Memorial Sloan Kettering Cancer Center

Weill Cornell Medicine

Characterizing double positive T cells in the tumor microenvironment: a tale of promiscuous cell fates

Sara Schad
Wolchok & Merghoub Lab
SITC 2020

LUDWIG CANCER RESEARCH

PARKER INSTITUTE FOR CANCER IMMUNOTHERAPY

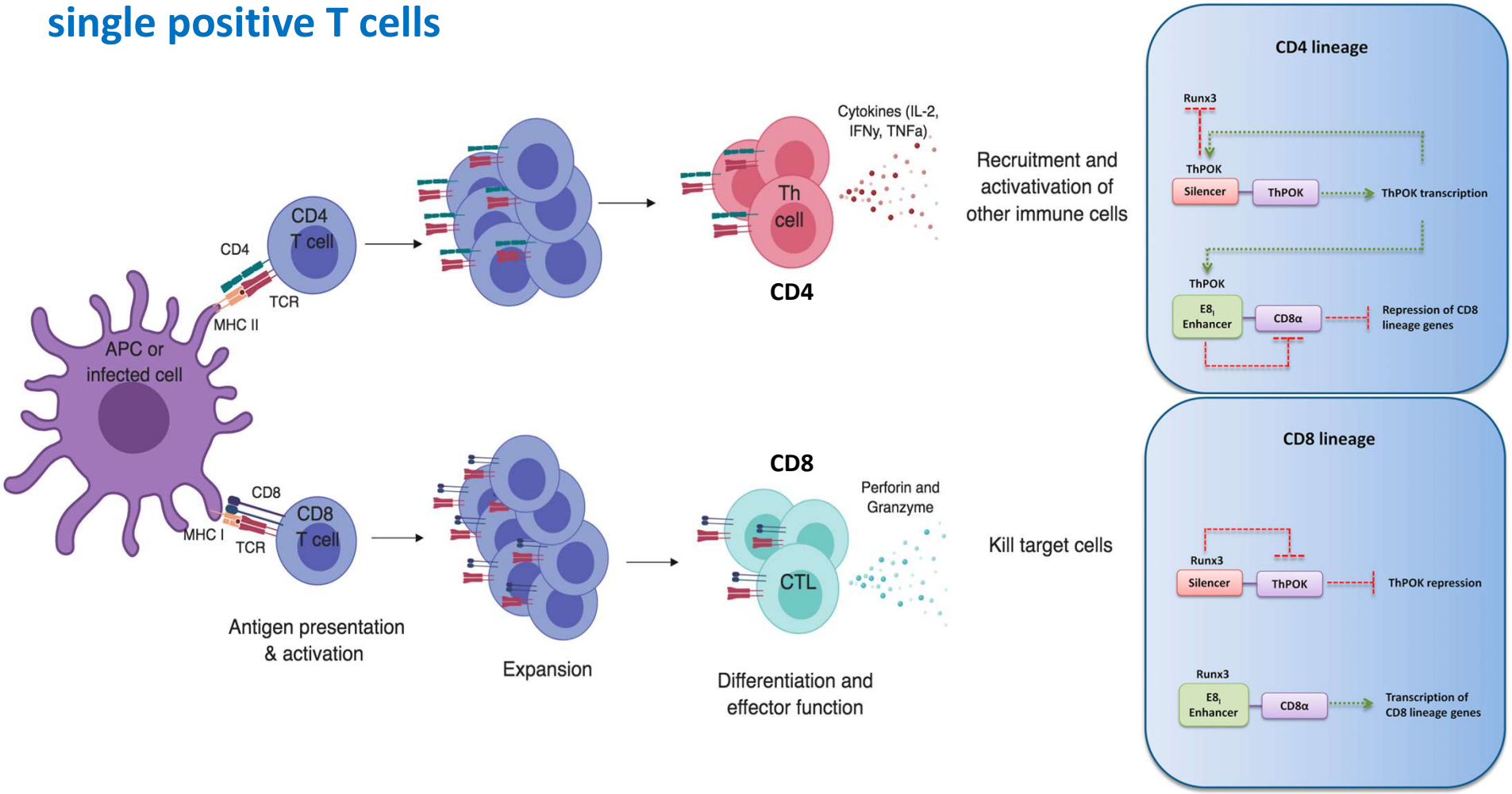
SWIM ACROSS AMERICA
MAKING WAVES TO FIGHT CANCER

Disclosures

US Provisional Patent:

Phosphatidylserine Targeting Agents And Uses Thereof For Adoptive T-Cell Therapies

ThPOK and Runx3 regulate the development of functionally distinct single positive T cells



Overgaard *et al.*, 2015

Polyfunctional CD4^{+}CD8^{+} Double Positive T cells exist in the periphery

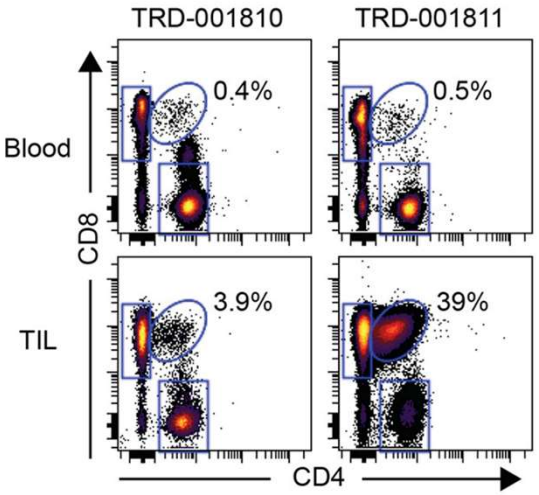
frontiers in Immunology

ORIGINAL RESEARCH
published: 26 November 2018
doi: 10.3389/fimmu.2018.02728

Renal Cell Carcinoma (RCC) Tumors Display Large Expansion of Double Positive (DP) CD4+CD8+ T Cells With Expression of Exhaustion Markers

Laurence C. Menard[1], Paul Fischer[1], Bijal Kakrecha[1], Peter S. Linsley[2], Erik Wambre[2], Maochang C. Liu[2], Blake J. Rust[2], Deborah Lee[1], Becky Penhallow[1], Nataly Manjarrez Orduno[1] and Steven G. Nadler[1]*

[1] Translational Medicine, Bristol-Myers Squibb, Princeton, NJ, United States, [2] Benaroya Research Institute at Virginia Mason, Seattle, WA, United States



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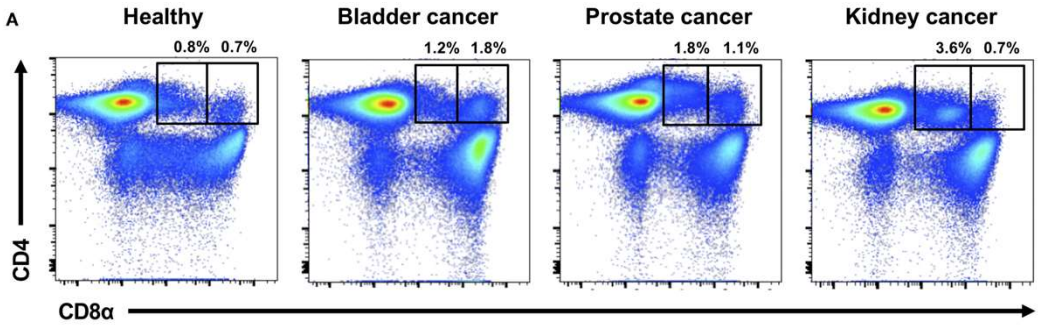
Double Positive CD4^{+}CD8^{+} T Cells Are Enriched in Urological Cancers and Favor T Helper-2 Polarization

*Perrine Bohner†, Mathieu F. Chevalier†, Valérie Cesson, Sonia-Christina Rodrigues-Dias, Florence Dartiguenave, Rodolfo Burruni, Thomas Tawadros, Massimo Valerio, Ilaria Lucca, Denise Nardelli-Haefliger, Patrice Jichlinski and Laurent Derré**

Urology Research Unit, Urology Department, University Hospital of Lausanne (CHUV), Lausanne, Switzerland



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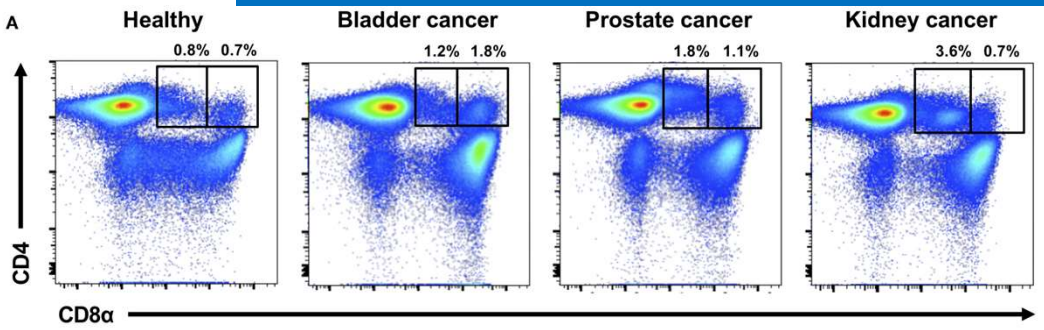
What signals are suppressing lineage commitment mechanisms in the periphery?



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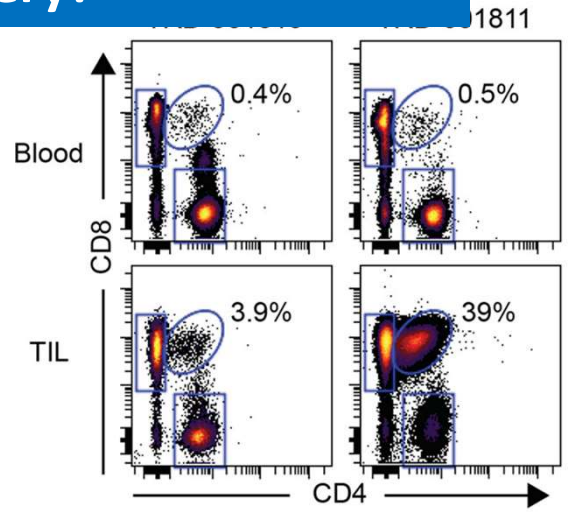

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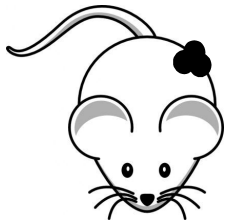
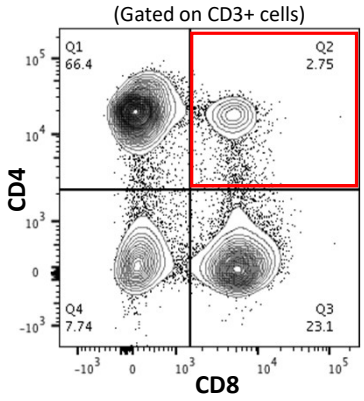
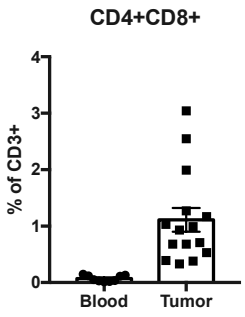
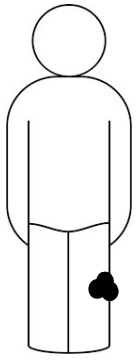
Heterogenous $CD4^{+}CD8^{+}$ double positive T cells accumulate in murine and human melanoma tumors

B16 Melanoma

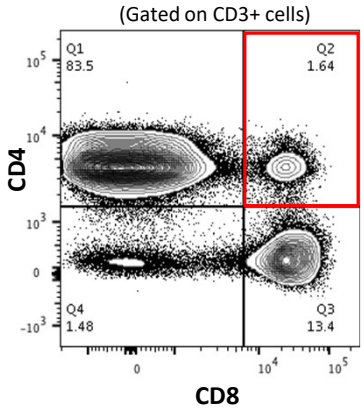


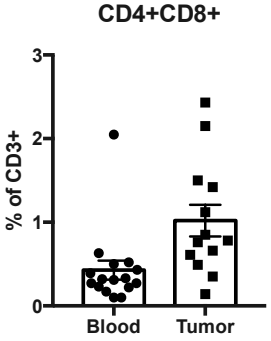






Melanoma resection





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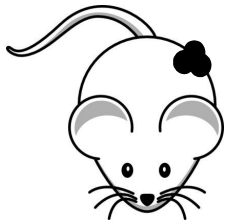

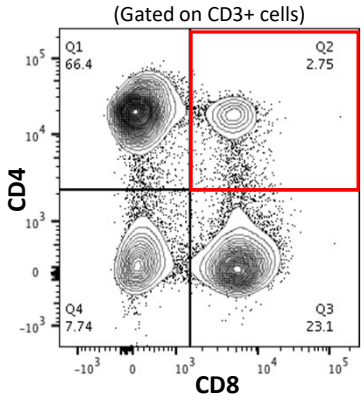

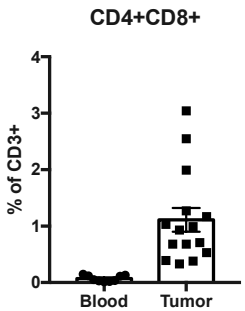

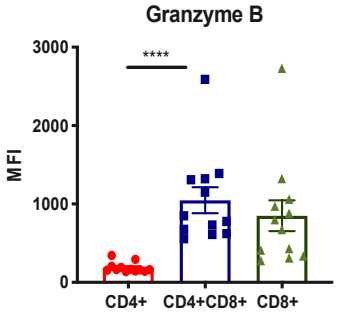

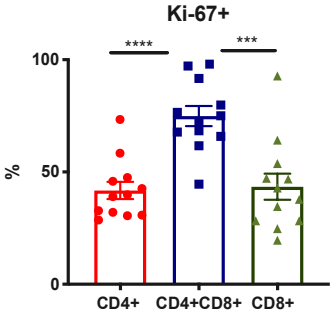

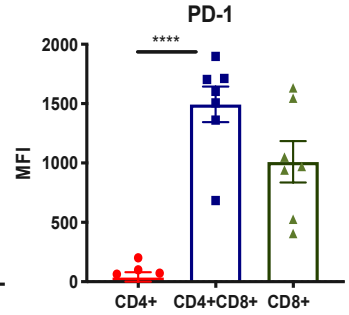

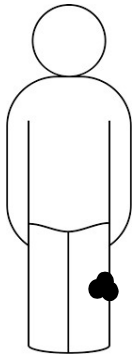

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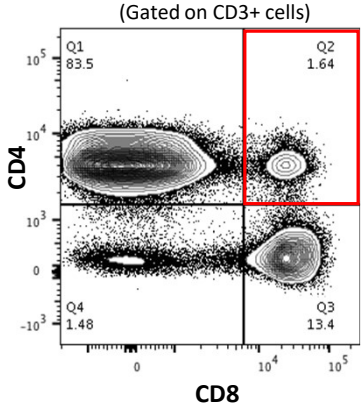
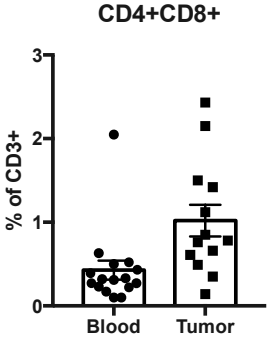
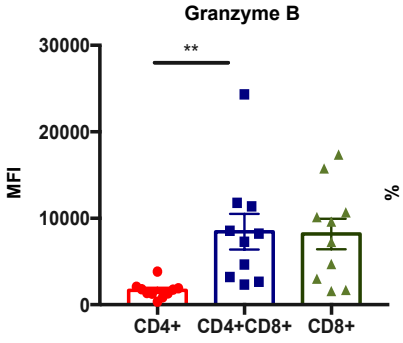
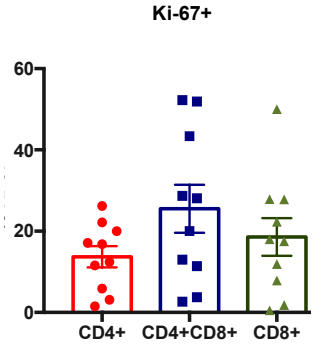
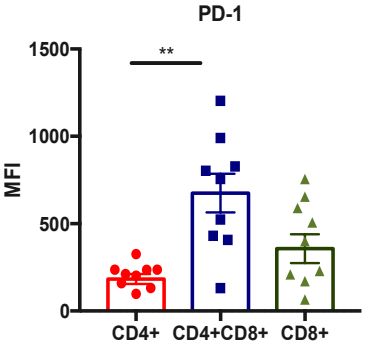




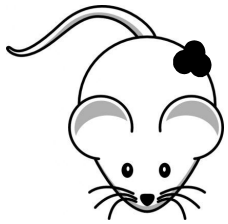


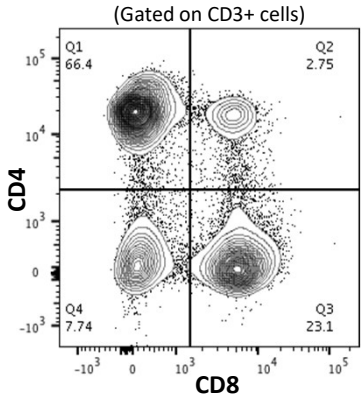


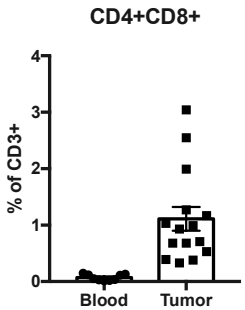


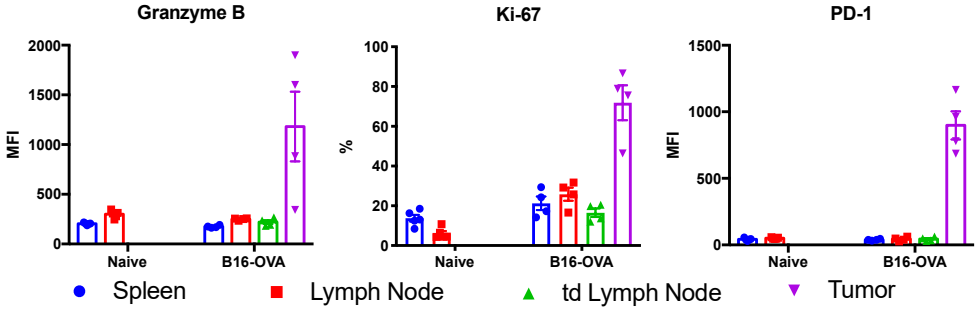
$CD4^+CD8^+$ double positive T cells display tumor specific phenotype with clonally expanded and shared TCR repertoire

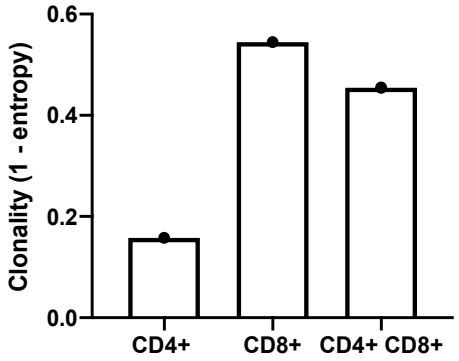
B16 Melanoma

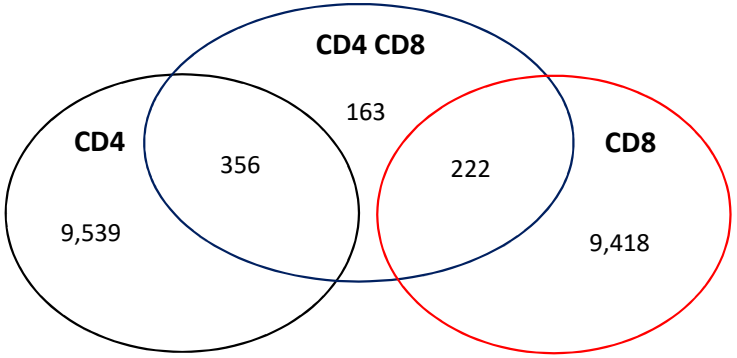












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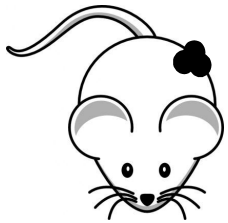
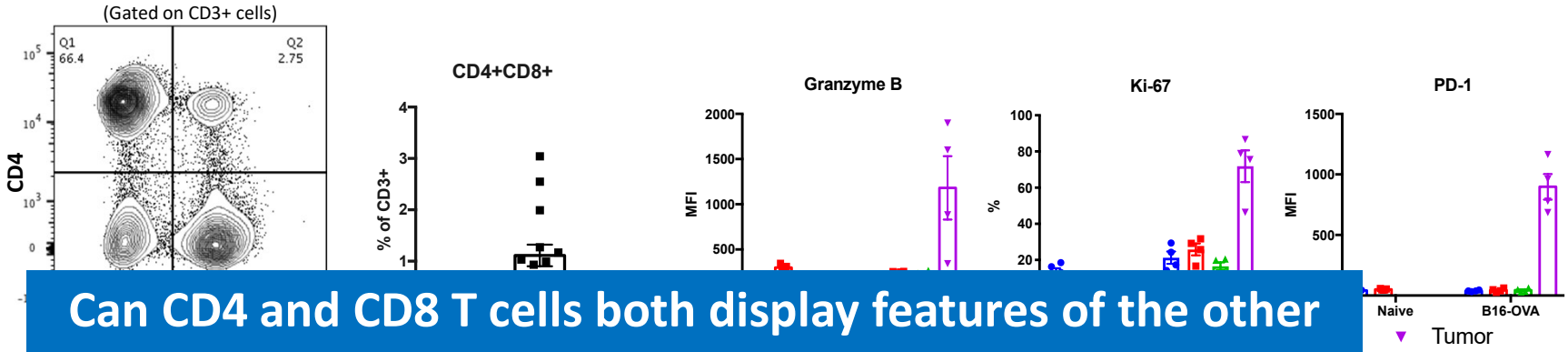
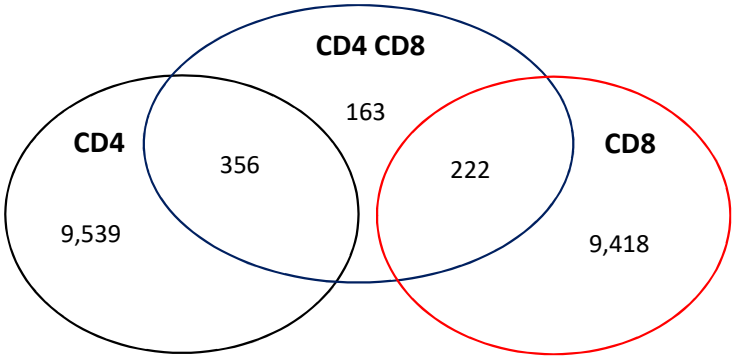
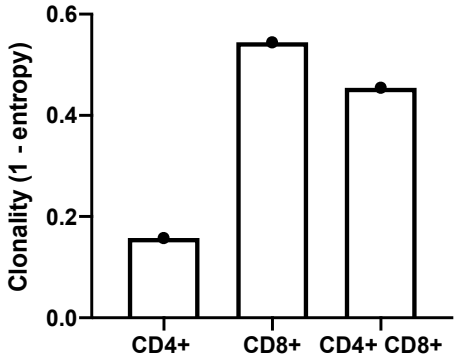


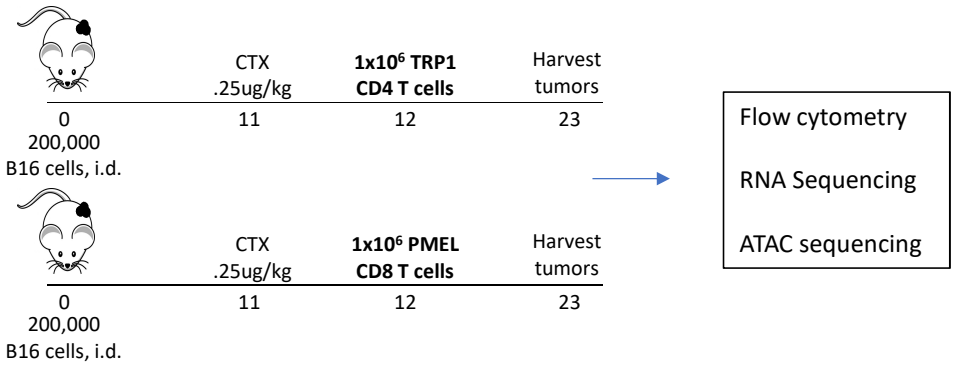


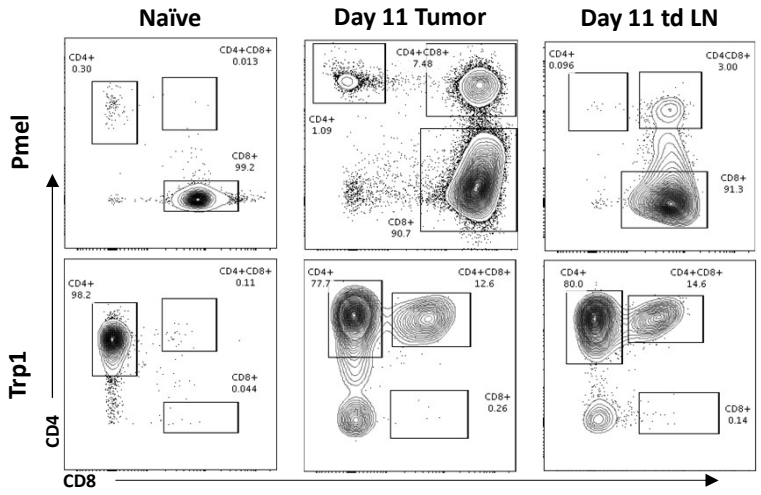
Can CD4 and CD8 T cells both display features of the other cell type?

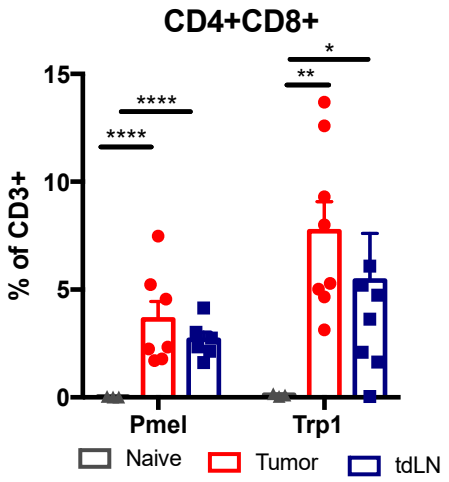




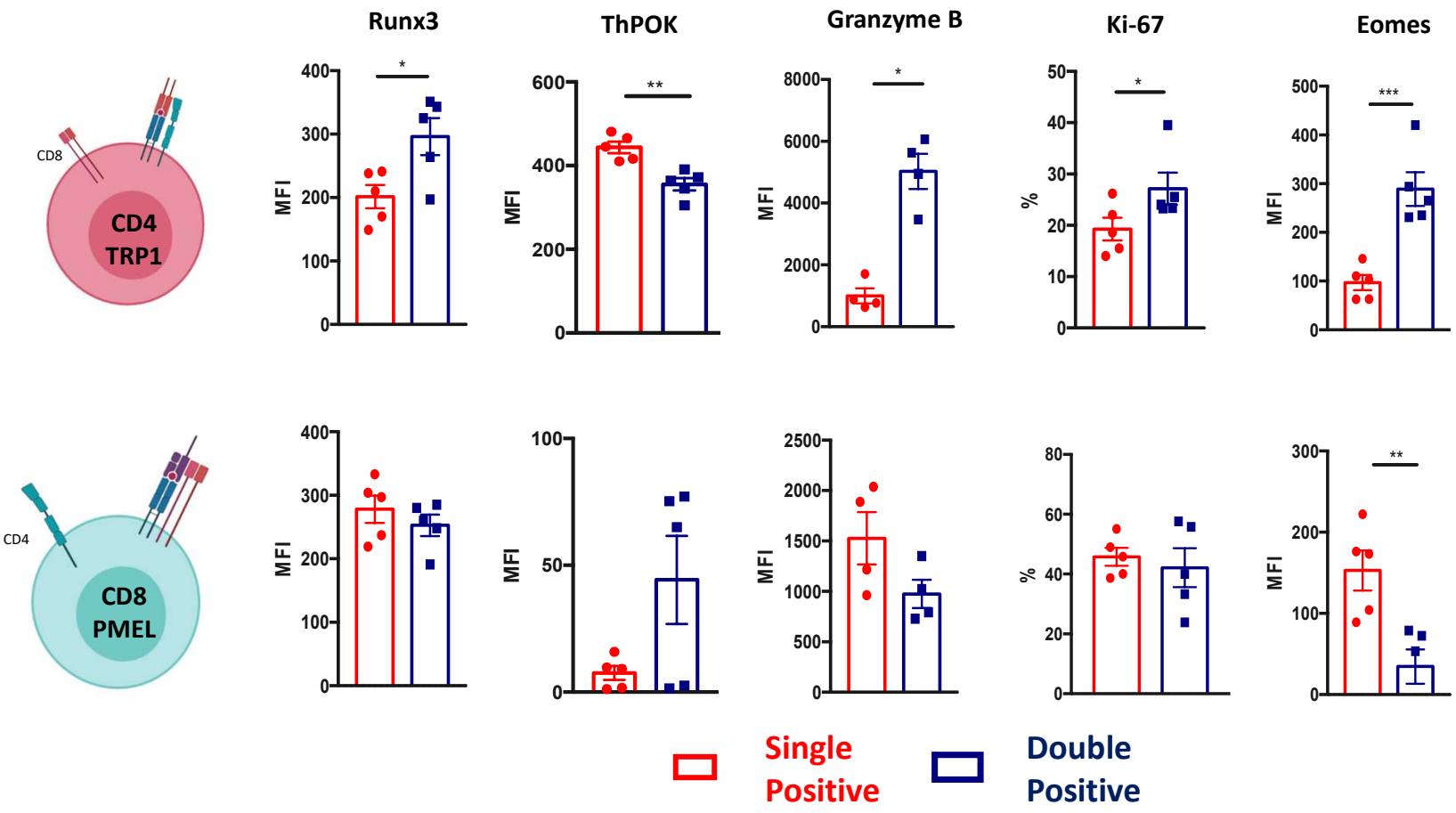
Antigen specific CD4 and CD8 T cells can re-express the opposite co-receptor







CD4 and CD8 derived CD4^{+}CD8^{+} T cells have distinct phenotypes



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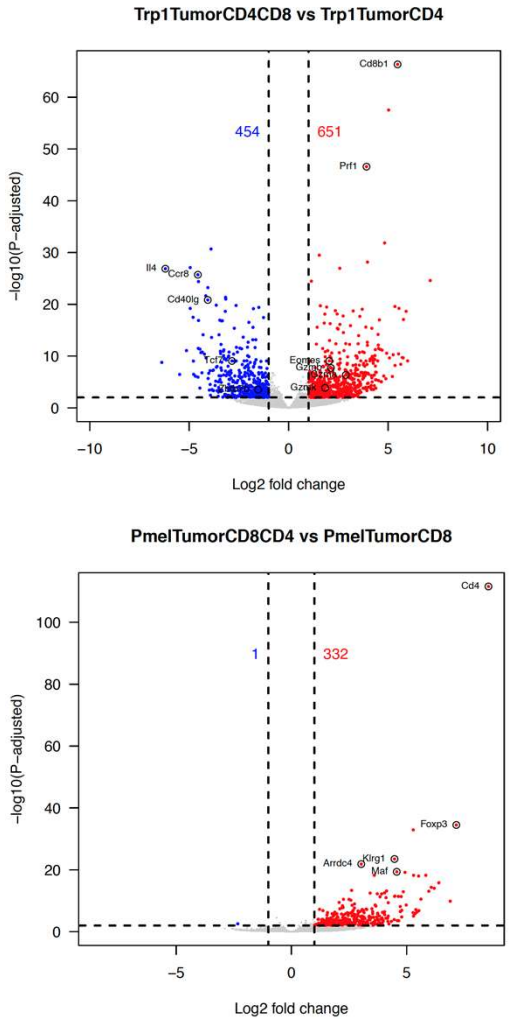

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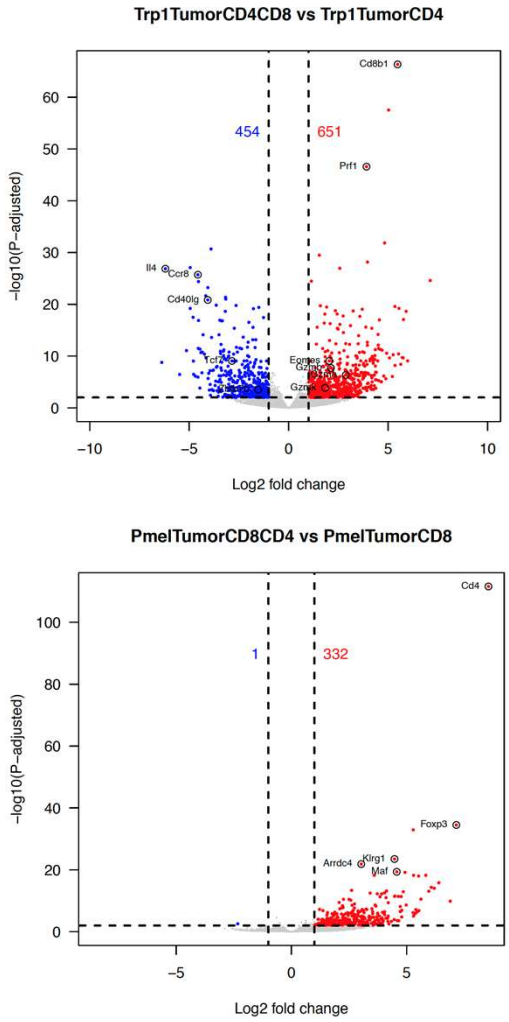

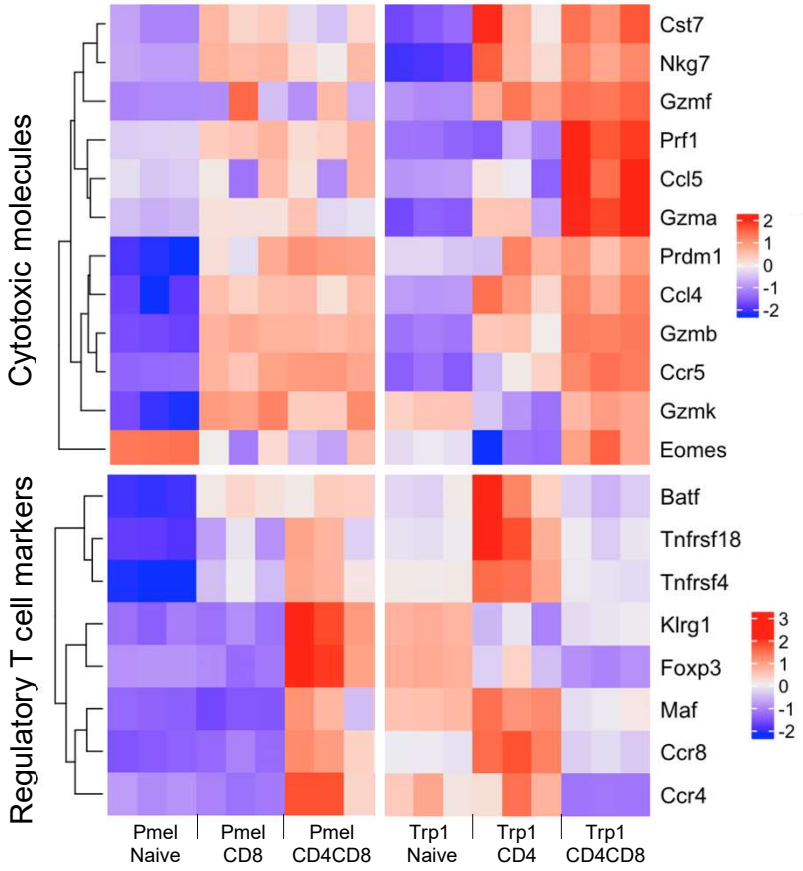

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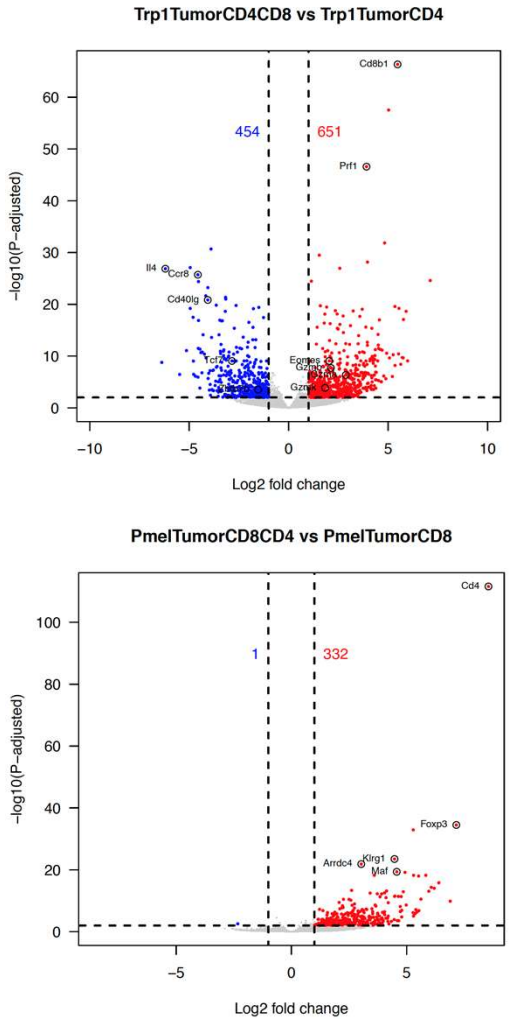
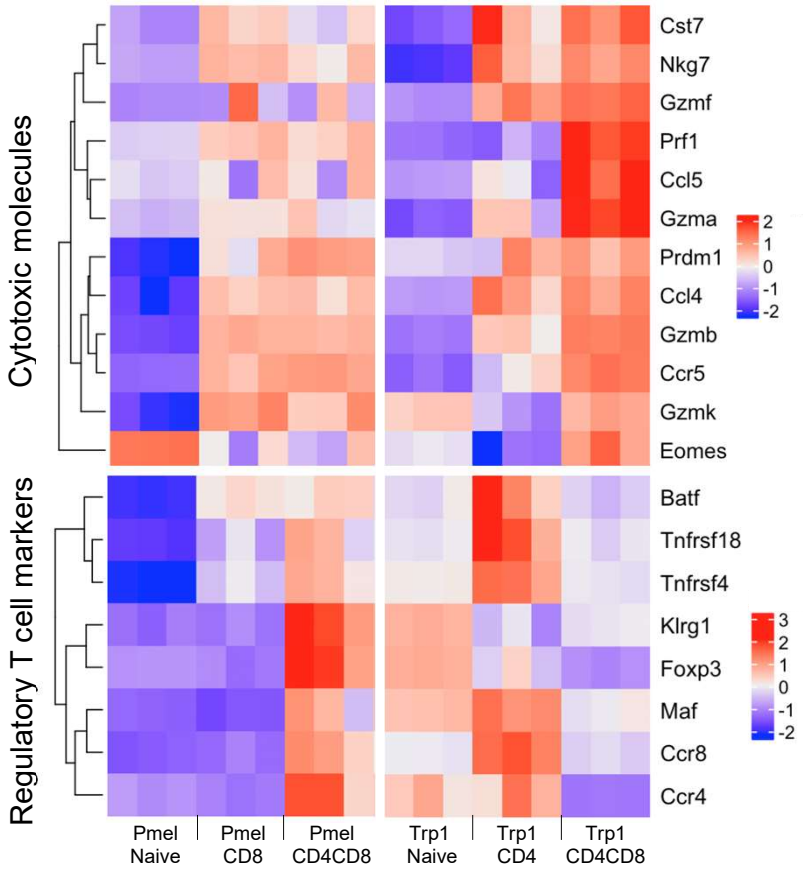
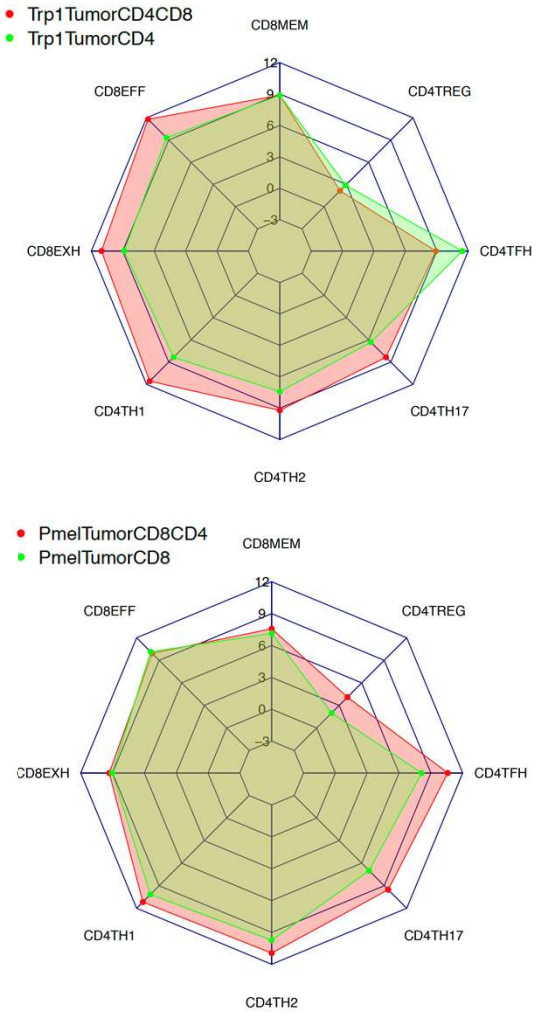
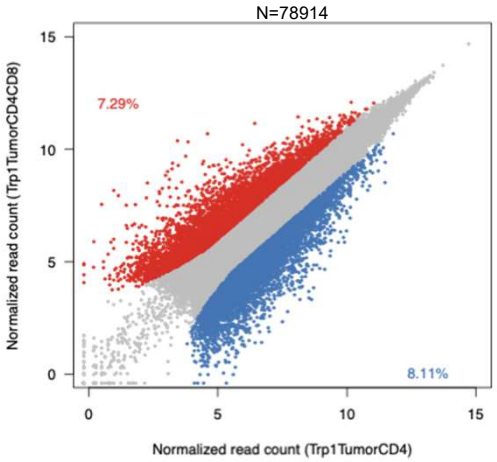
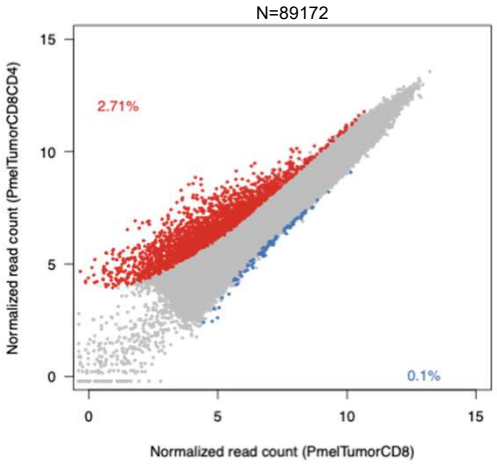


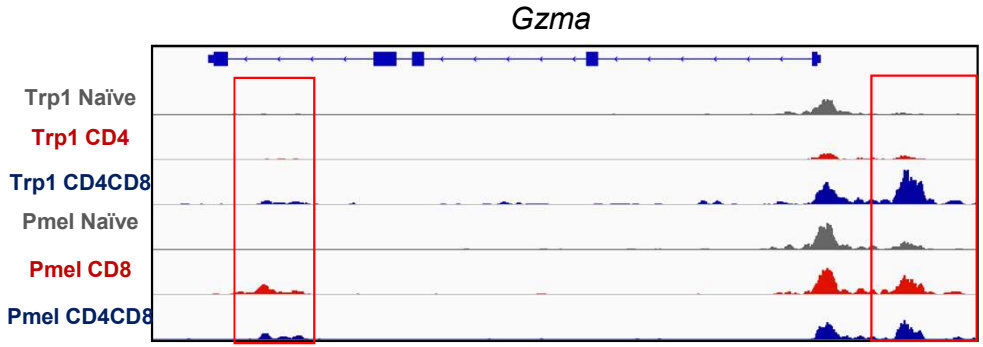


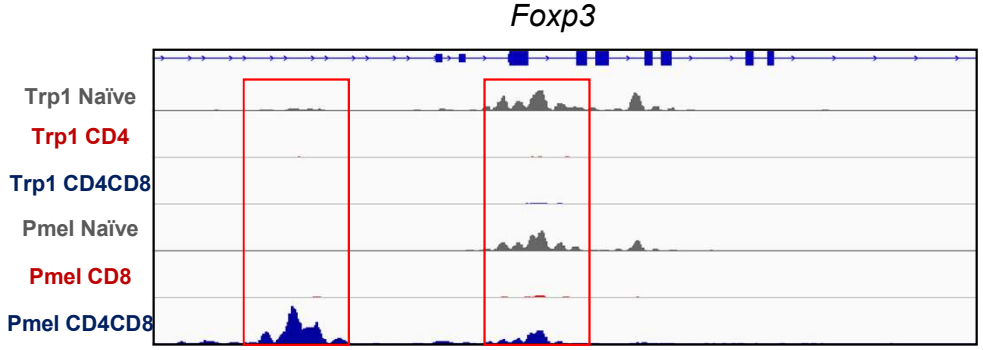


CD4^{+}CD8^{+} T cells differentiate with unique chromatin states

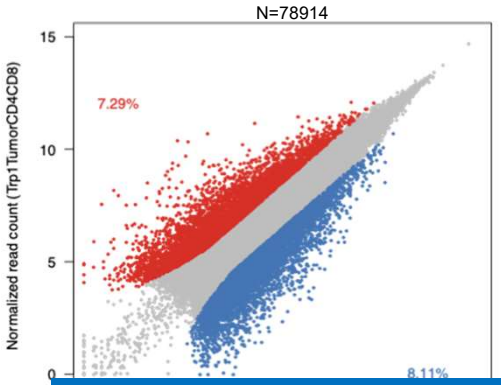


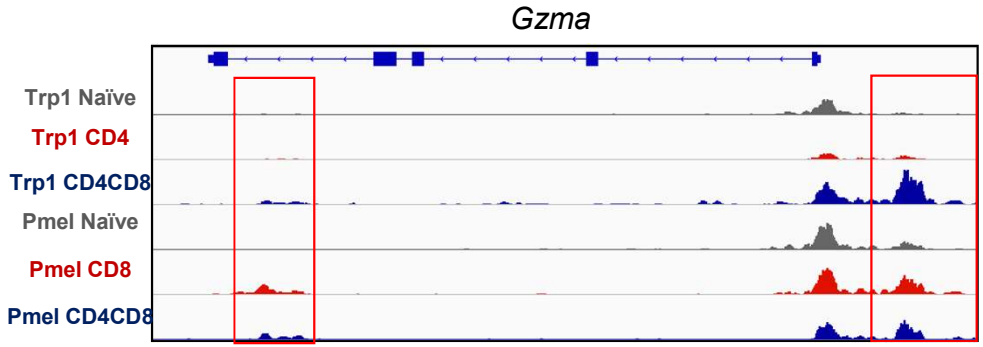




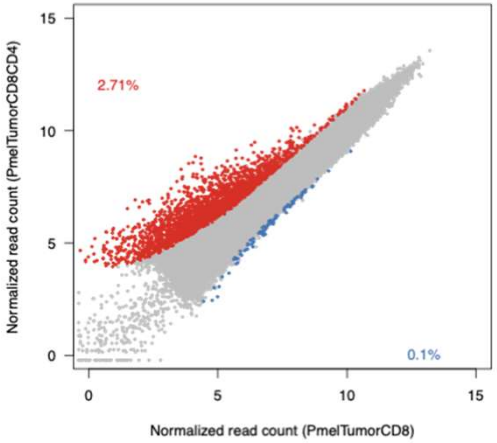


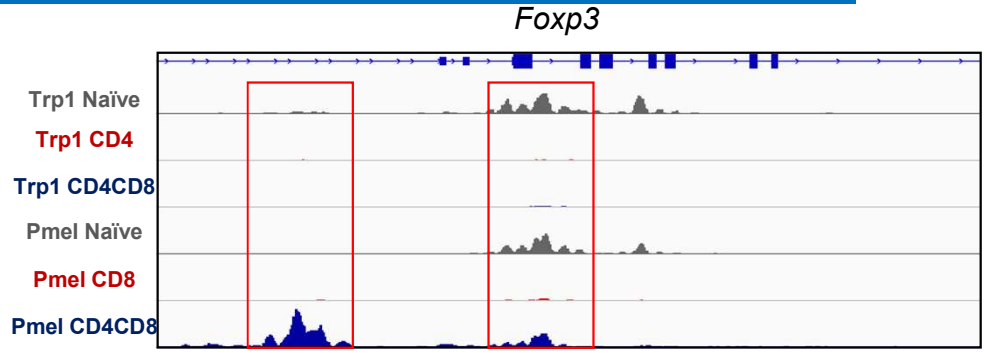
$CD4^+CD8^+$ T cells differentiate with unique chromatin states





Do CD4 derived $CD4^+CD8^+$ T cells have enhanced cytotoxic capability?

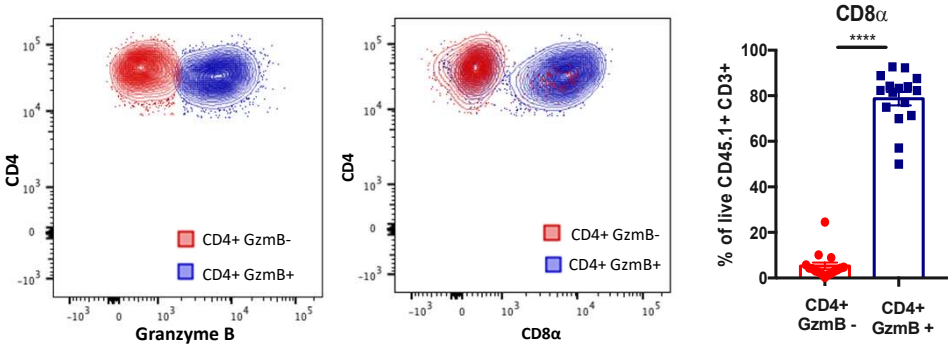




CD8 expression identifies a population of highly cytotoxic CD4 T cells

	CTX .25ug/kg	**1x10^6 TRP1 CD4 T cells**	Harvest tumors
0	11	12	23

200,000 B16 cells, i.d.



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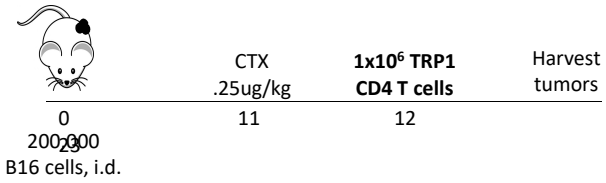
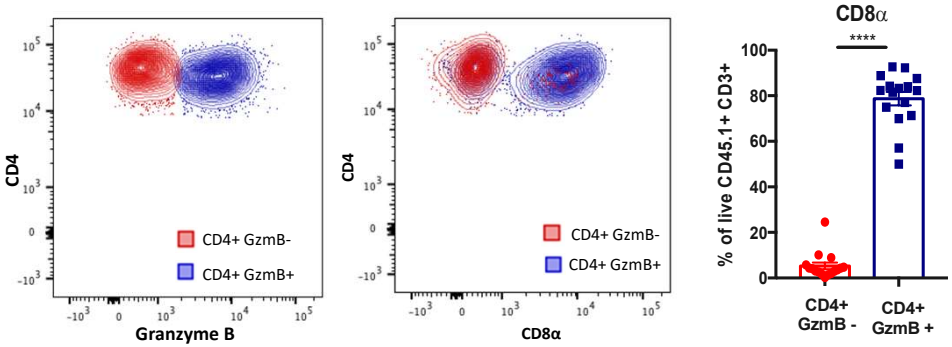
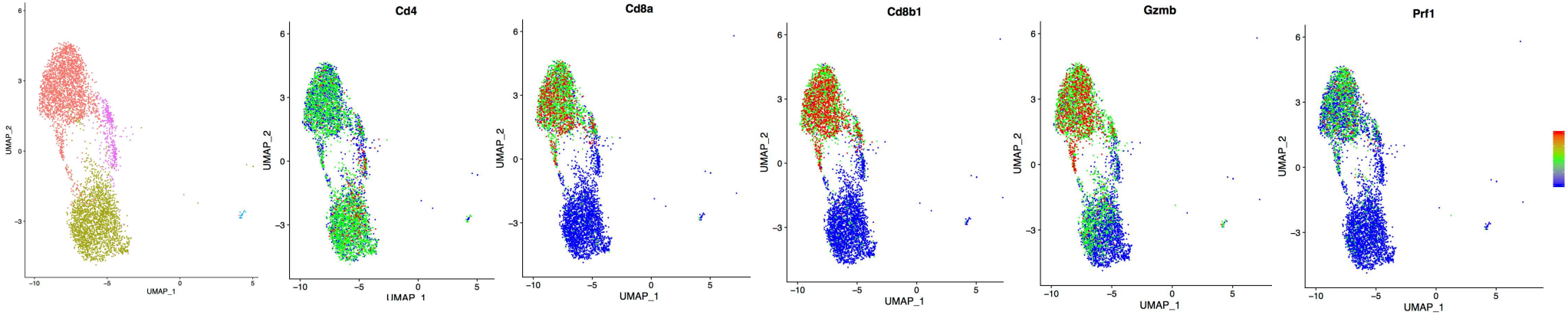
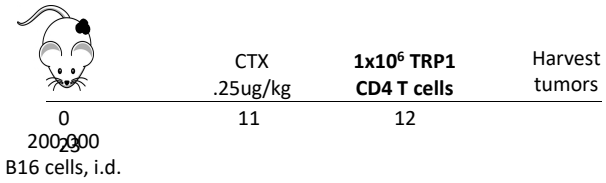
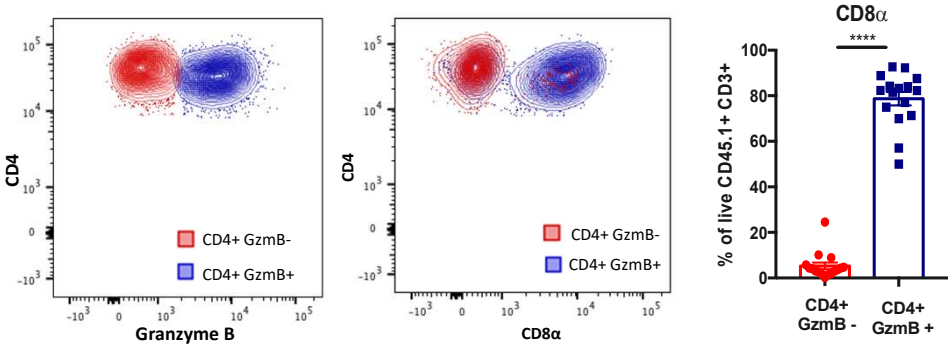


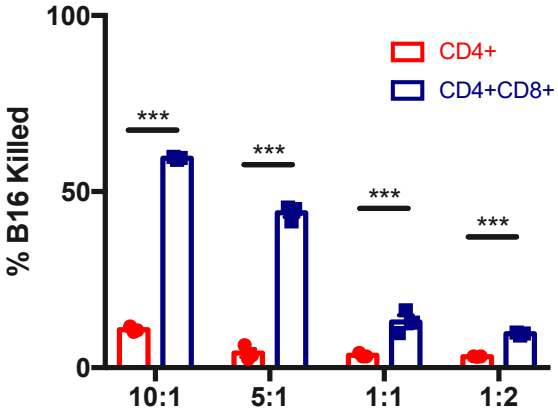


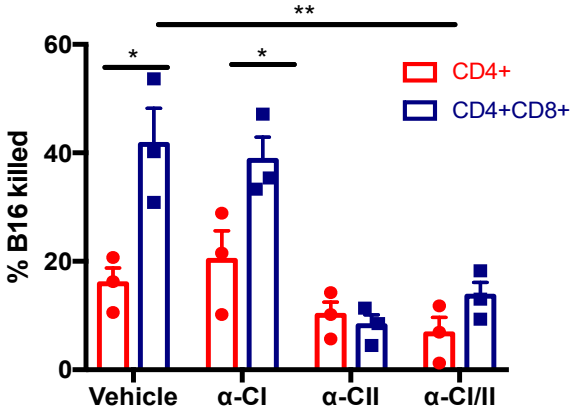


CD8 expression identifies a population of highly cytotoxic CD4 T cells



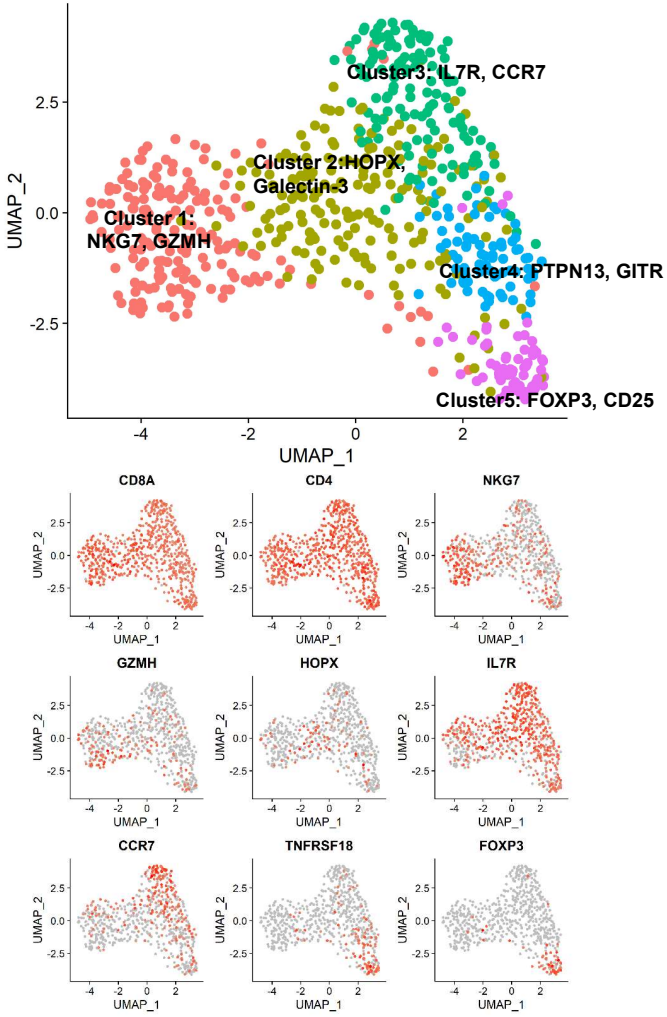






Can we identify unique $CD4^+CD8^+$ T cell states in polyclonal T cells?

Identifying unique CD4^{+}CD8^{+} T cell states in human lung tumors



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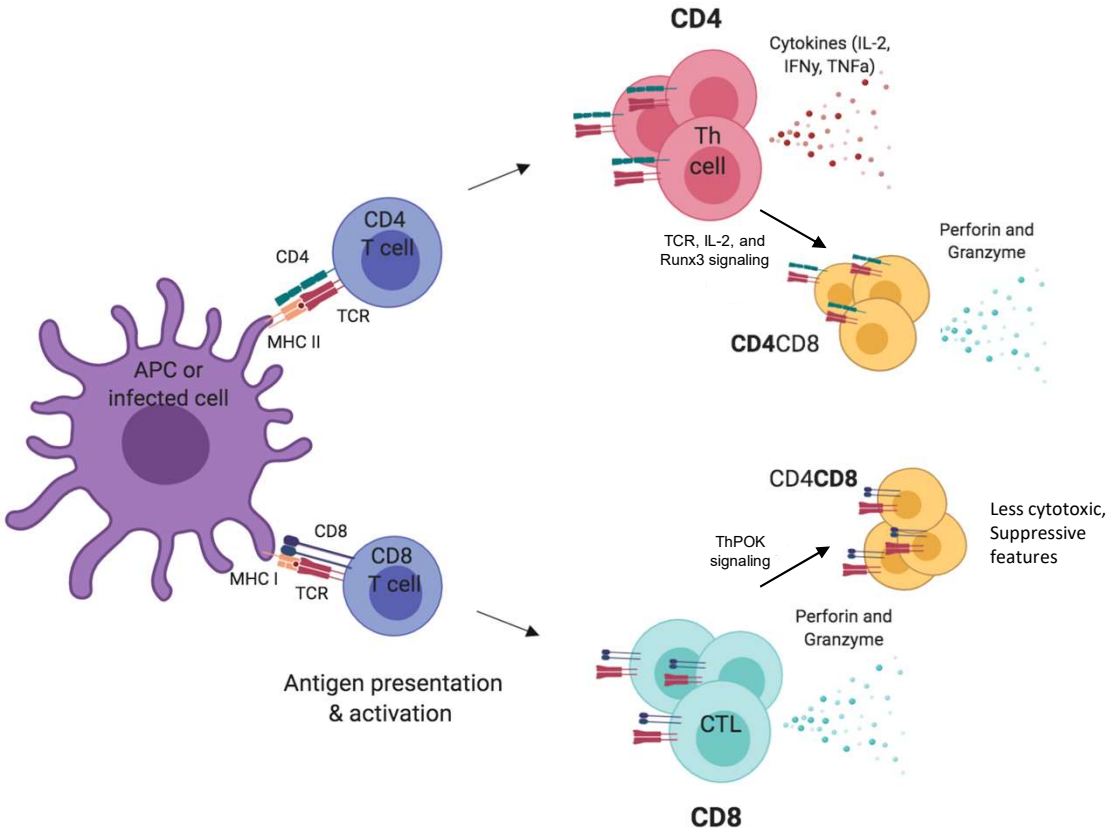
Working model



Thank you!

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