



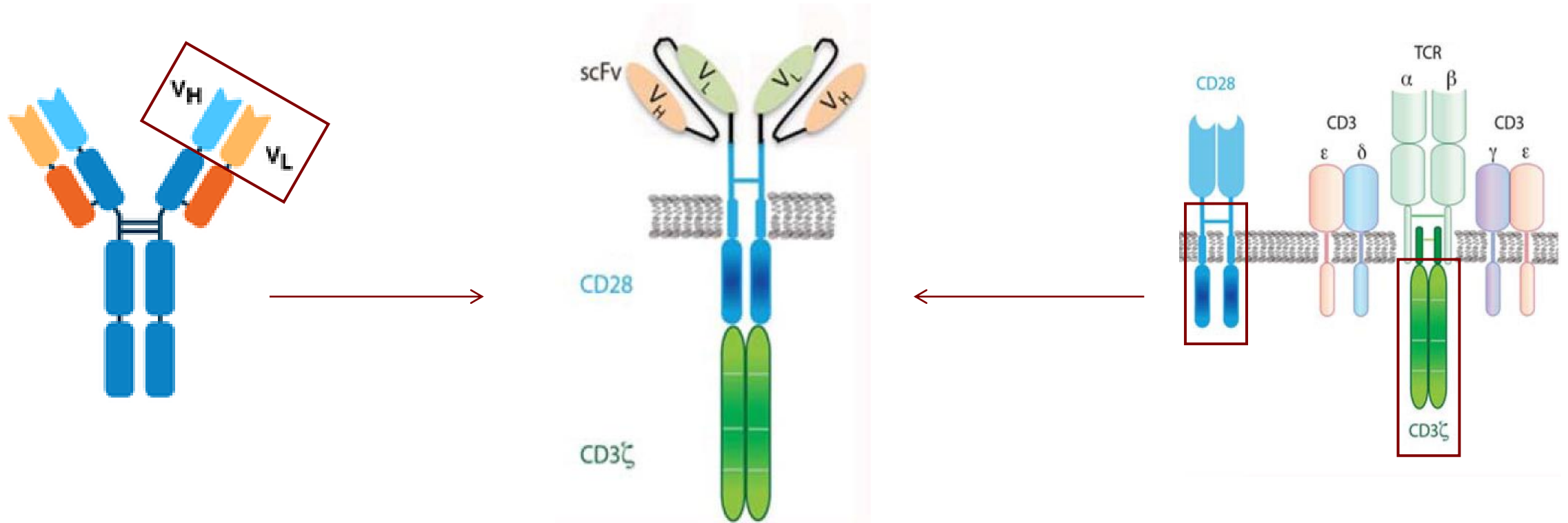
Society for Immunotherapy of Cancer

TiPS derived TCR^{-/-} CAR⁺ CD8 $\alpha\beta$ T cells

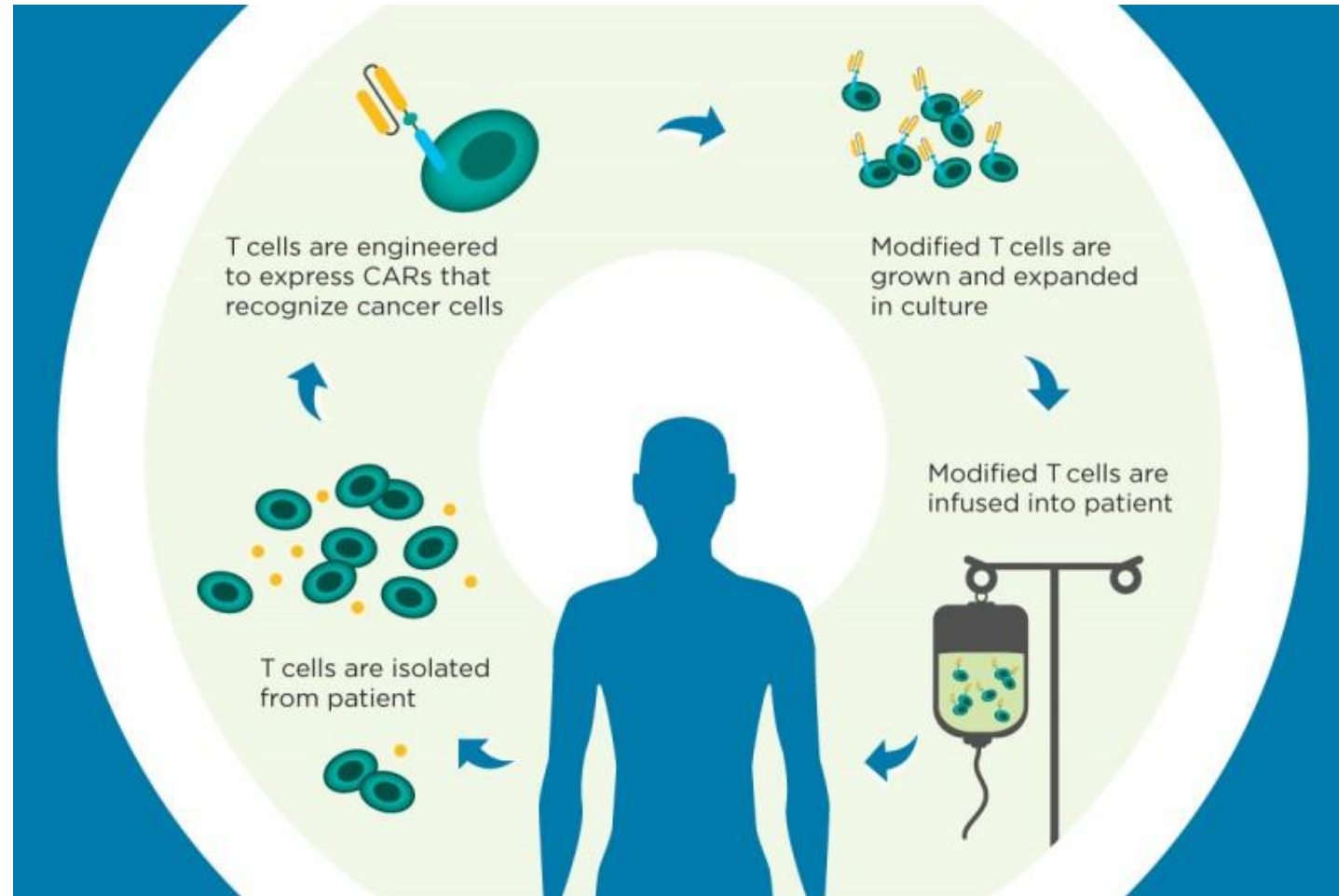
September 26, 2022

Sjoukje van der Stegen, PhD

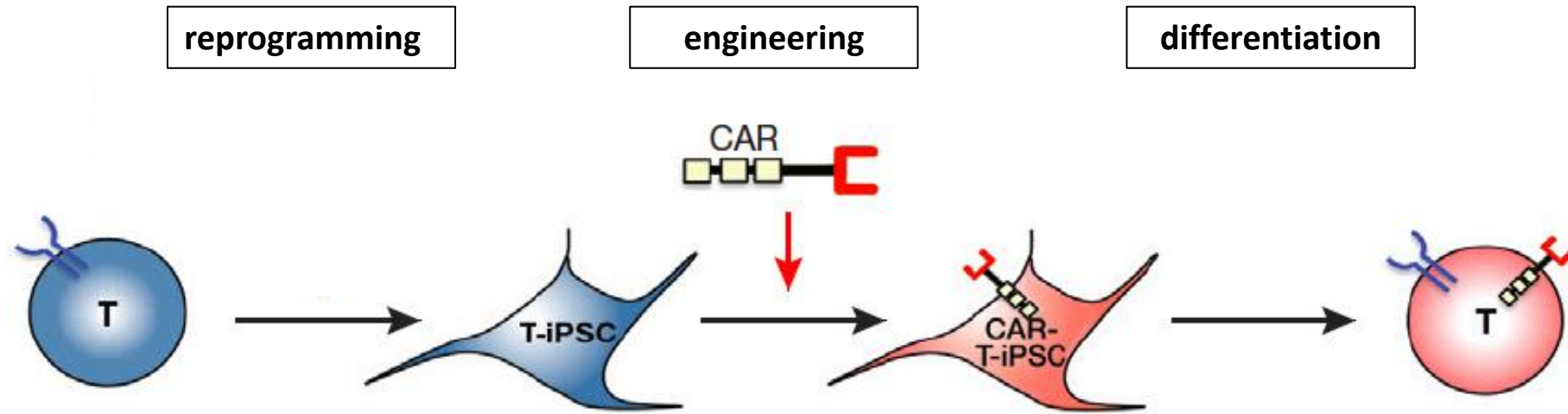
CAR T cell therapy



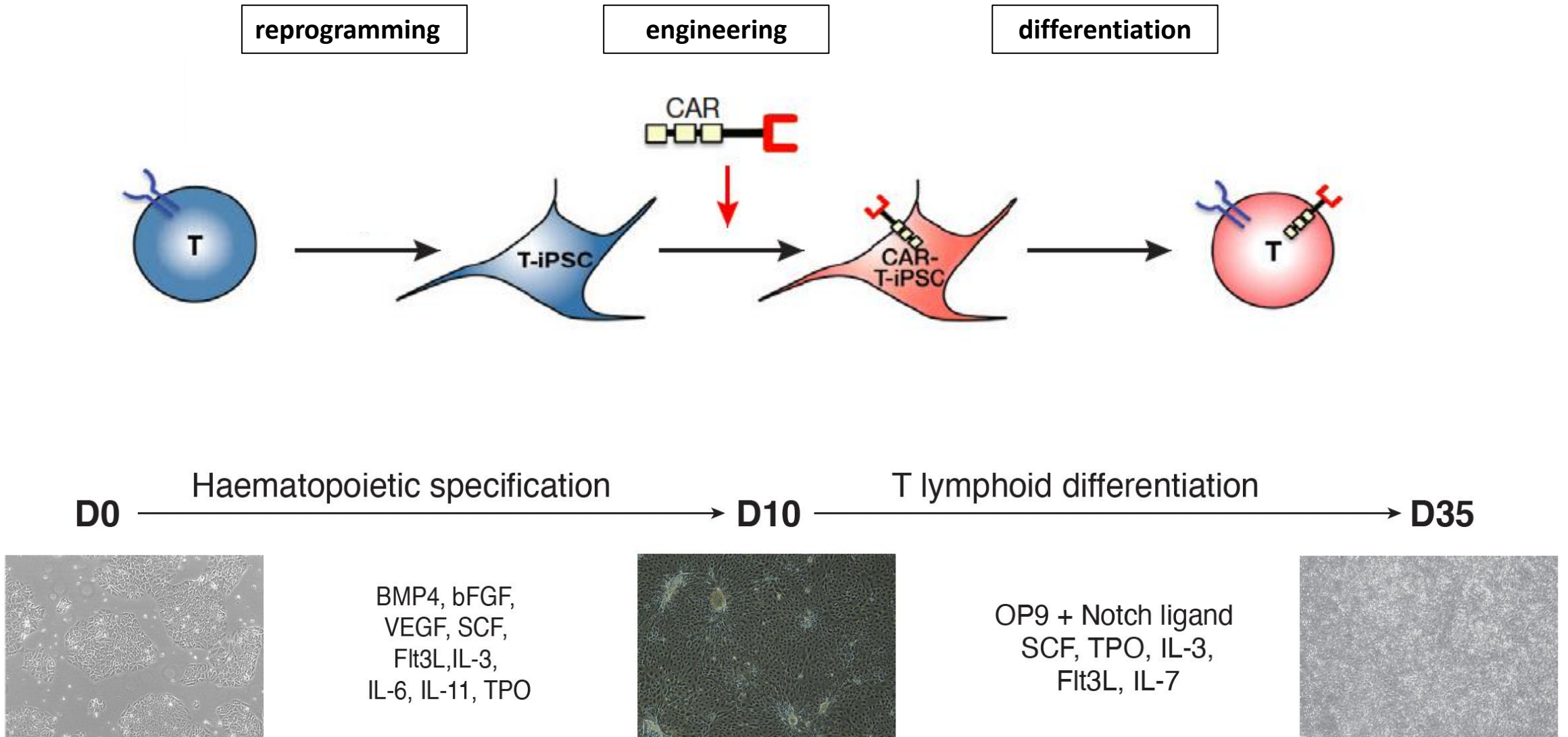
CAR T cell therapy



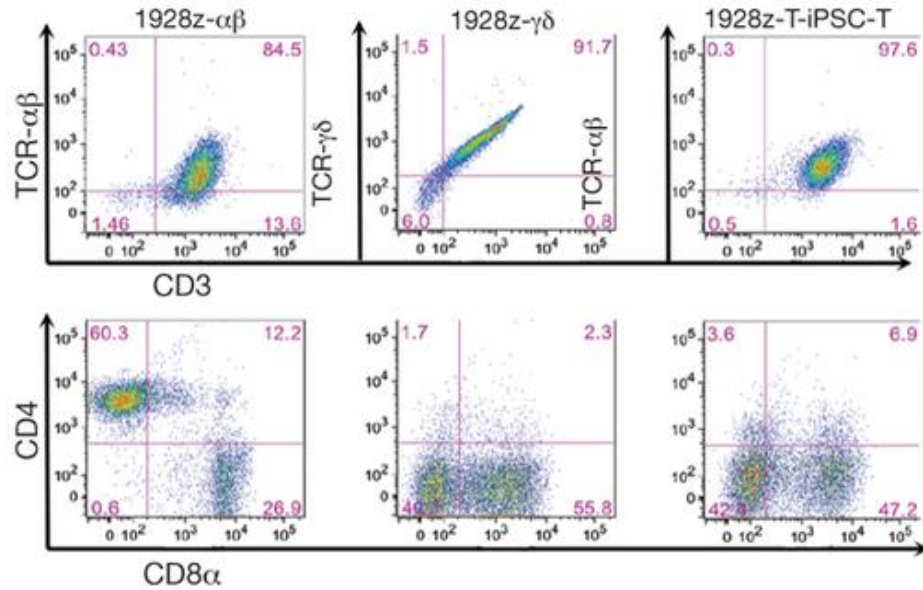
In vitro T cell differentiation



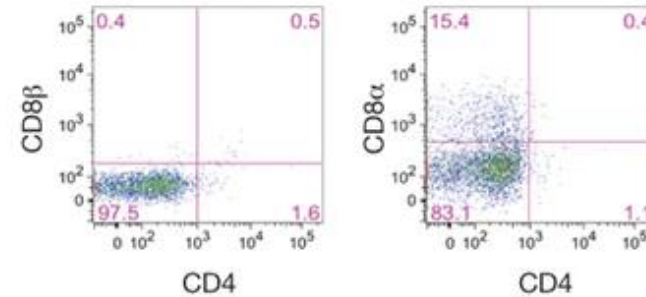
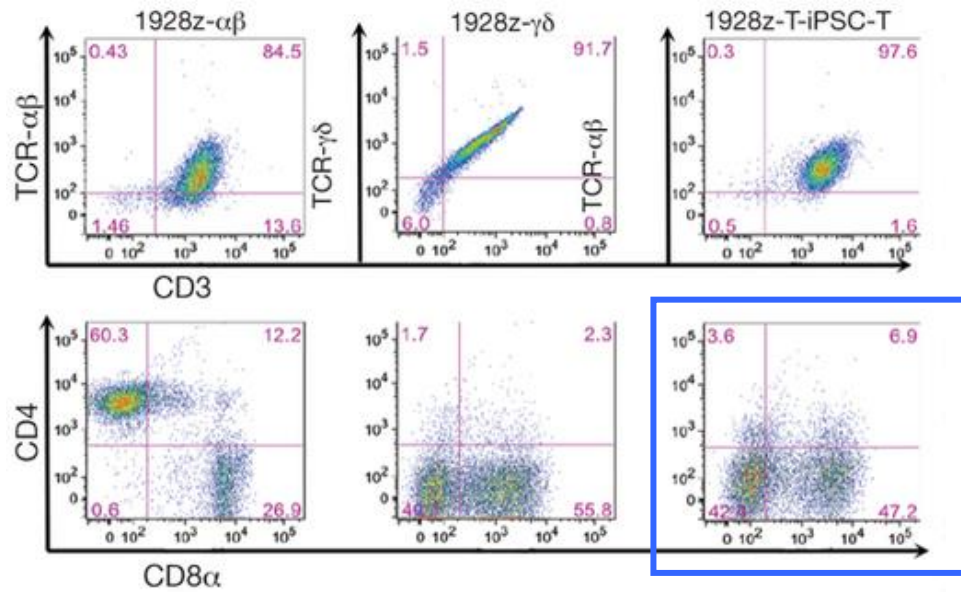
In vitro T cell differentiation



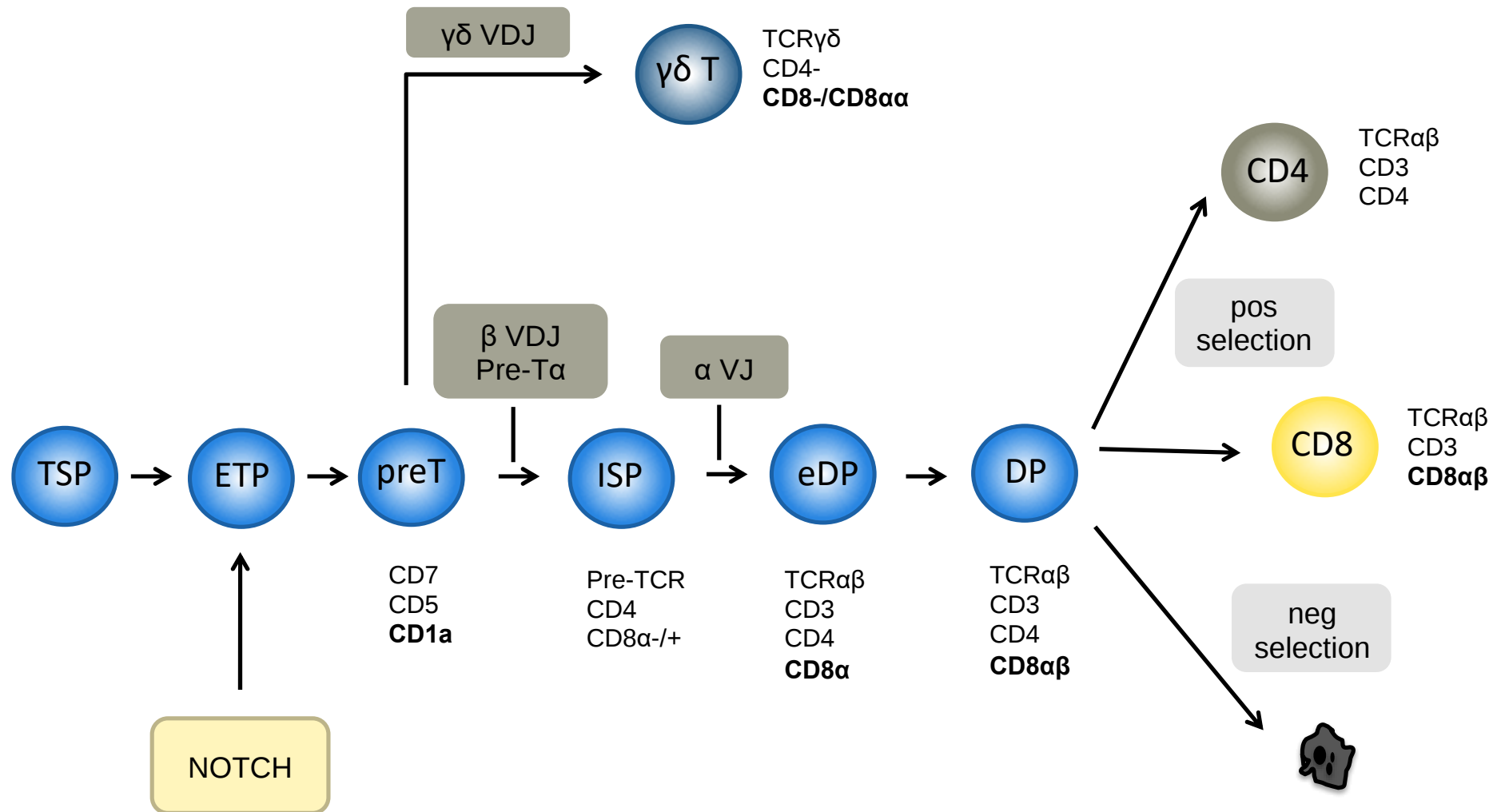
CAR-TiPS produce innate-like effector cells



CAR-TiPS produce innate-like effector cells



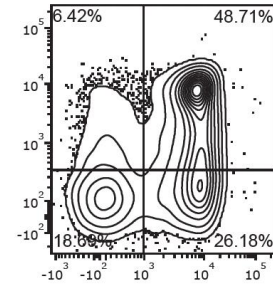
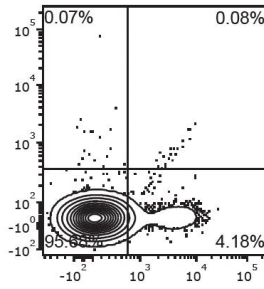
Human T cell development



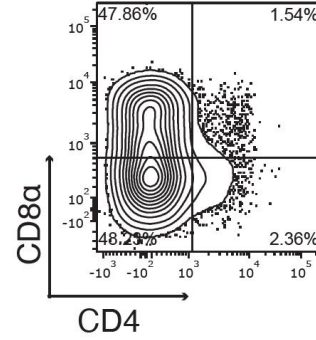
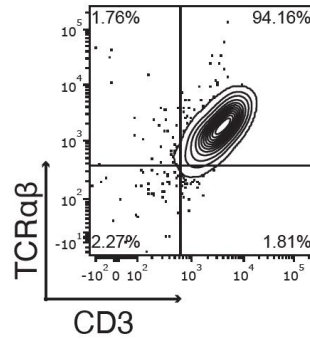
Notch and TCR/CAR redirect T lineage commitment

DLL1

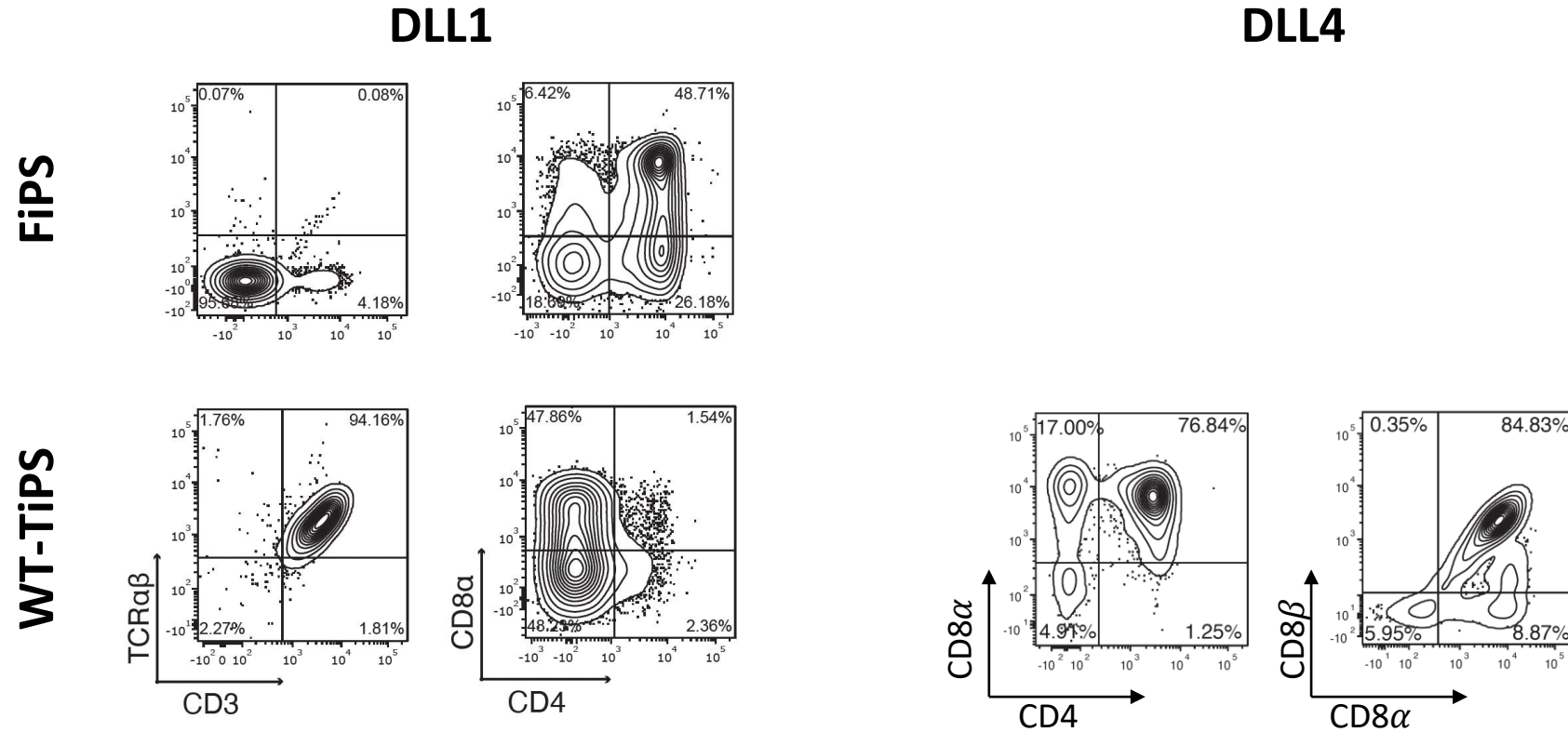
FiPS



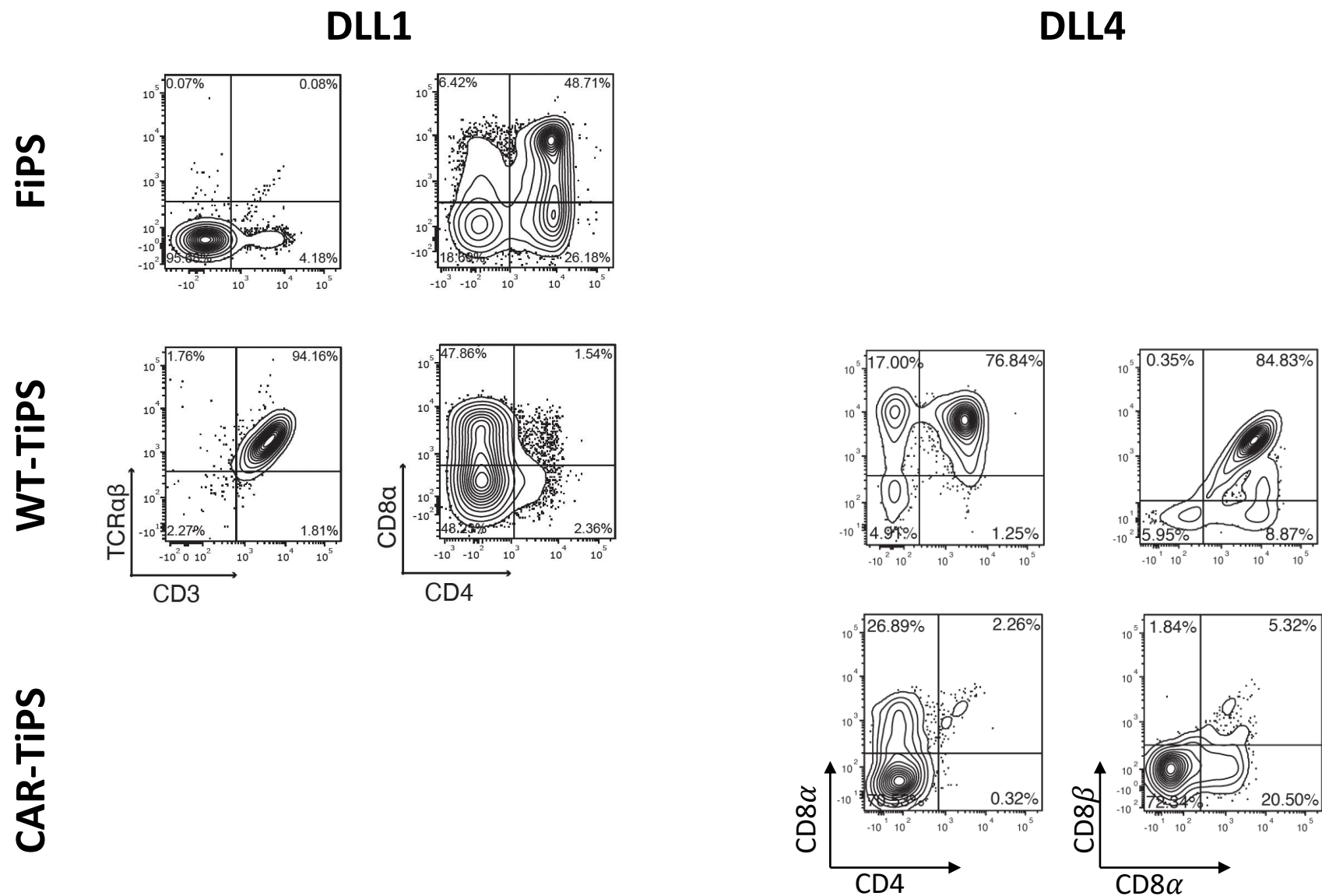
WT-TiPS



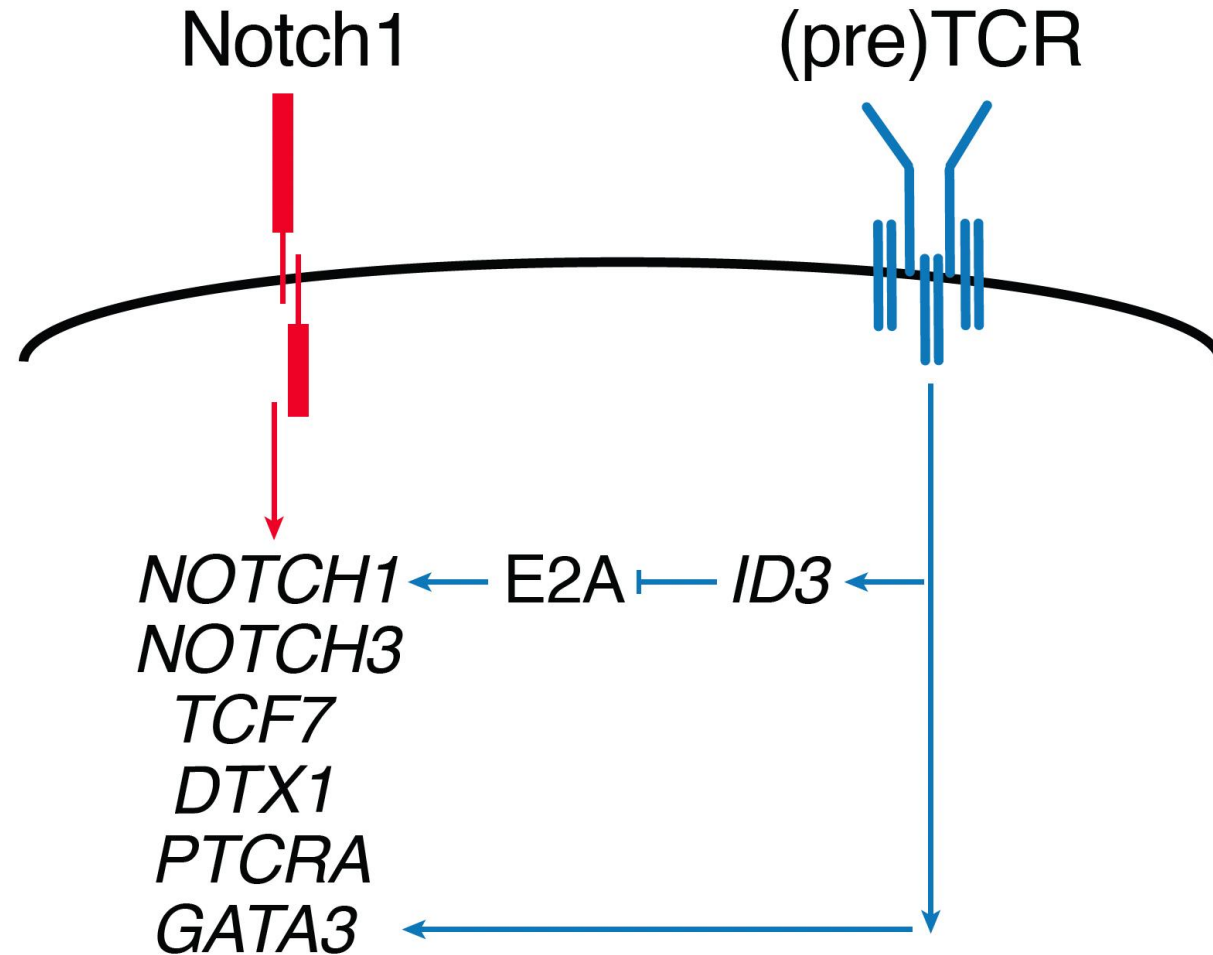
Notch and TCR/CAR redirect T lineage commitment



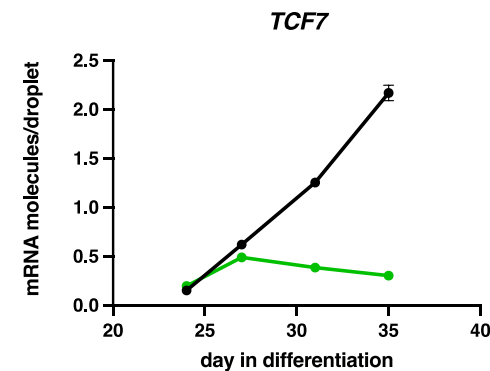
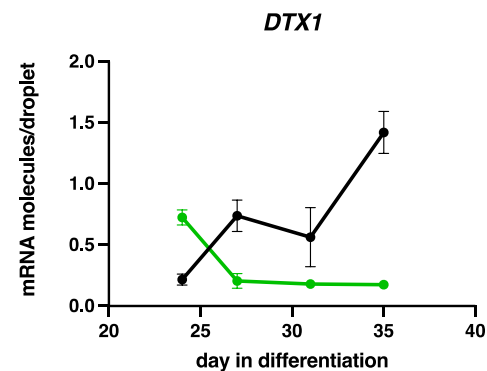
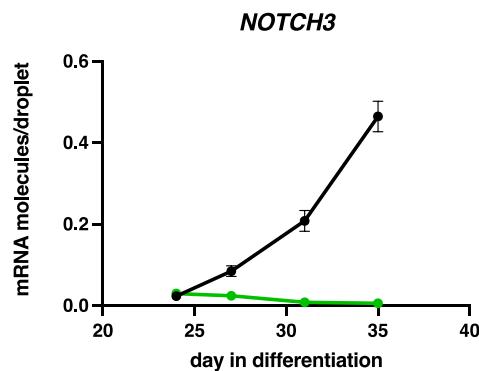
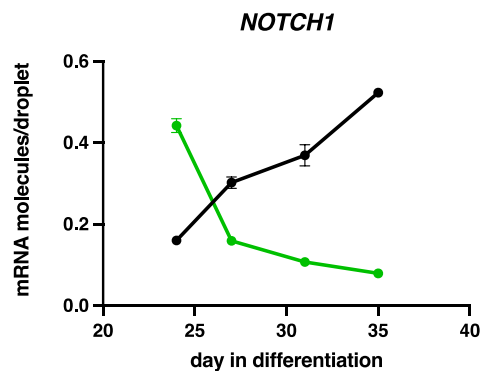
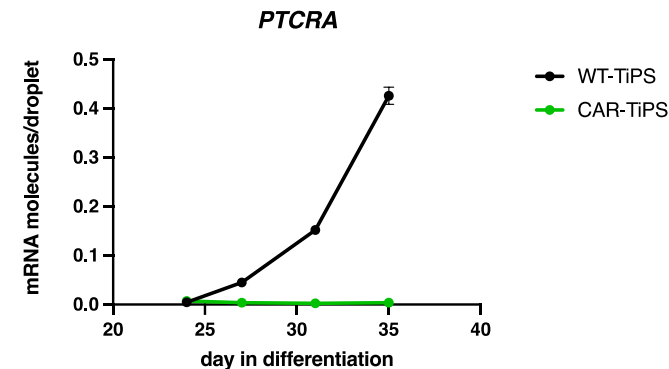
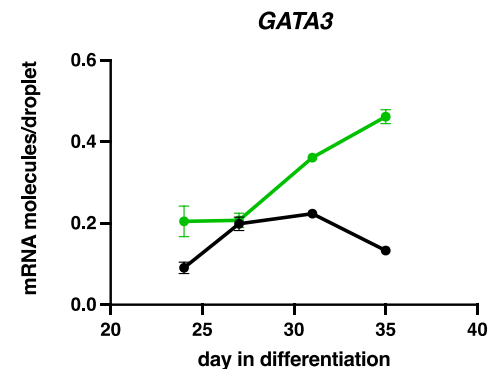
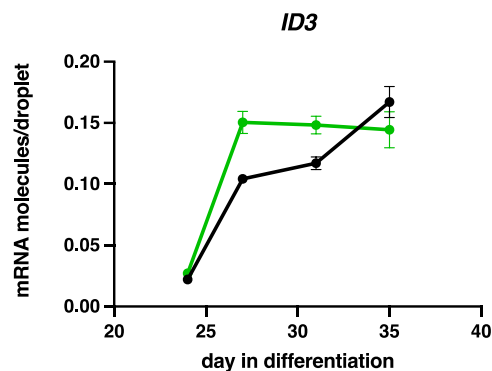
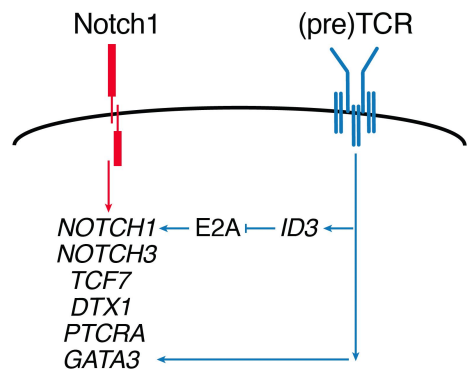
Notch and TCR/CAR redirect T lineage commitment



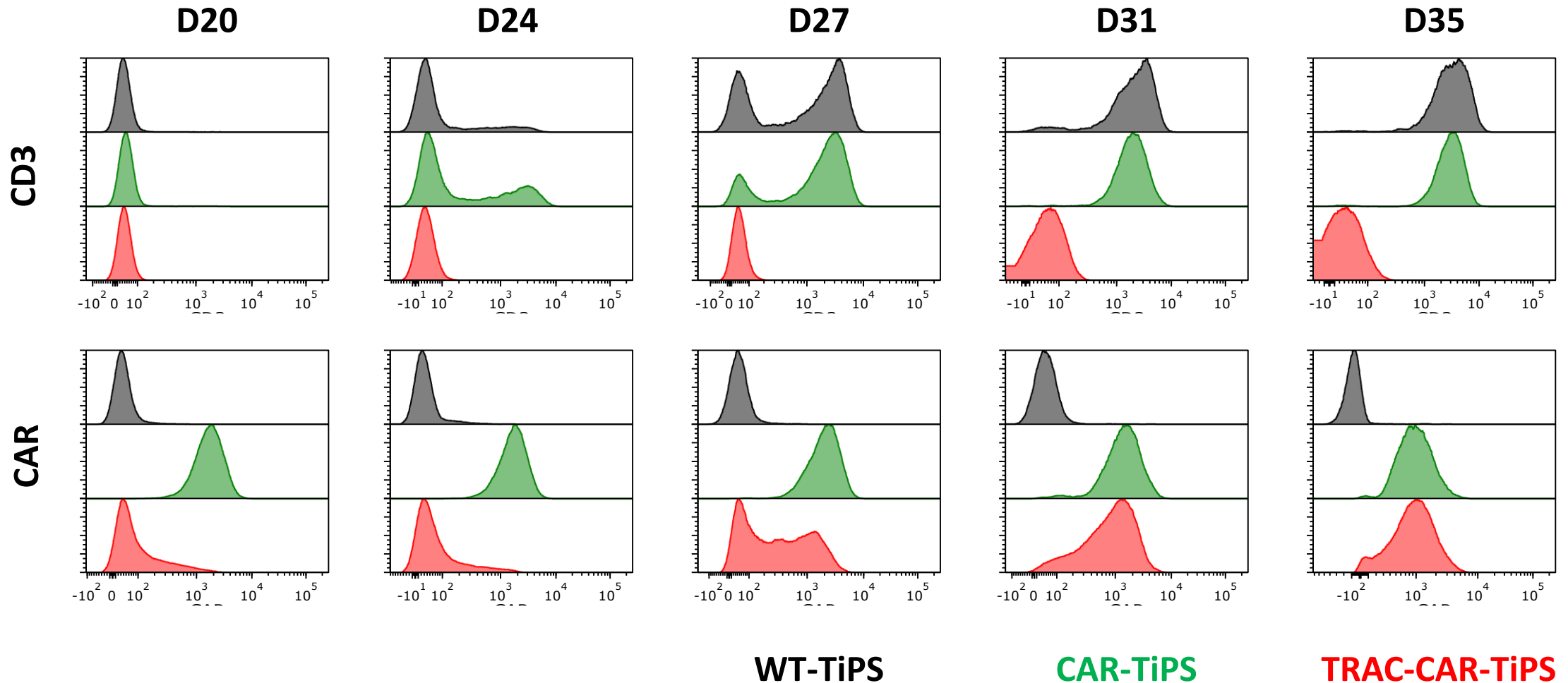
(pre)TCR signaling interacts with Notch



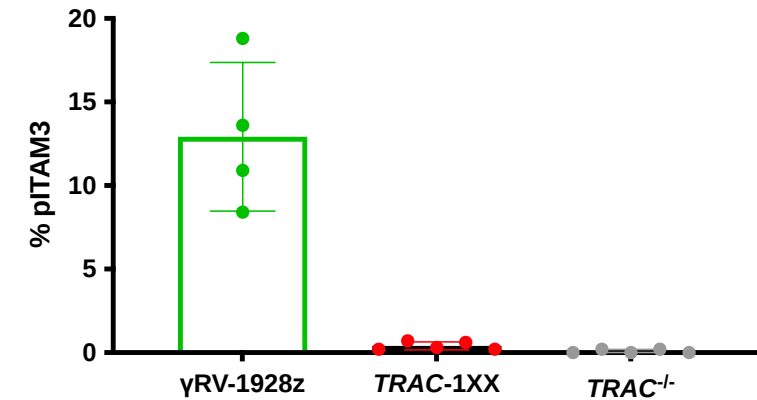
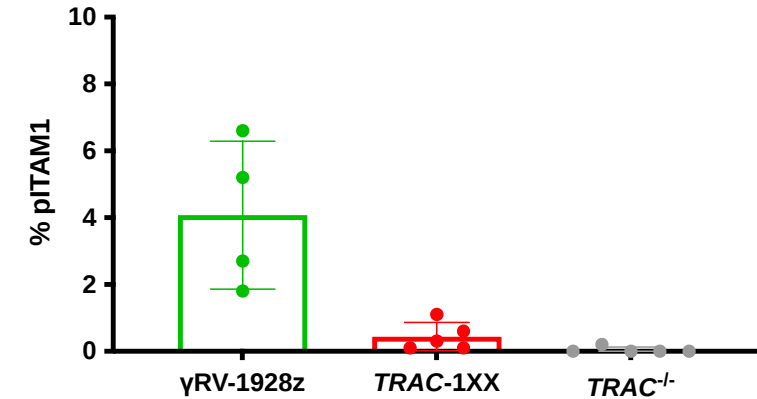
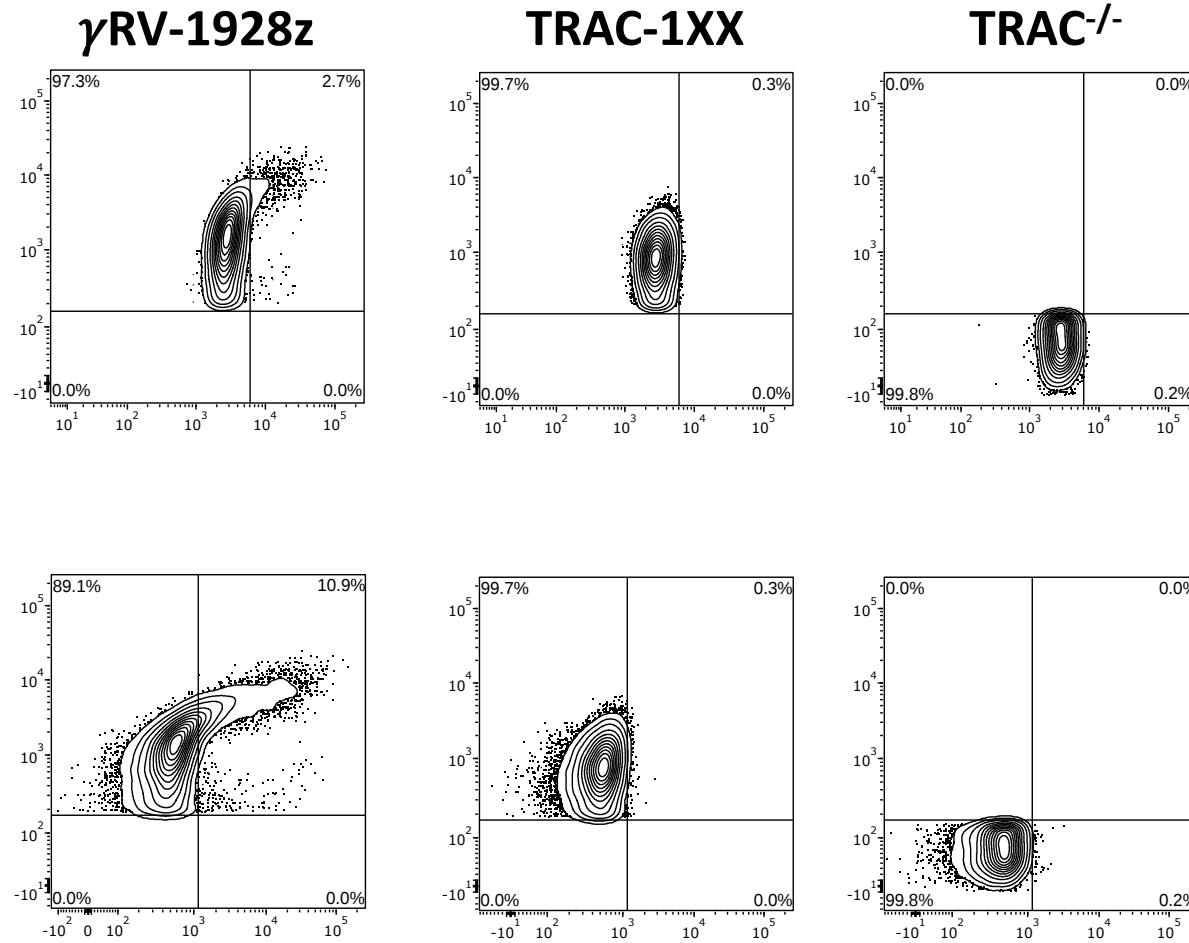
CAR expression affects downstream Notch signaling



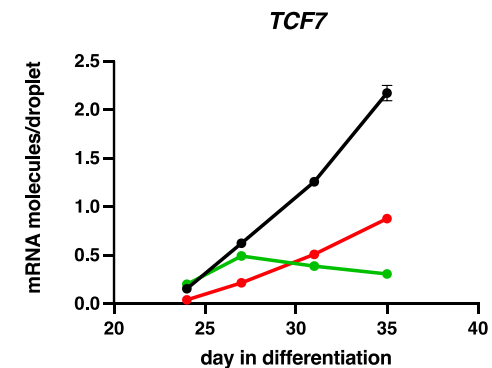
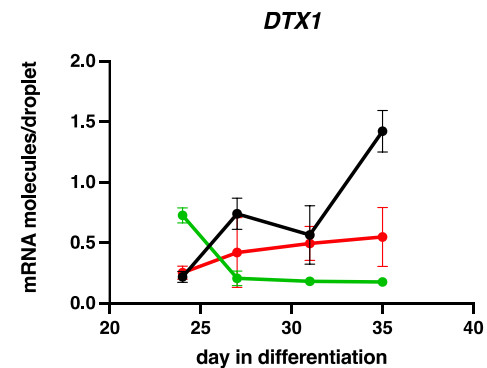
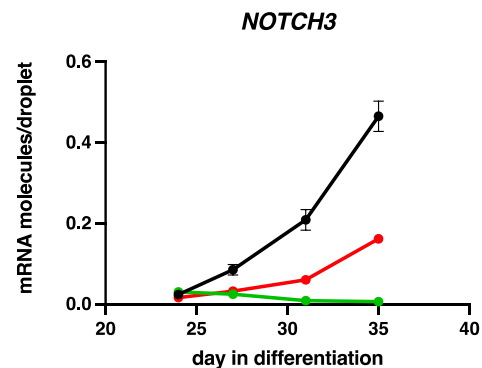
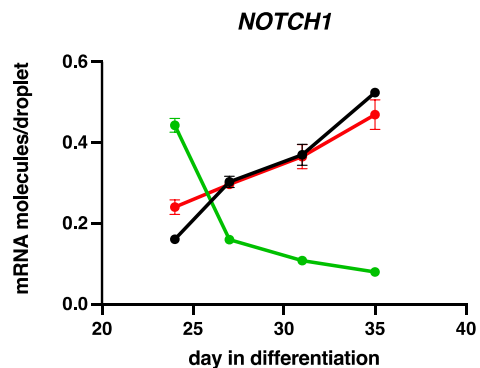
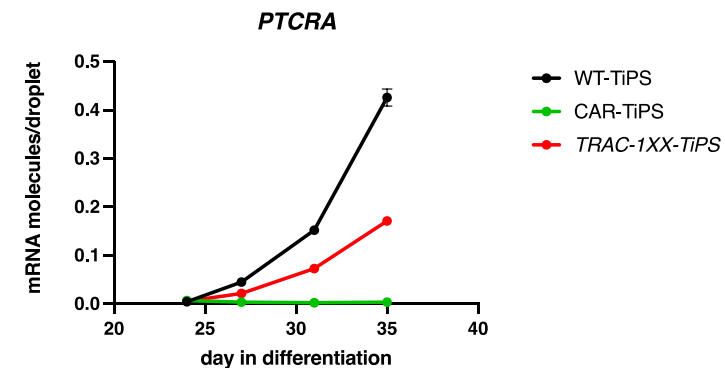
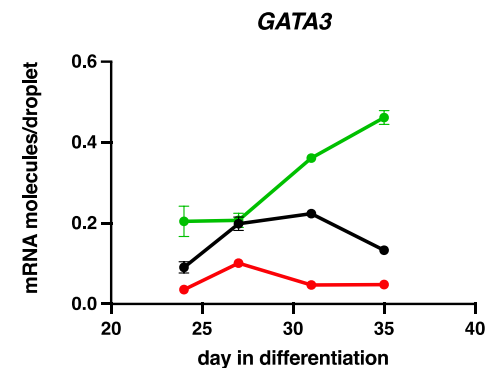
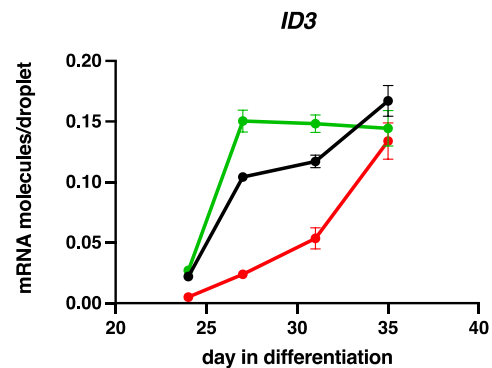
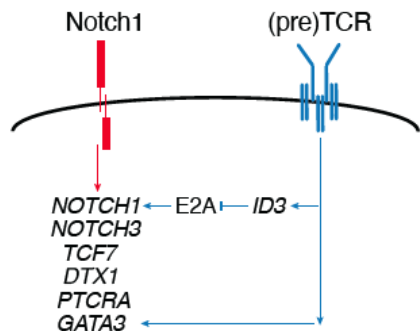
TRAC controls CAR expression in differentiation



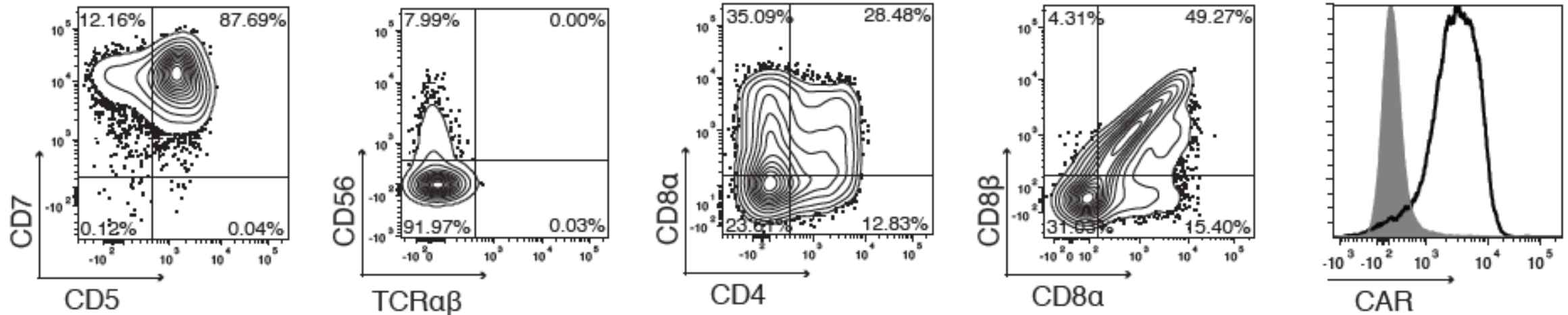
TRAC-1XX has reduced tonic ITAM phosphorylation



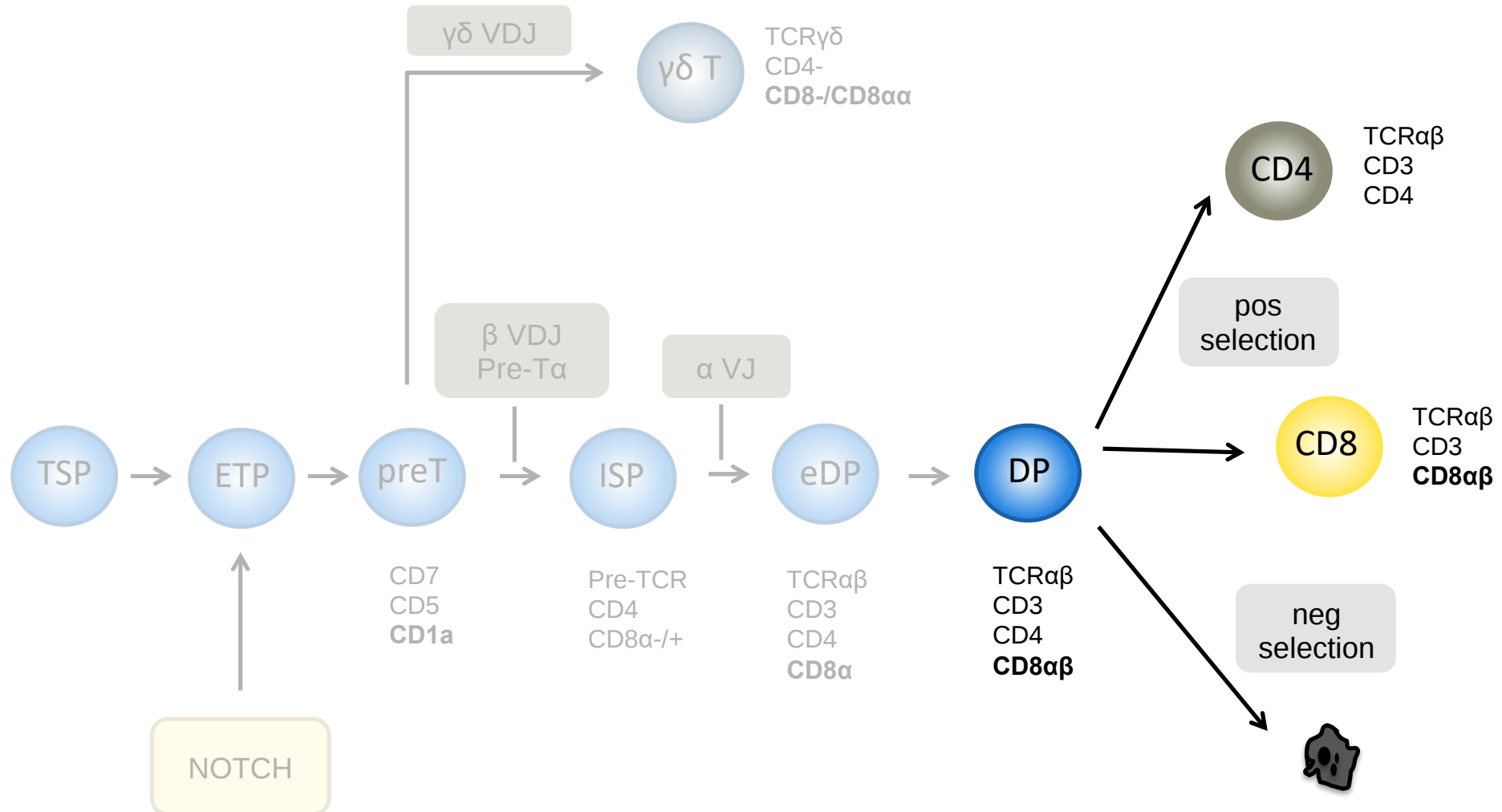
TRAC-1XX rescues Notch signaling



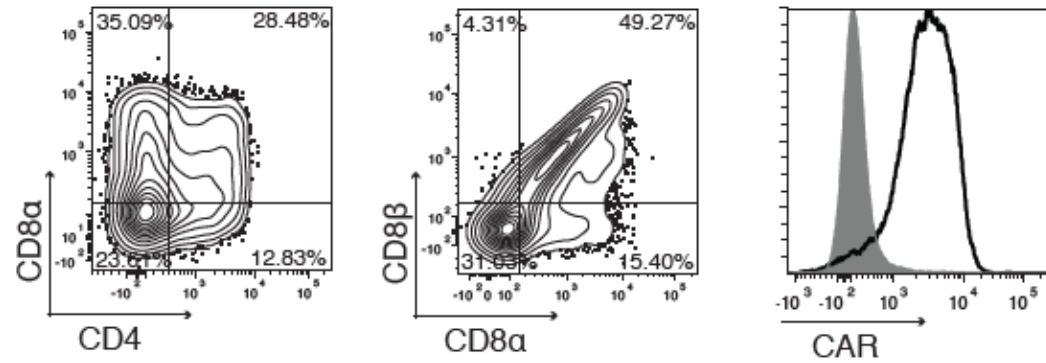
Controlled CAR supports DP development



Maturation to the SP stage

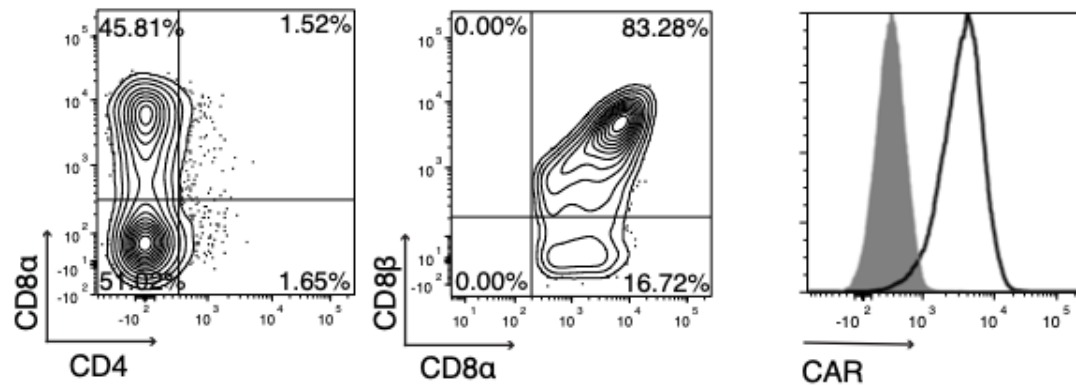


CAR engagement facilitates CD8 $\alpha\beta$ SP development

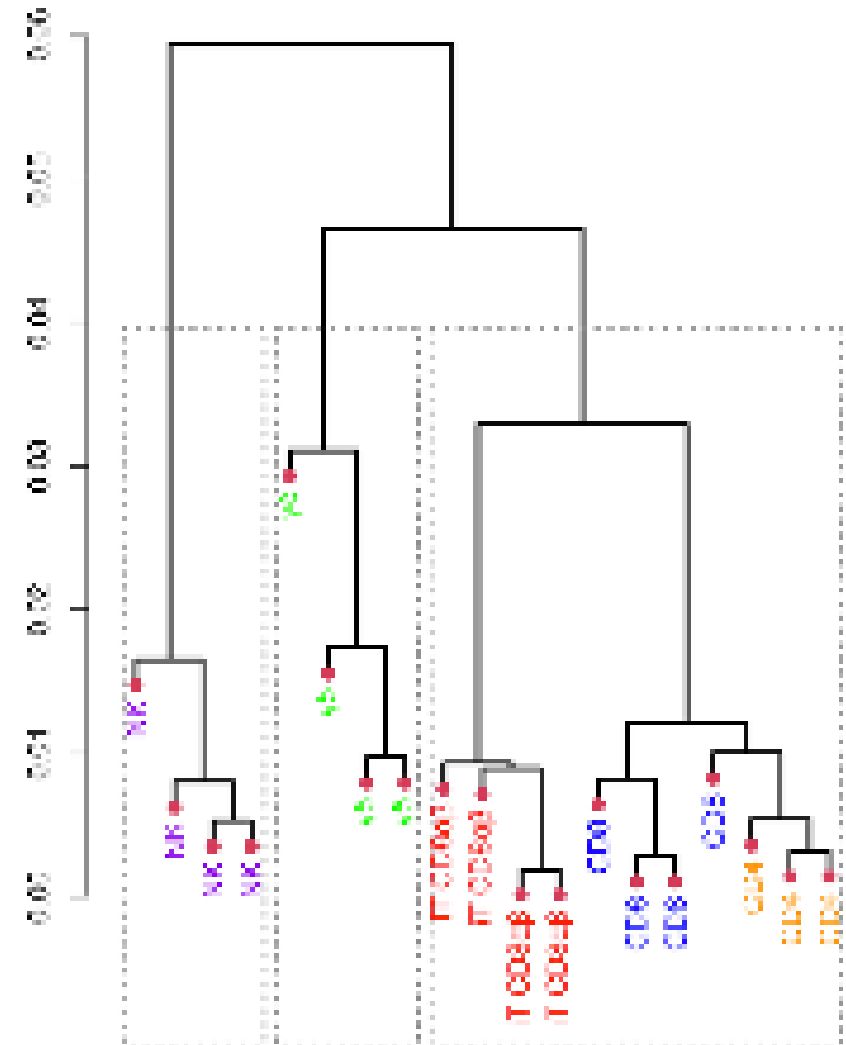
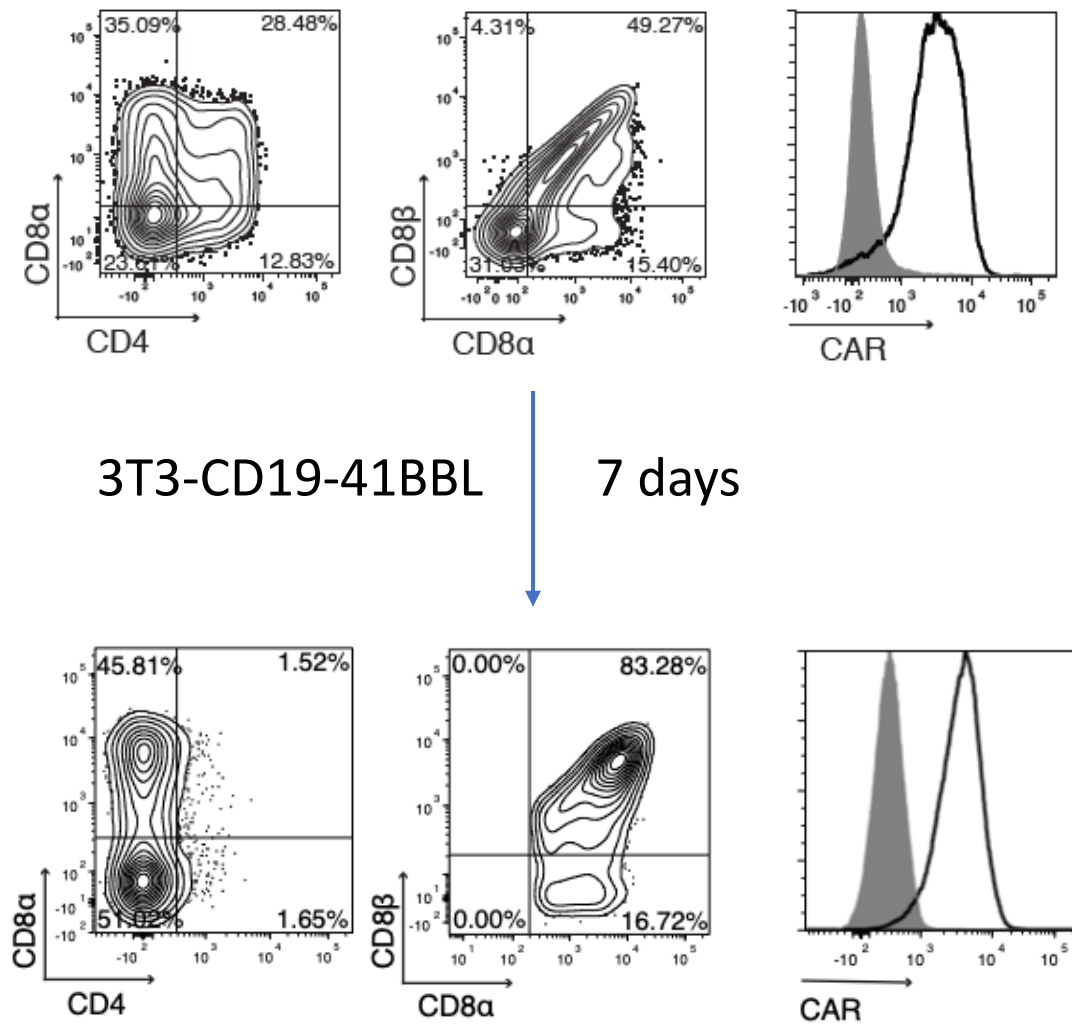


3T3-CD19-41BBL

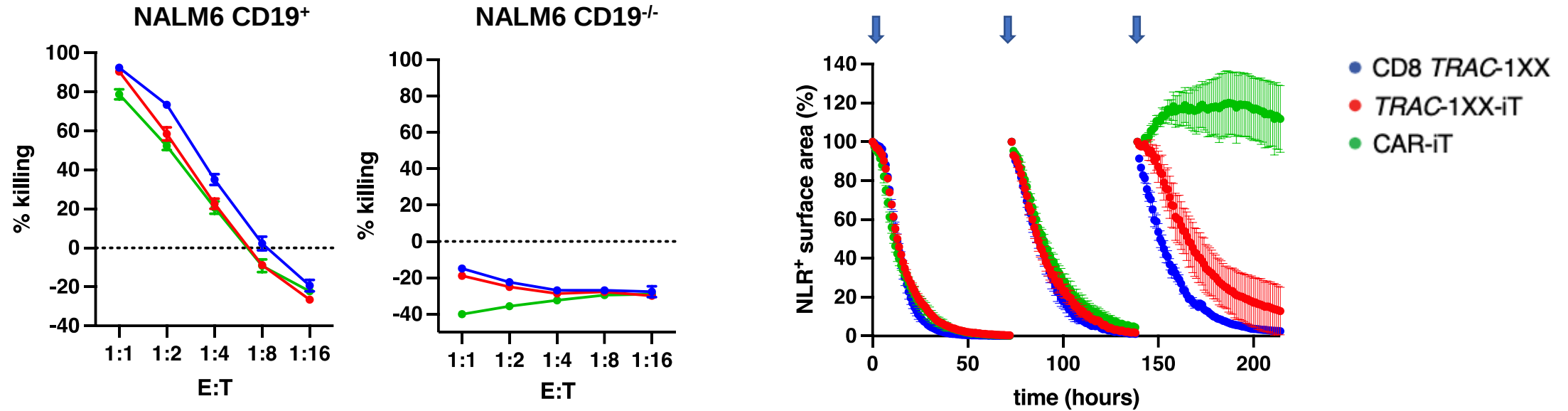
7 days



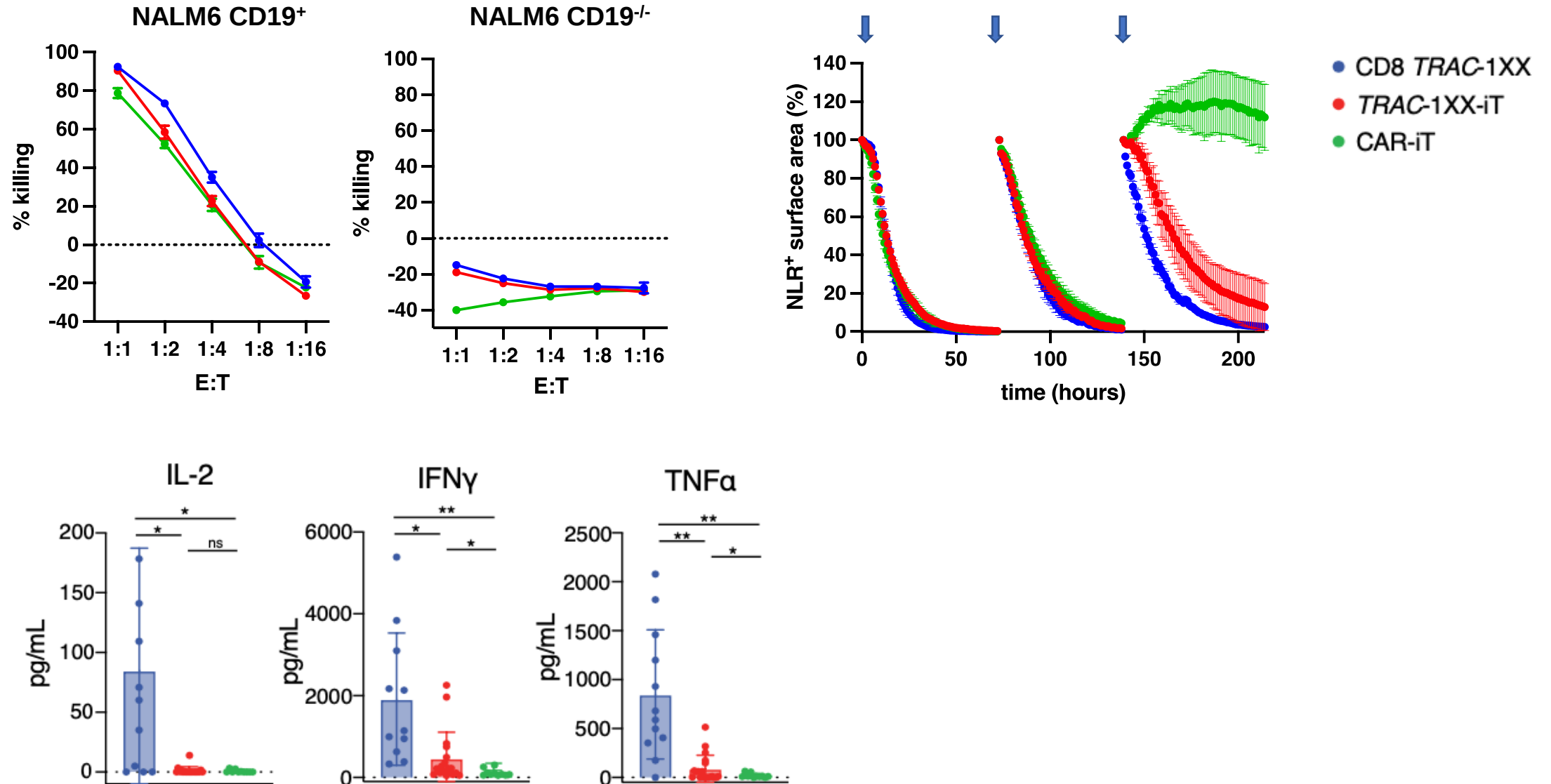
CAR engagement facilitates CD8 $\alpha\beta$ SP development



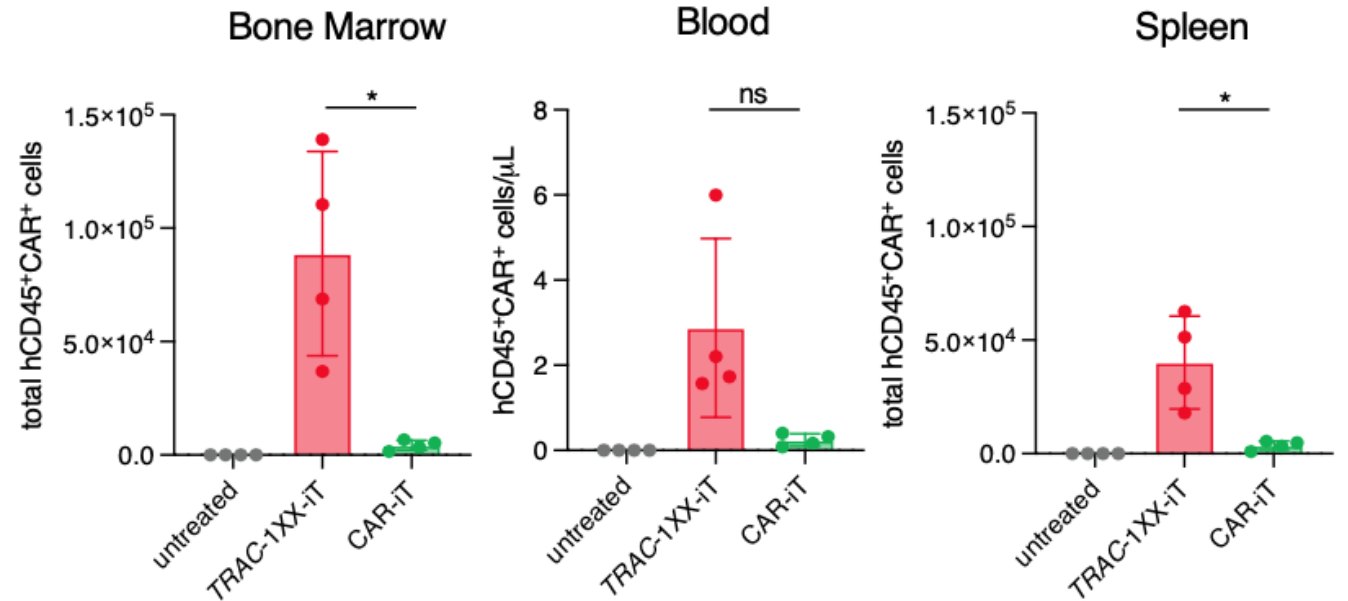
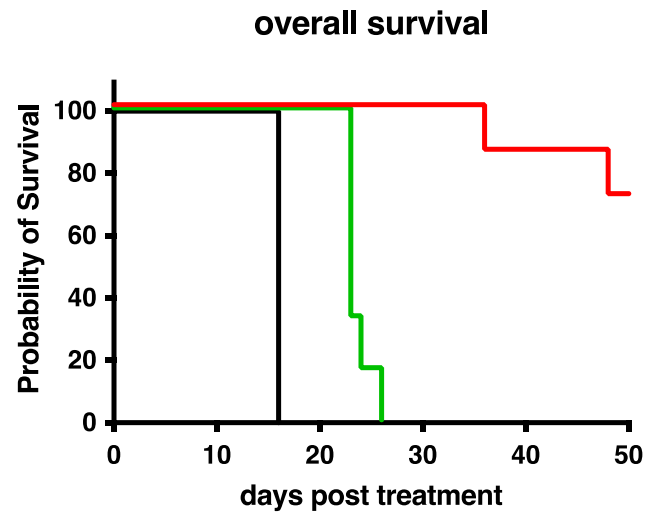
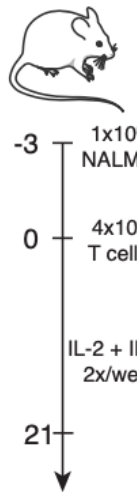
TRAC-1XX-iT have improved function over CAR-iT



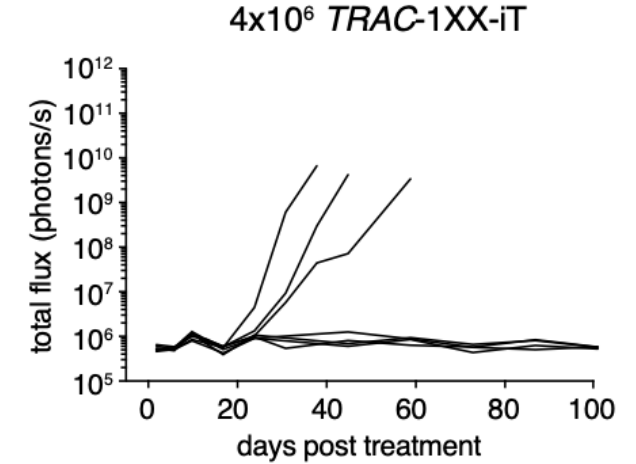
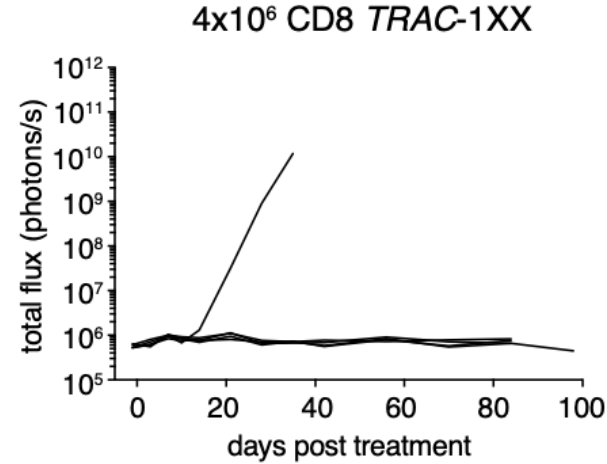
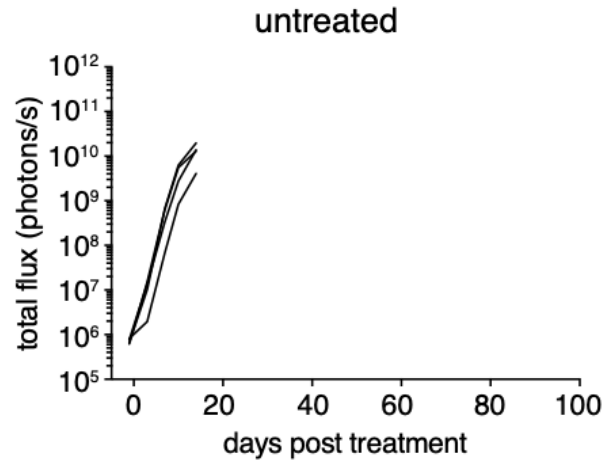
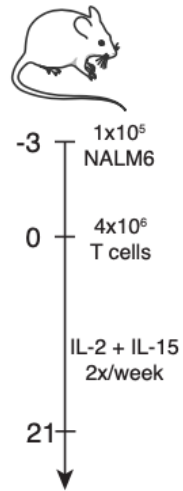
TRAC-1XX-iT have improved function over CAR-iT



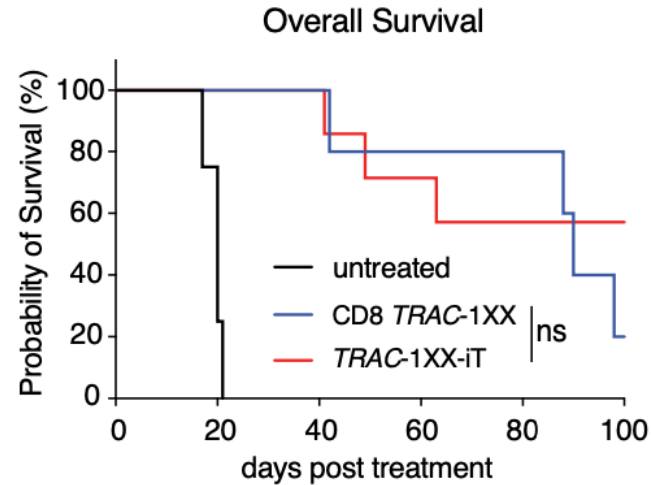
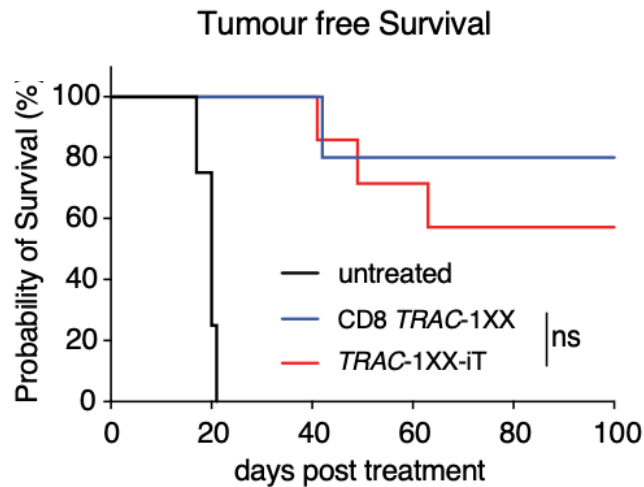
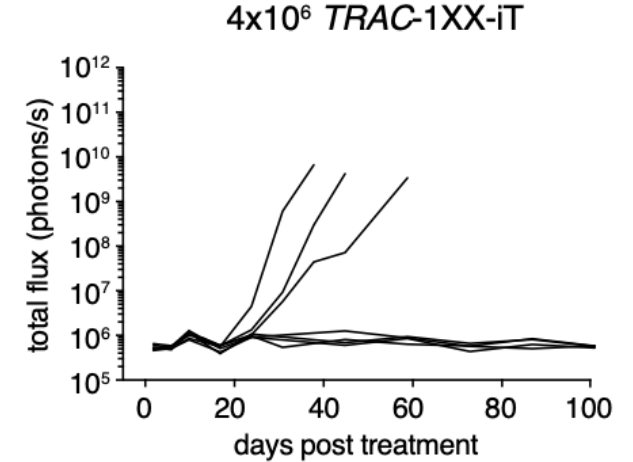
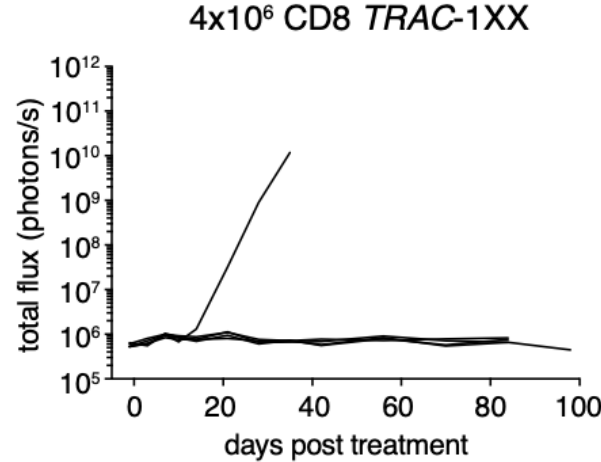
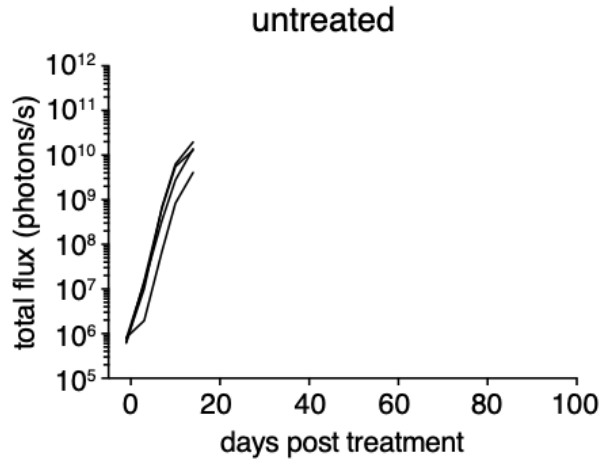
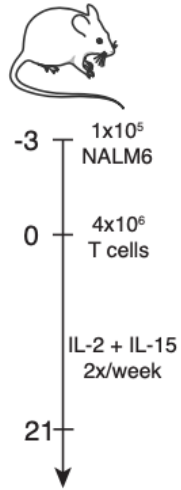
TRAC-1XX-iT have improved function over CAR-iT



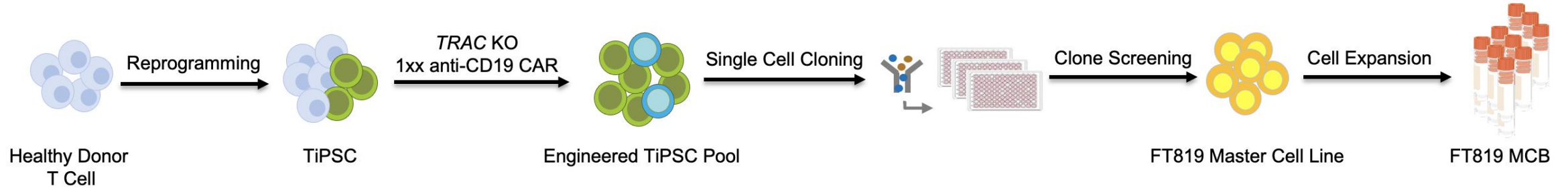
TRAC-1XX-iT can cure systemic leukemia without inducing GvHD



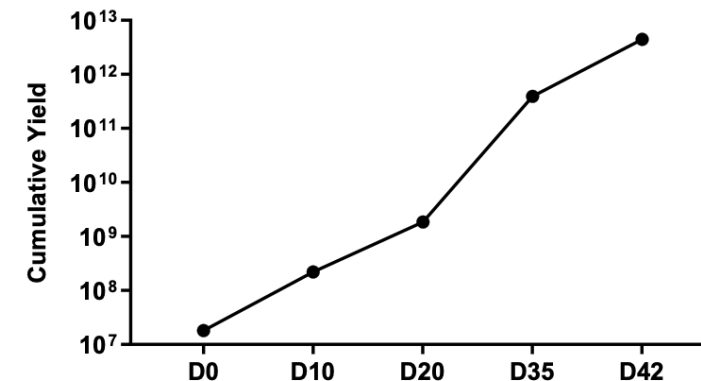
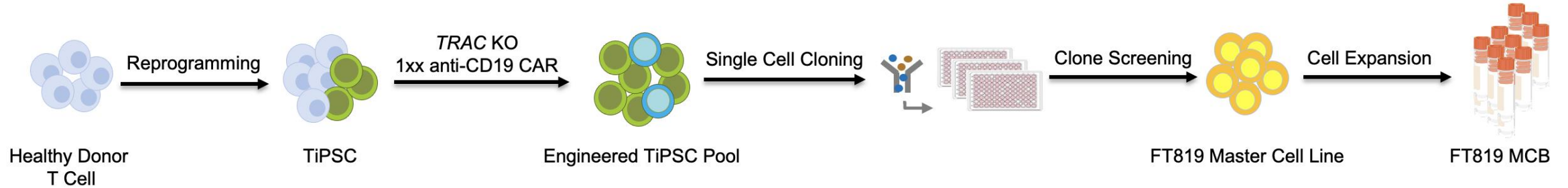
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FT819: *TRAC*-1XX-iT production for Phase I clinical trial



FT819: *TRAC*-1XX-iT production for Phase I clinical trial



TiPS-derived TCR^{-/-} CAR⁺ CD8 $\alpha\beta$ T cells

- TCR and CAR diminish Notch1 downstream signaling
- Delayed and titrated CAR signaling can drive T cell differentiation
- CAR engagement facilitates maturation from DP to CD8 $\alpha\beta$ SP
- *TRAC*-1XX-iT have superior function over CAR-iT
- *TRAC*-1XX-iT can cure systemic leukemia model
- *TRAC*-1XX-iT do not induce GvHD

Michel Sadelain Lab

- Michel Sadelain
- Pieter Lindenbergh
- Roseanna Petrovic
- Hongyao Xie
- Mame Diop
- Vera Alexeeva
- Yuzhe Shi
- Jorge Mansilla-Soto
- Mohamad Hamieh
- Justin Eyquem
- Annalisa Cabriolu
- Maria Themeli

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- Isabelle Riviere

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- Tom Lee
- Ramzey Abujarour
- Bob Valamehr



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