T cell exhaustion in Hematological malignancies

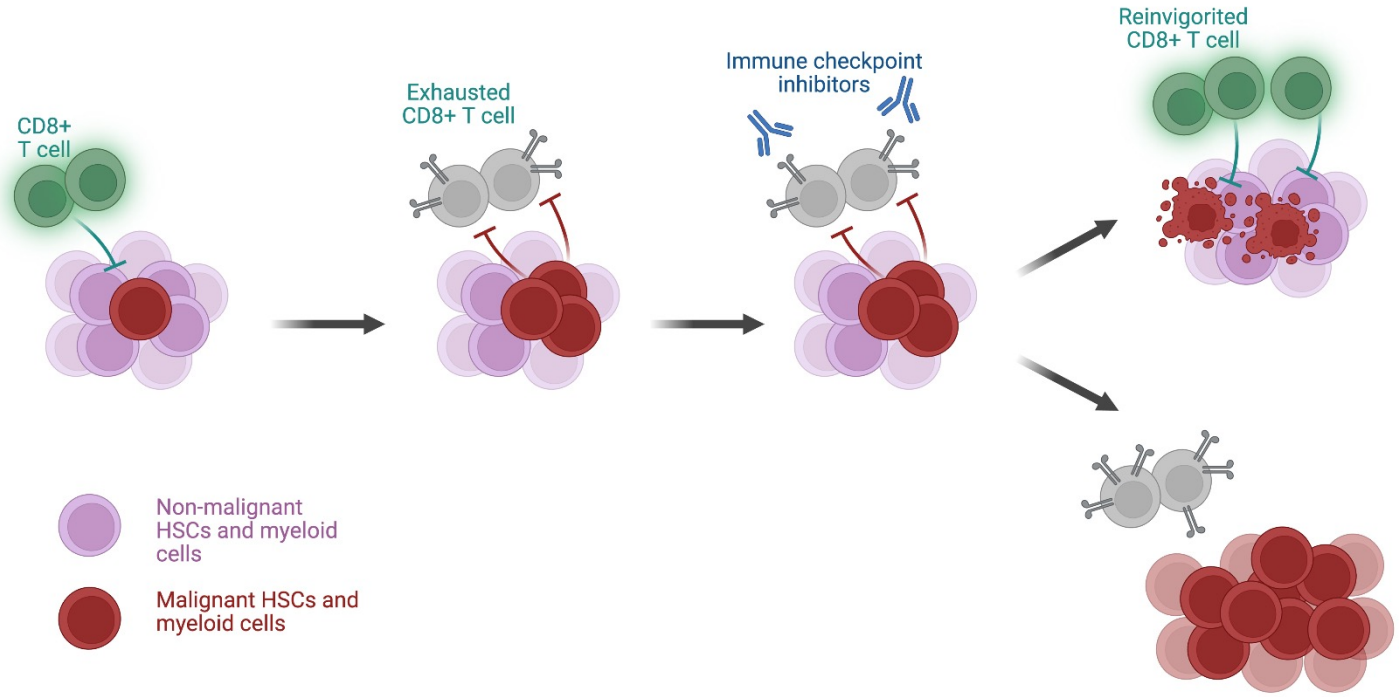
Lara Tavernari

Firenze | 4-6 marzo 2026
Palazzo degli Affari

Disclosures of Lara Tavernari

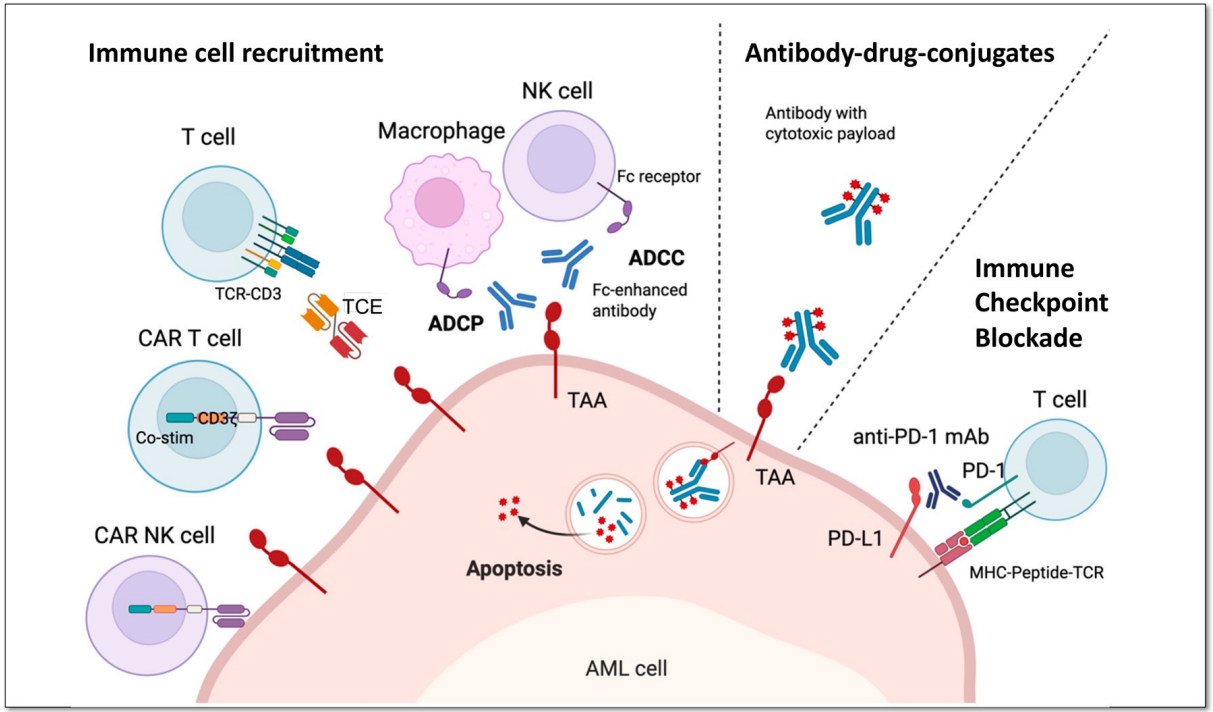
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
NONE							

T cell exhaustion in haematological malignancies



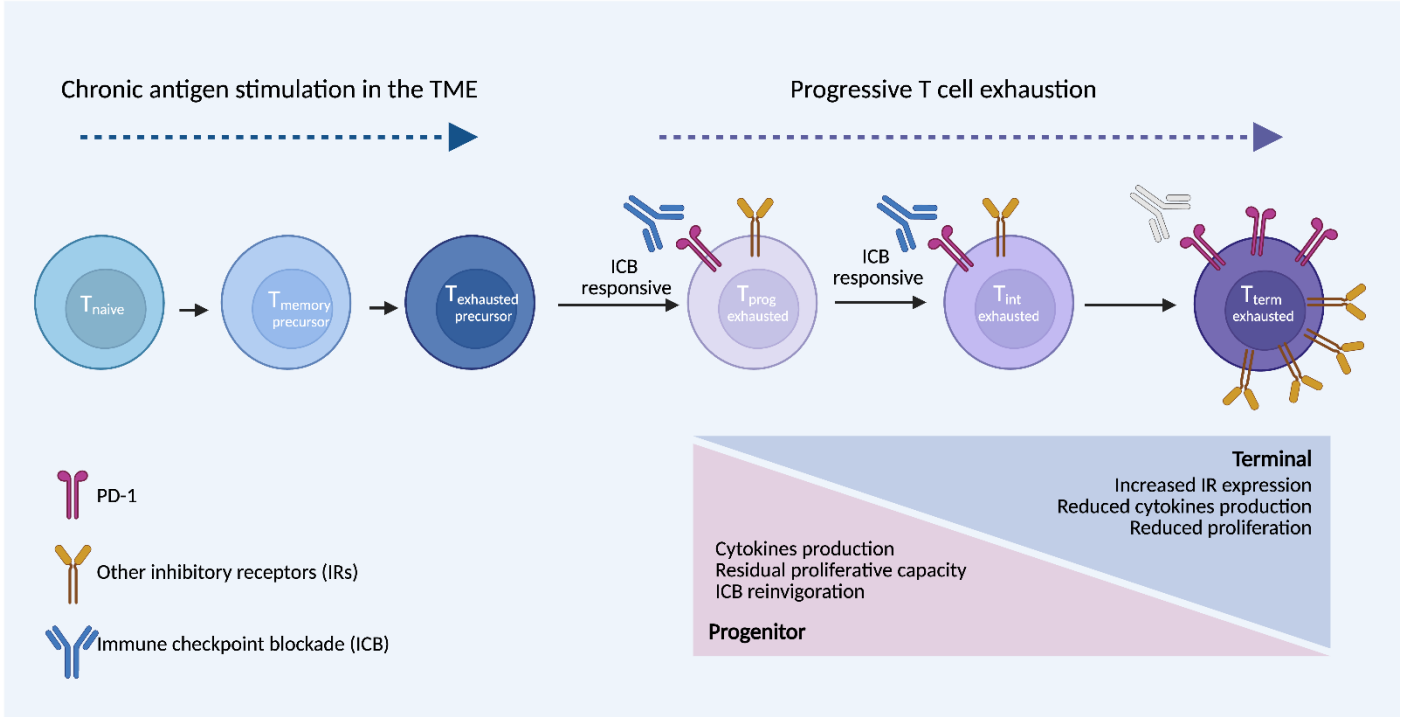
Created with BioRender

T cells: disease-fighting effectors and therapeutic strategies



Subklewe M, Seminars in Hematology, 2025

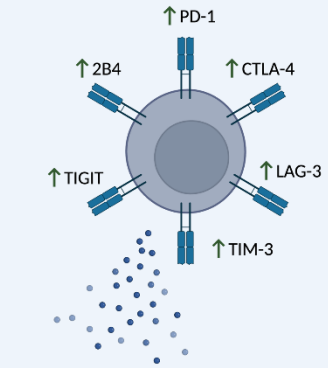
T cell exhaustion



Created with BioRender, adapted from:
Pauken K.E. et al, Trends Immunol, 2015; McLane L.M. et al, Ann Rev, 2019; Franco F, Nature Metabolism, 2020

T cell exhaustion and senescence

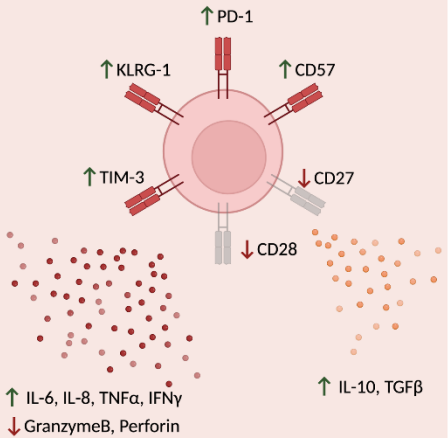
EXHAUSTION



Features

- ↓ Proliferation
- ↓ Cytotoxic activity
- ↓ cell cycle arrest
- ↓ glycolisis, ↑ ROS

SENESCENCE

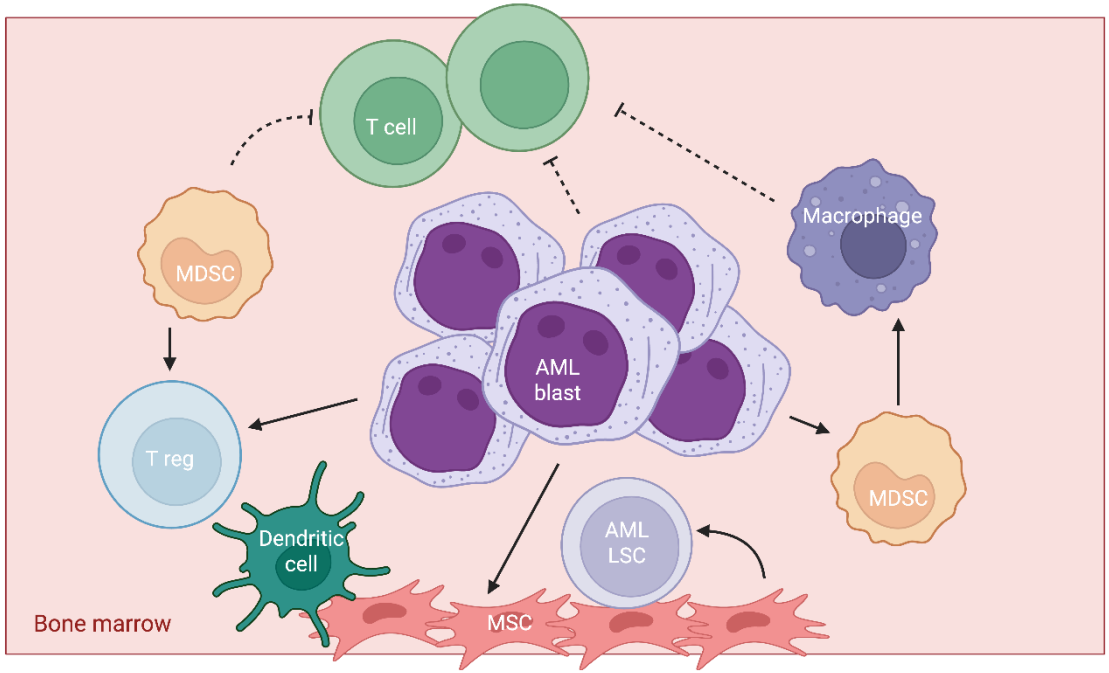


Features

- ↓↓ Proliferation
- ↑ Proinflammatory cytokines
- ↑ Inhibitory factors
- ↓ cell cycle arrest
- ↓ glycolisis, ↑ ROS

Created with BioRender

Immune escape mechanisms in AML

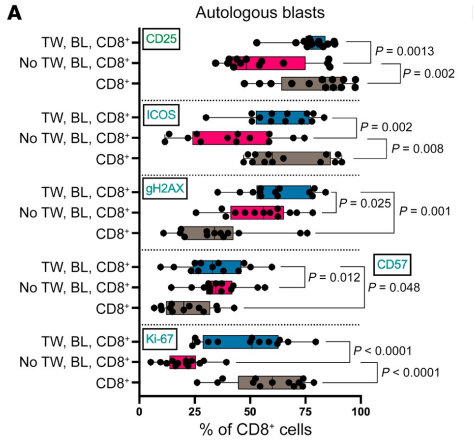


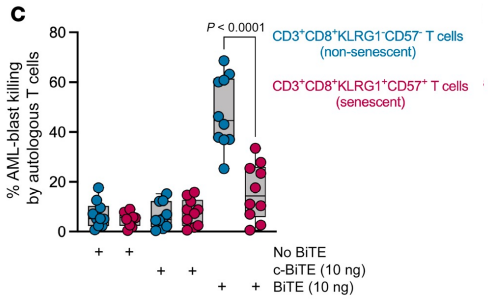
Created with BioRender

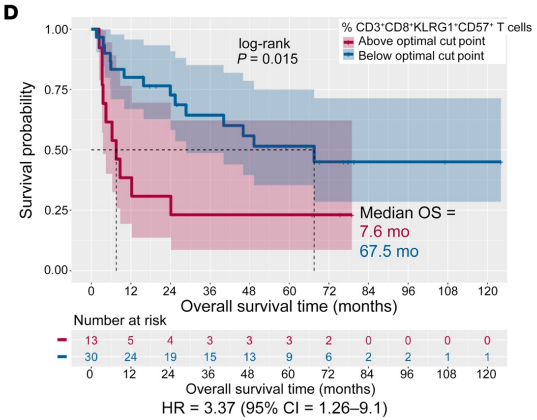
Immune escape mechanisms in AML

Tumor-intrinsic

Alteration of T cells through direct contact with blasts





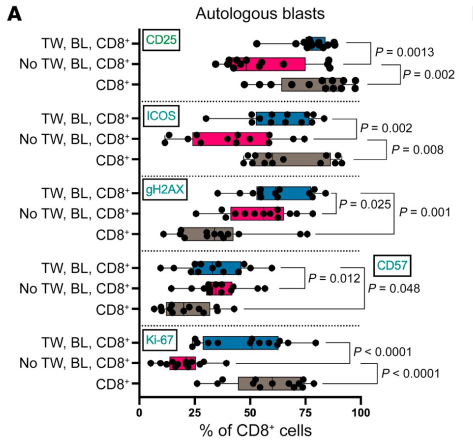


Rutella S et al, Journal of Clinical Investigation, 2022

Immune escape mechanisms in AML

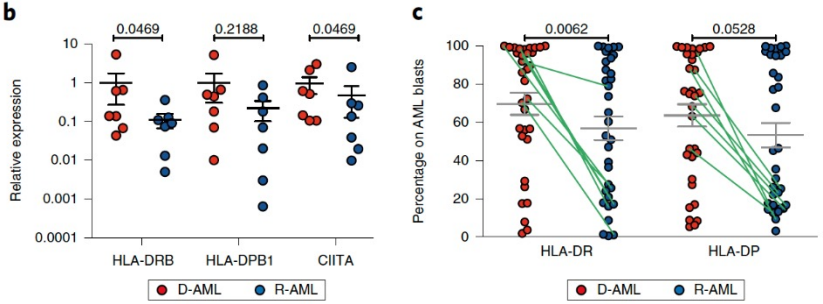
Tumor-intrinsic

Alteration of T cells through direct contact with blasts



Rutella S et al, Journal of Clinical Investigation, 2022

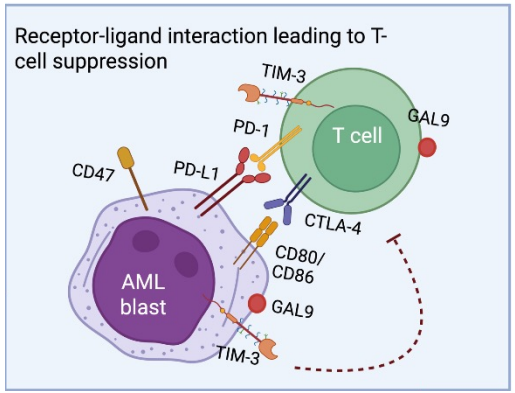
Loss of T cell AML recognition



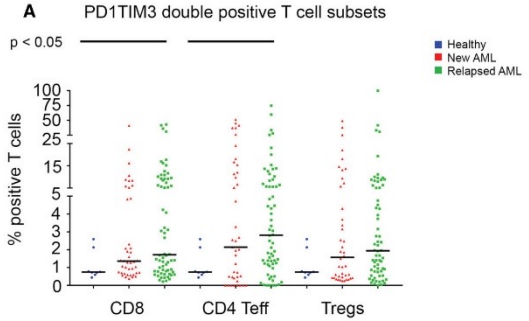
Toffalori C et al, Nature Medicine, 2019

Immune escape mechanisms in AML

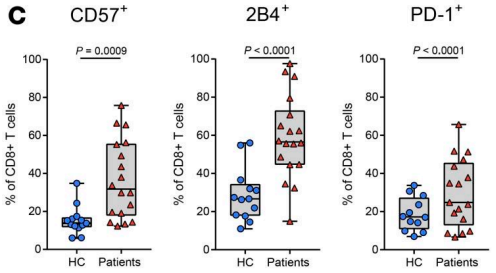
T cell mediated:



Inhibitory receptor expression on T cells

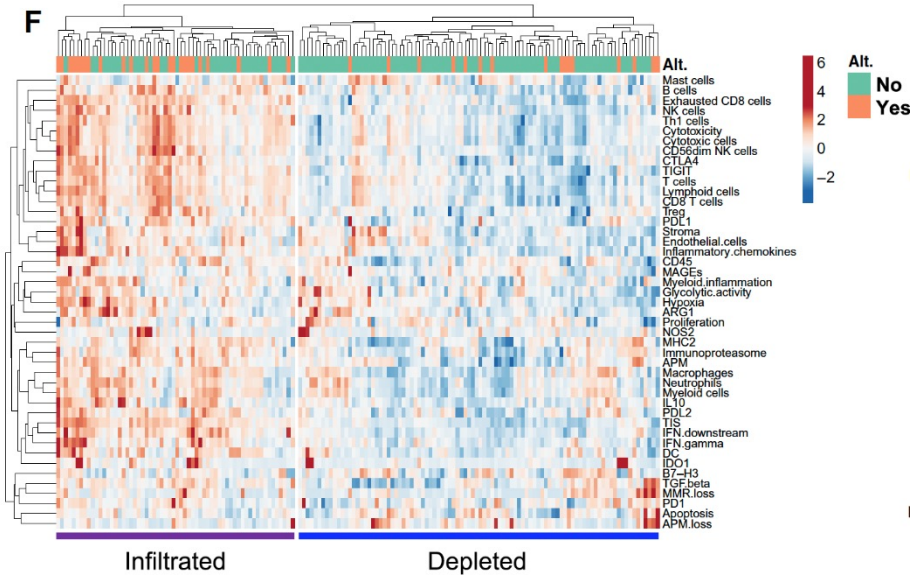


Williams P et al, Cancer, 2019



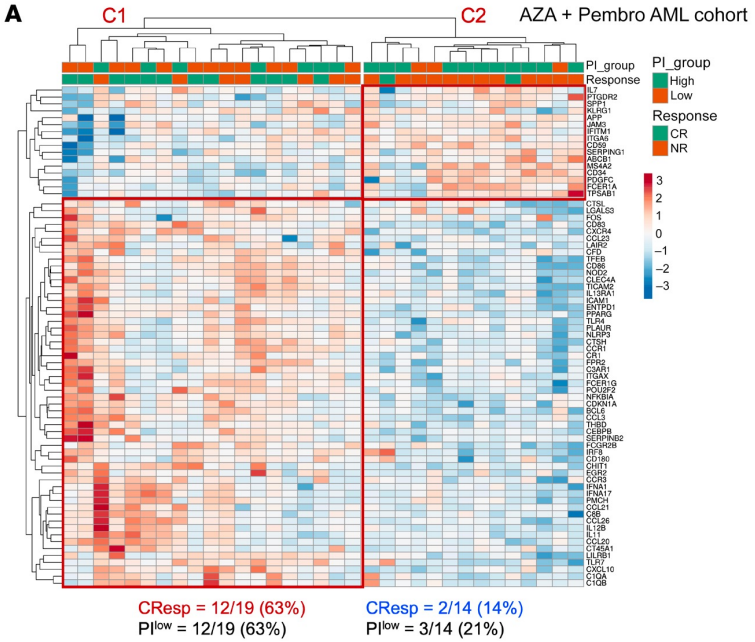
Knau H et al, JCI insight, 2018

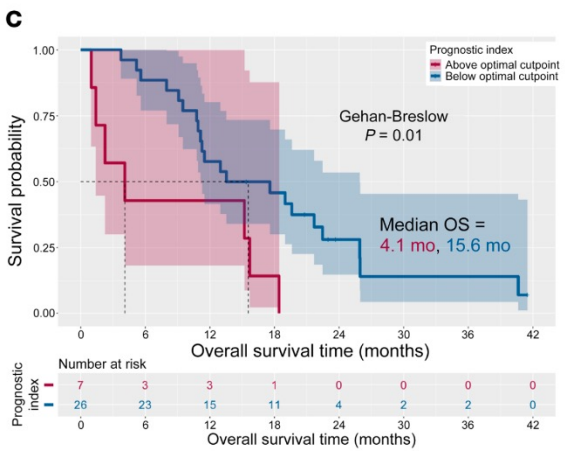
Characterization of the immune landscape in AML: immune-infiltrated and immune-depleted microenvironment



Vadakekolathu J et al, Science Translational Medicine, 2020

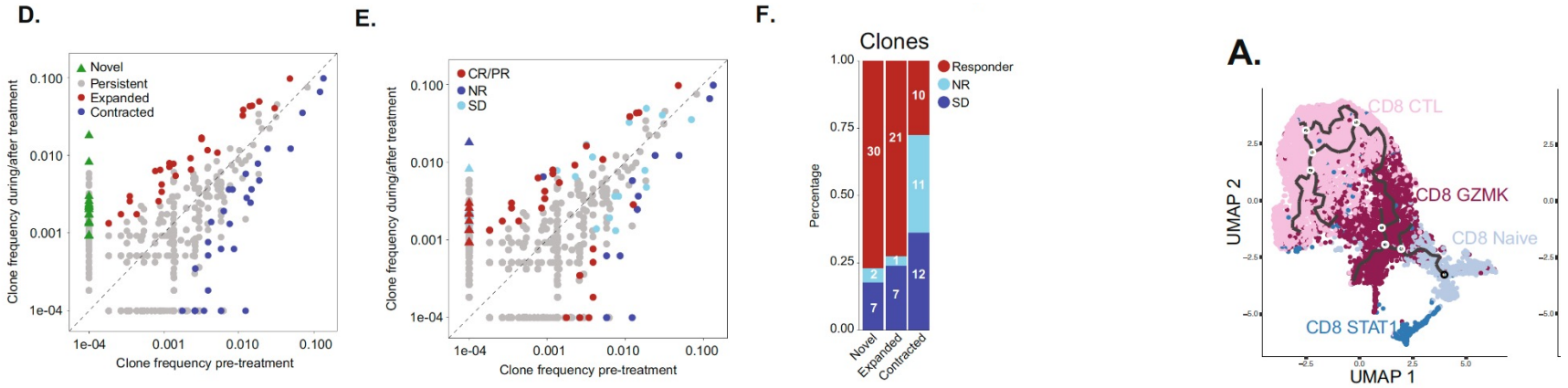
Characterization of the immune landscape in AML: Immune effector dysfunction signatures





Rutella S et al, Journal of Clinical Investigation, 2022

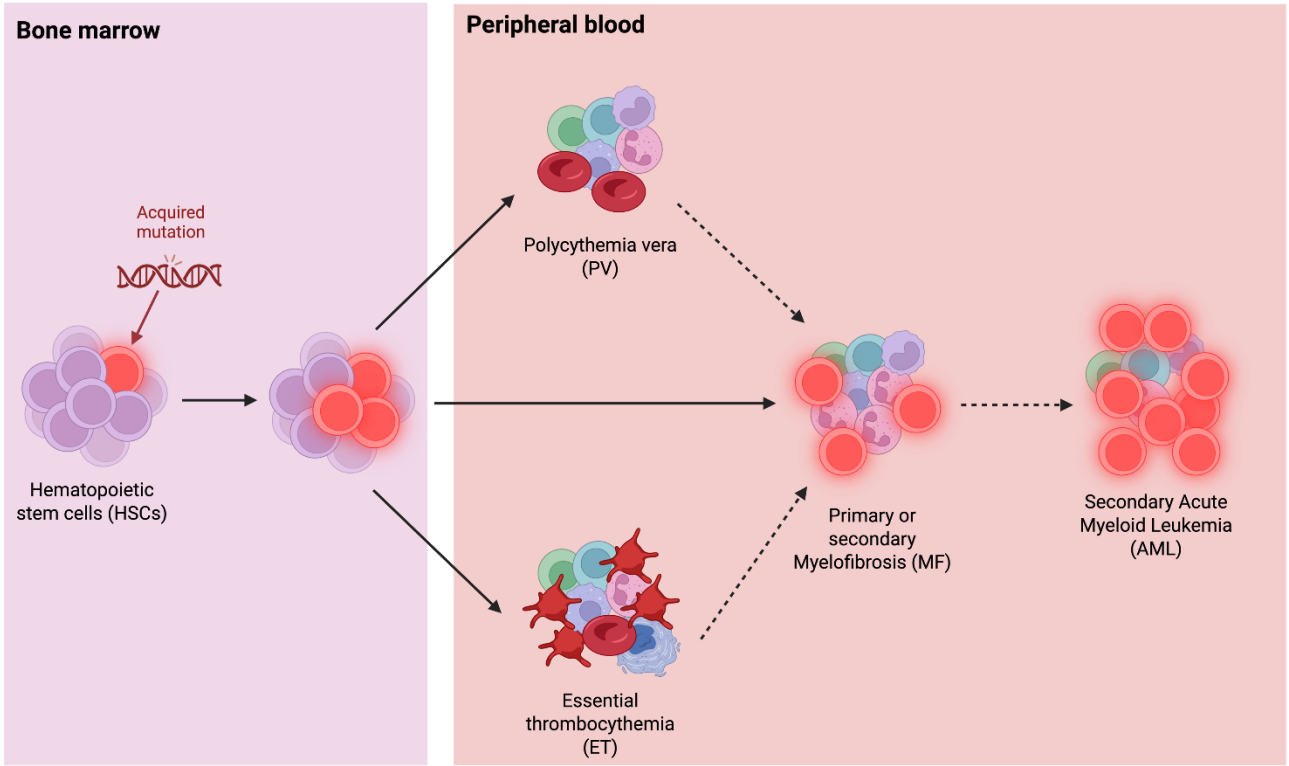
TCR repertoire expansion in immunotherapy-responder patients



Abbas H.A. et al, Nature Communications, 2021

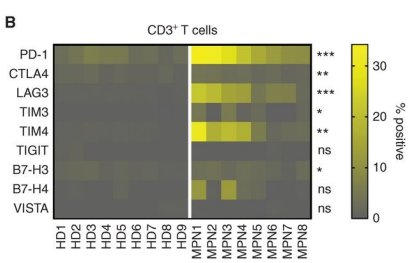
The real question is not whether checkpoint inhibitors work in AML, but in which state T cells are when we intervene

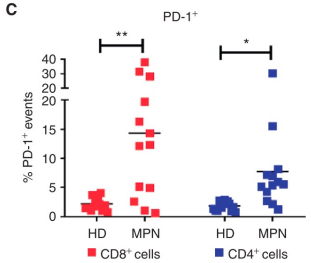
Myeloproliferative neoplasms (MPN) as a model of chronic T-cell dysfunction

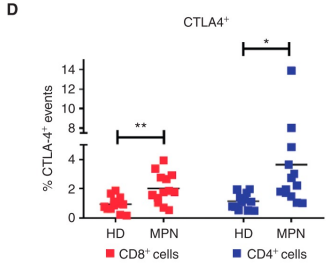


Created with BioRender

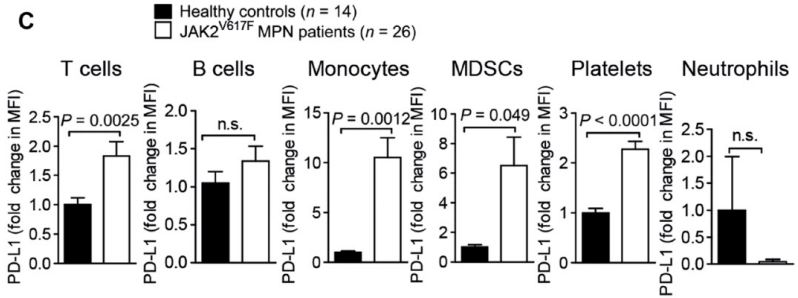
Immunobiology in MF





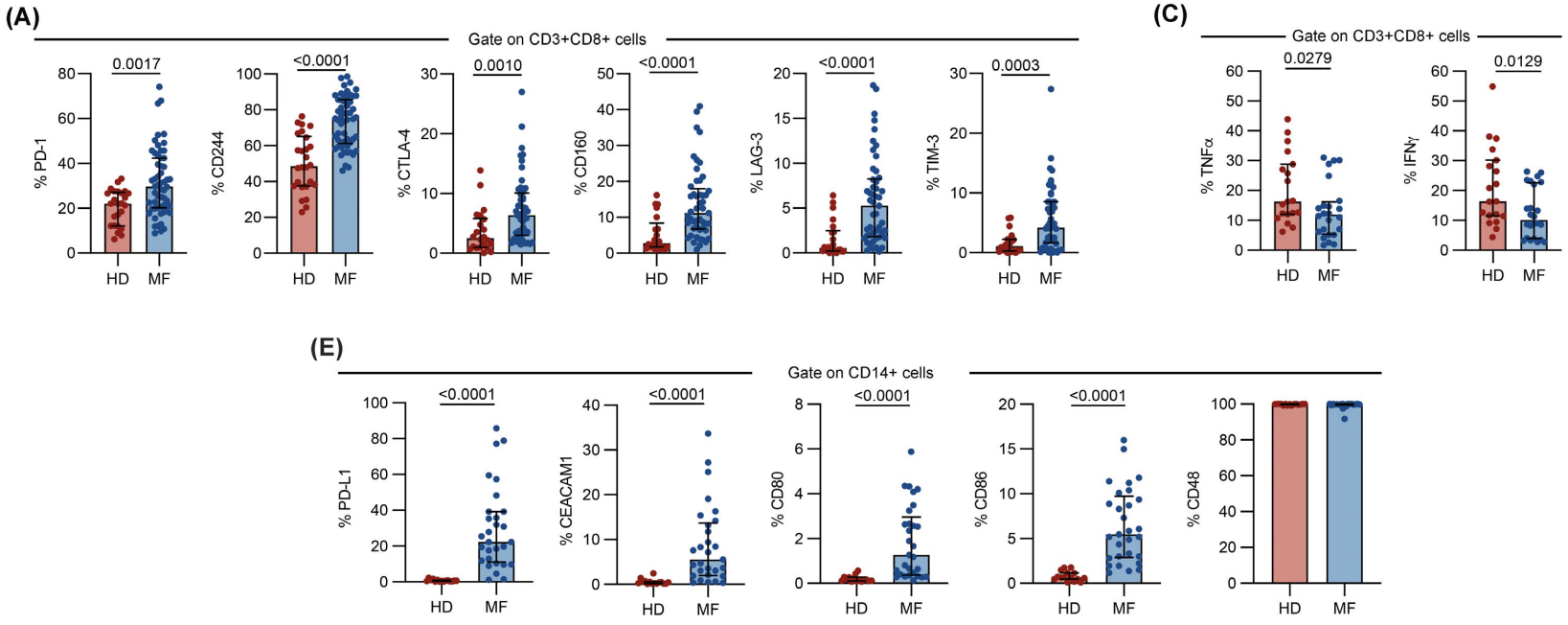


Bozkus C. et al, Cancer Discovery, 2019



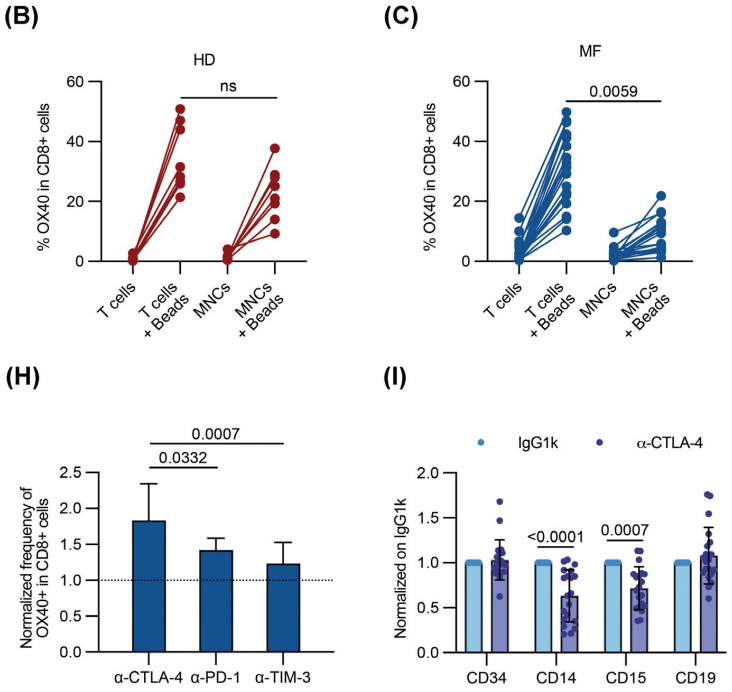
Prestipino A. et al, Science Translational Medicine, 2018

MF patients exhibit circulating exhausted cytotoxic T cell



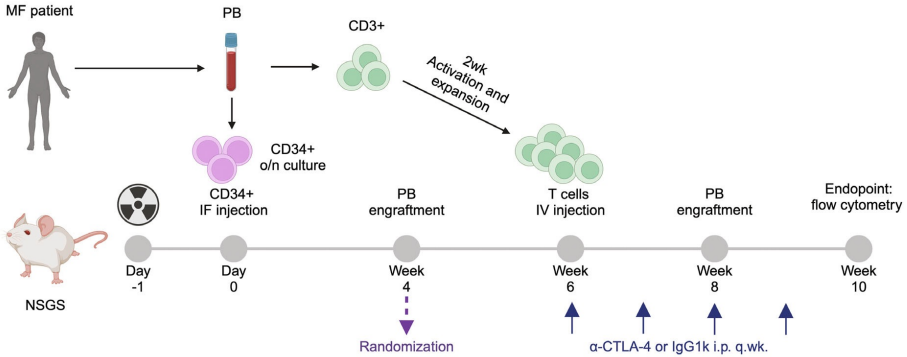
Tavernari L. et al, American Journal of Hematology, 2024

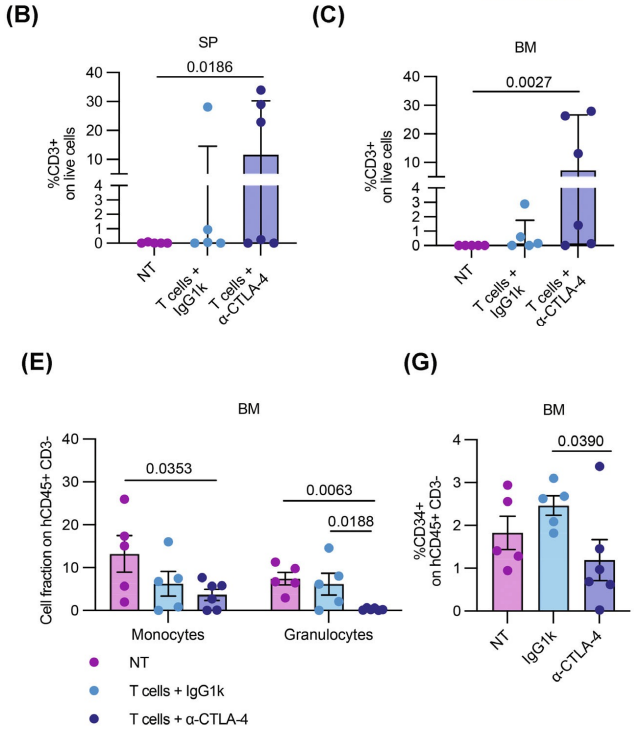
MF malignant cells impair T cell function



Tavernari L. et al, American Journal of Hematology, 2024

In vivo treatment with anti-CTLA-4 reinvigorate MF T cells

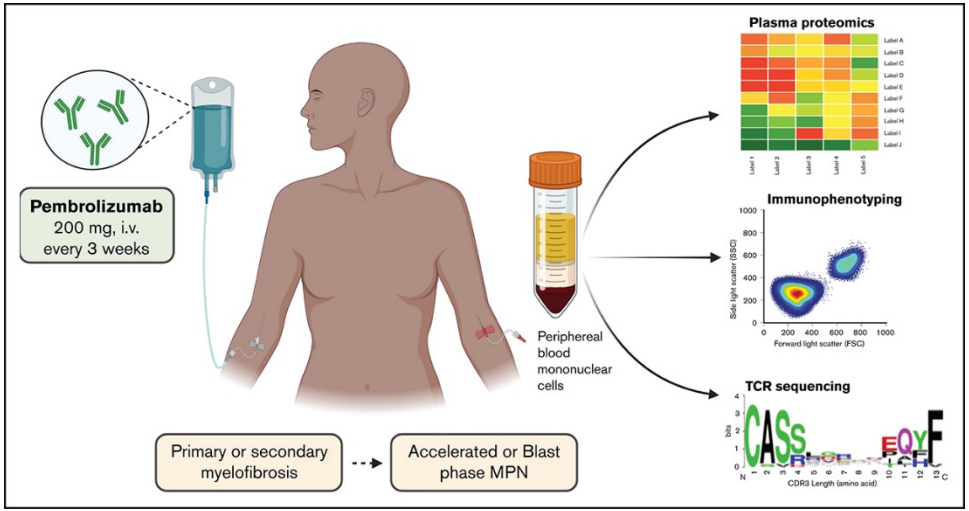




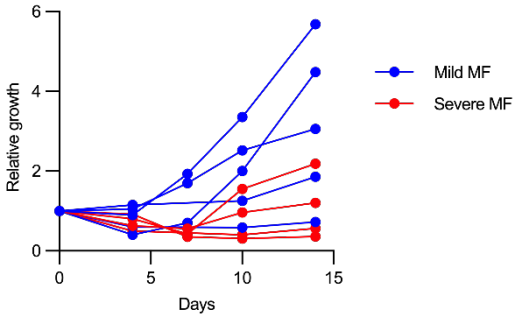
Tavernari L. et al, American Journal of Hematology, 2024

Anti-PD1 trial in MF failed to prove efficacy

Trial NCT03065400
Pembrolizumab in advanced MPN (DIPSS plus intermediate2 or high)



Hobbs G. et al, Blood Advances, 2021



Tavernari L. et al, American Journal of Hematology, 2024

Conclusions

T cell exhaustion is not a binary state – it is a continuum

Effective T cell must:

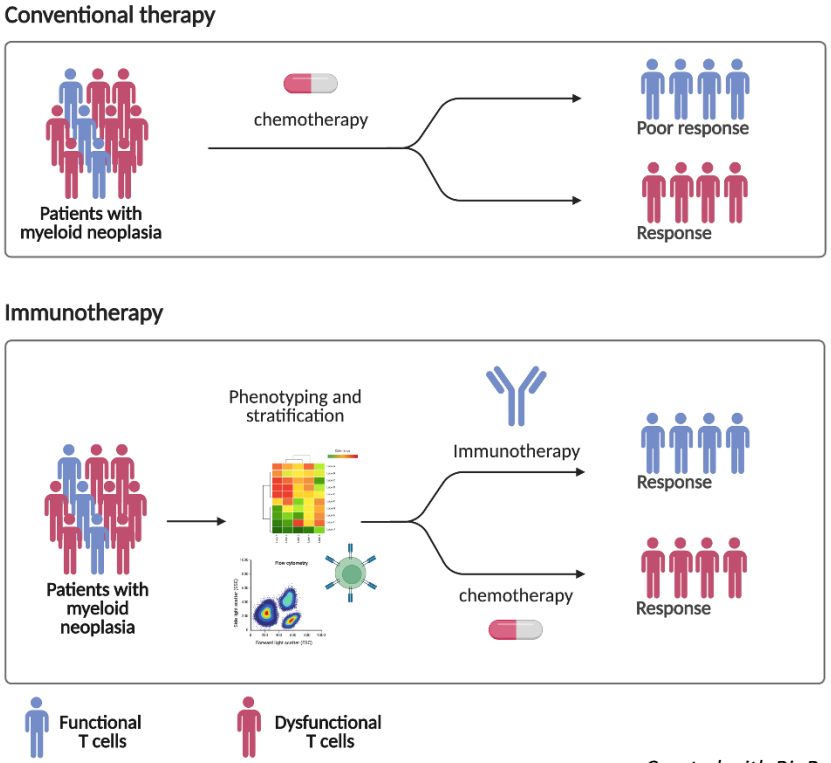
1. Recognize tumor antigen efficiently
2. Receive adequate costimulation
3. Maintain functional plasticity
4. Avoid collapse into terminal states

Targeting a single checkpoint is rarely sufficient

Conclusions

Understanding T cell biology allows us to:

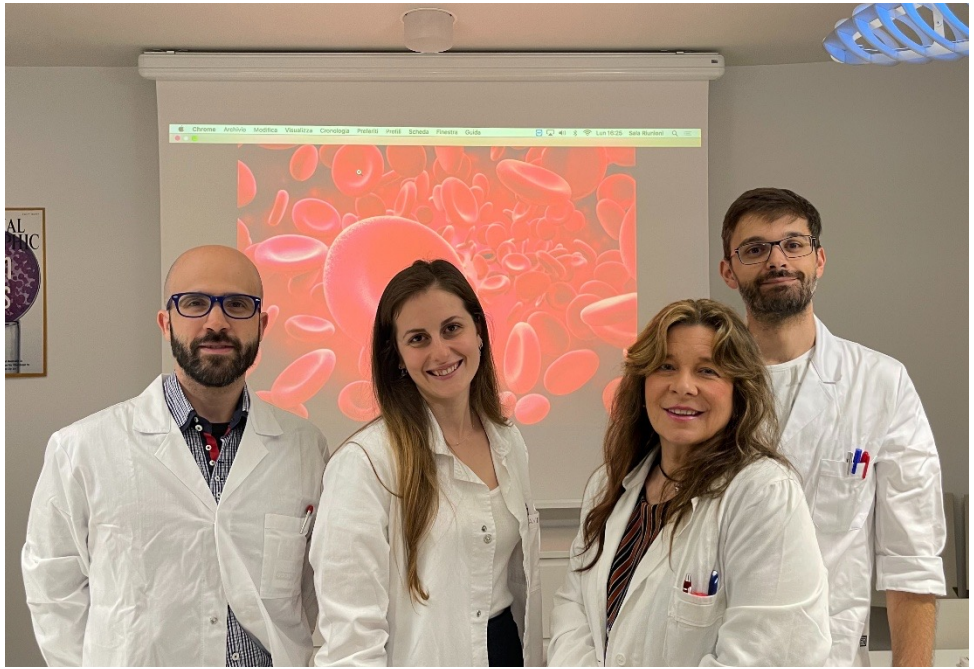
1. Stratify patients
2. Choose the right timing for intervention
3. Design rational therapeutic combinations



Created with BioRender

The real question is not only how to eliminate the leukaemia cell – but in which state the immune system is when we decide to act

Acknowledgments



Centro di Medicina Rigenerativa
Centre for Regenerative Medicine
"Stefano Ferrari"
UNIMORE

Rossella Manfredini
Ruggiero Norfo
Sebastiano Rontauroli

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Modena
UNIMORE

Mario Luppi
Leonardo Potenza
Enrico Tagliafico
Monica Maccaferri

UNIVERSITÀ DEGLI STUDI FIRENZE
Azienda Ospedaliero Universitaria Careggi

A.M. Vannucchi
Paola Guglielmelli

AIRC
Metastatic disease: the key unmet need in oncology
Mynerva
MYeloid NEoplasm Research Venture Airc