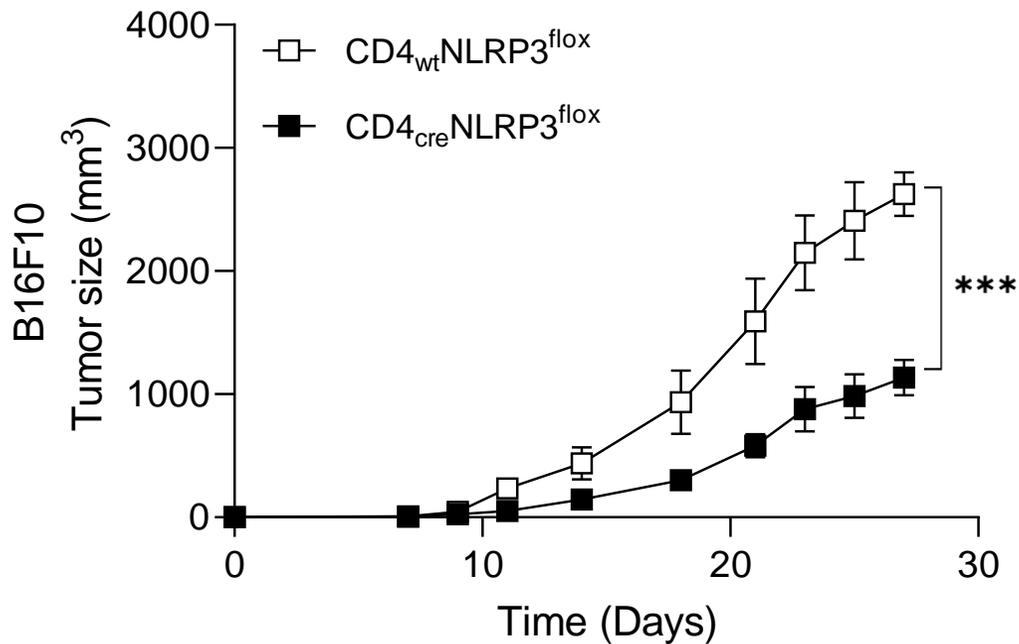
Méthodologie



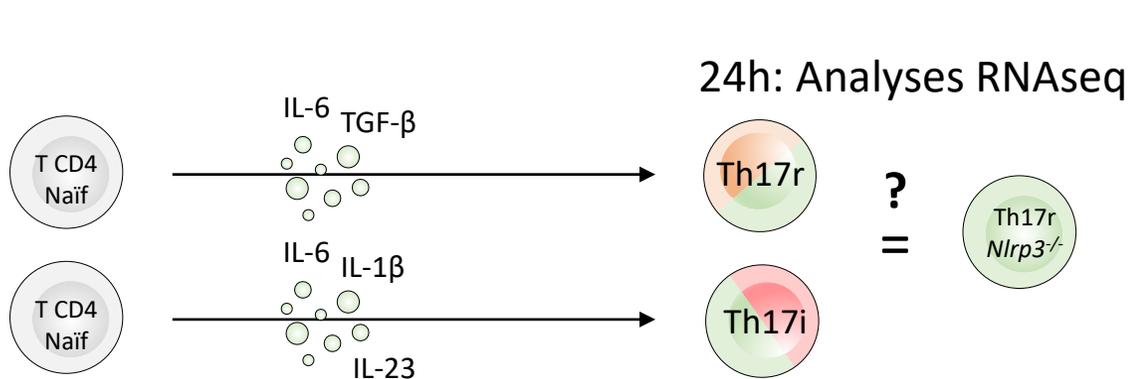


Résultats

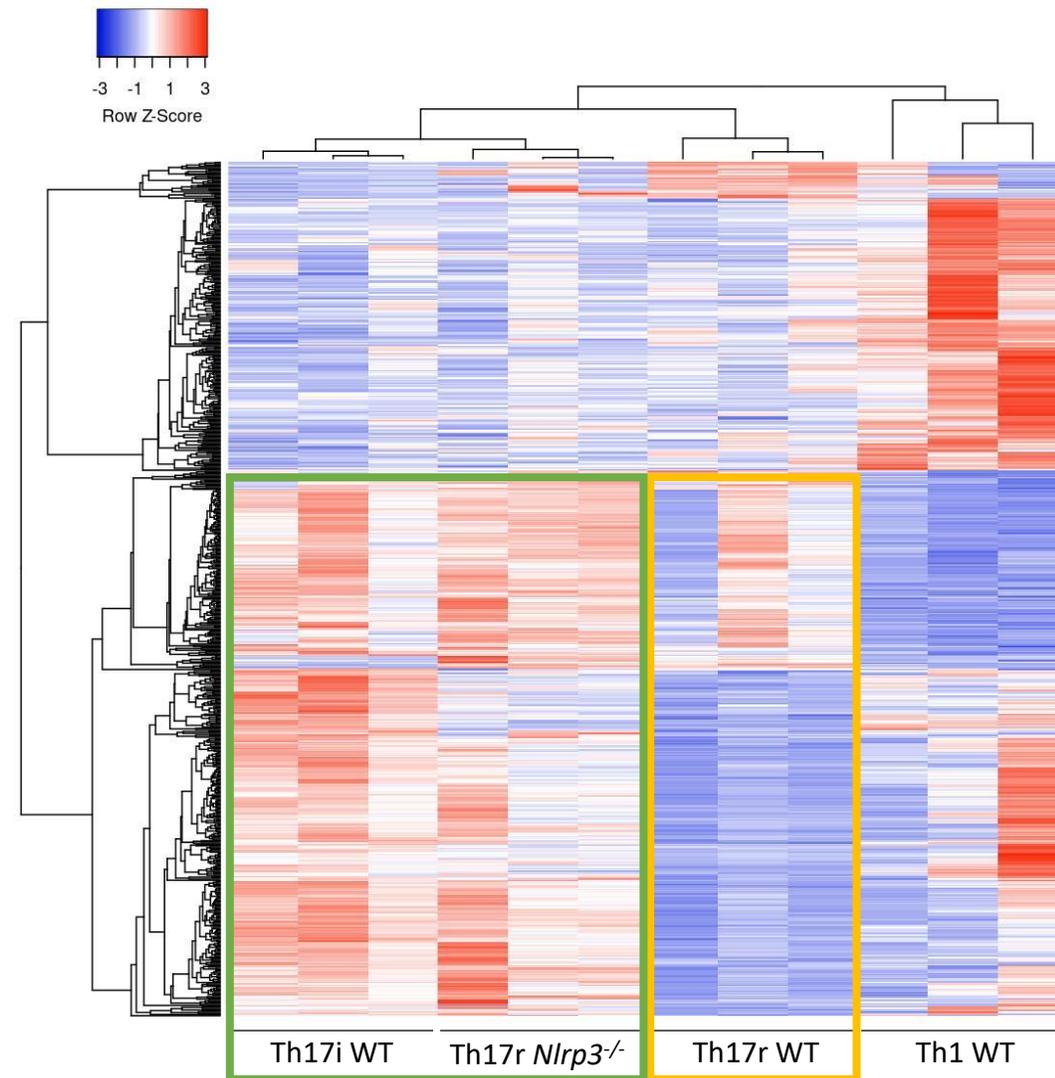
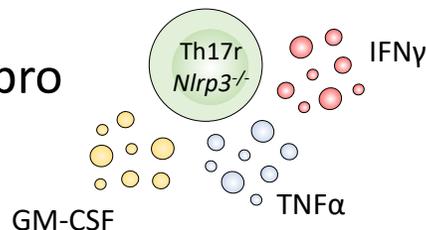
Les Th17 TILs de souris $CD4_{cre} NLRP3^{flox}$ surexpriment l'IFN γ



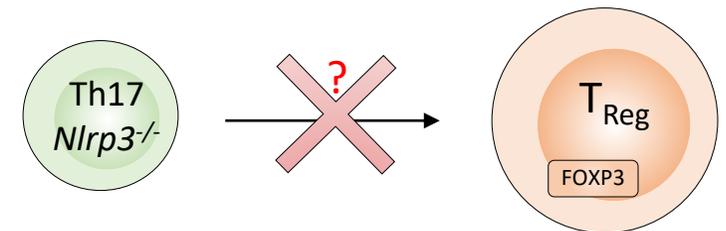
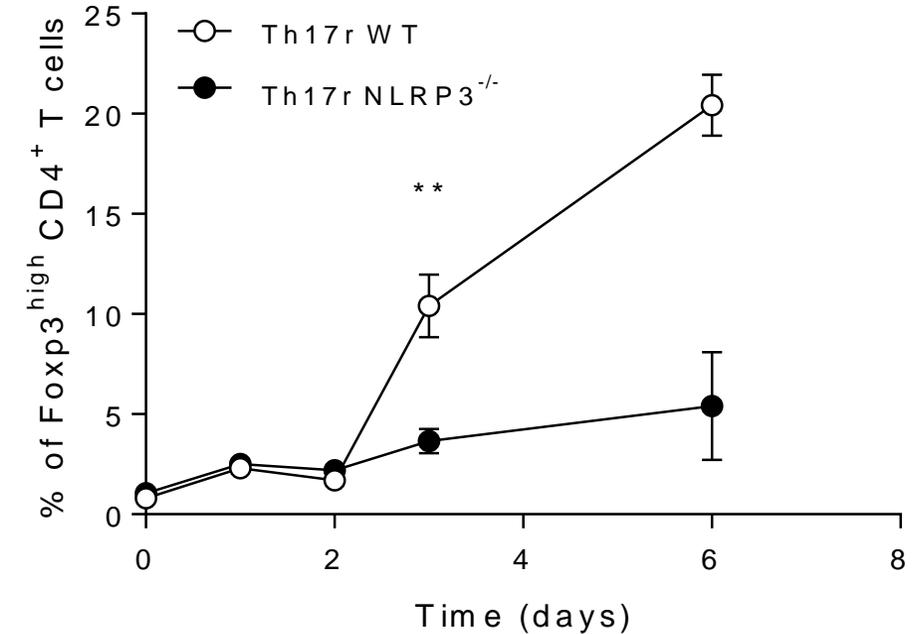
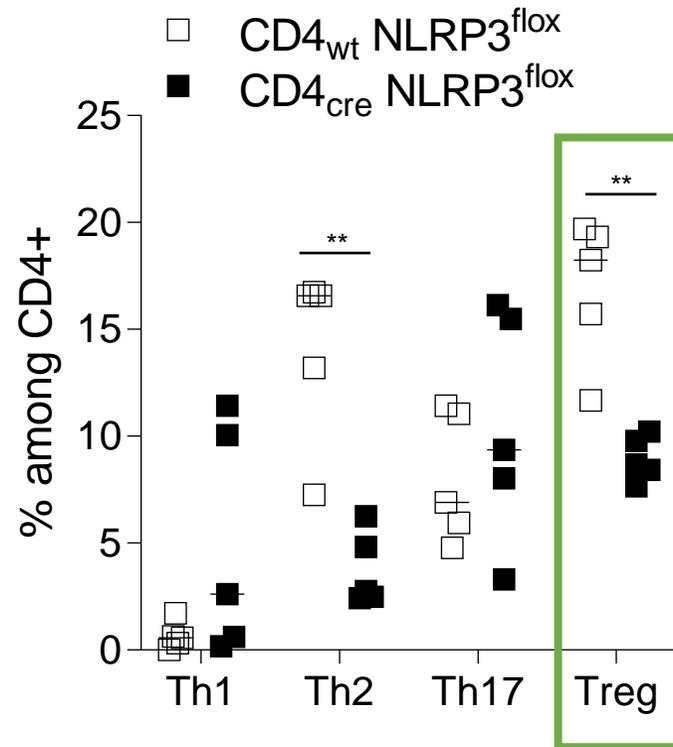
Les Th17r *NLRP3*^{-/-} surexpriment des gènes caractéristiques du profil Th17i



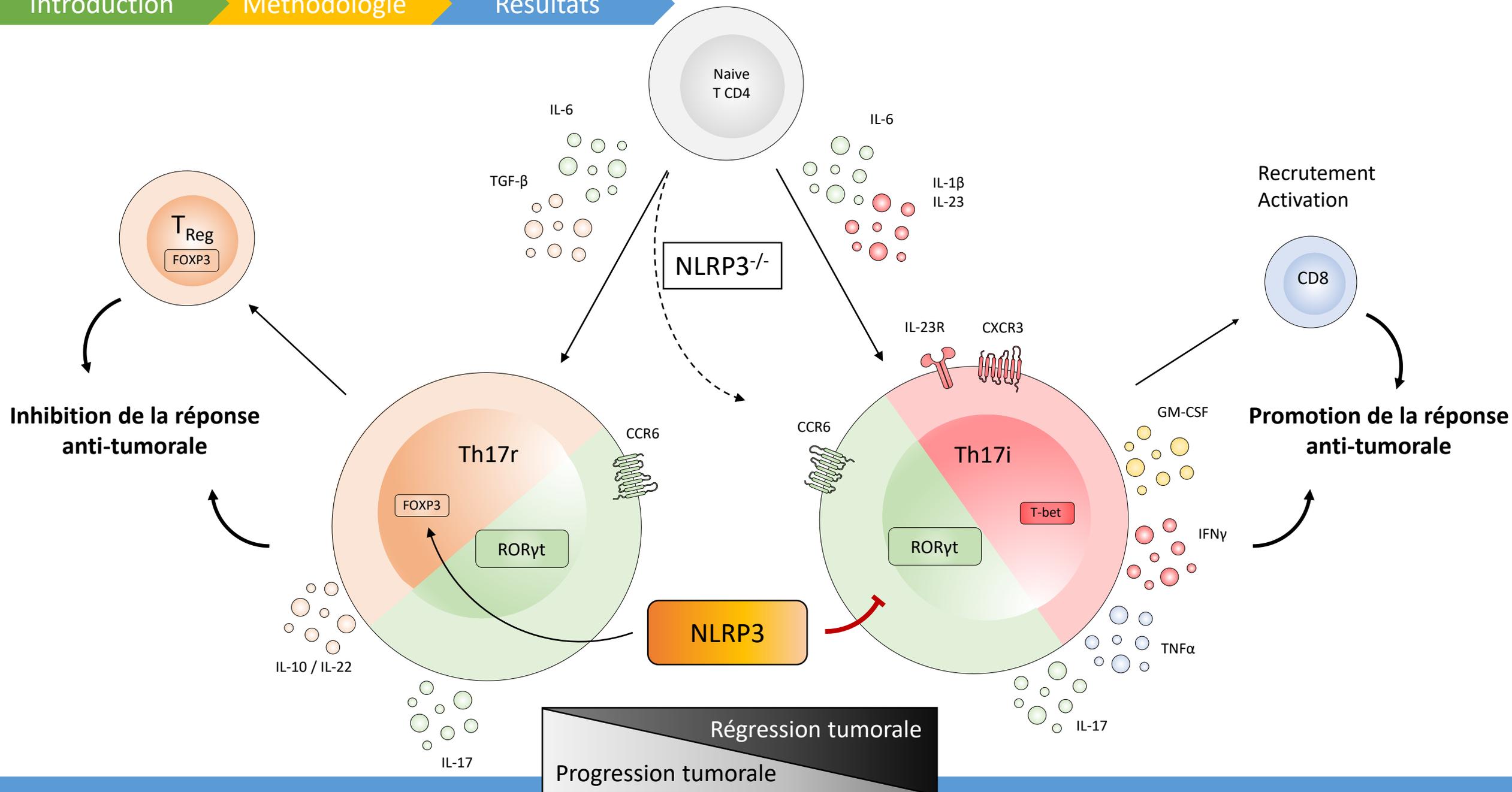
- Les Th17 *Nlrp3*^{-/-} ont un profil transcriptionnel proche des Th17i
- Les Th17 *Nlrp3*^{-/-} expriment des gènes caractéristiques du profil Th17i
- Traduit par l'expression de cytokines pro inflammatoires



Les Th17 *Nlrp3*^{-/-} ne se transdiffèrent plus en T_{Reg}

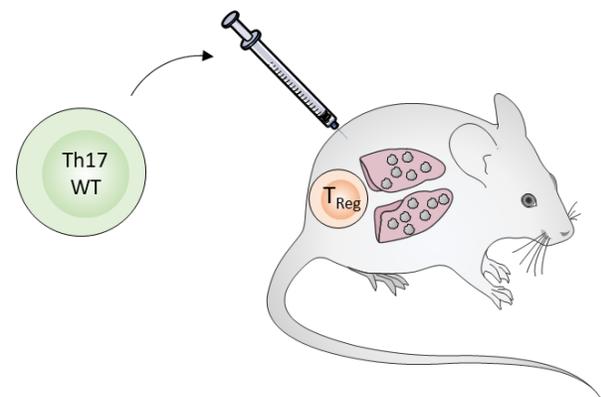


- Les T_{Reg} ne sont pas impactés par la déficience en NLRP3
- La déficience en NLRP3 empêche les Th17 d'alimenter le pool de T_{Reg}

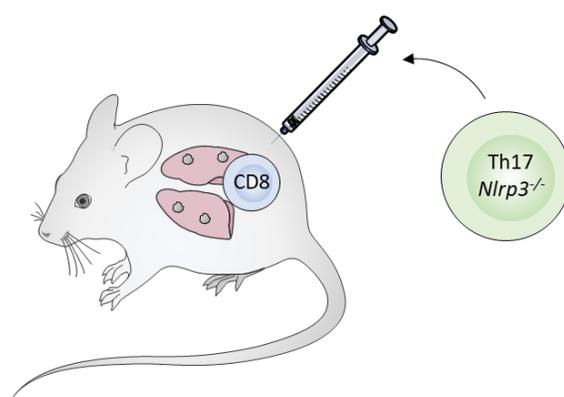


Les Th17 *Nlrp3*^{-/-} sont efficaces en thérapie cellulaire

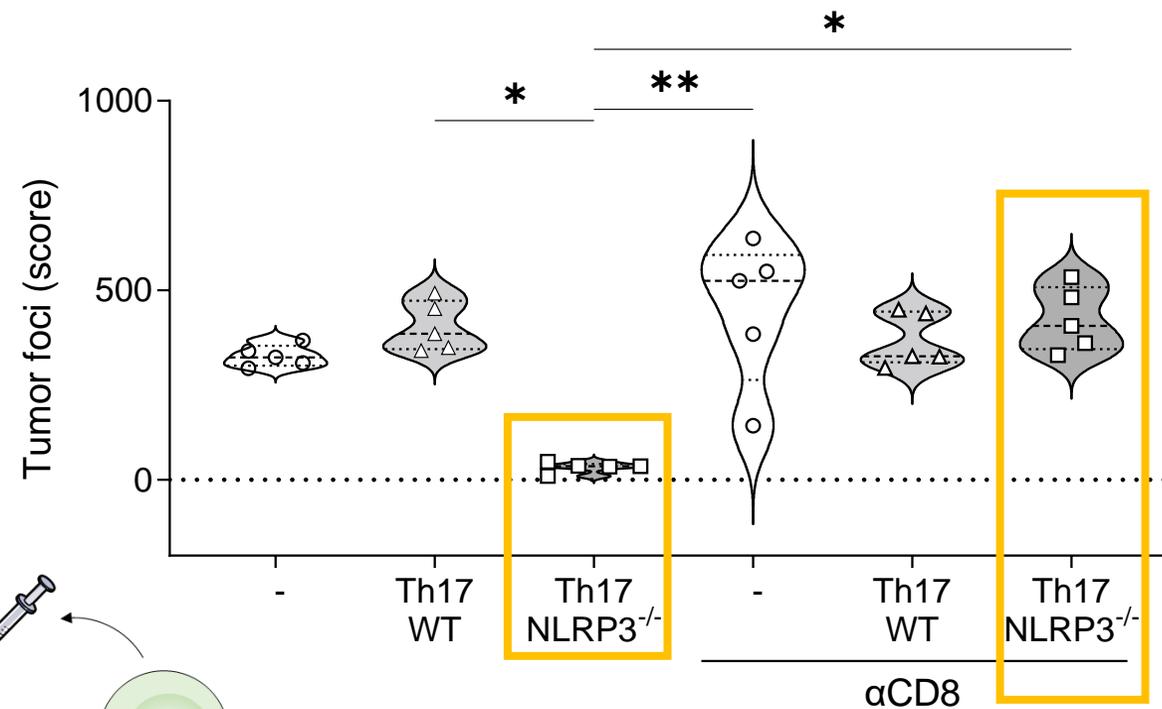
- Les Th17 *Nlrp3*^{-/-} ont un effet anti-tumoral dépendant des LT CD8⁺



Pas d'effet sur la croissance tumorale

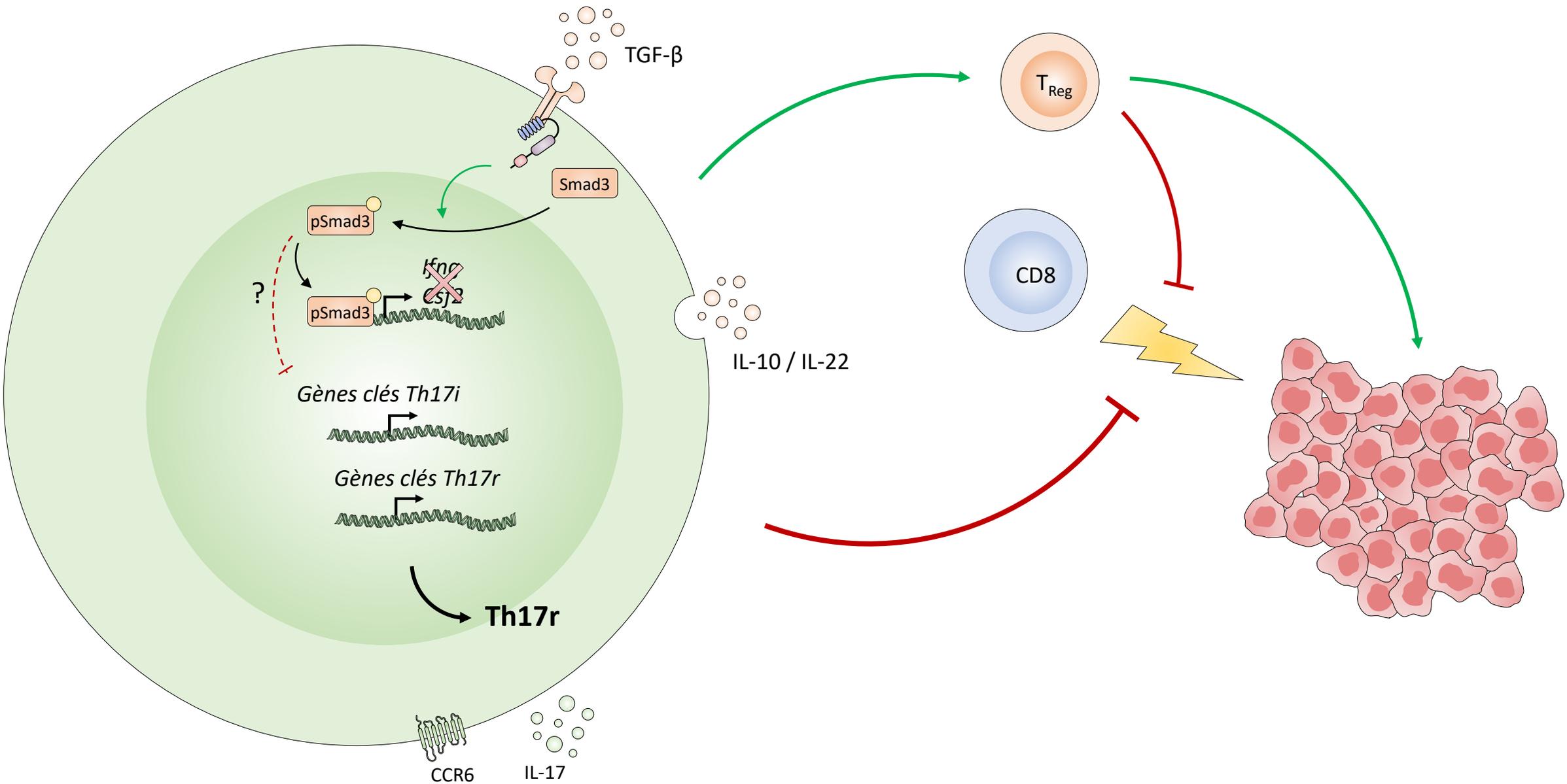


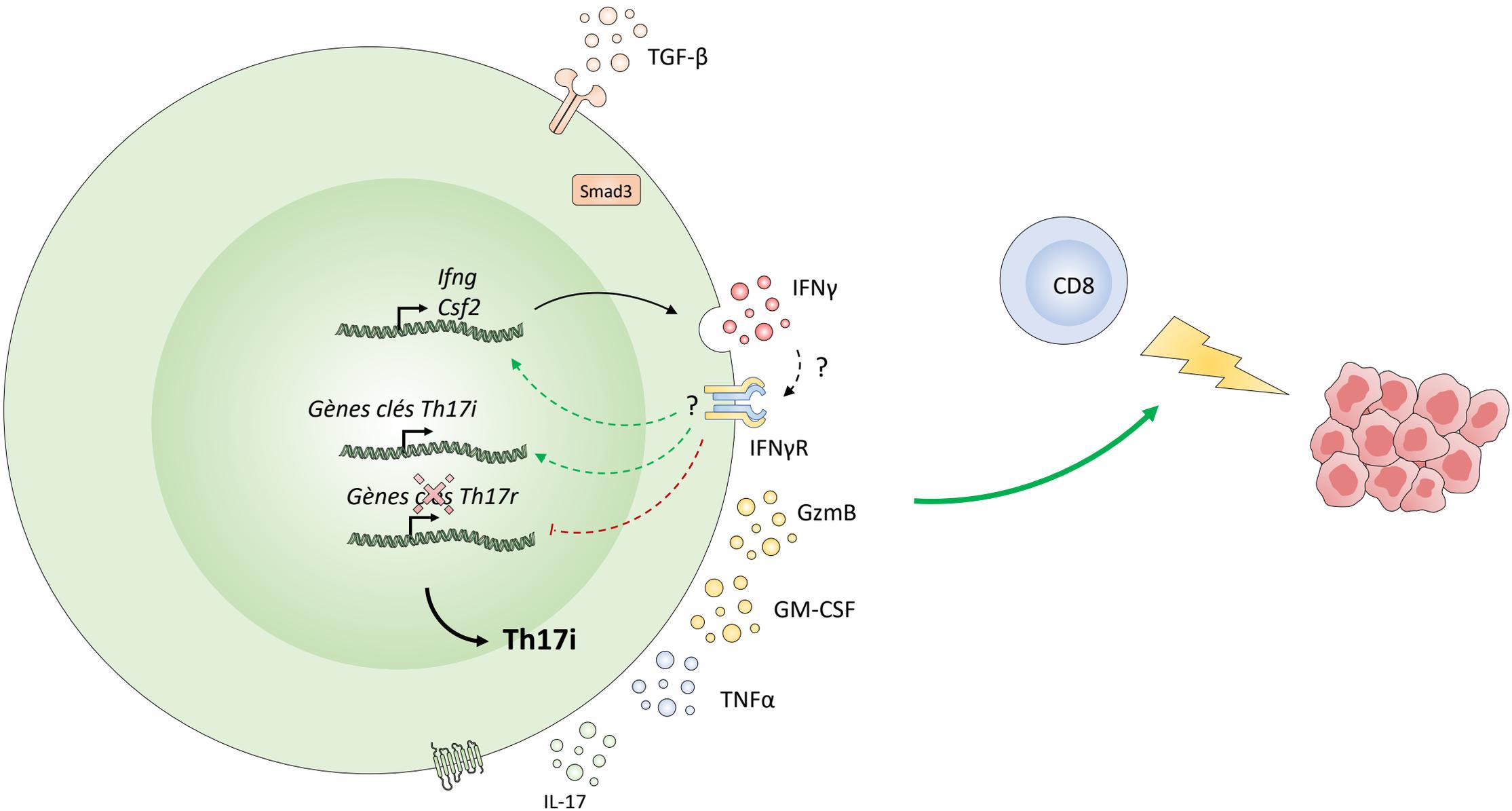
Diminution de la croissance tumorale





Discussion







Conclusion



NLRP3 inhibe le phénotype
Th17i



NLRP3 est nécessaire pour la
transdifférenciation
Th17/T_{Reg}



Les Th17 *Nlrp3*^{-/-} favorisent
la réponse anti-tumorale
dépendante des LT CD8

Remerciements

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