



Reimagined
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Society for Immunotherapy of Cancer



A combination of functional biomarkers improves identification of the tumor-specific reactive T cell repertoire

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Disclosures

Arianna Draghi, MD

I have no disclosures to declare.

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Introduction

How to differentiate tumor-specific reactive T cells from bystander T cells?

Bystander CD8⁺ T cells are abundant and phenotypic

Yannick Simoni , Etien

Nature 557, 575–579(2

PD-1 identifies the patient-specific CD8⁺ tumor-reactive repertoire infiltrating human tumors

Alena Gros,¹ Paul F. Robbins,¹ Xin Yao,¹ Yong F. Li,¹ Simon Turcotte,¹ Eric Tran,¹ John R. Wundt,¹ Arnold Mixon,¹ Shawn Farid,¹ Mark E. Dudley,¹ Ken-ichi Hanada,¹ Jorge R. Almeida,² Sam Dai,¹ Daniel C. Douek,² James C. Yang,¹ and Steven A. Rosenberg¹

CD137 Accurately Identifies and Enriches for Naturally Occurring Tumor-Reactive T Cells in Tumor Activation-induced expression of CD137 permits detection, isolation, and expansion of the full repertoire of CD8⁺ T cells responding to antigen without requiring

Qunhui Ye, De-Gang

DOI:

Cutting edge: CD69 interference with sphingosine-1-phosphatase receptor function

phosphate receptor function cell retention

Laura K Mackay¹, Asolina Braun², Bethany L, Sammy Bedou

Co-expression of CD39 and CD103 identifies tumor-reactive CD8 T cells in human solid tumors

Thomas Duhon , Rebekka Duhon, Ryan Montler, Jake Moses, Tarsem Moudgil, Noel F. de Miranda, Cheri P. Goodall, Tiffany C. Blair, Bernard A. Fox, Jason E. McDermott, Shu-Ching Chang, Gary Grunkemeier, Rom Leidner, Richard Bryan Bell & Andrew D. Weinberg 

Nature Communications 9, Article number: 2724 (2018) | Cite this article

Assessment of Antitumor T-Cell Responses by Flow Cytometry After Coculture of Tumor Cells with Autologous Tumor-Infiltrating Lymphocytes

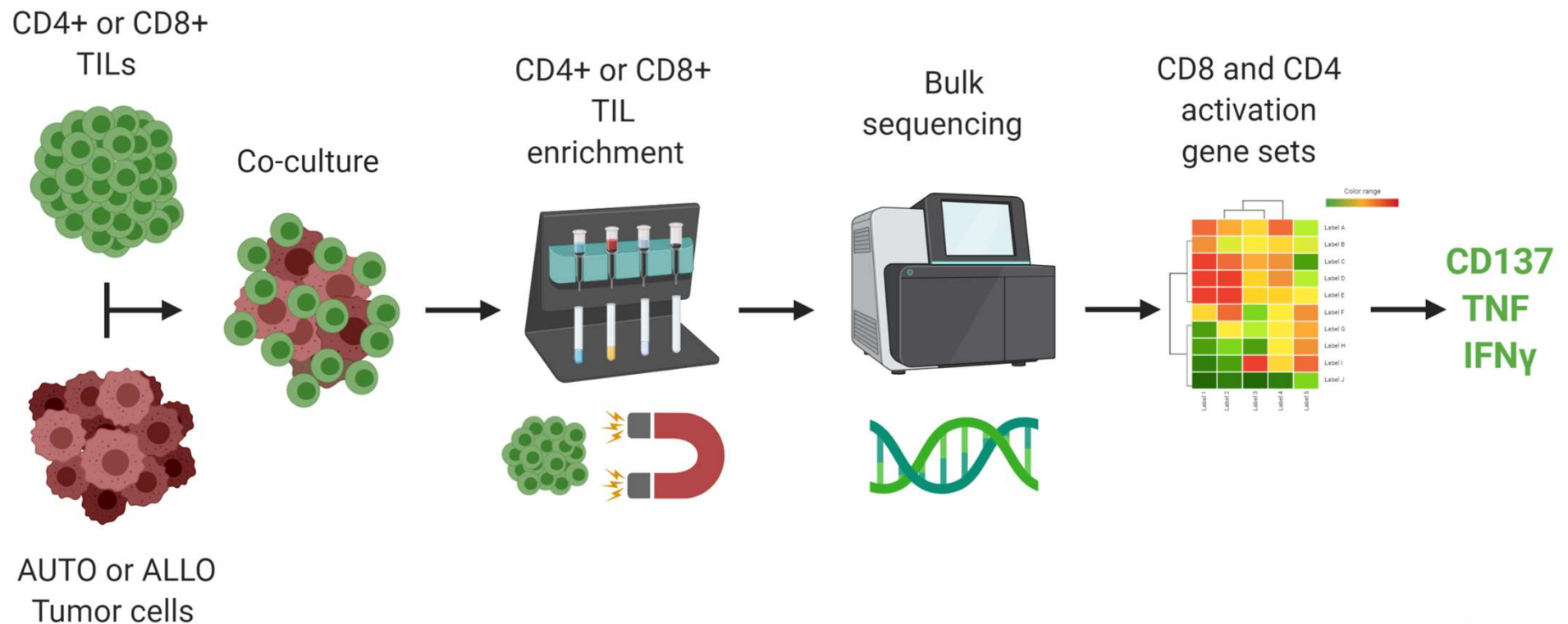
Sensitive and viable identification of antigen-specific CD8⁺ T cells by a flow cytometric assay for degranulation

Michael R. Betts , Jason M. Brenchley, David A. Price, Stephen C. De Rosa, Daniel C. Douek, Mario Roederer, Richard A. Koup

Improve the detection of the repertoire of tumor-specific reactive T cells

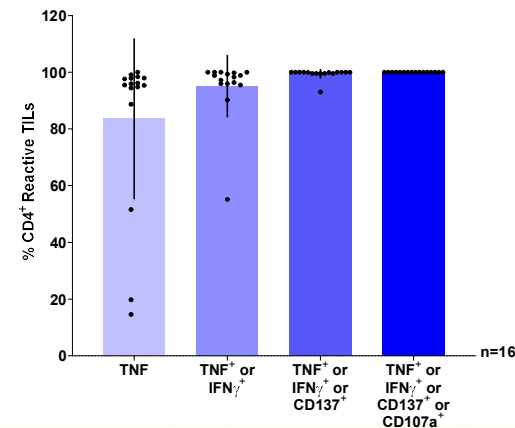
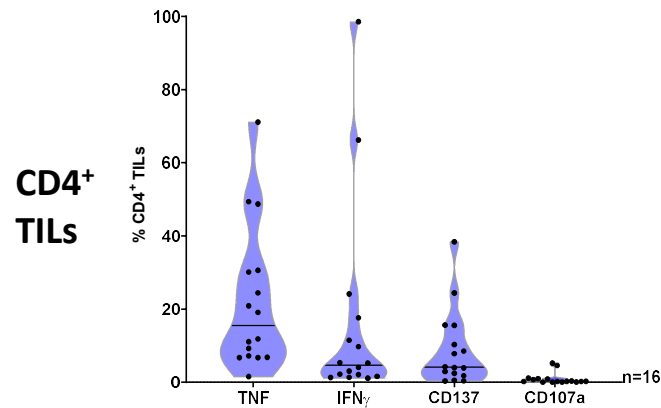
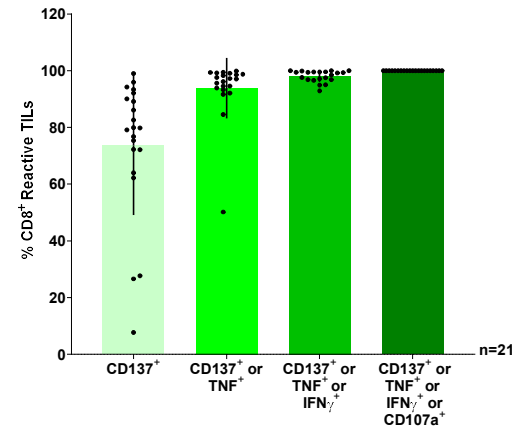
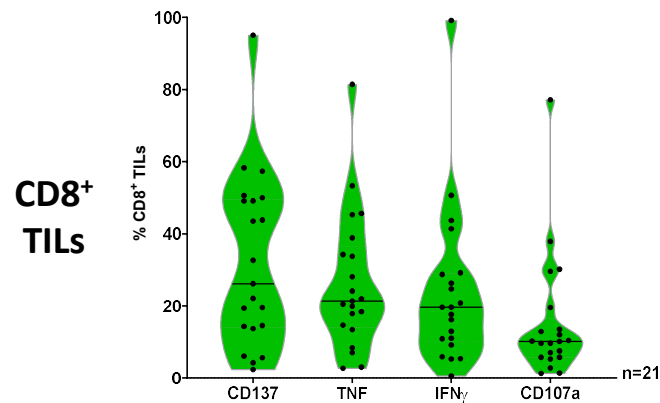
Methodology

In vitro tumor-specific activation setup

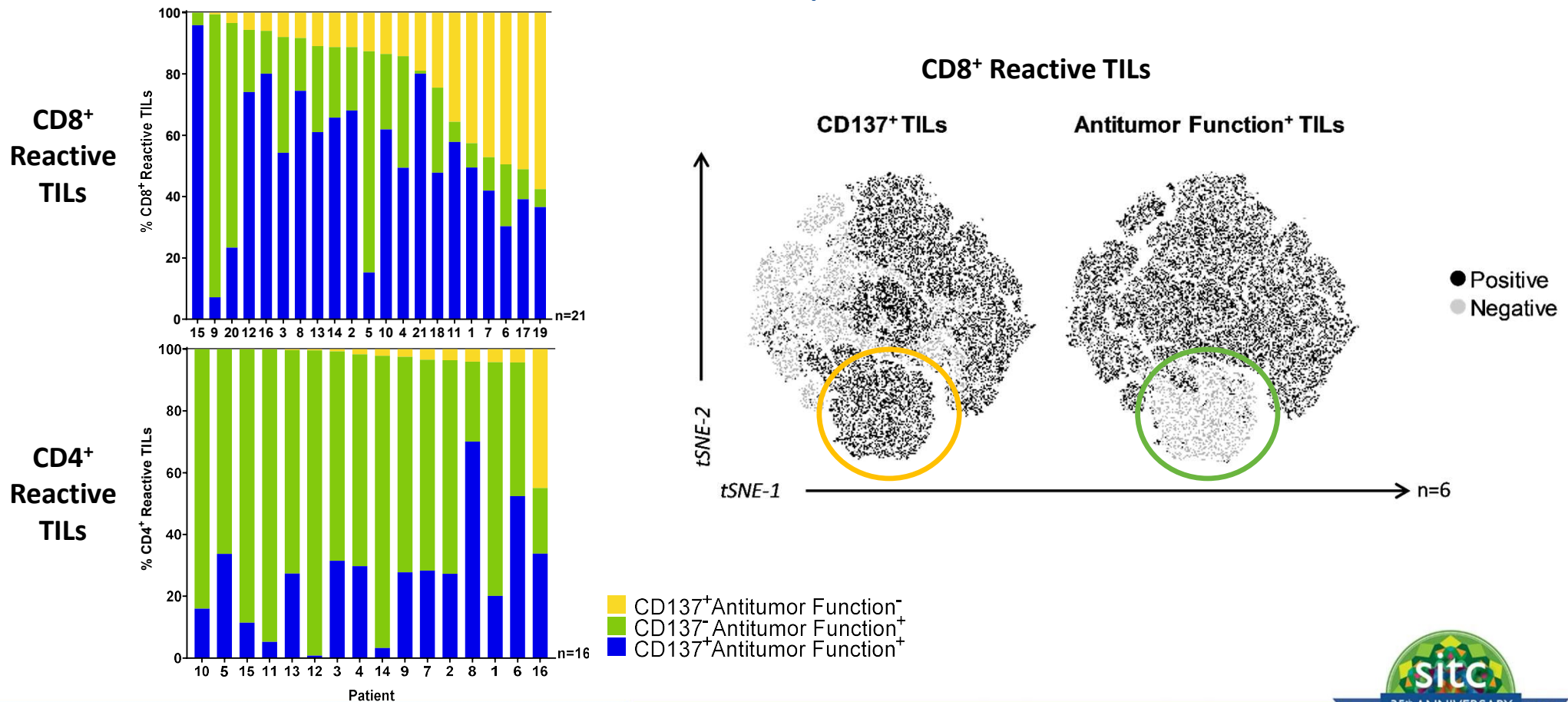


Created with BioRender.com

Combined intracellular detection of CD137, TNF and IFN γ improves the identification of tumor-specific reactive TILs *in vitro*

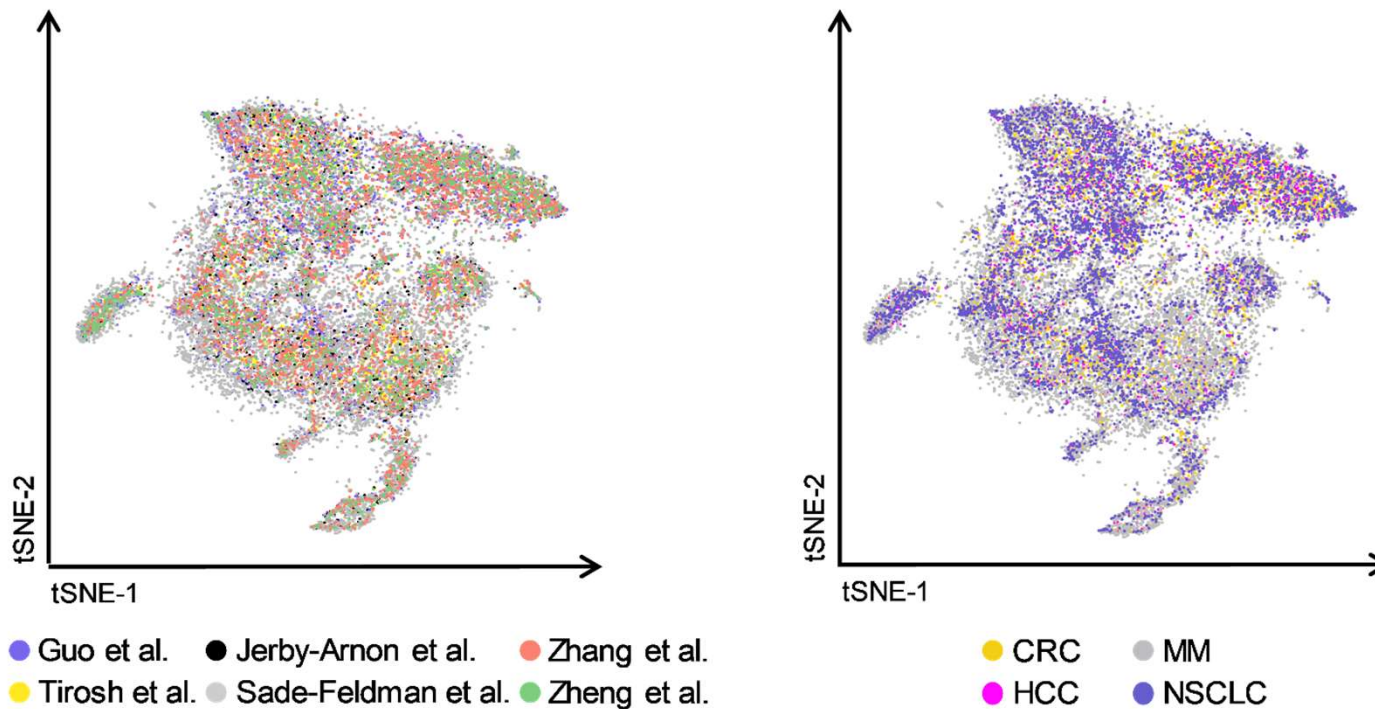


Combined intracellular detection of CD137, TNF and IFN γ improves the identification of tumor-specific reactive TILs *in vitro*



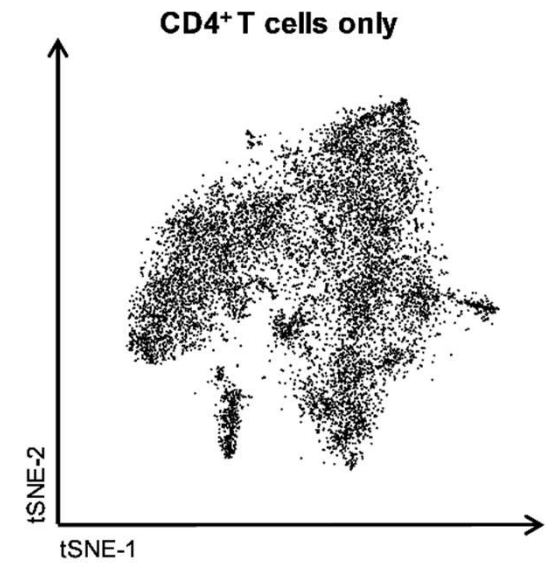
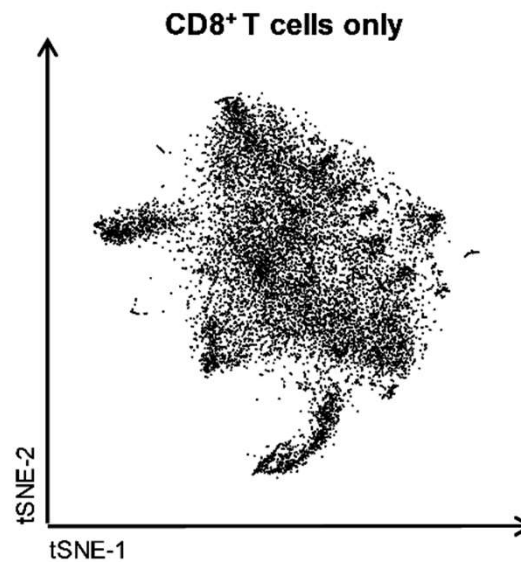
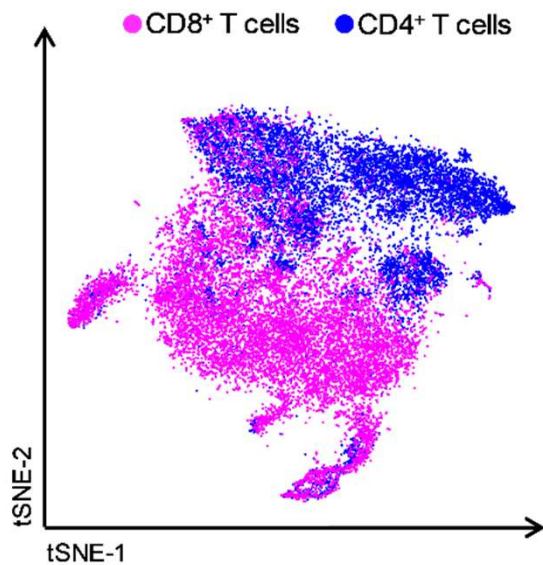
Methodology

Processing of T cell transcriptomics single-cell data from public repositories

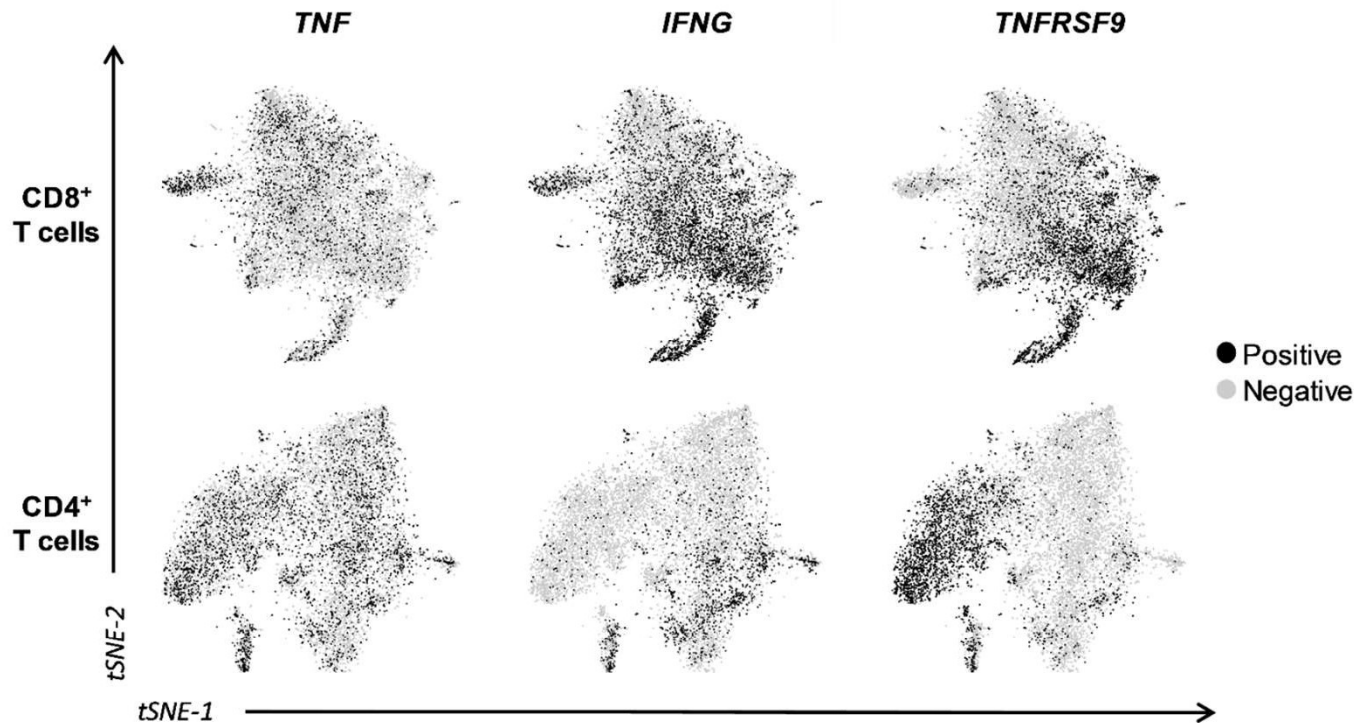


Methodology

Processing of T cell transcriptomics single-cell data from public repositories

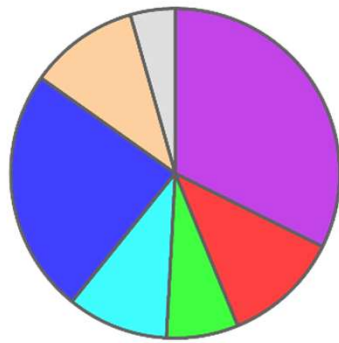


TNFRSF9, TNF and IFNG expression identifies multiple functional clusters of tumor-specific reactive TILs *in situ*



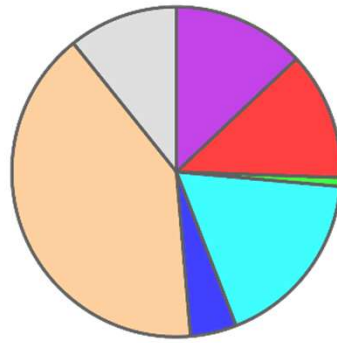
CD137 (*TNFRSF9*), TNF (*TNF*) and IFN γ (*IFNG*) expression identifies multiple functional clusters *in vitro* and *in situ*

CD8⁺ Reactive TILs
In vitro



n=21

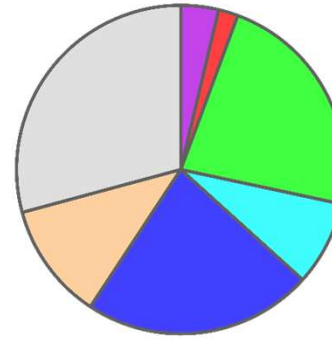
CD4⁺ Reactive TILs
In vitro



n=16

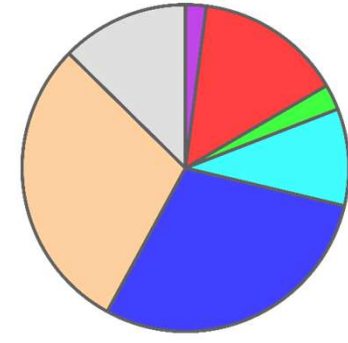
- CD137⁺ TNF⁺ IFN γ ⁺
- CD137⁺ TNF⁺ IFN γ ⁻
- CD137⁺ TNF⁻ IFN γ ⁺
- CD137⁻ TNF⁺ IFN γ ⁺
- CD137⁺ TNF⁻ IFN γ ⁻
- CD137⁻ TNF⁺ IFN γ ⁻
- CD137⁻ TNF⁻ IFN γ ⁺

CD8⁺ Reactive TILs
In situ



Total= 7605 cells

CD4⁺ Reactive TILs
In situ

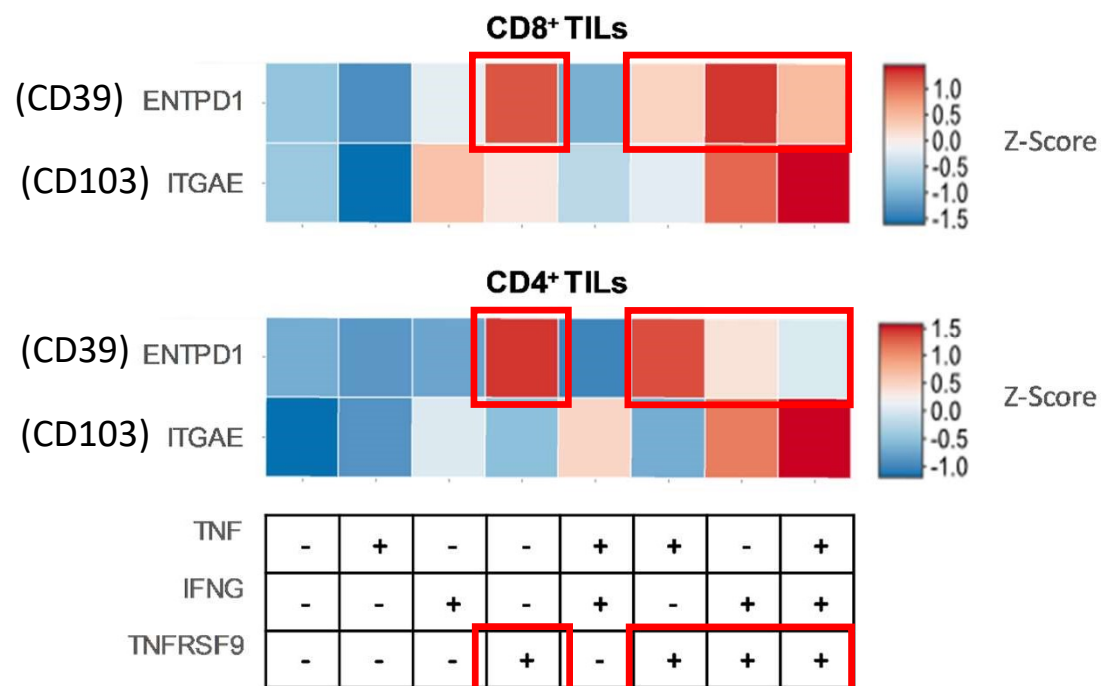


Total= 5272 cells

- TNFRSF9⁺ TNF⁺ IFNG⁺
- TNFRSF9⁺ TNF⁺ IFNG⁻
- TNFRSF9⁺ TNF⁻ IFNG⁺
- TNFRSF9⁻ TNF⁺ IFNG⁺
- TNFRSF9⁺ TNF⁻ IFNG⁻
- TNFRSF9⁻ TNF⁺ IFNG⁻
- TNFRSF9⁻ TNF⁻ IFNG⁺

Not Disclosed

ENTPD1 expression overlaps with *TNFRSF9* expression.



Take home message

The simultaneous detection of **CD137 (*TNFRSF9*)**, **TNF (*TNF*)** and **IFN γ (*IFNG*)** is potentially able to identify the full **tumor-specific reactive T cell repertoire** while identifying multiple distinct functional clusters of tumor-specific reactive T cells *in vitro* and *in situ*

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