

20TH

**INTERNATIONAL
ULTMANN
CHICAGO
LYMPHOMA
SYMPOSIUM**

APRIL 21-22, 2023



**Immune
Microenvironment in
Lymphoma**

Immune Microenvironment in lymphoma

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Chair, Lymphoma Group

Mayo Clinic

Disclosures for

Stephen Ansell, MD, PhD

In compliance with ACCME policy, Mayo Clinic requires the following disclosures to the activity audience:

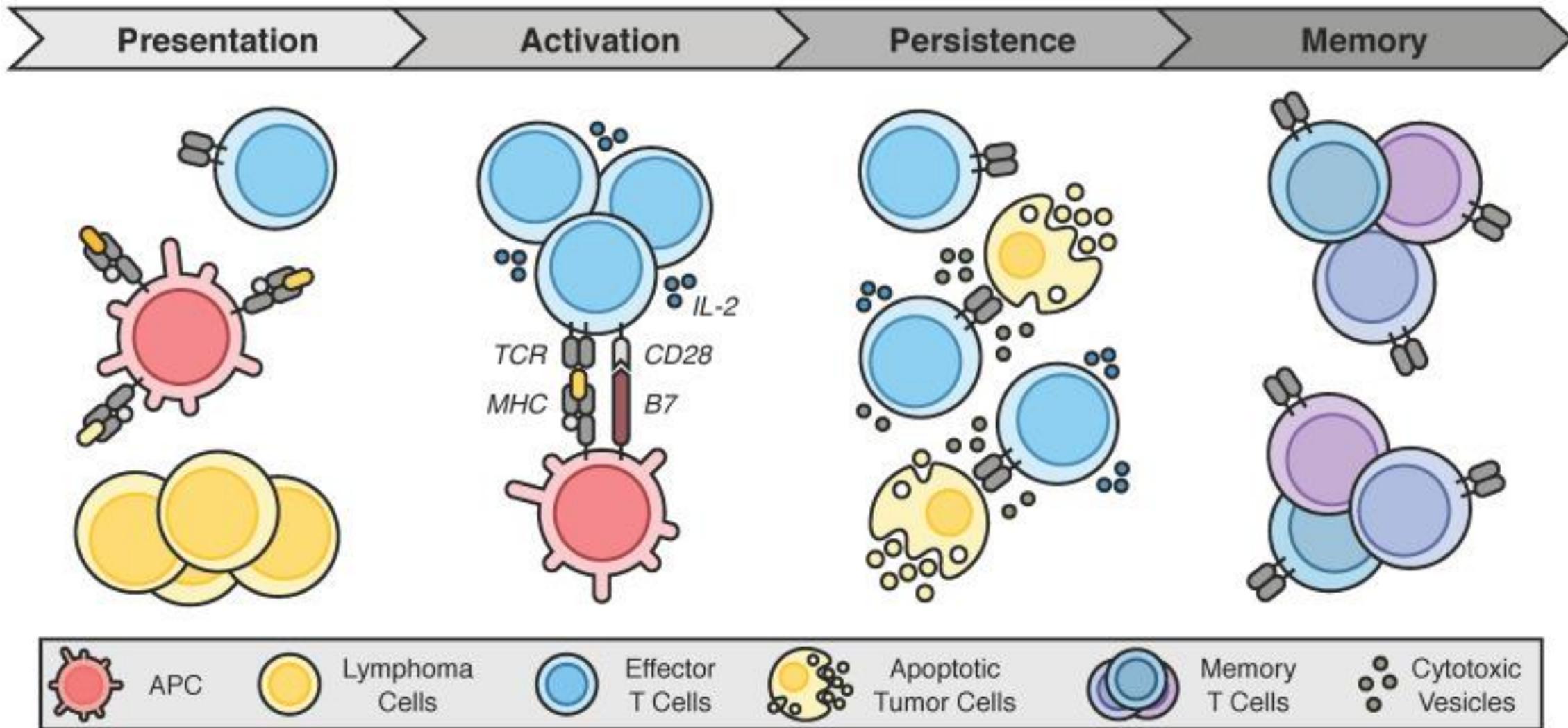
Research Support/P.I.	PI – SeaGen, BMS, Affimed, Regeneron, Pfizer, Takeda, AstraZeneca, ADC Therapeutics for clinical trials
Employee	N/A
Consultant	N/A
Major Stockholder	N/A
Speakers' Bureau	N/A
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N/A = Not Applicable (no conflicts listed)

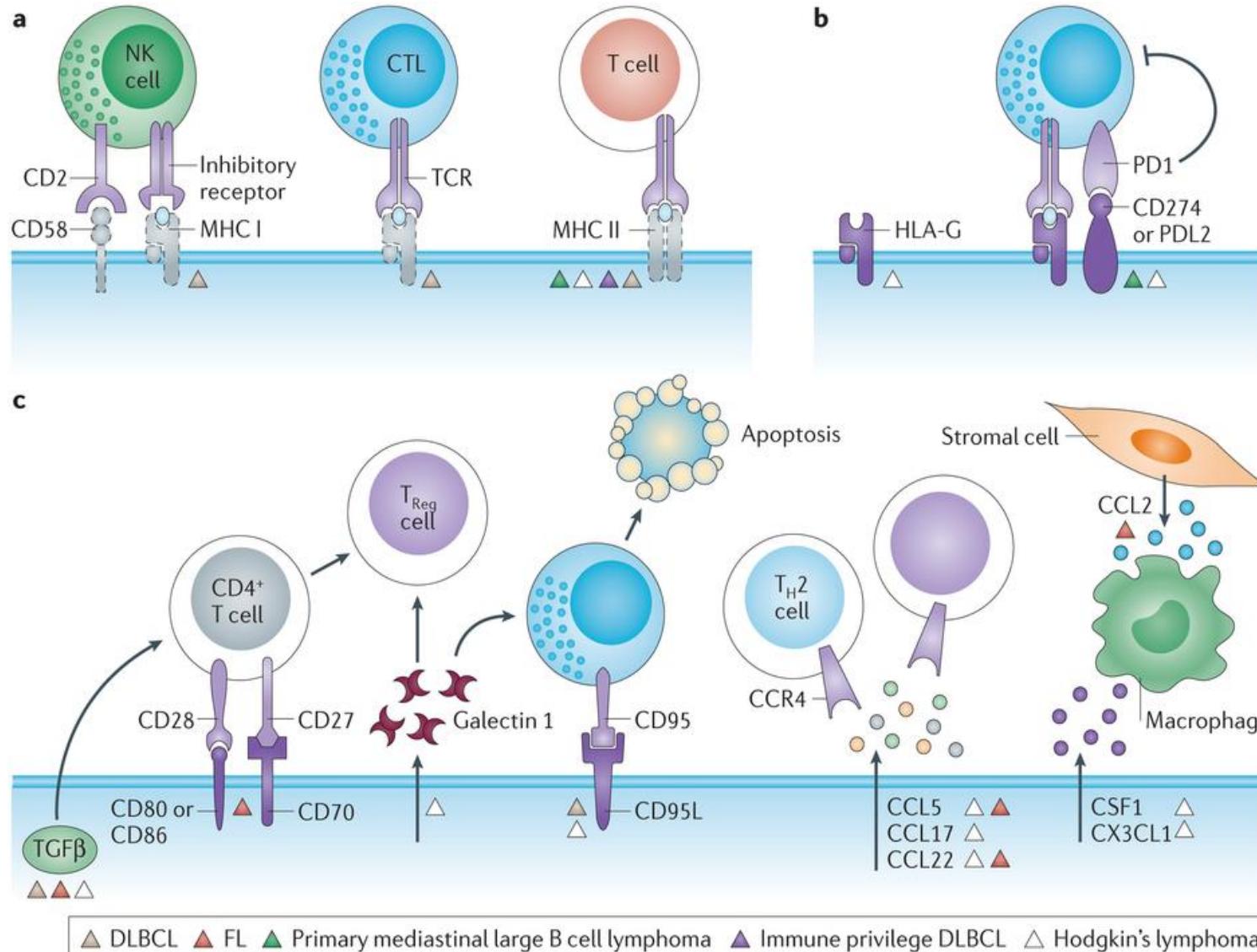
Learning Objectives -

- Define the components of an effective T-cell mediated immune response.
- Identify barriers to an effective immune response in lymphoma
- Describe strategies to overcome the immune defects –
 - immune checkpoint blockade
 - Inducing T-cell activation
 - engaging the innate Immune response

An Effective T-cell Response to Lymphoma

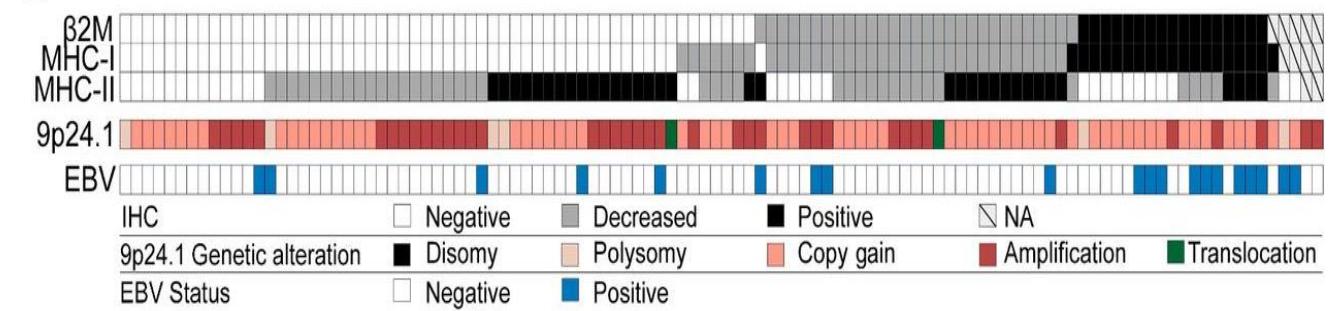
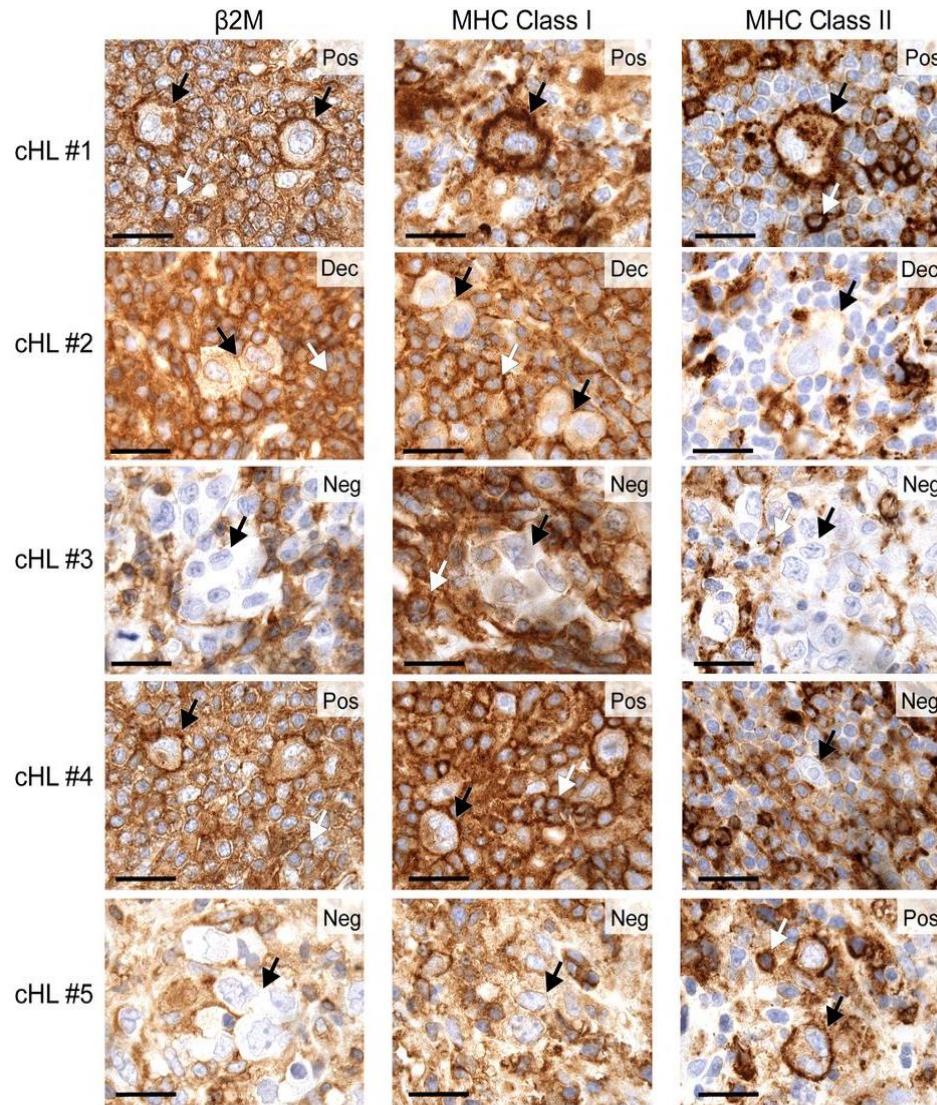


Four Mechanisms accounting for an inadequate T-cell response in lymphoma



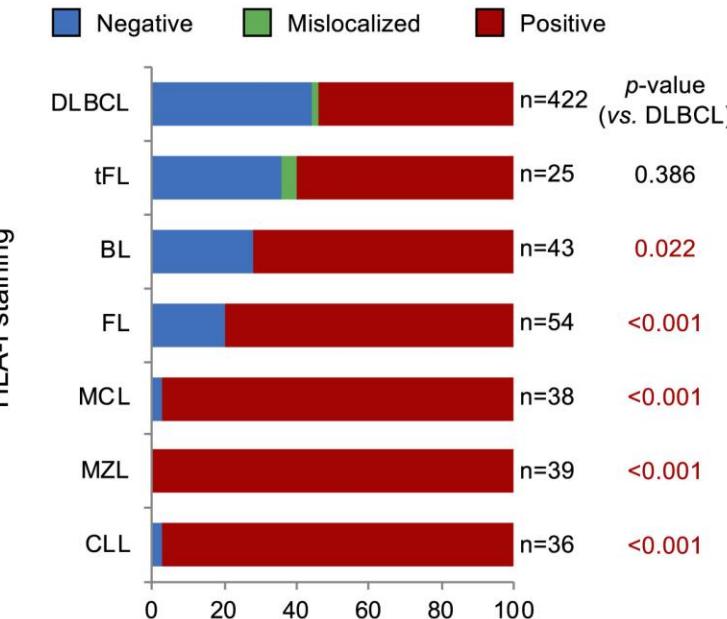
1. Loss of antigen presentation
2. Suppressive ligands
3. Suppressive cell populations
4. Suppressive cytokines

1. Loss of β2M, MHC class I and II expression in classical Hodgkin Lymphoma

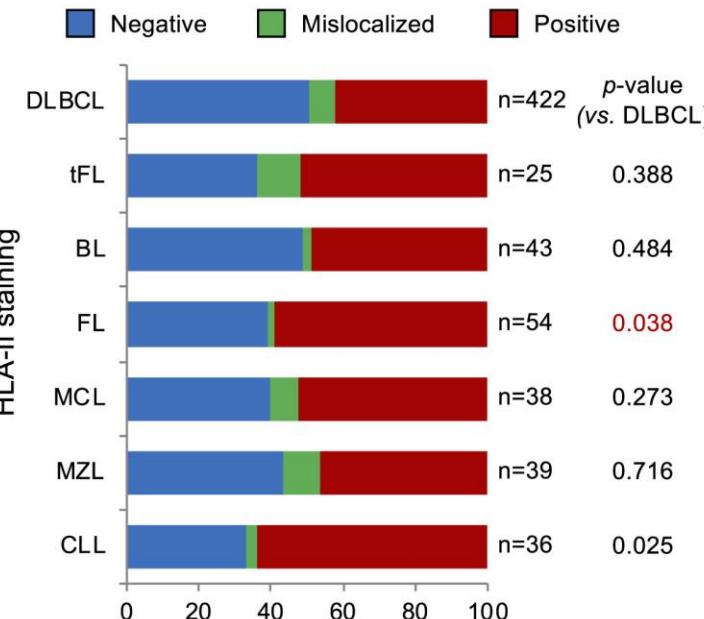


1. Loss of MHC-I expression is significantly more frequent in DLBCL

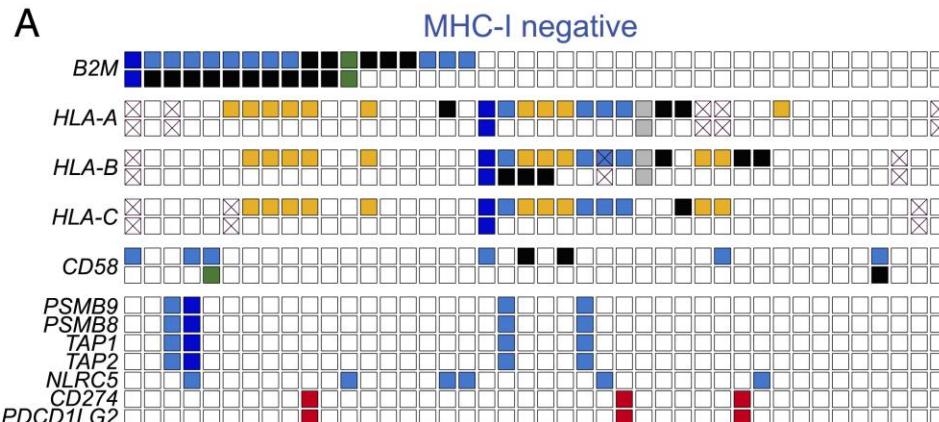
A



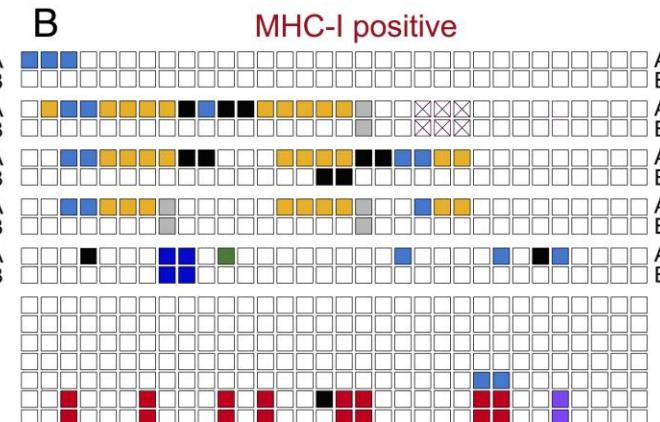
B



A



B



■ Amplification

■ Deletion

■ Germline homozygosity

■ Missense mutations (B2M and CD58)

■ not determined

■ cnLOH / Allelic imbalance

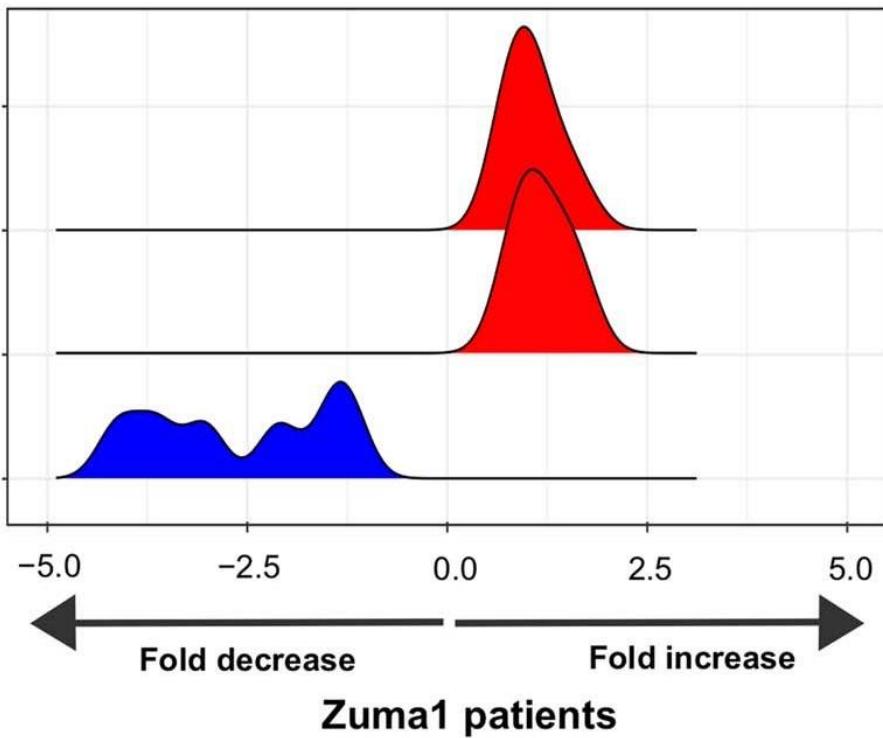
■ Gain

■ Homozygous deletion

■ Truncating mutations

1. Antigen processing and peptide antigen presentation pathways in pretreatment, CR vs. non-CR, tumor biopsies from CAR T-cell patients

c

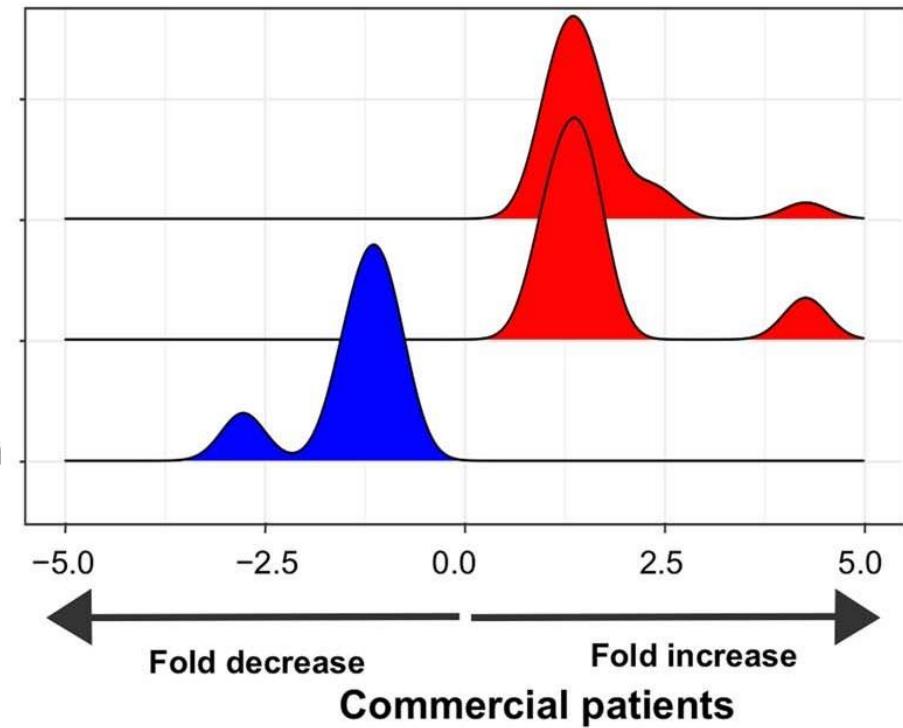


Positive regulation of leukocyte cell-cell adhesion

Lymphocyte costimulation

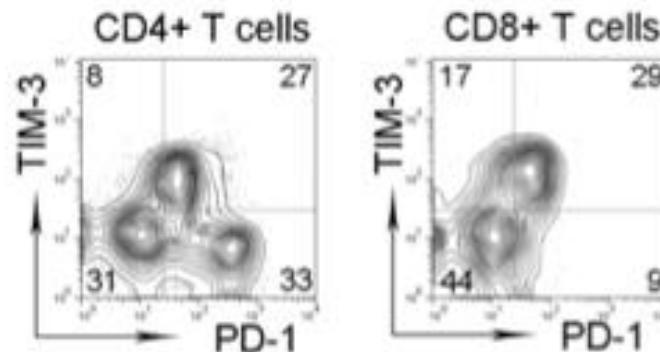
Antigen processing and presentation of peptide antigen

d

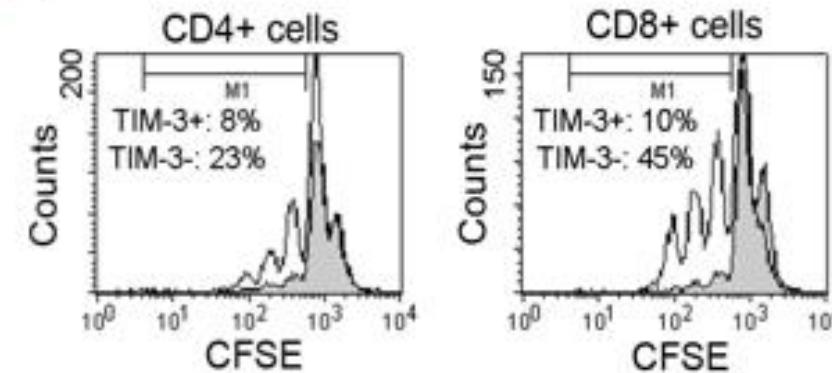


2. Exhausted T-cells in lymphoma are susceptible to suppression

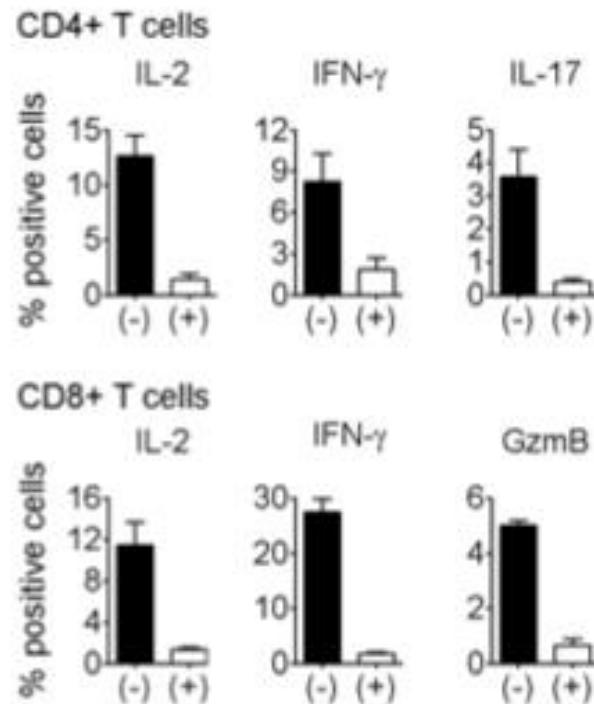
A.



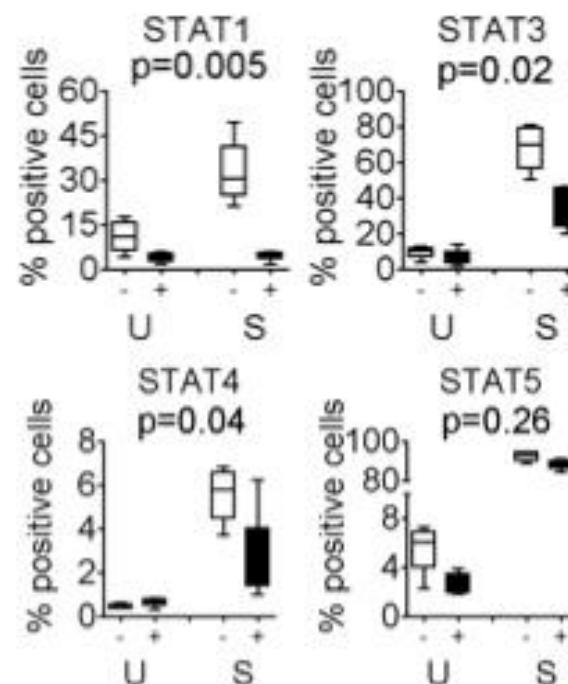
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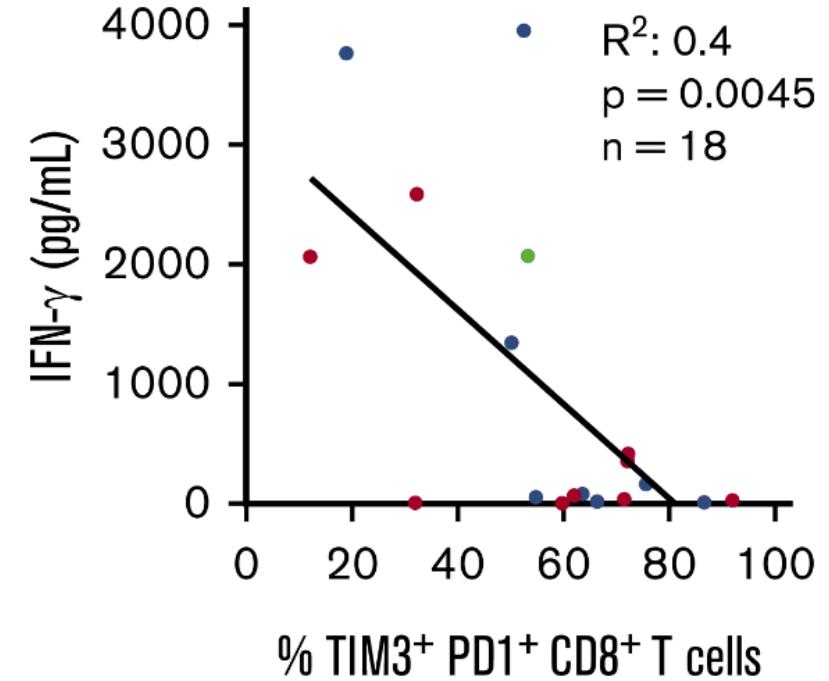
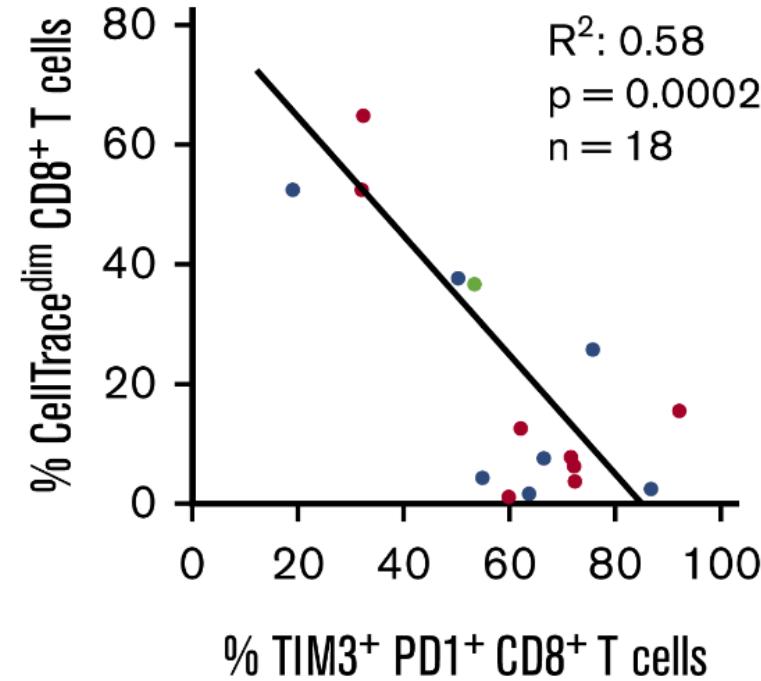
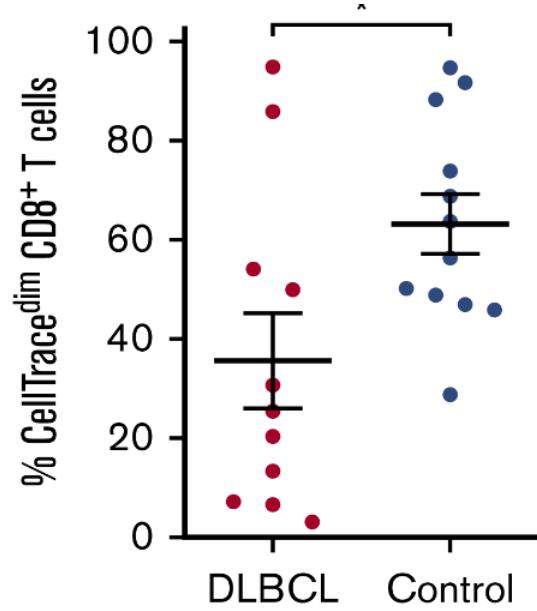
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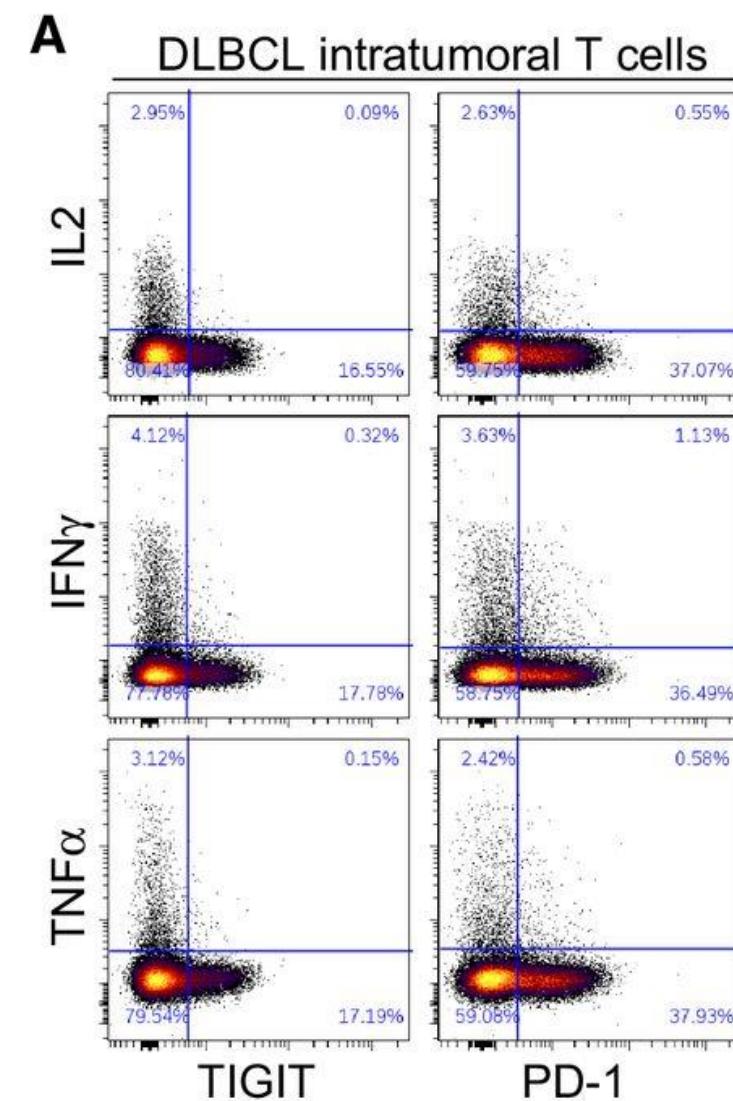
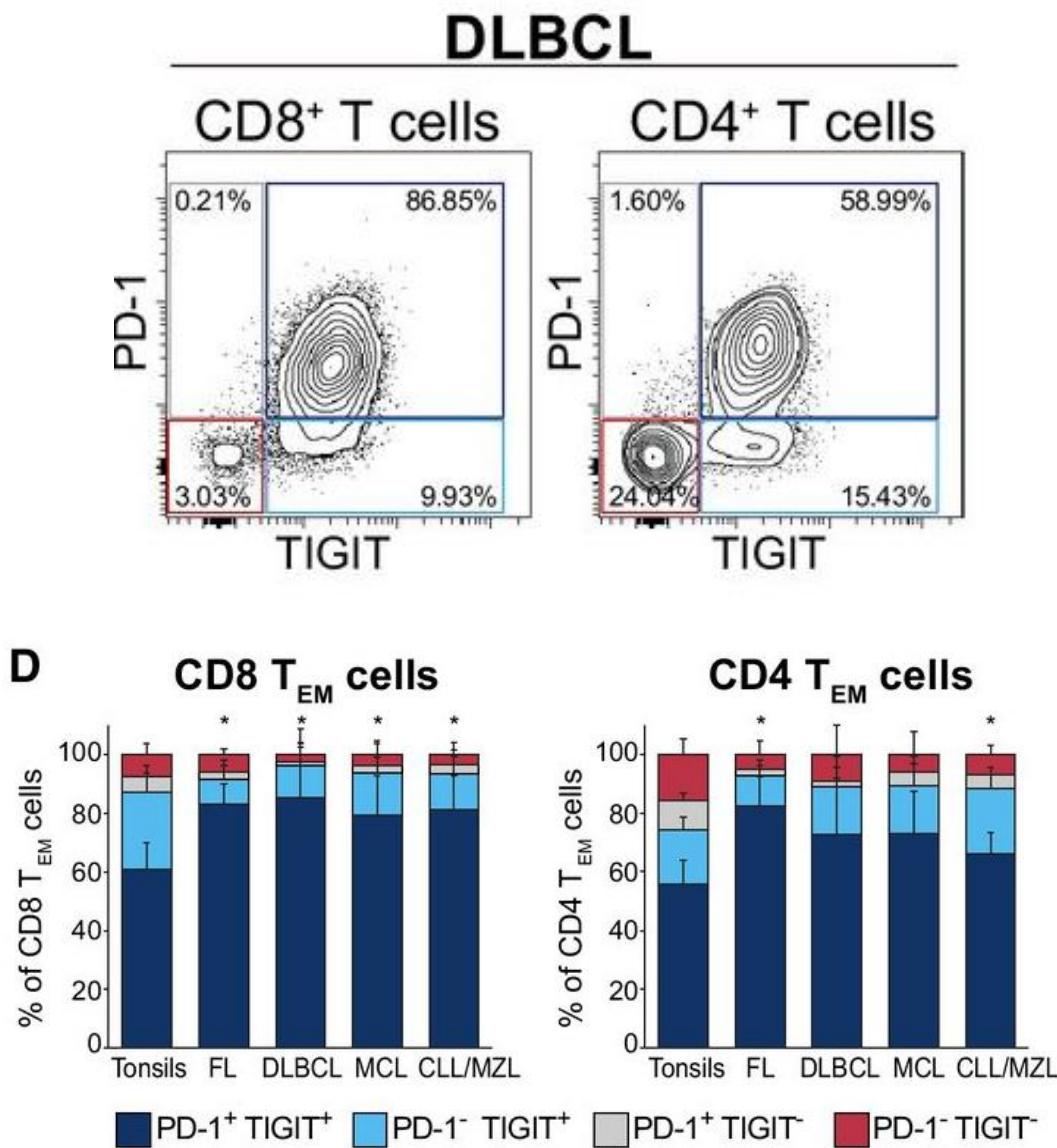
D.



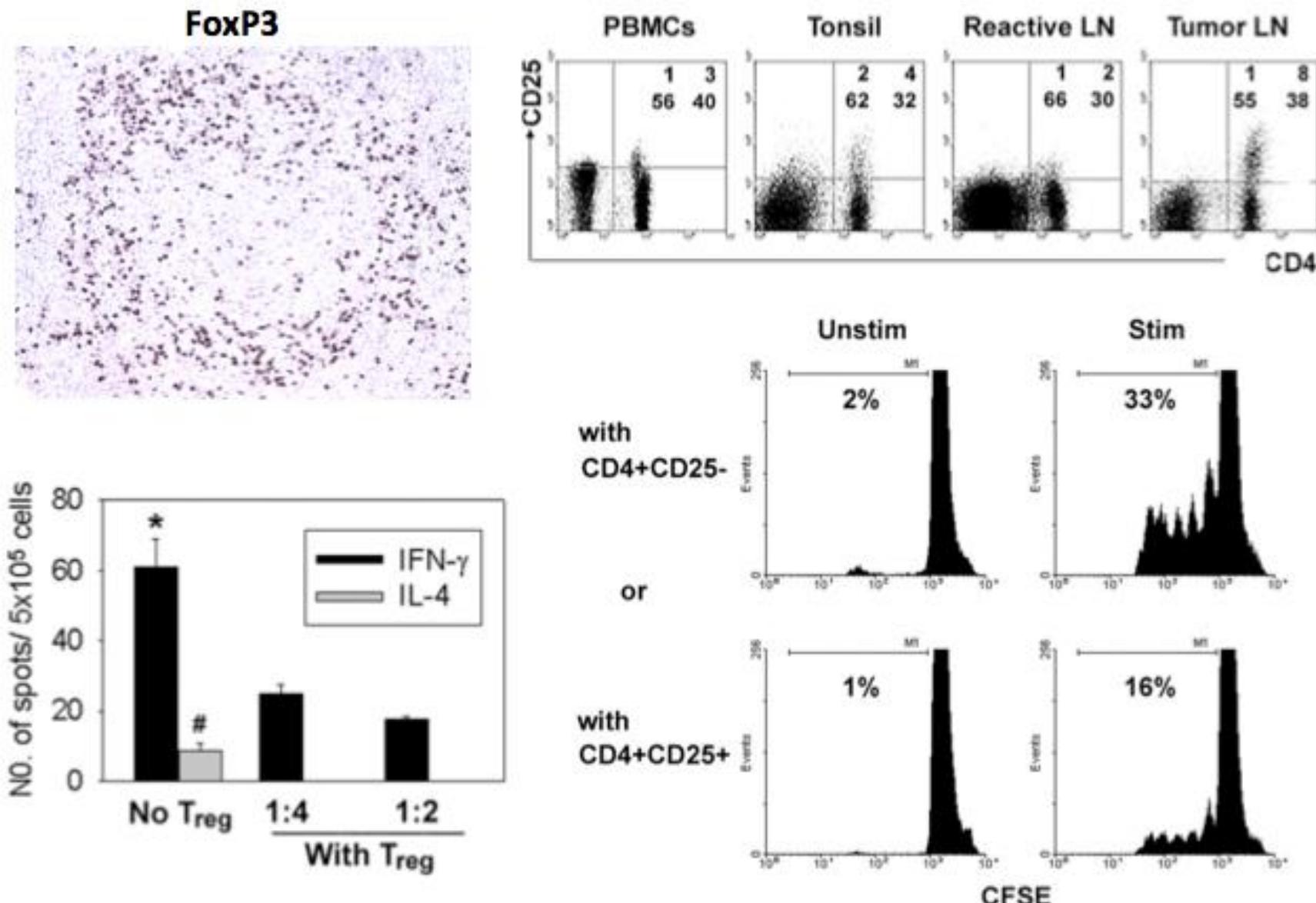
2. Functional characterization of PD1⁺TIM3⁺ tumor-infiltrating T cells in DLBCL



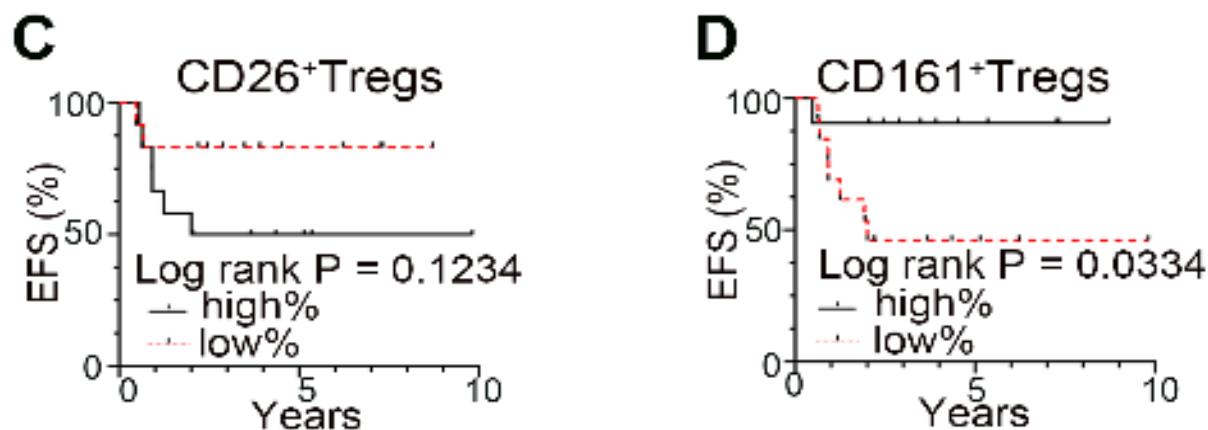
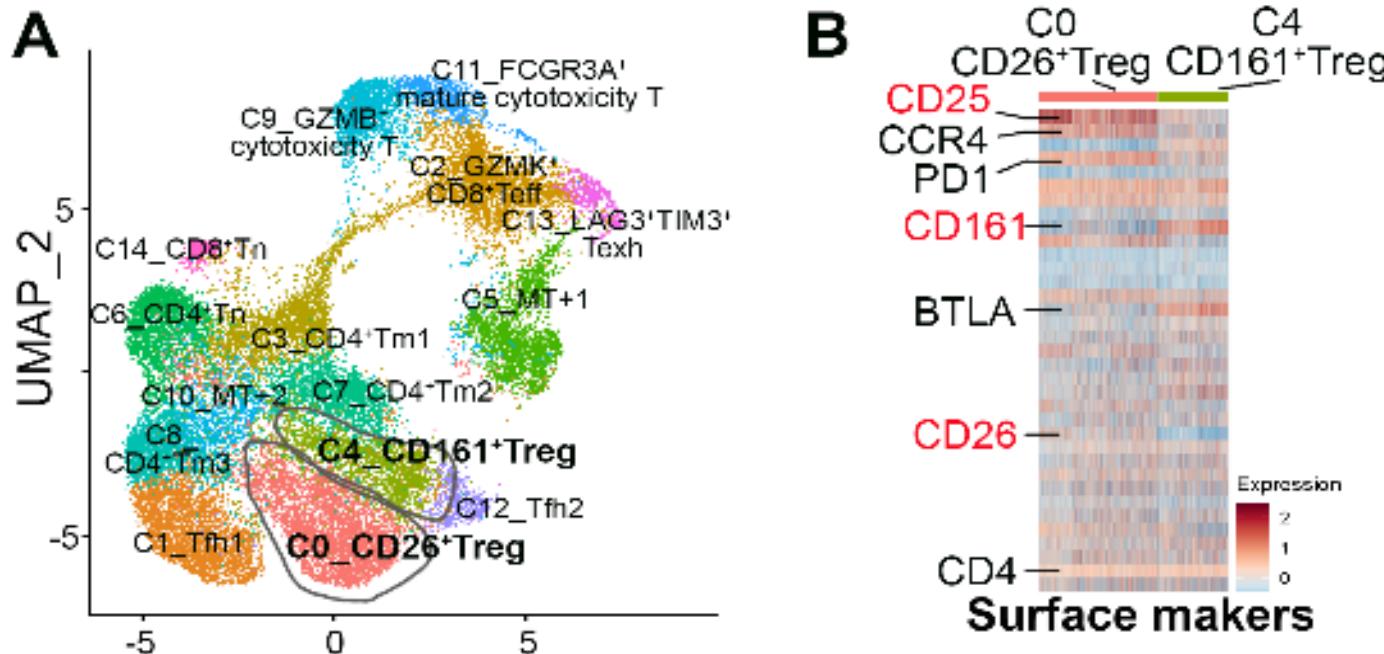
2. TIGIT and PD-1 Identify T-Cells with Reduced Effector Function



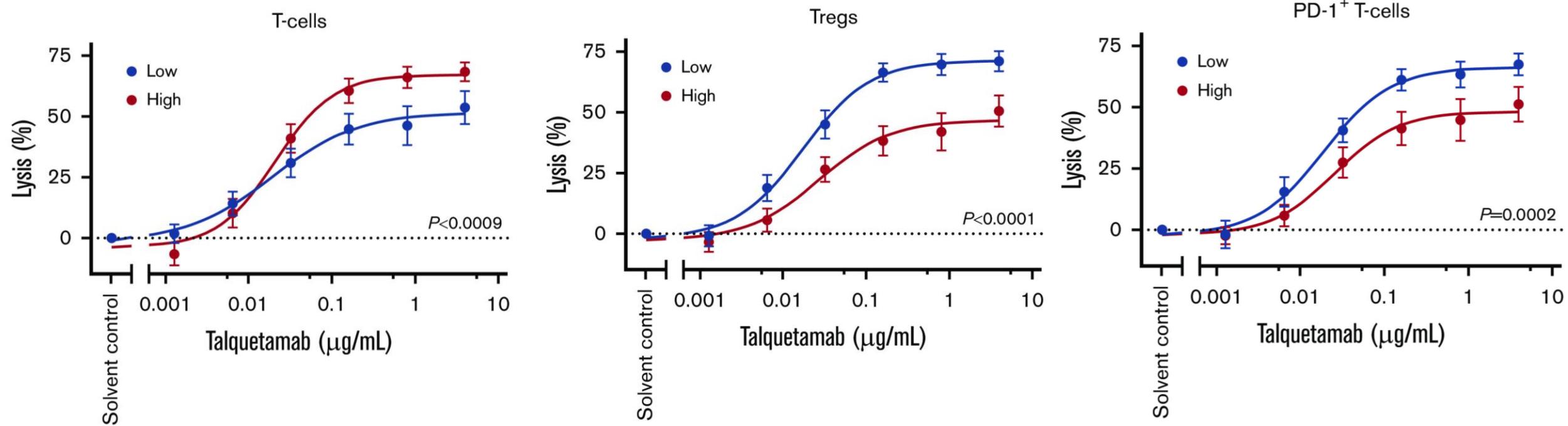
3. Increased regulatory T-cells in lymphoma



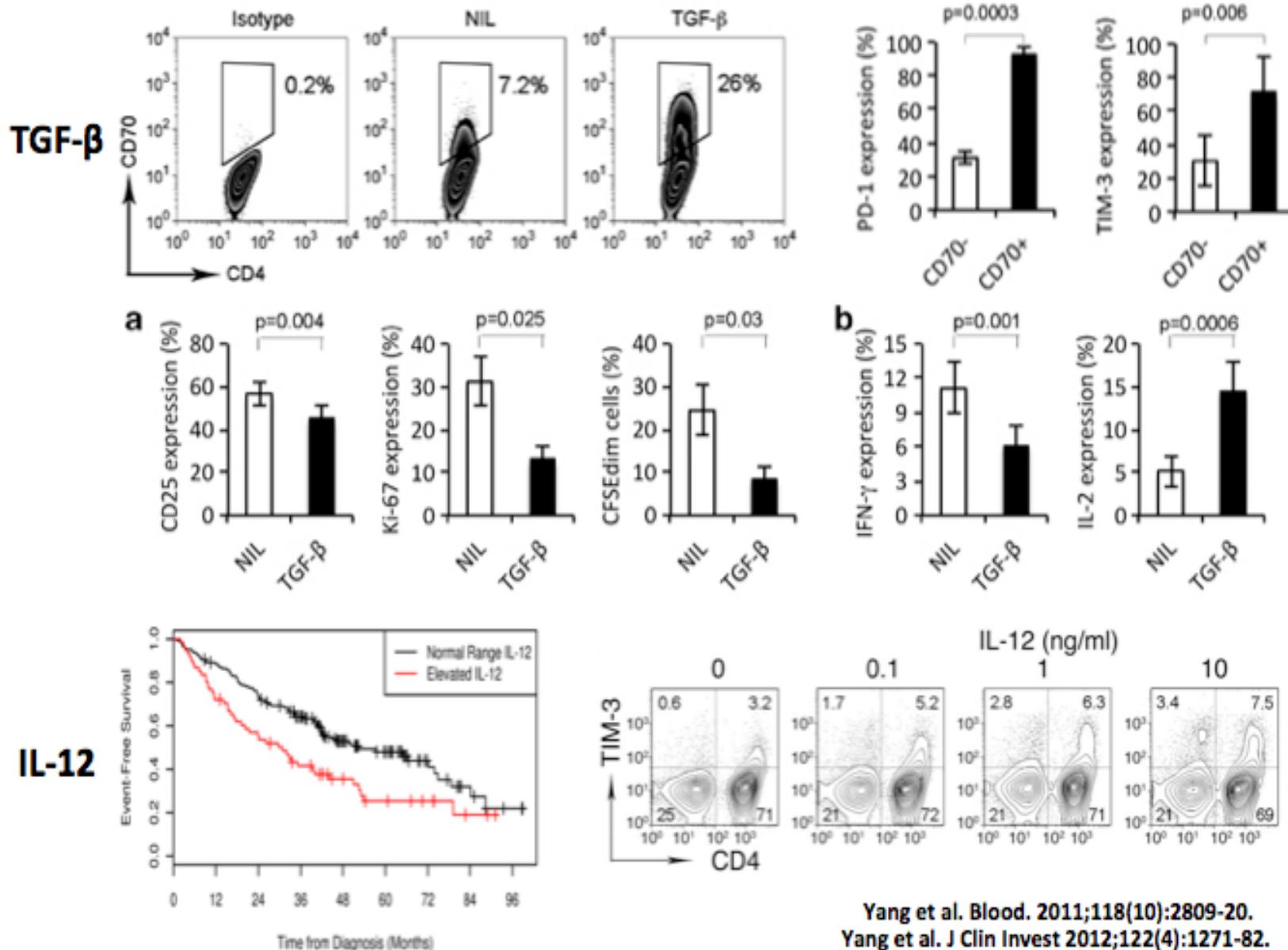
3. CD26+ and CD161+ Treg cells have different effects in lymphoma



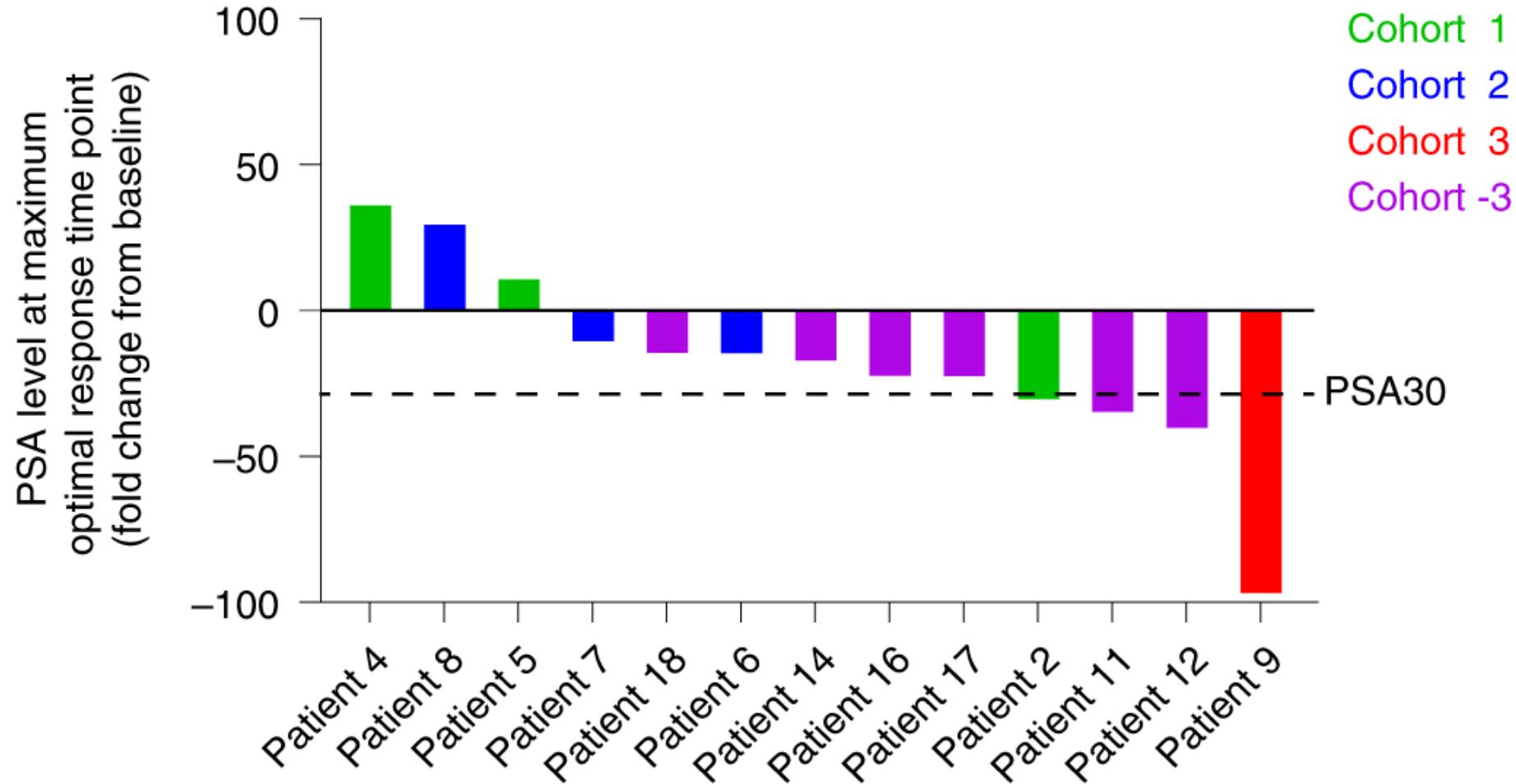
3. Determinants of tumor lysis by the bispecific antibody talquetamab



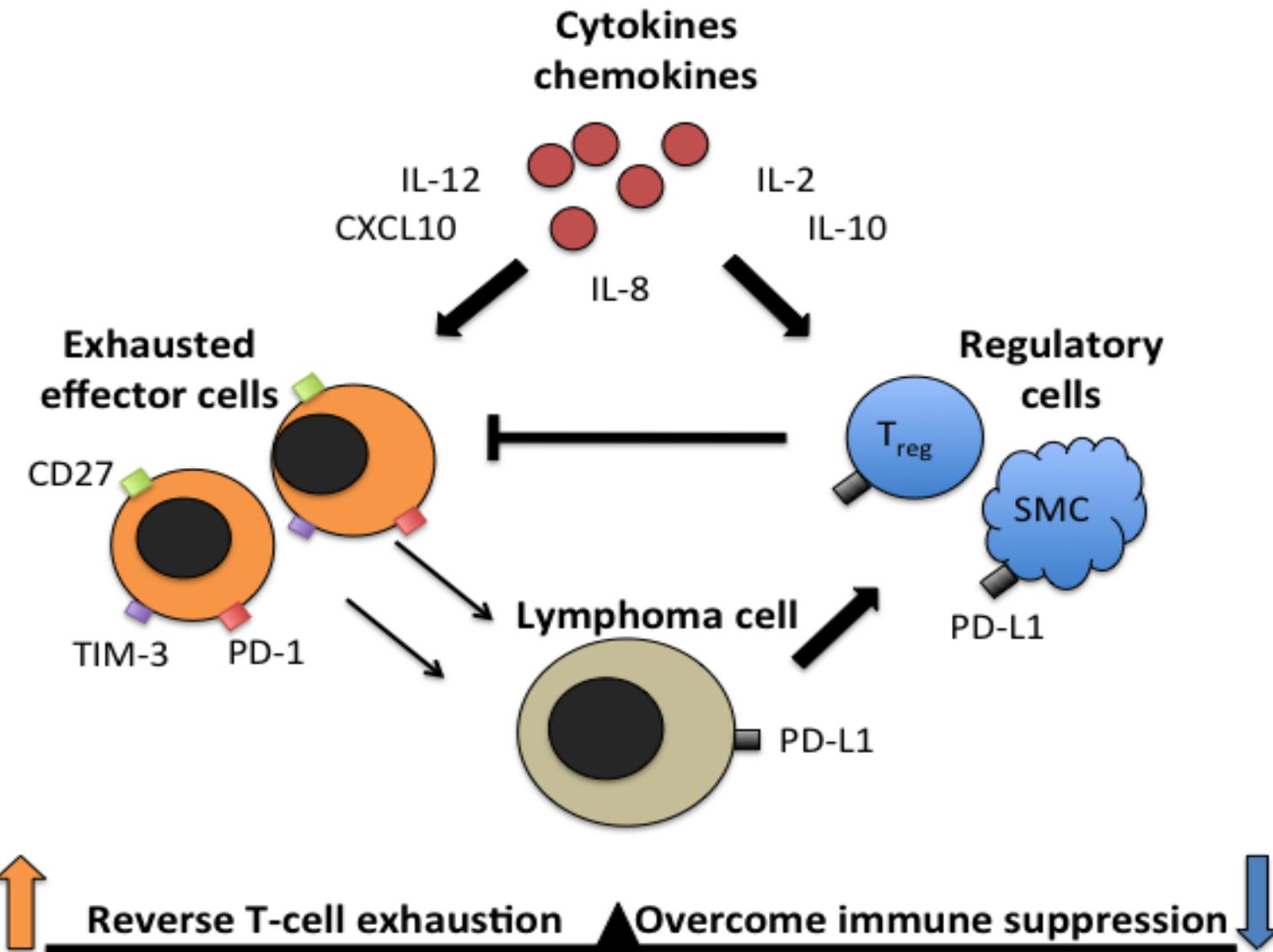
4. Immunostimulatory cytokines induce T-cell exhaustion



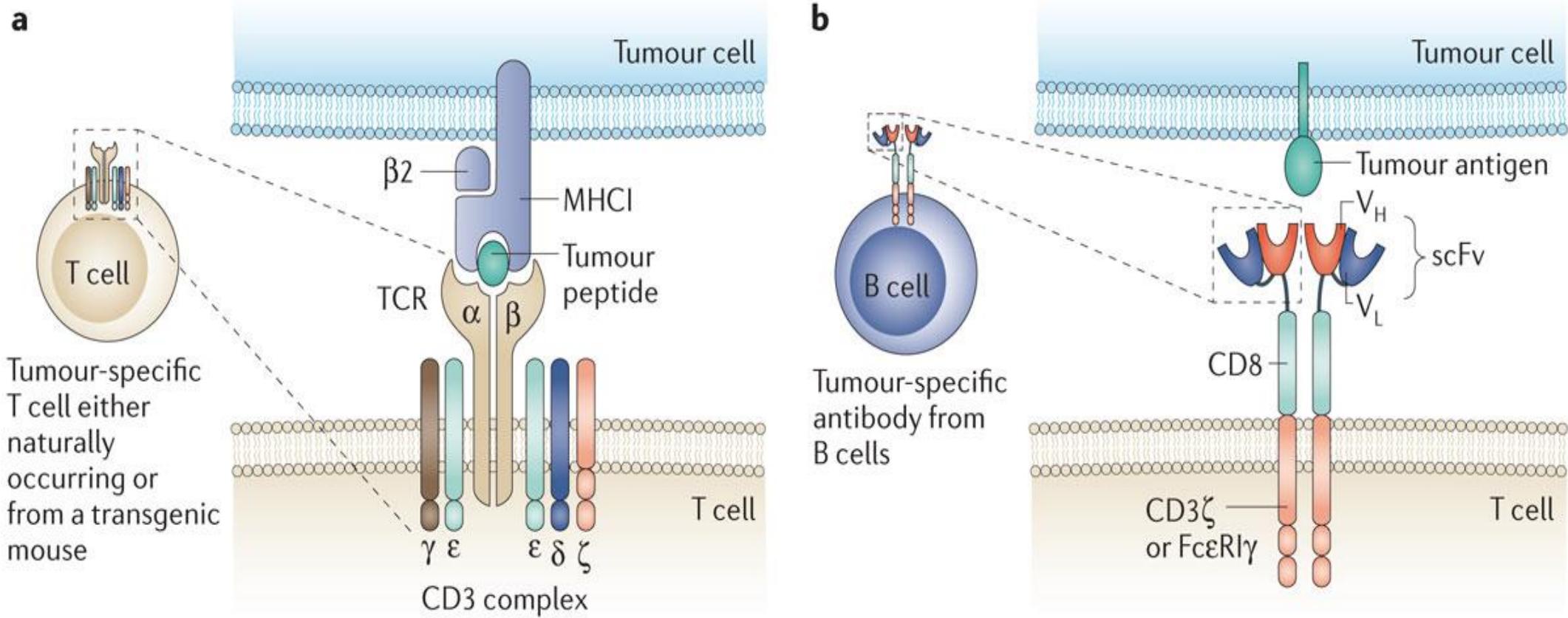
Responses following CART-PSMA-TGF β R Double Negative cell infusion



How can we activate the anti-tumor immune response in lymphoma?

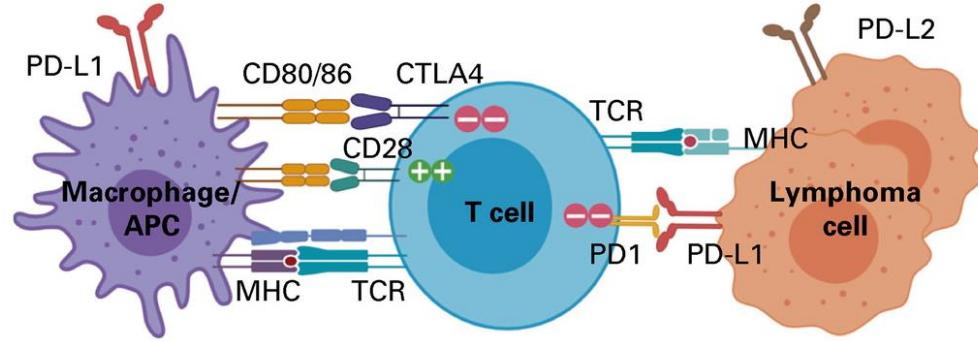


Strategy 1: Chimeric Antigen Receptor T-cells – Improve Target Recognition

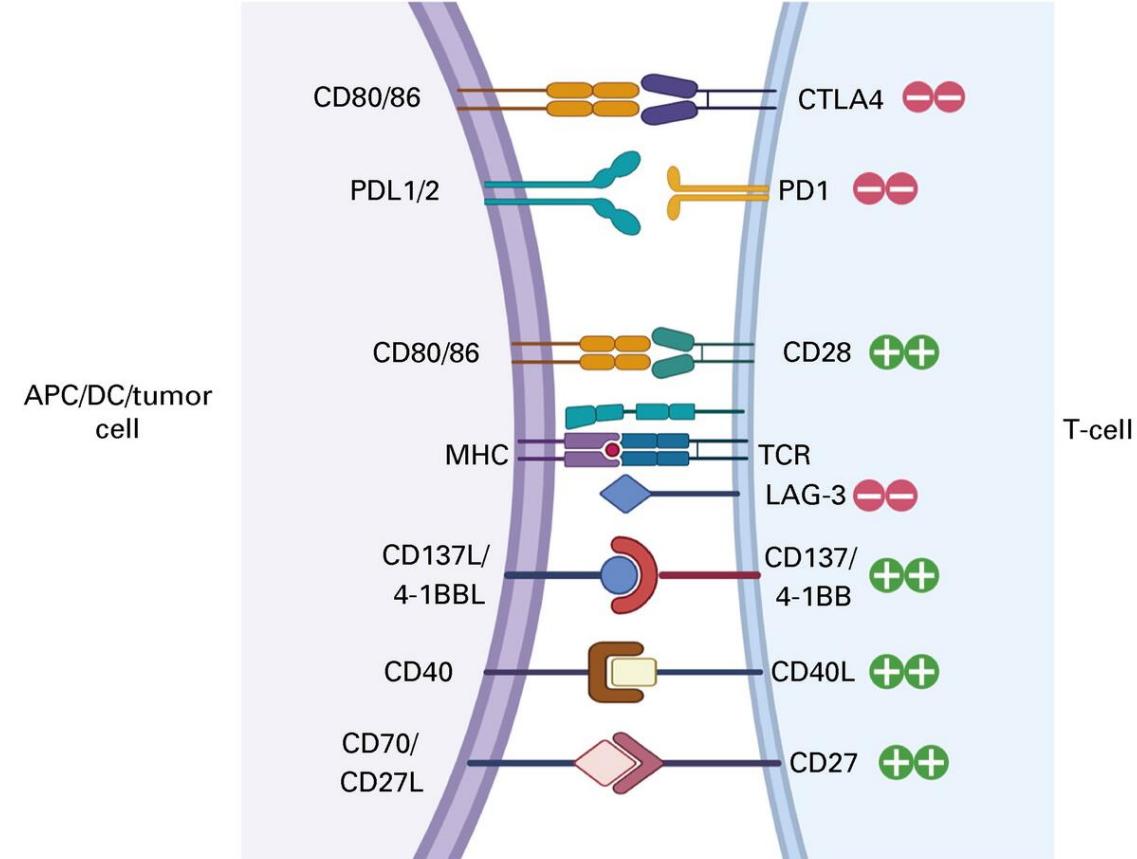


Strategy 2: Target immune checkpoints – prevent immune suppression

A

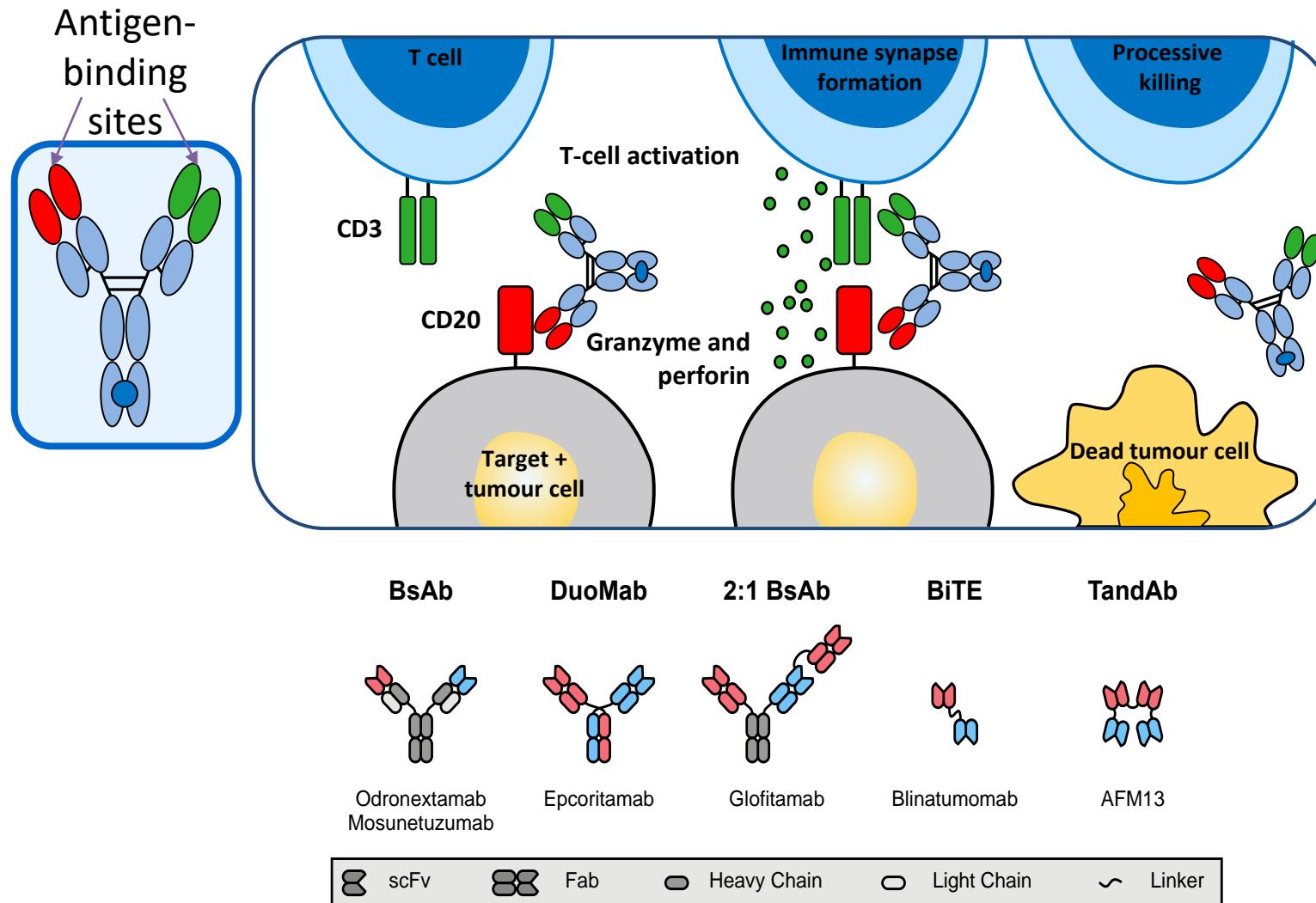


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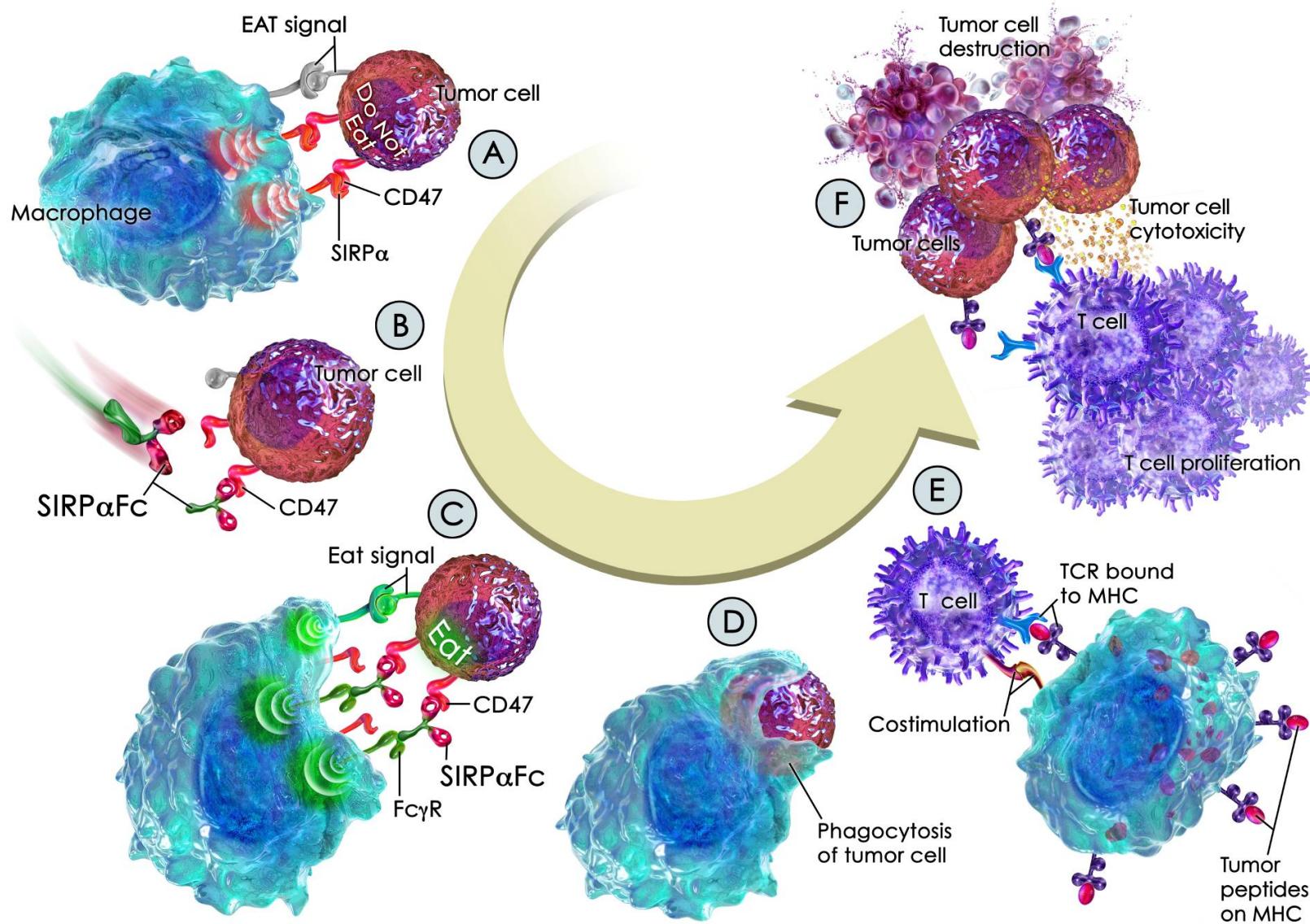


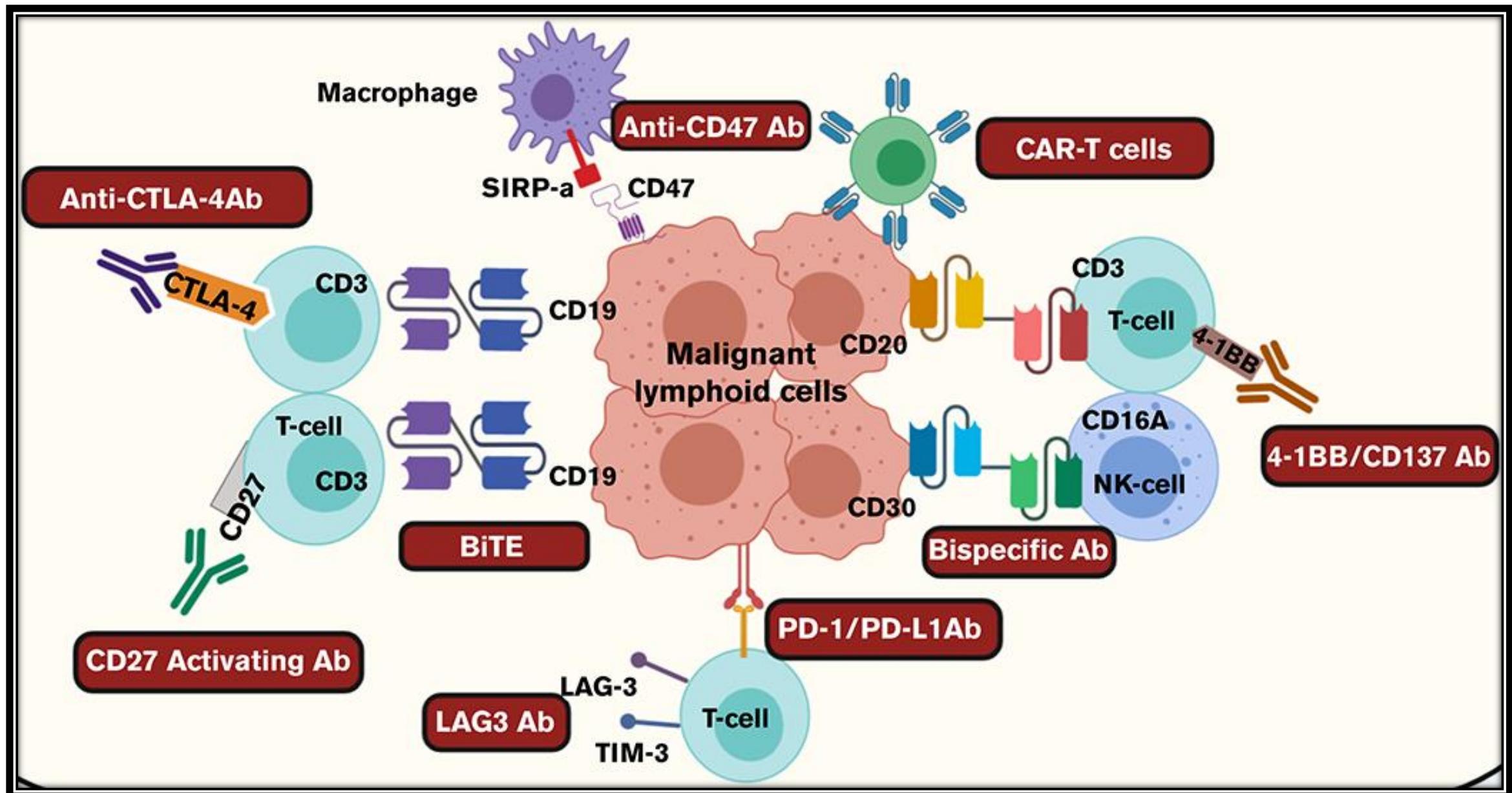
Strategy 3: Bispecific antibodies –

Force T-cell activation



Strategy 4: Engage the Innate Immune System





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