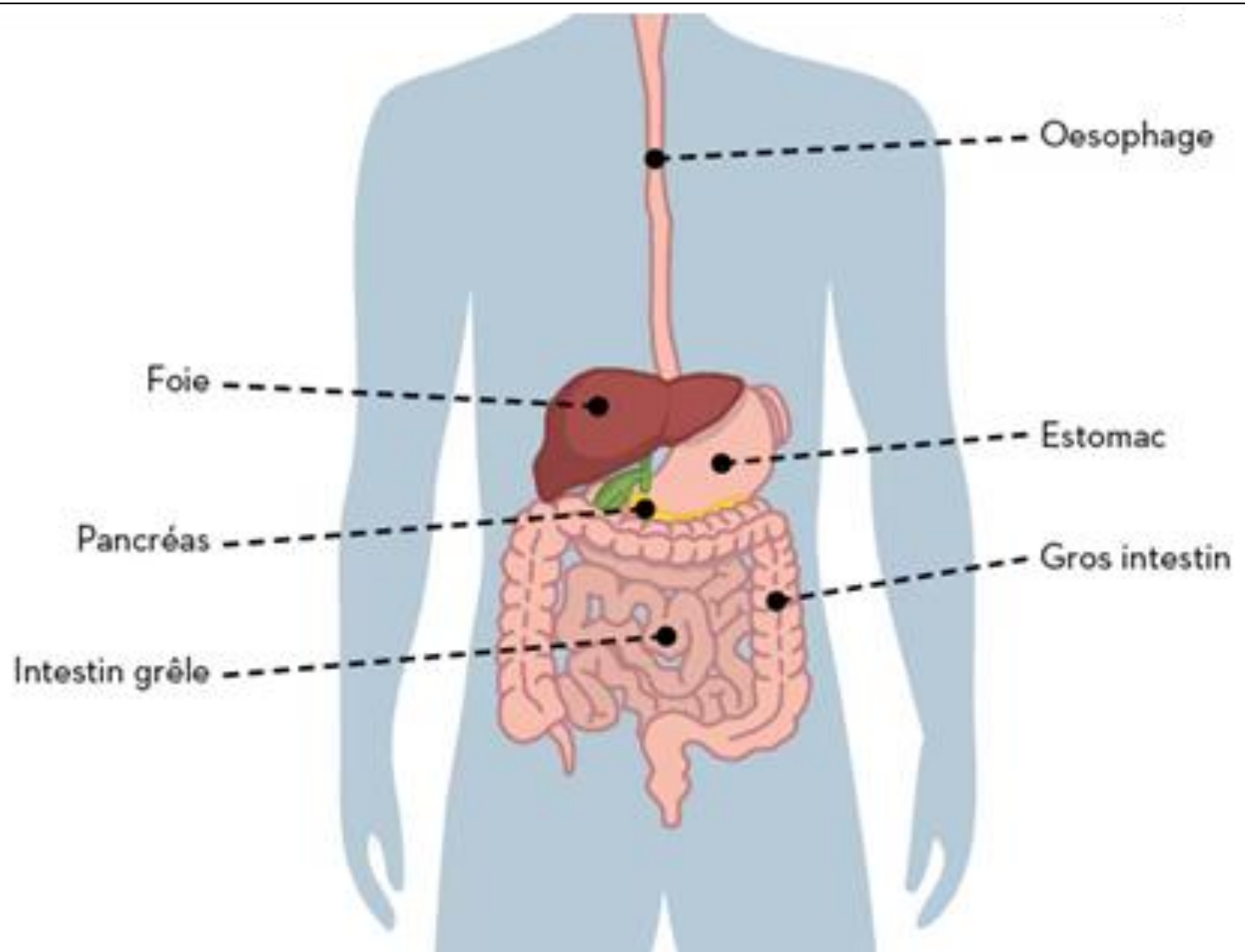


Impact de l'Oxaliplatine sur les lymphocytes T régulateurs

Dr Frédérique VEGRAN
Email: frederique.vegran@inserm.fr

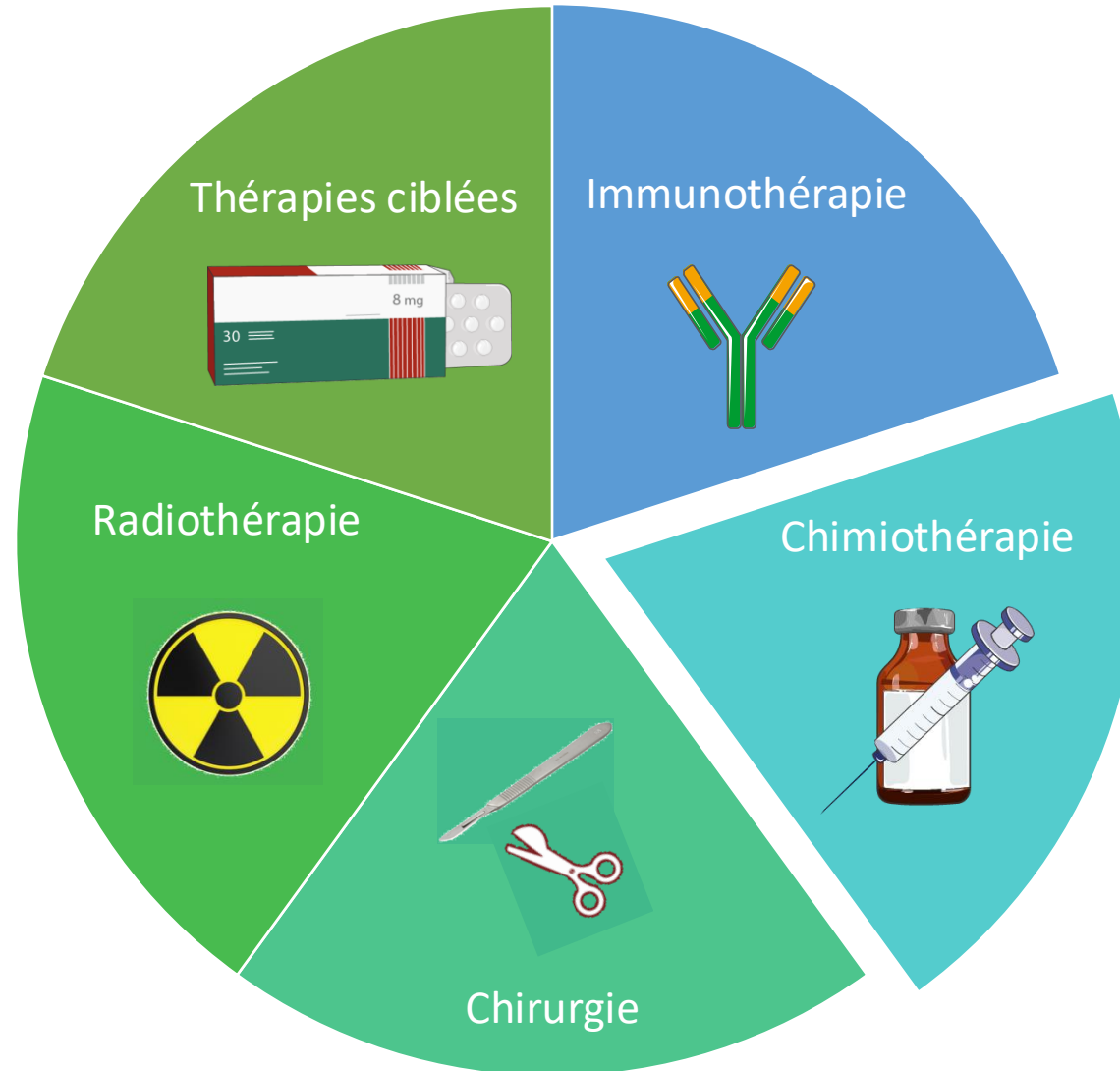
Cancers digestifs en Europe



Survie à 5 ans

Œsophage	20%
Foie et voies biliaires	25-30%
Estomac	20%
Pancréas	<10%
Intestin grêle	40-50%
Colon et rectum	60%

Traitements des Cancers digestifs



Anti-métabolites

- 5-fluorouracile

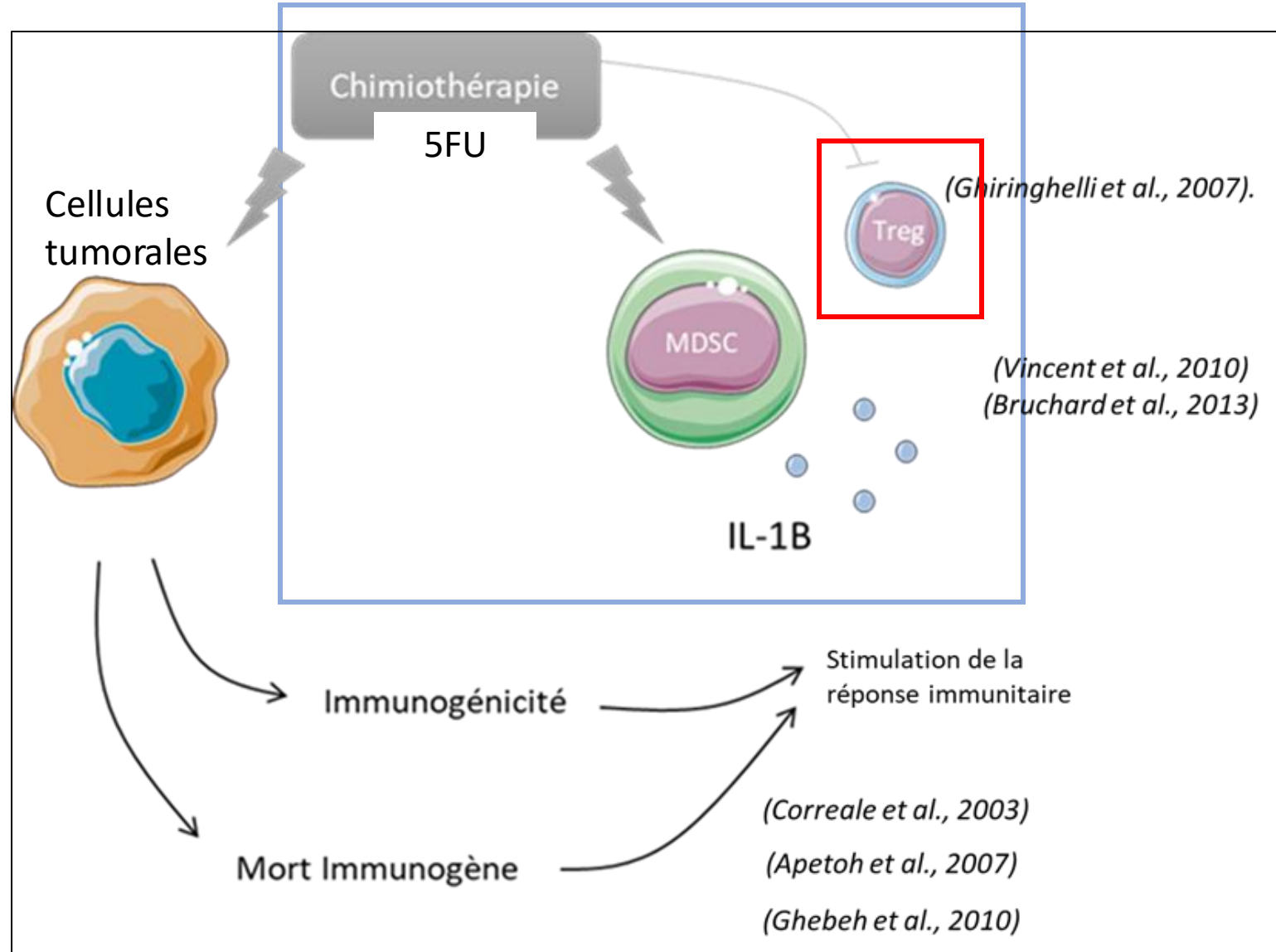
Poisons du fuseau

- Taxanes

Agents de dommages à l'ADN

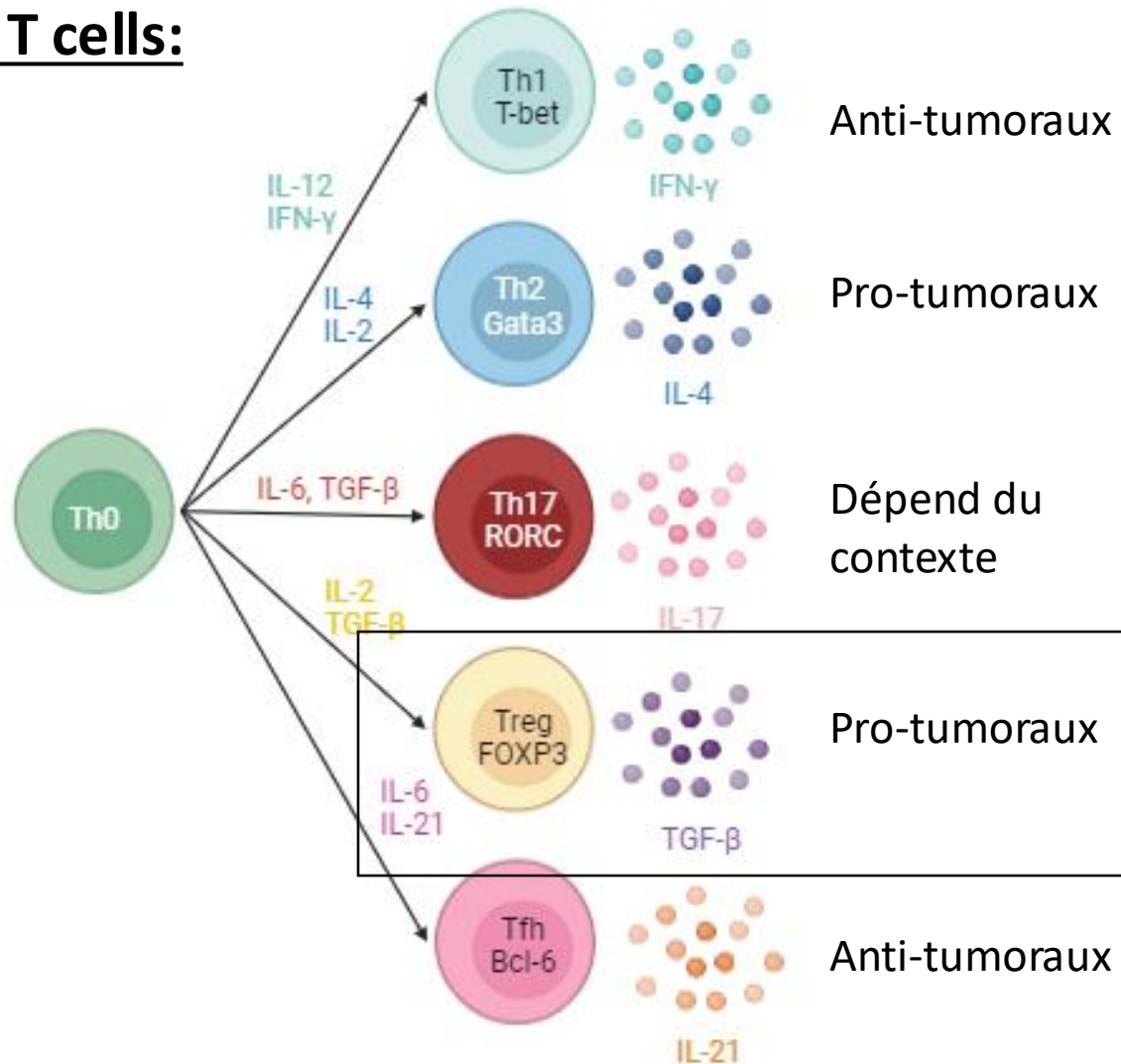
- Agents alkylants
- Sels de platine : **Oxaliplatine**

Chimiothérapies et système immunitaire



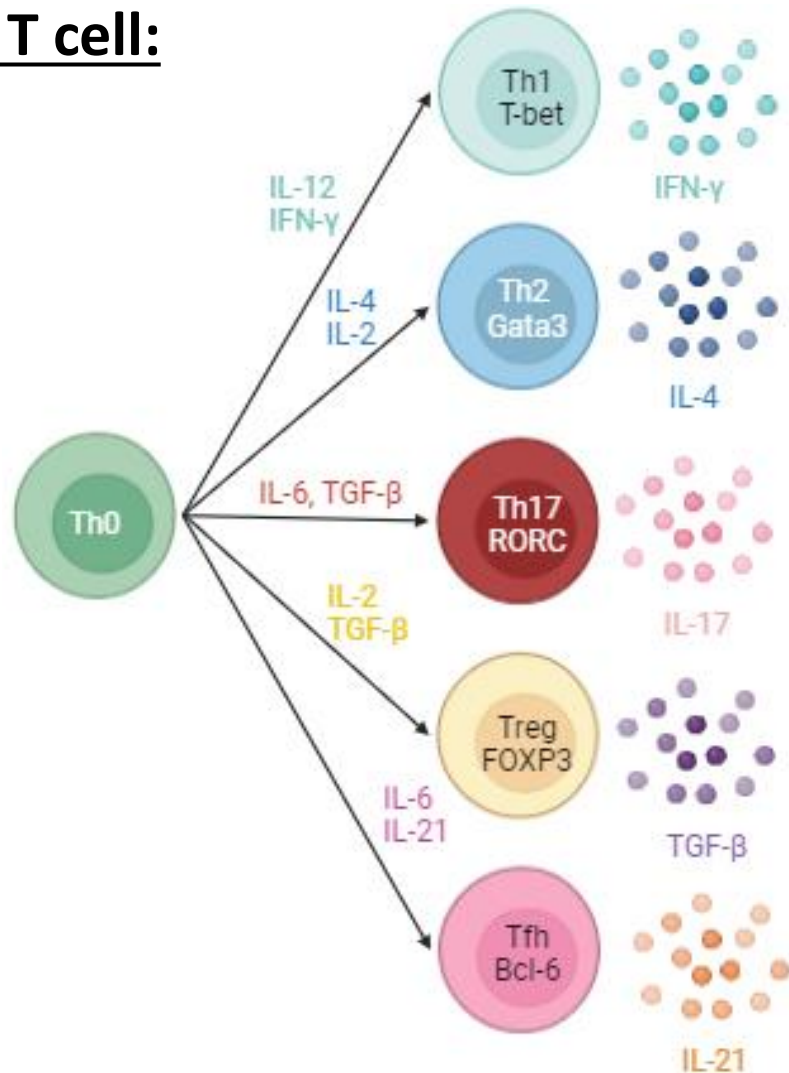
Lymphocytes T CD4+

CD4+ T cells:

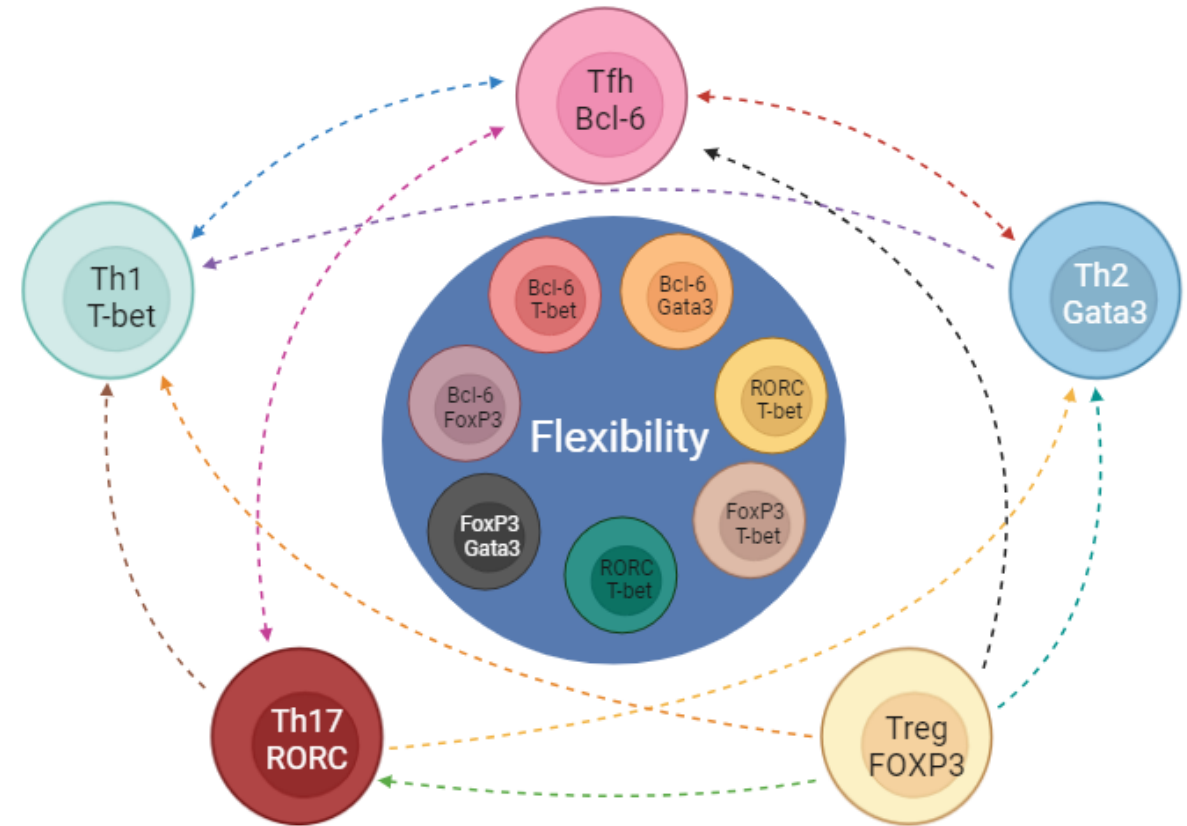


Plasticité des lymphocytes T CD4

CD4+ T cell:



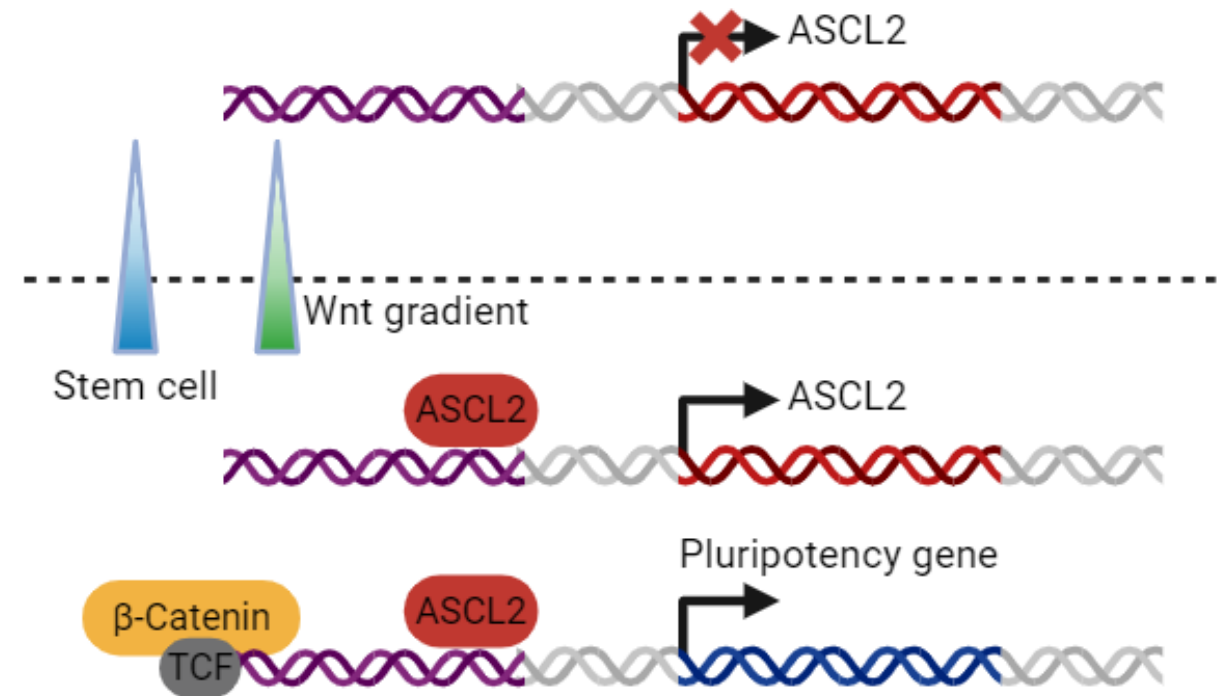
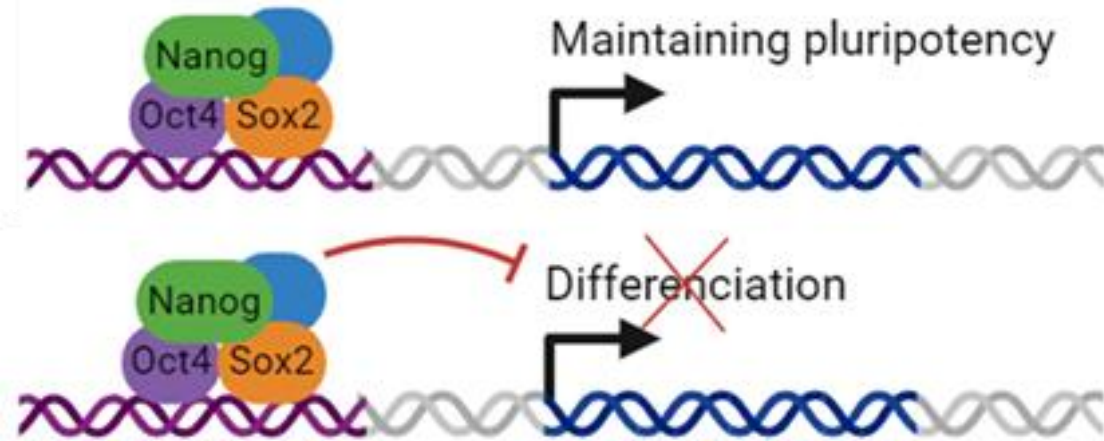
Russ et al., 2013



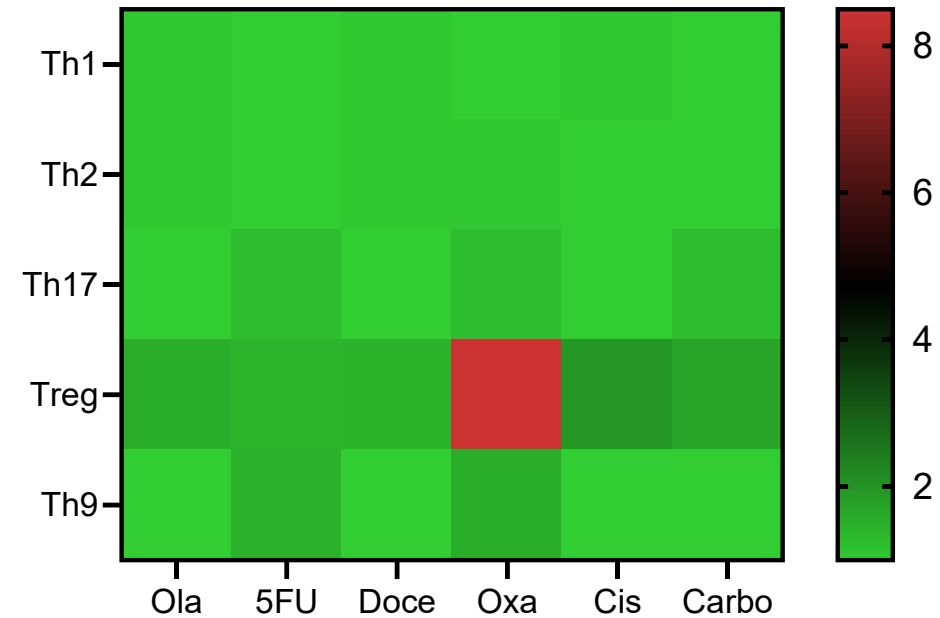
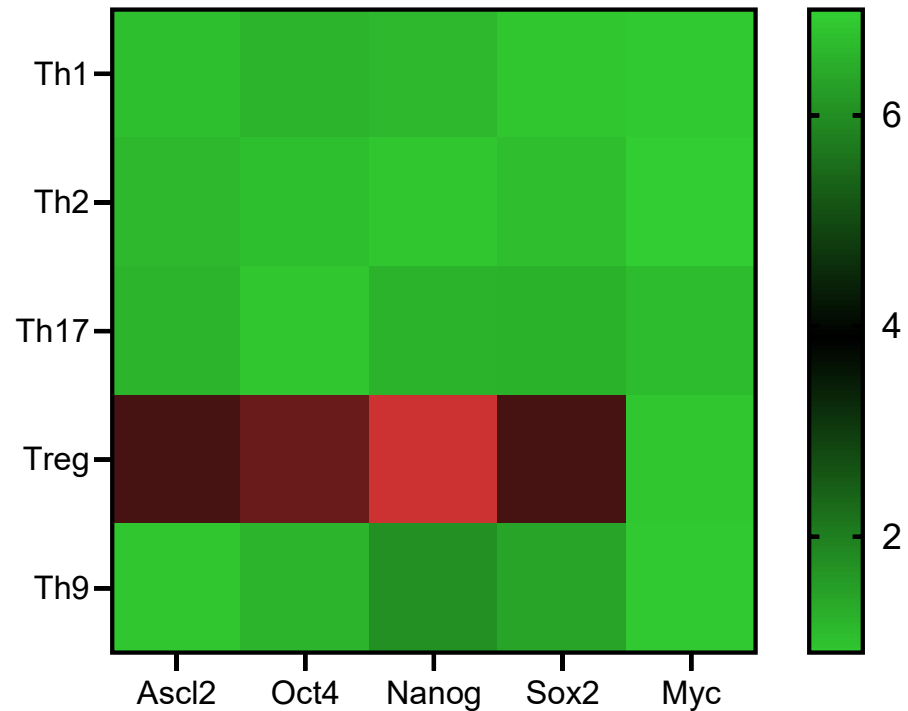
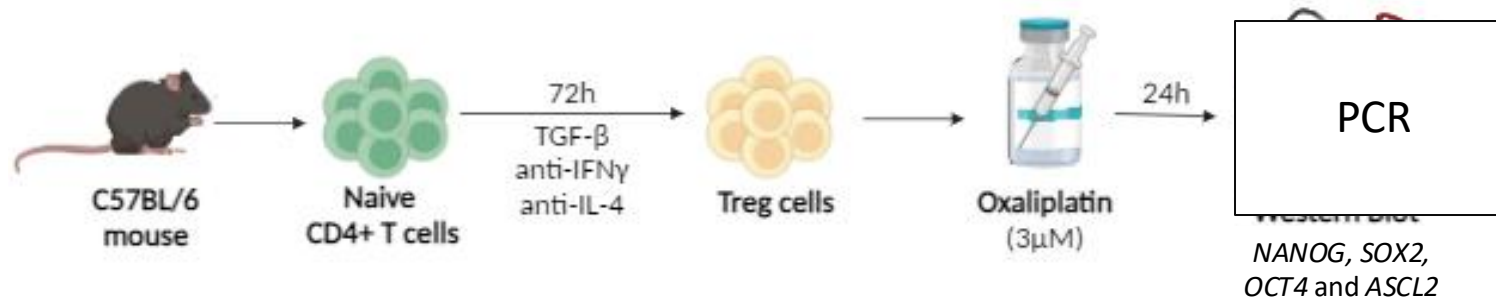
Nakayama et al., 2012

Régulation moléculaire de la pluripotence

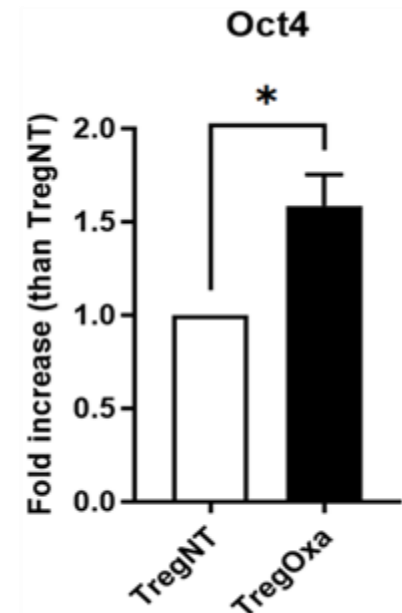
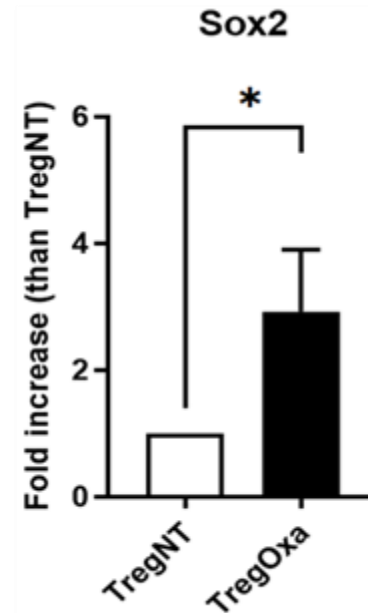
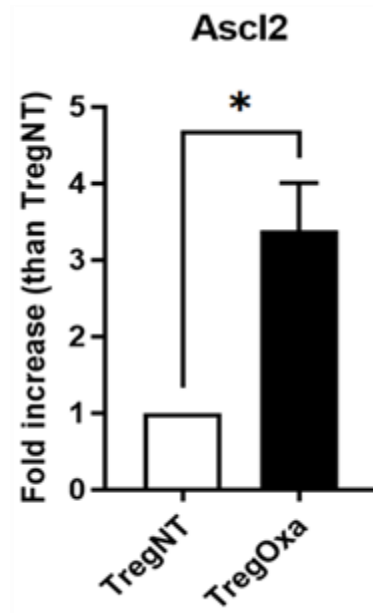
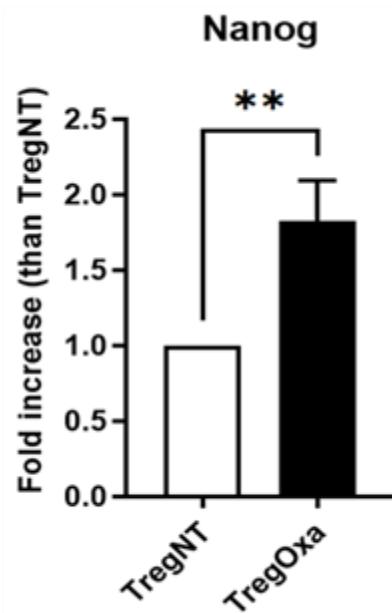
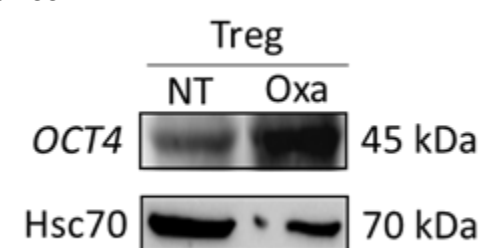
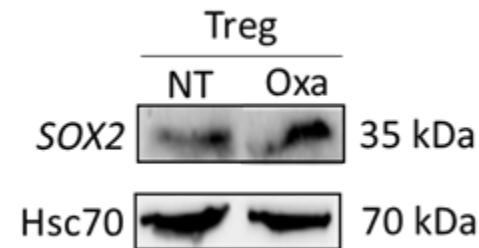
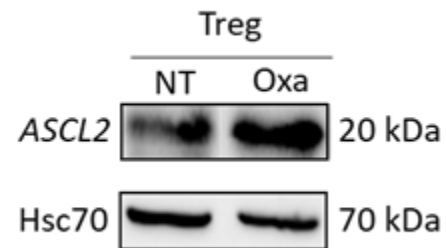
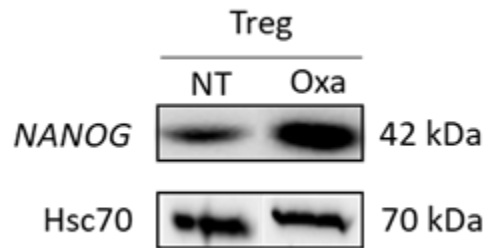
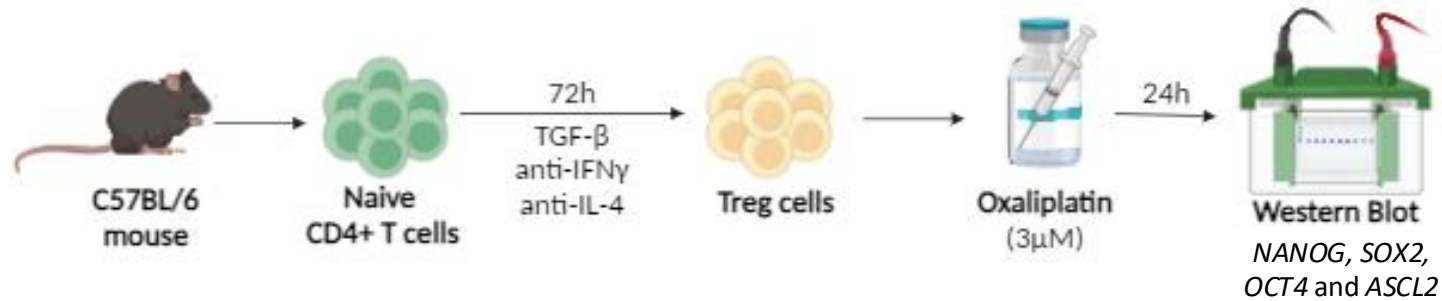
Factors involved in maintaining pluripotency:



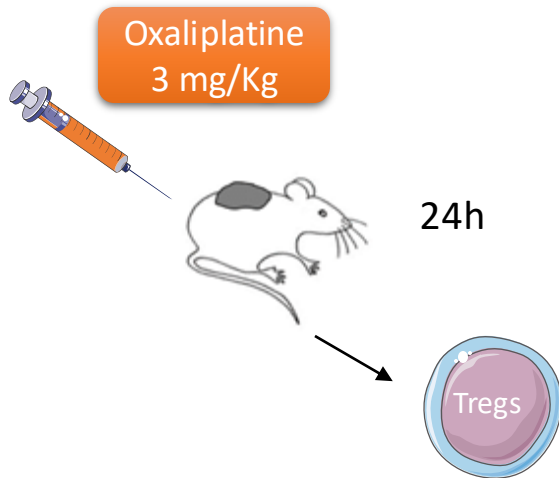
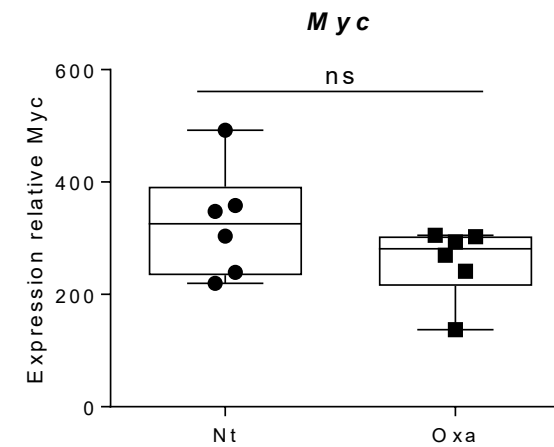
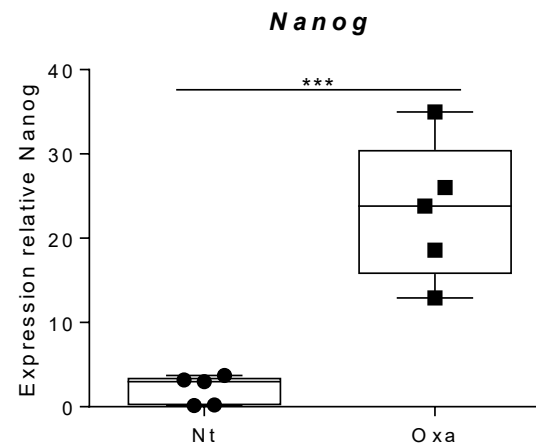
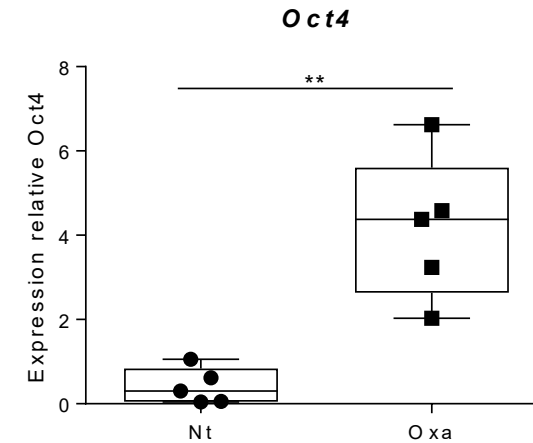
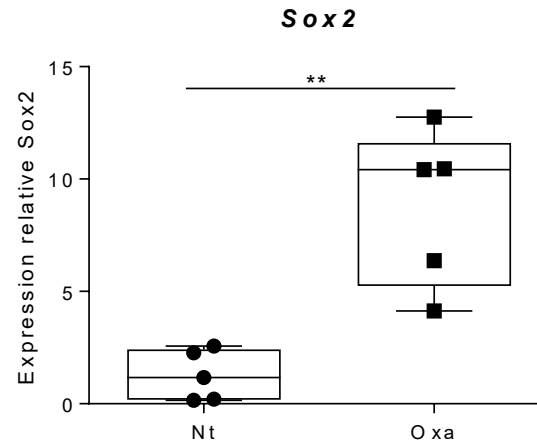
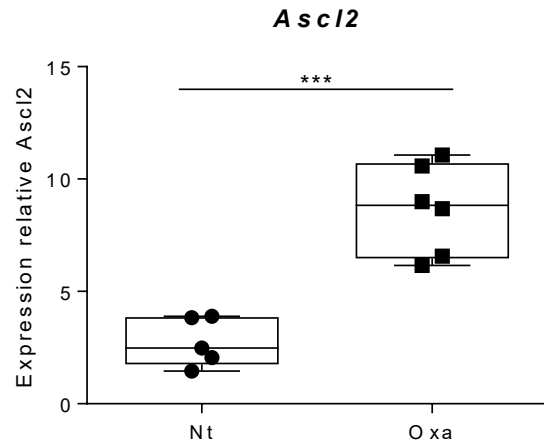
L'oxaliplatine induit l'expression des facteurs de pluripotence dans les Tregs *in vitro*



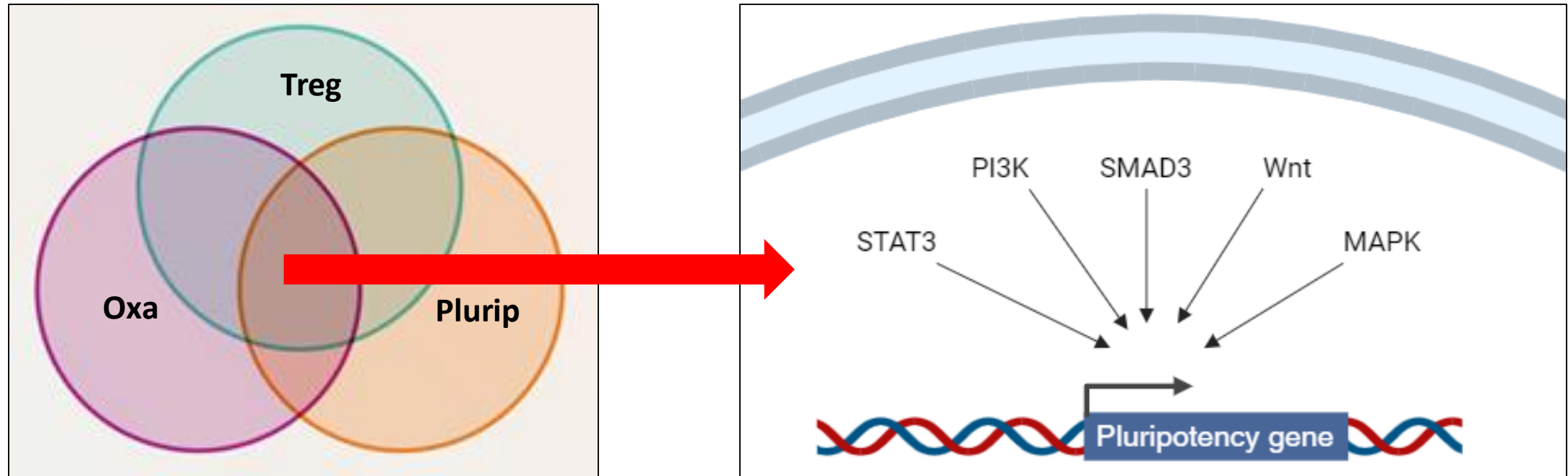
L'oxaliplatine induit l'expression des facteurs de pluripotence dans les Tregs *in vitro*



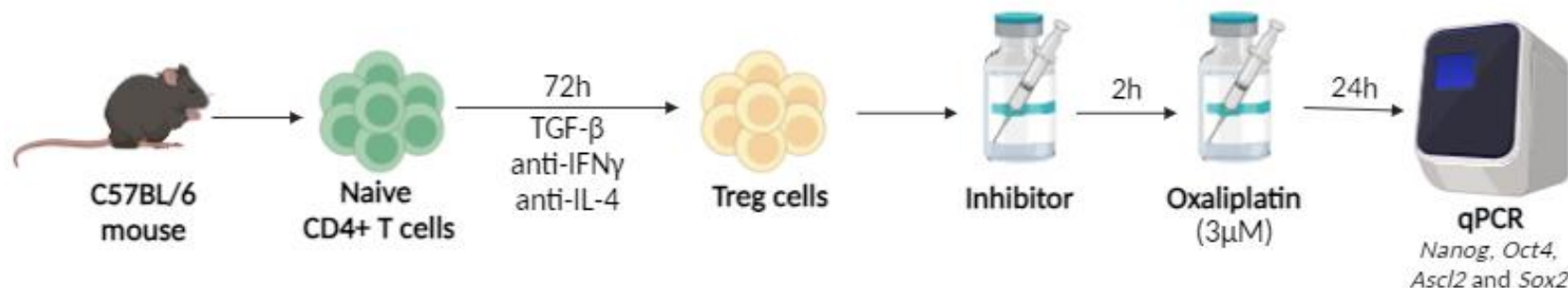
L'oxaliplatine induit l'expression des facteurs de pluripotence dans les Tregs *in vivo*



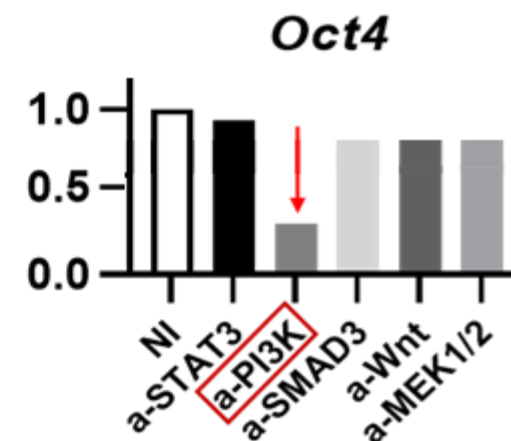
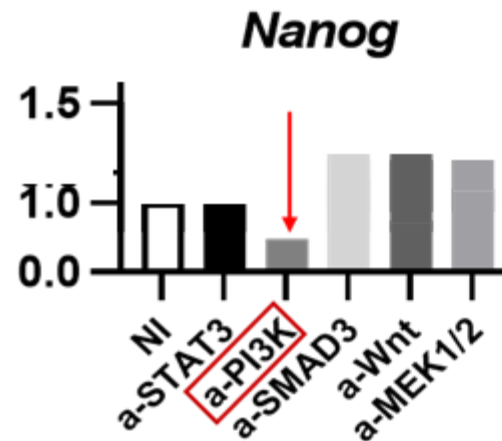
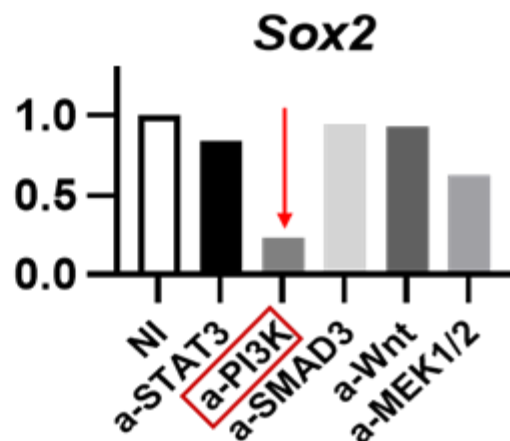
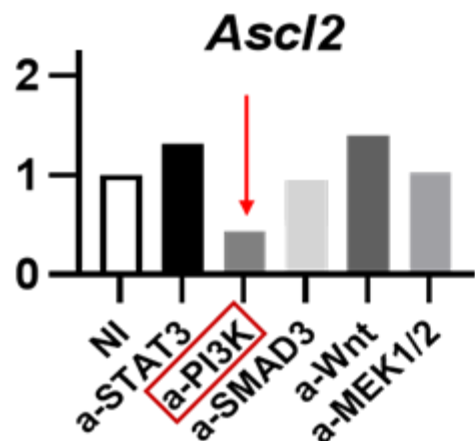
Mécanismes moléculaires



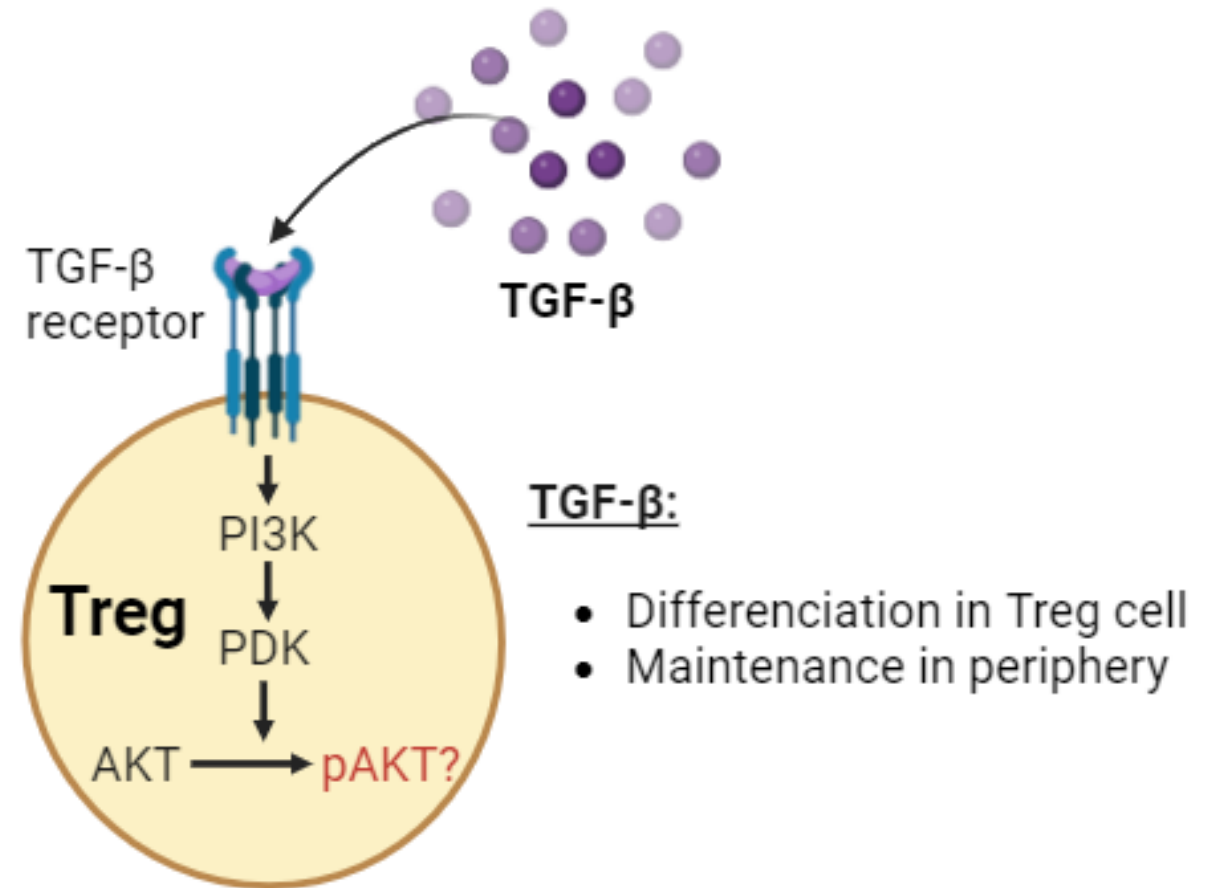
Rôle potentiel de la voie PI3K



Inhibitor:
a-STAT3: STA21
a-PI3K: LY294002
a-SMAD3: S1S3
a-Wnt: JW67
a-MEK1/2: Trametinib

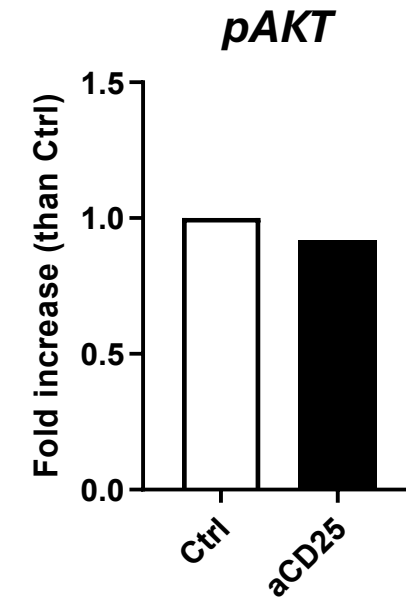
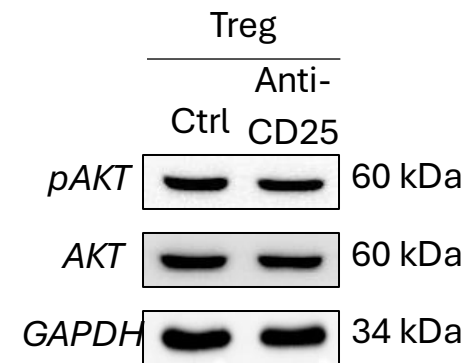
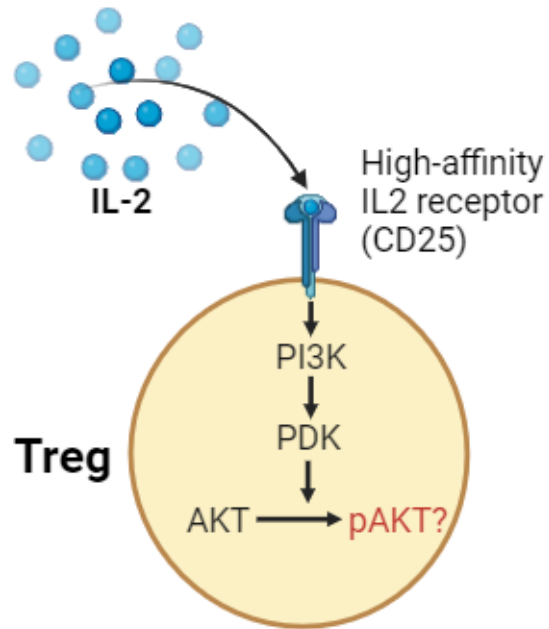
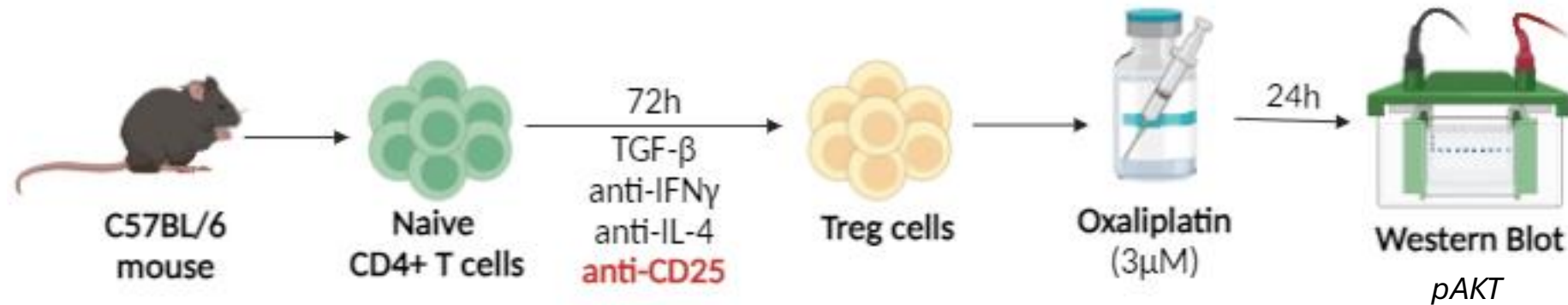


Pourquoi est-ce spécifique aux Tregs ?

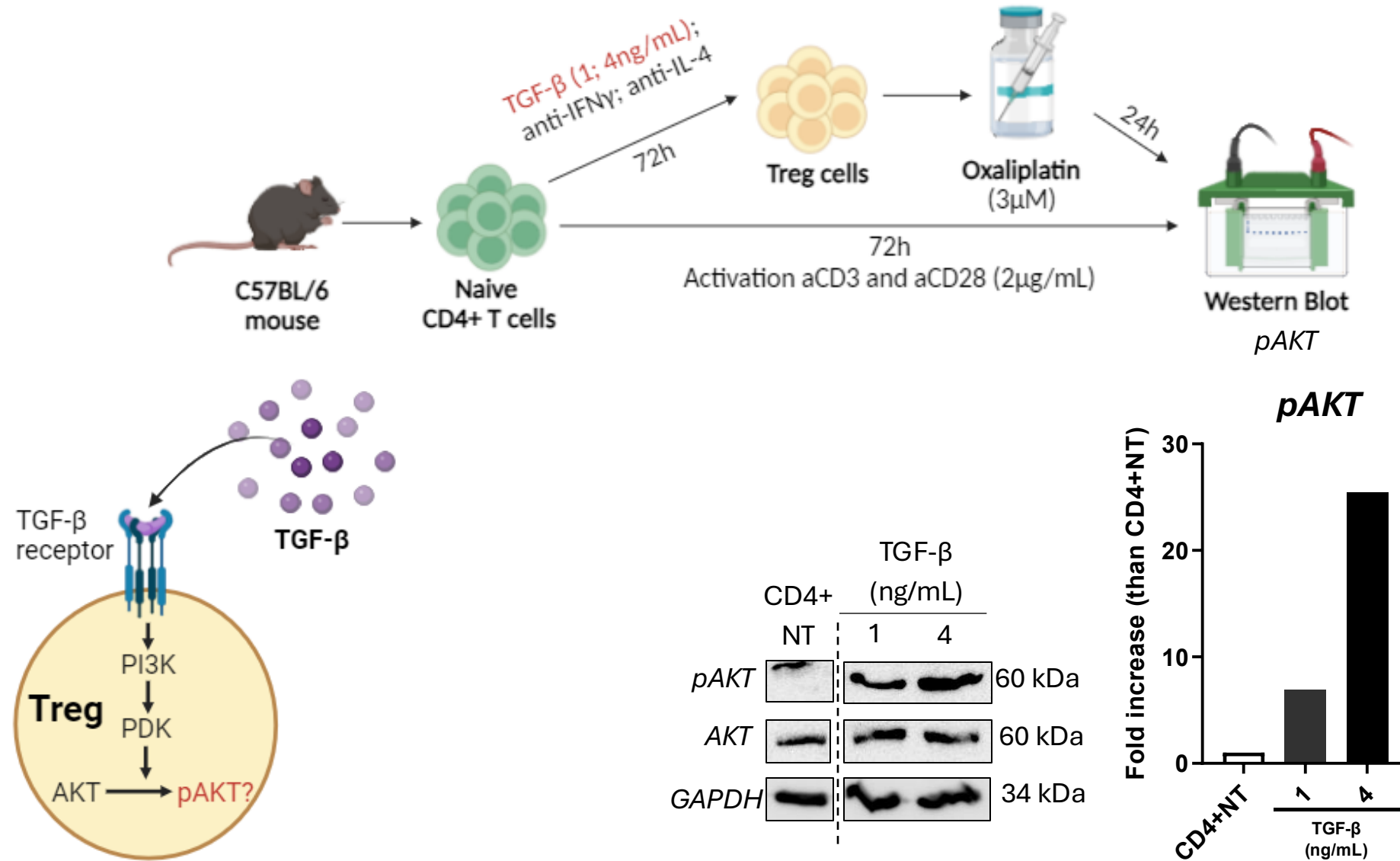


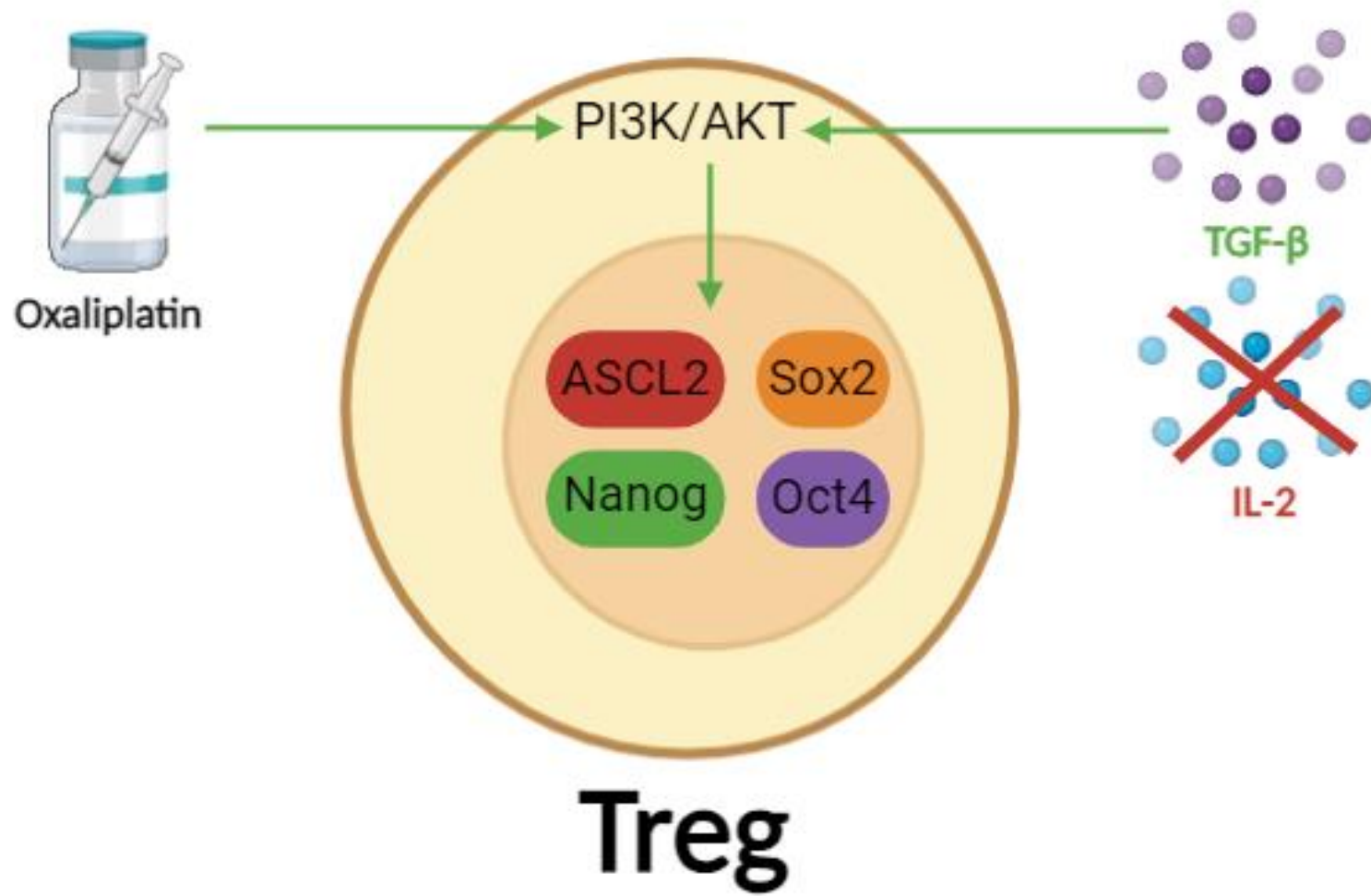
Choi et al., 2020

La signalisation par l'IL-2 ne semble pas impliquée



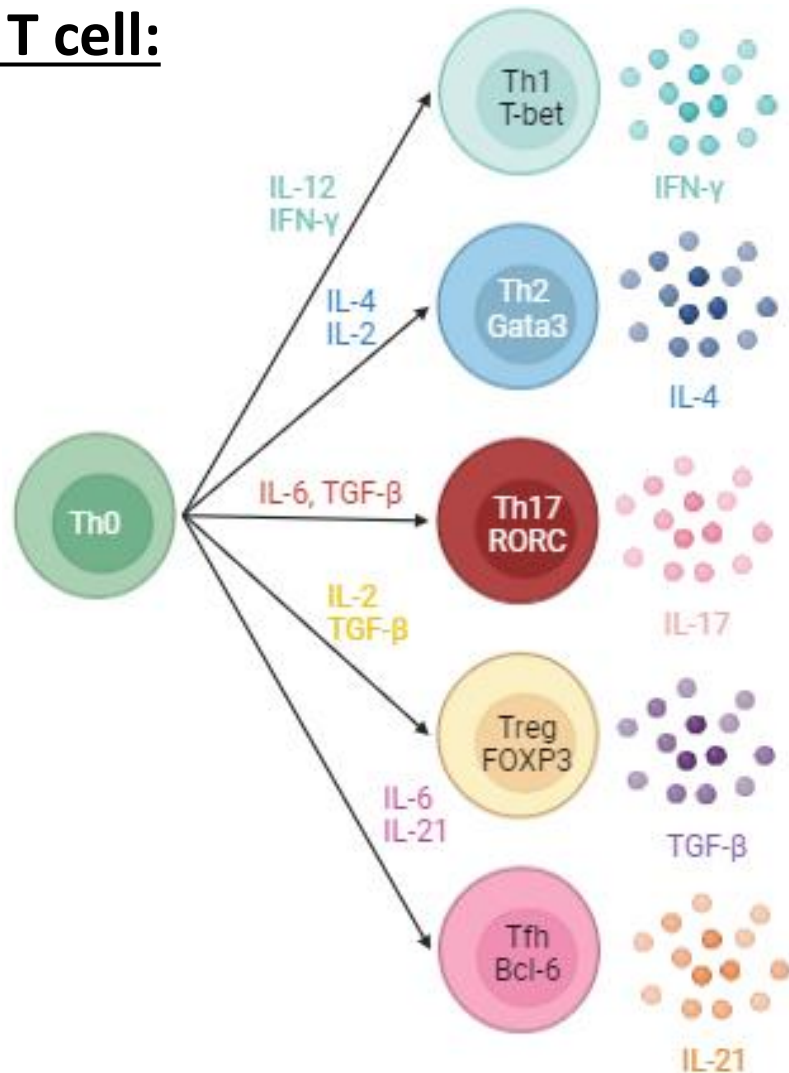
La voie du TGF β semble impliquée



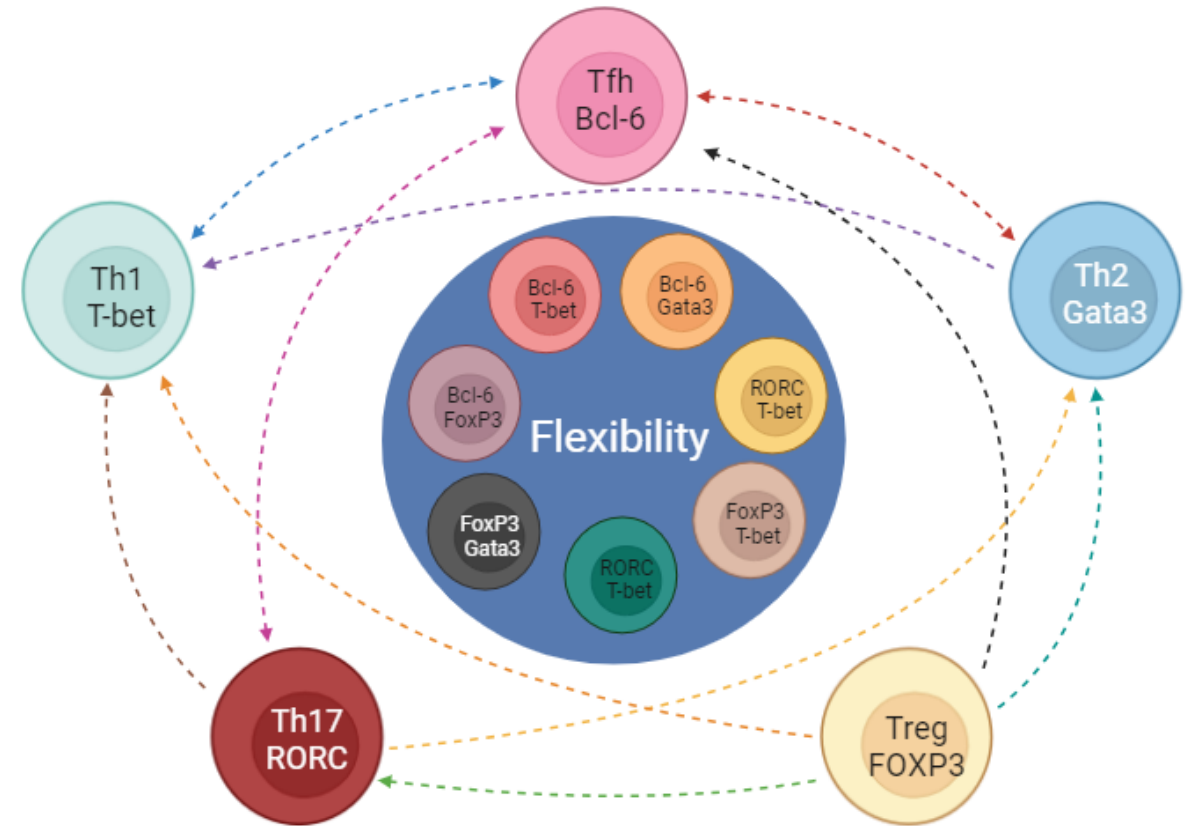


Plasticité des lymphocytes T CD4

CD4+ T cell:

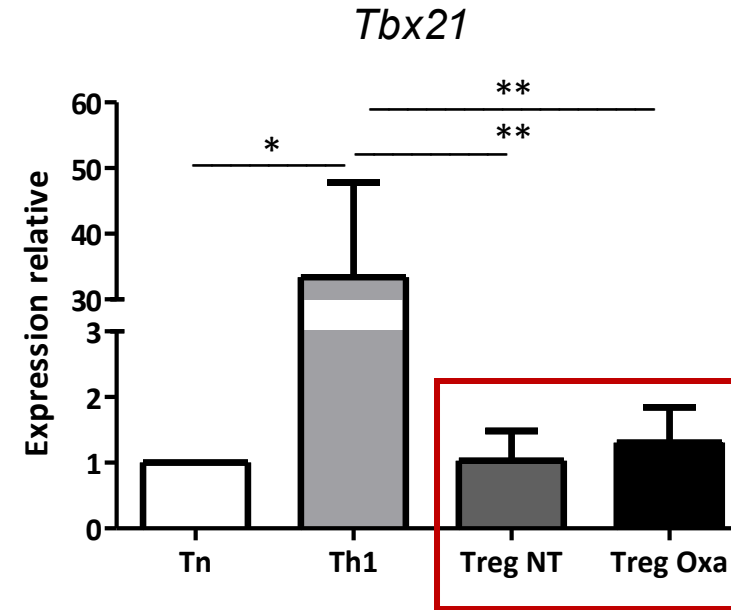
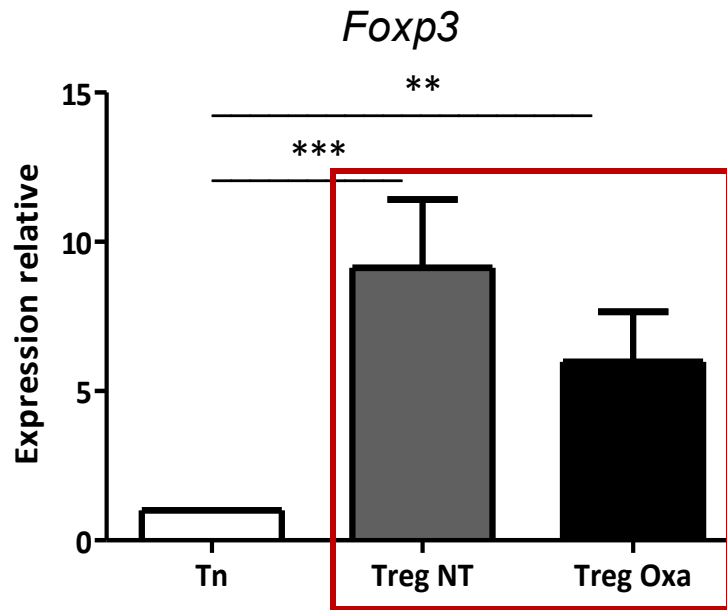
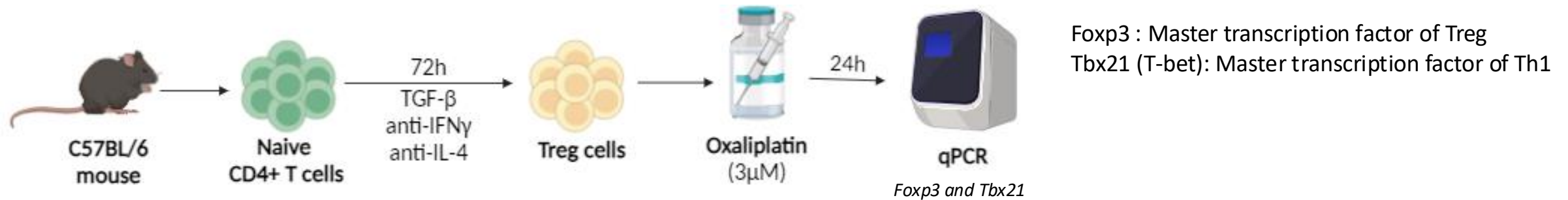


Russ et al., 2013



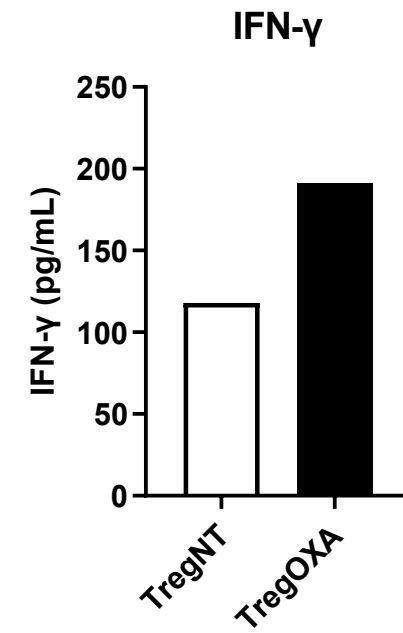
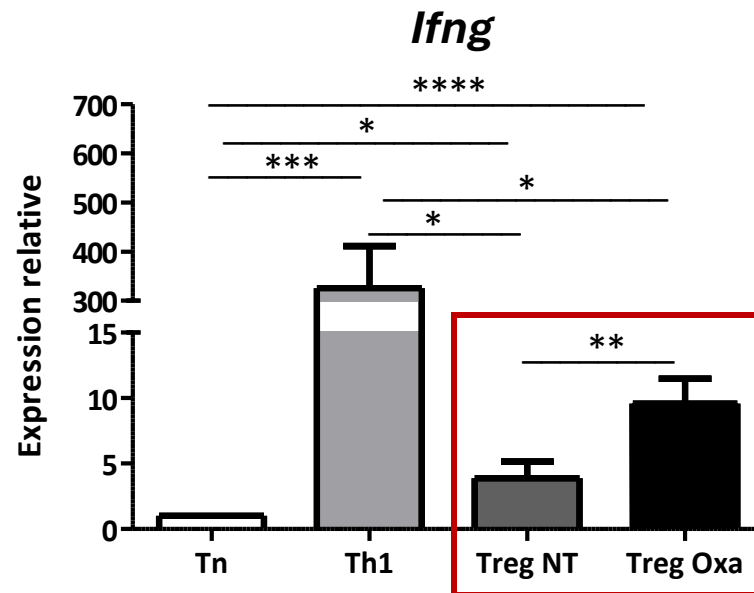
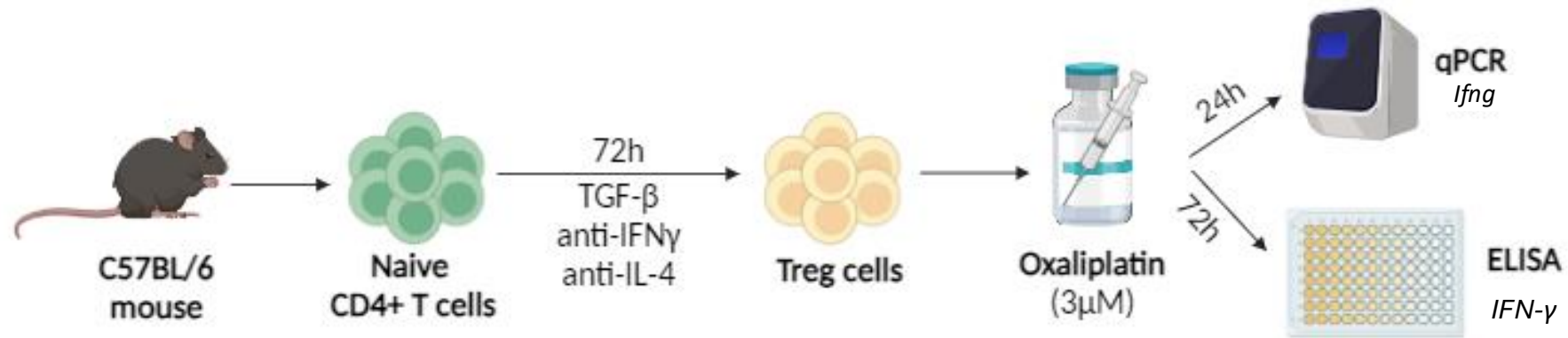
Nakayama et al., 2012

L'oxaliplatine ne permet pas la transdifférenciation des Tregs

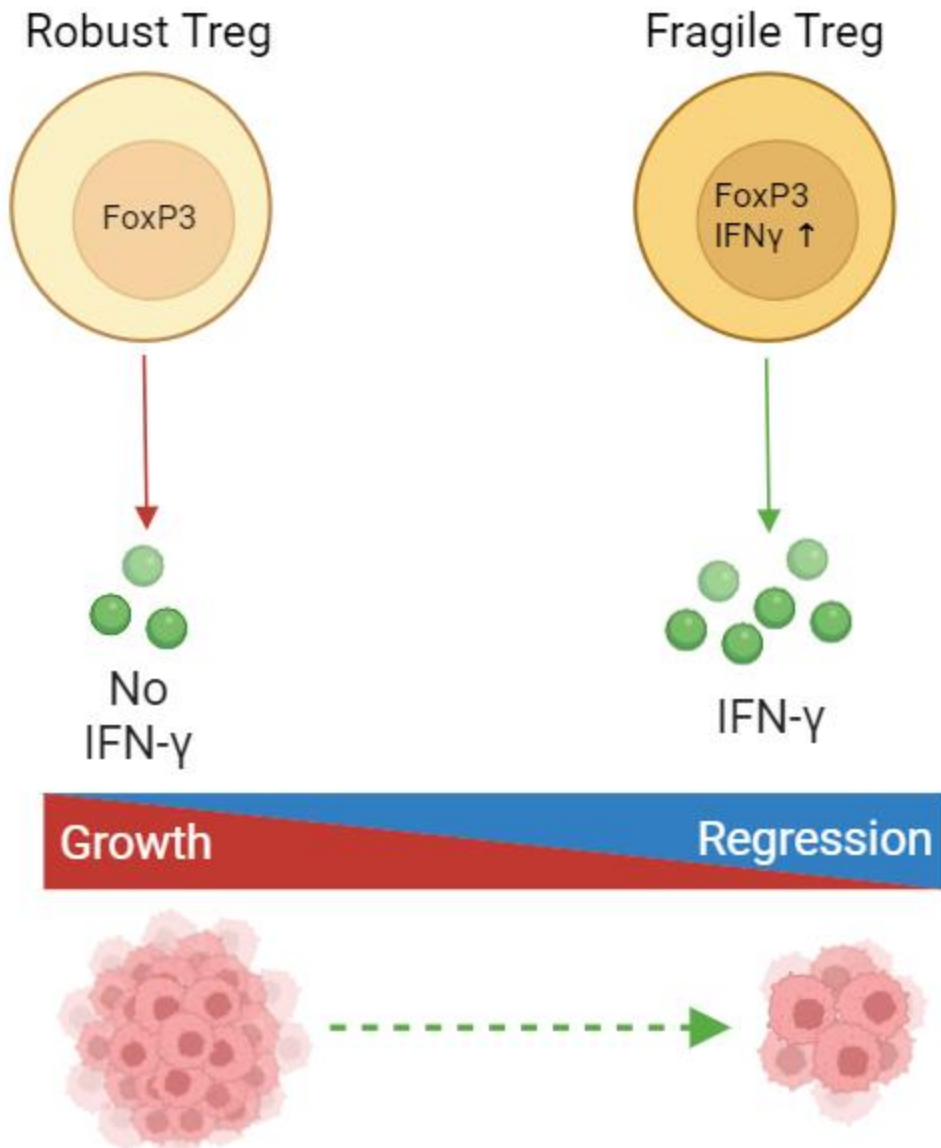


➔ Results not shown: Screening for other markers: Gata3 (Th2), RORC (Th17) and Bcl-6 (Tfh): same results

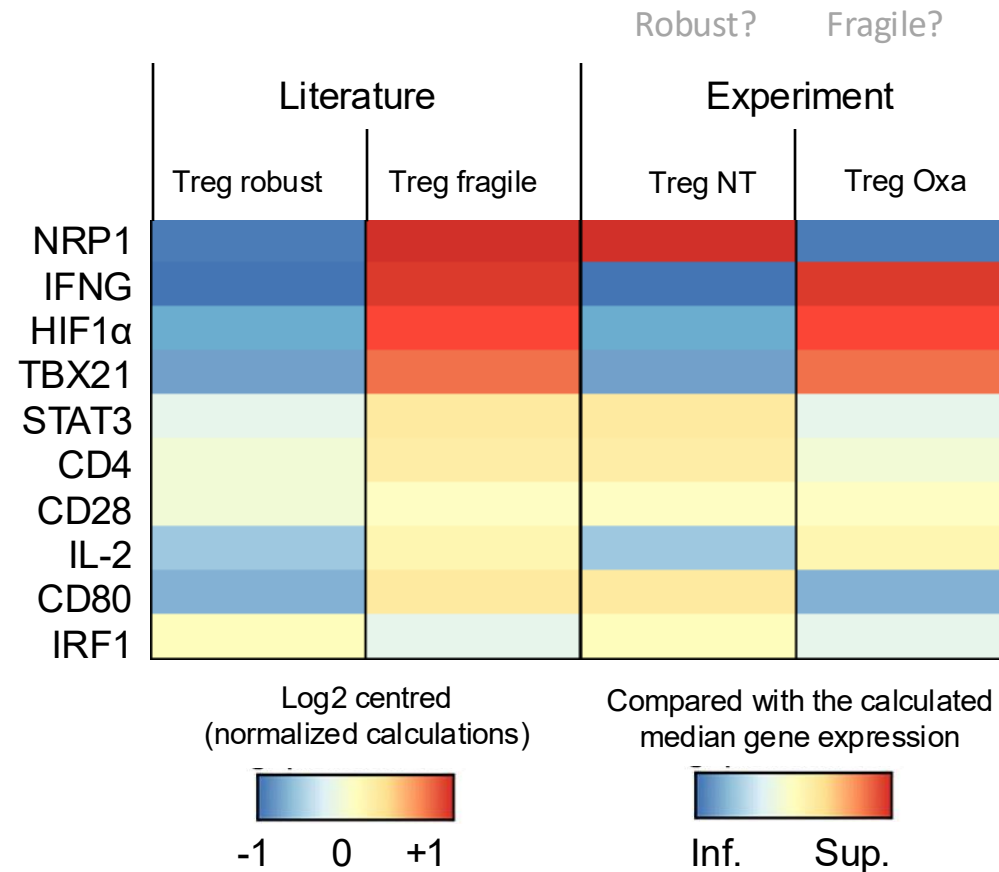
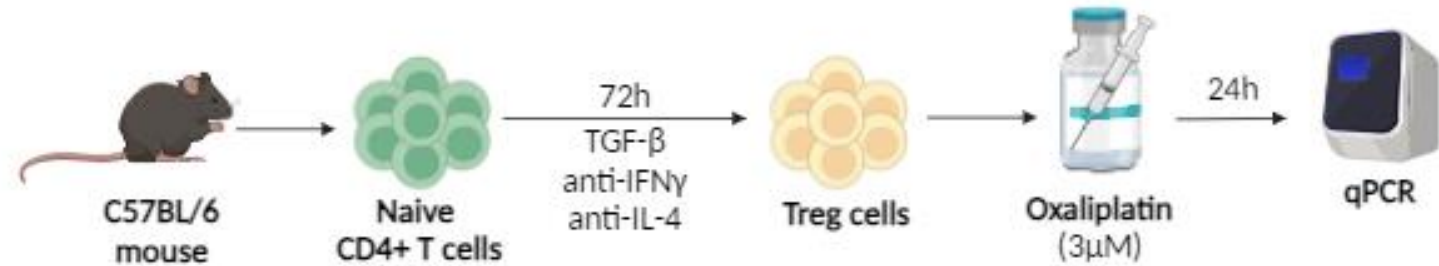
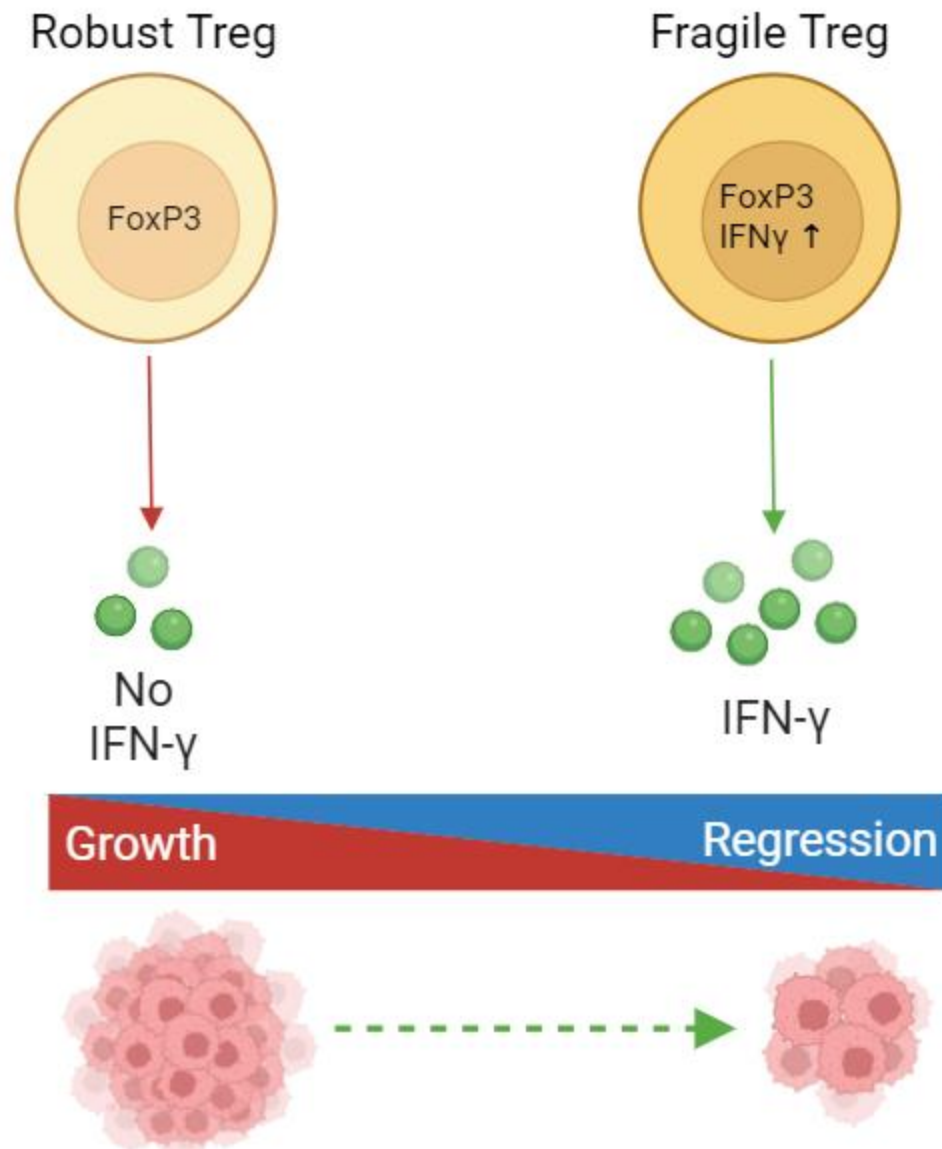
L'oxaliplatine induit la production d'IFN γ par les Tregs



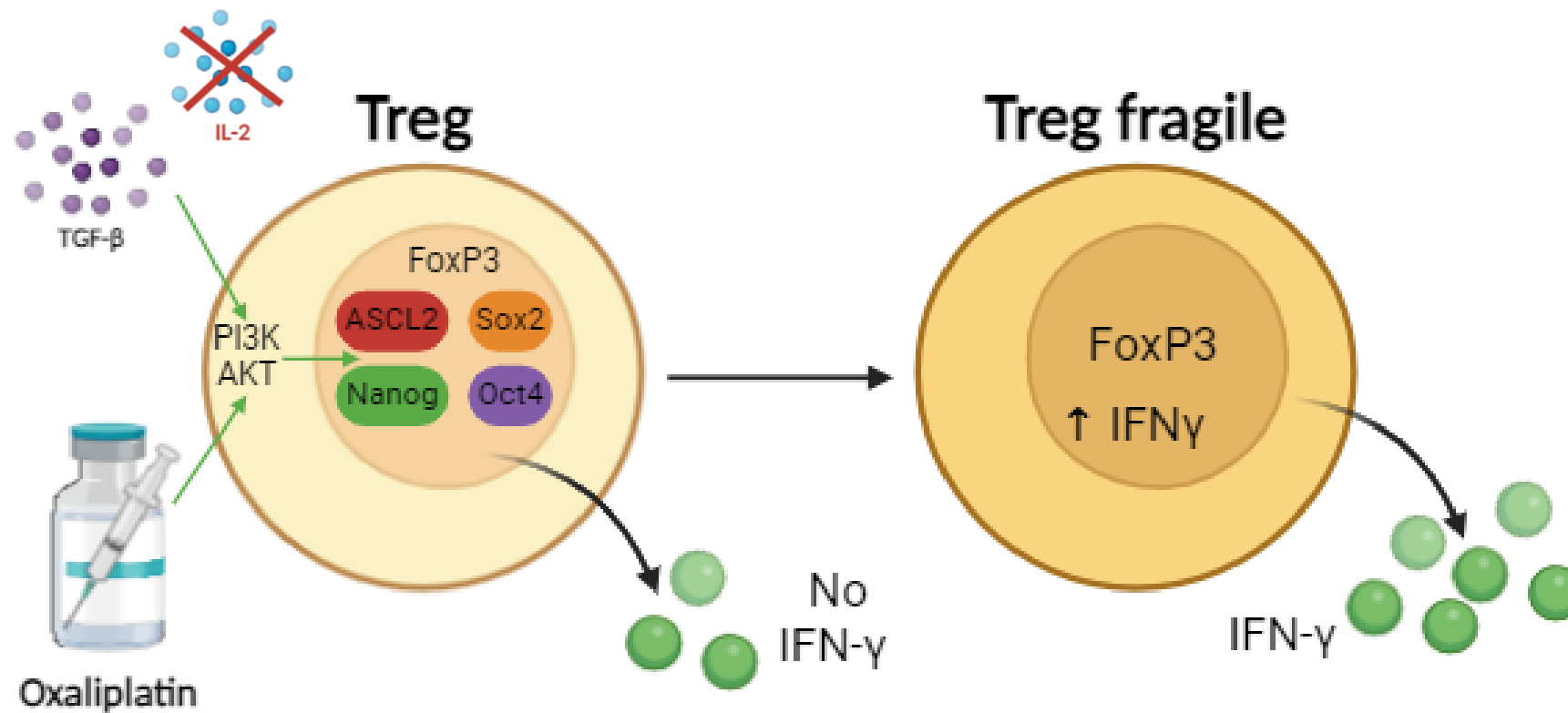
Treg robuste/Treg fragile



L'oxaliplatine induit un phenotype "fragile"



Résumer



Merci pour votre attention!

Remerciements:

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