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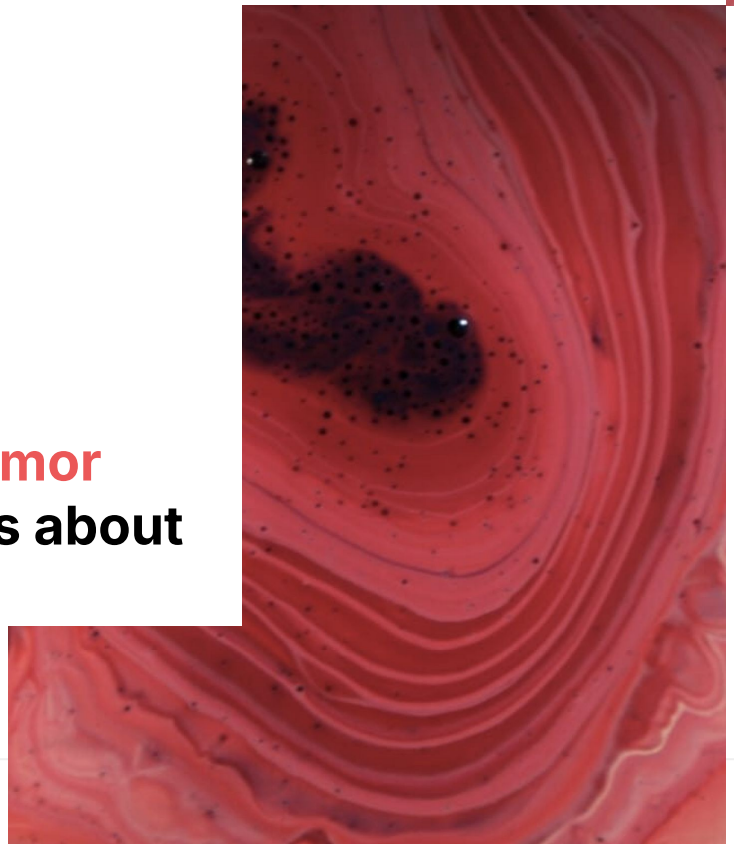
Precision Immune Monitoring

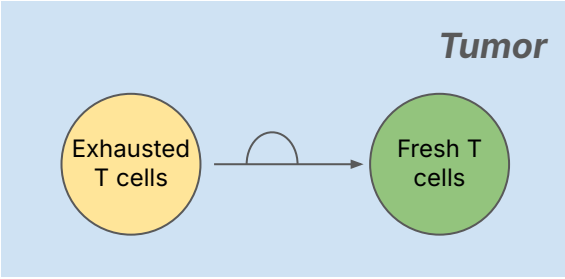
What looking beyond the tumor microenvironment taught us about immunotherapy



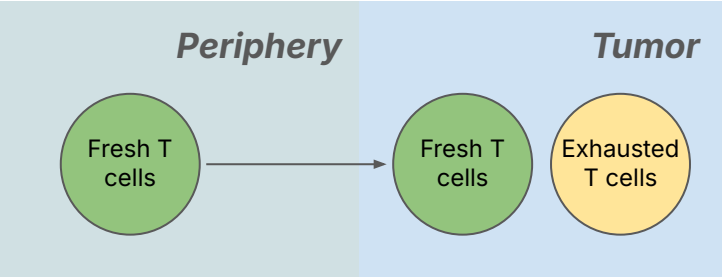
How does immunotherapy work?

Immunotherapy …

… reinvigorates exhausted T cells in the tumor microenvironment



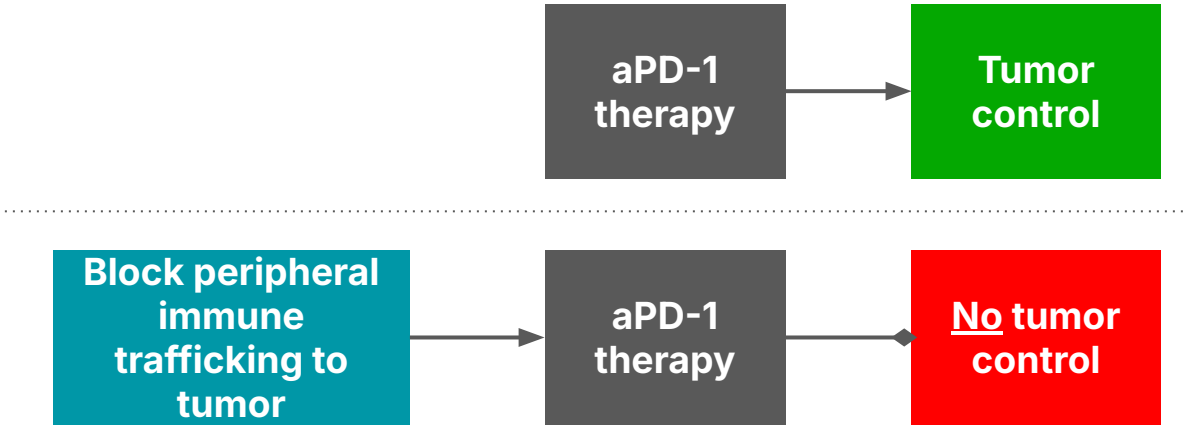
… brings new, non-exhausted T cells to the tumor microenvironment



Spitzer et al. showed that peripheral immune cells are required for immunotherapy in mouse models

Cell

Mouse model of colorectal cancer



Other studies have replicated these findings in different mouse models

Chamoto et al. PNAS 2017 PNAS

Fransen et al. JCI Insight 2018 JCI insight

Dammeijer et al. Cancer Cell 2020 Cancer Cell

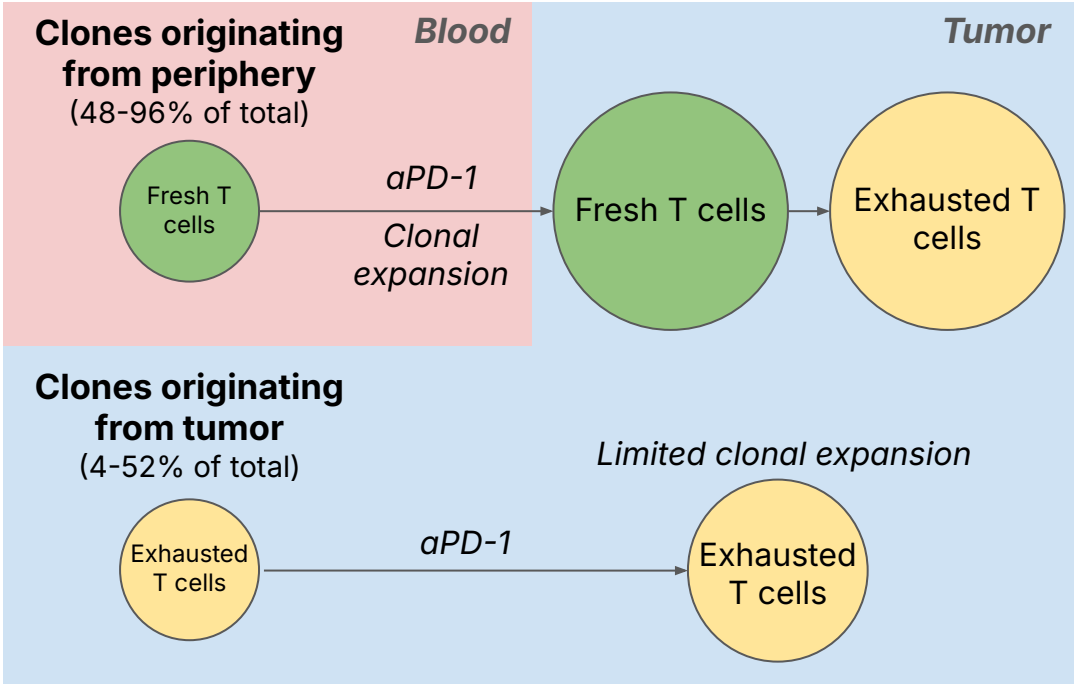
Human studies confirmed immunotherapy induces tumor infiltration by fresh peripheral T cell clones

Tumor-resident T cell clones are present in blood before immunotherapy

↓

Tumor infiltration by fresh peripheral CD8 T cell clones

Immunotherapy controls tumors by improving tumor infiltration by fresh clones from the blood



Yost et al. Nat Med 2019 nature medicine
Wu et al. Nature 2020 nature
Valpione et al. Nat Cancer 2020 nature cancer
Fairfax et al. Nat Med 2020 nature medicine

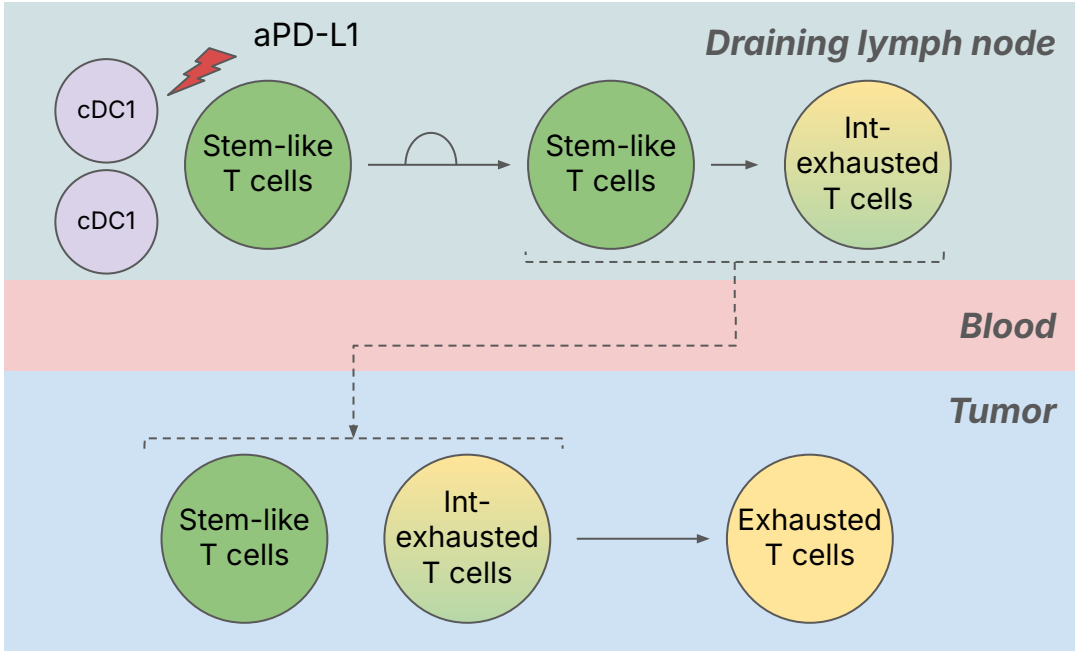
Several labs showed that these fresh T cells are activated in lymph nodes before entering the blood

Schenkel et al.
Immunity 2021

Immunity

Connolly et al.
Sci Immunol 2021

Science Immunology



Rahim, Okholm, Jones et al.
Cell 2023

Cell

How does immunotherapy work?

Immunotherapy …

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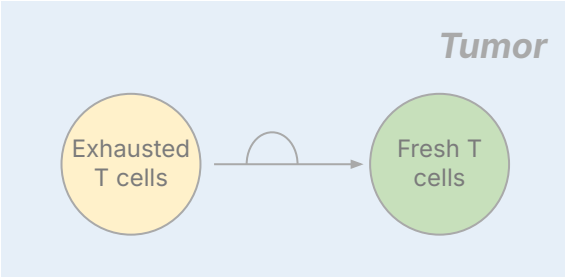
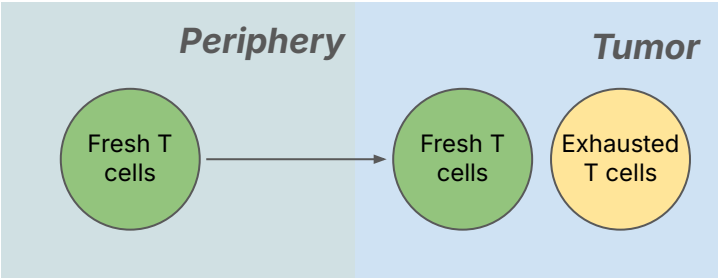


… brings new, non-exhausted T cells to the tumor microenvironment

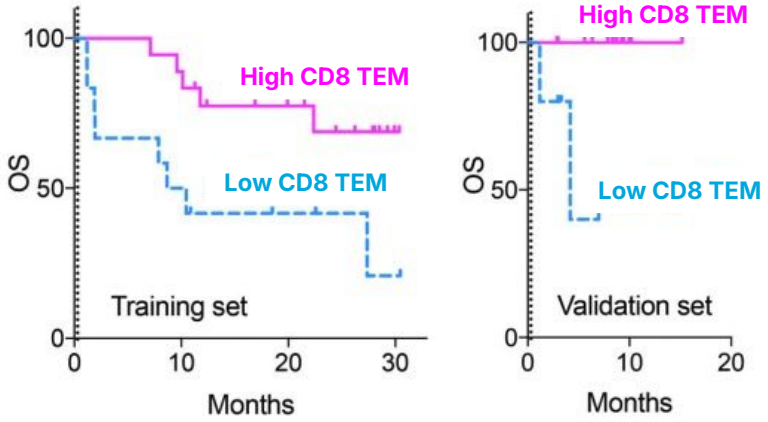


Peripheral T cells are associated with better clinical outcomes in humans

Clinical response / OS associated with:

After one cycle of immunotherapy

- Peripheral T cell clonal turnover
- Frequency of peripheral CD8 TEM cells
- Expression of cytotoxic / effector genes in peripheral CD8 T cell clones



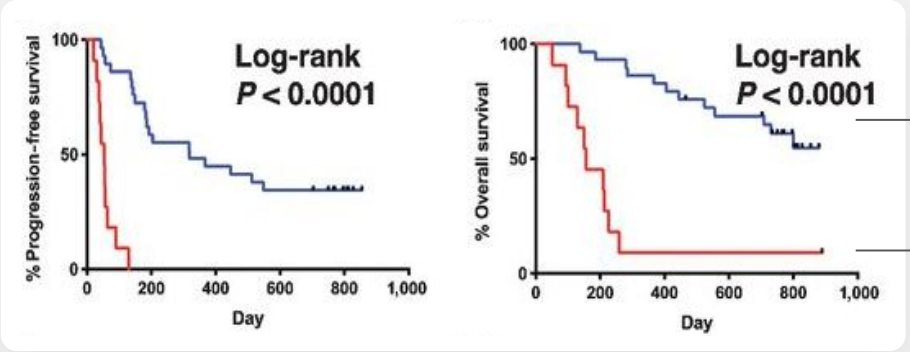
Wu et al. Nature 2020 nature
Valpione et al. Nat Cancer 2020 nature cancer
Fairfax et al. Nat Med 2020 nature medicine

Baseline blood can stratify response to anti–PD-1 checkpoint inhibitor therapy

Non-Small Cell Lung Cancer

CANCER IMMUNOLOGY RESEARCH

Kagamu, et. al. 2020



+45%
Progression Free Survival

+ 50%
Overall Survival

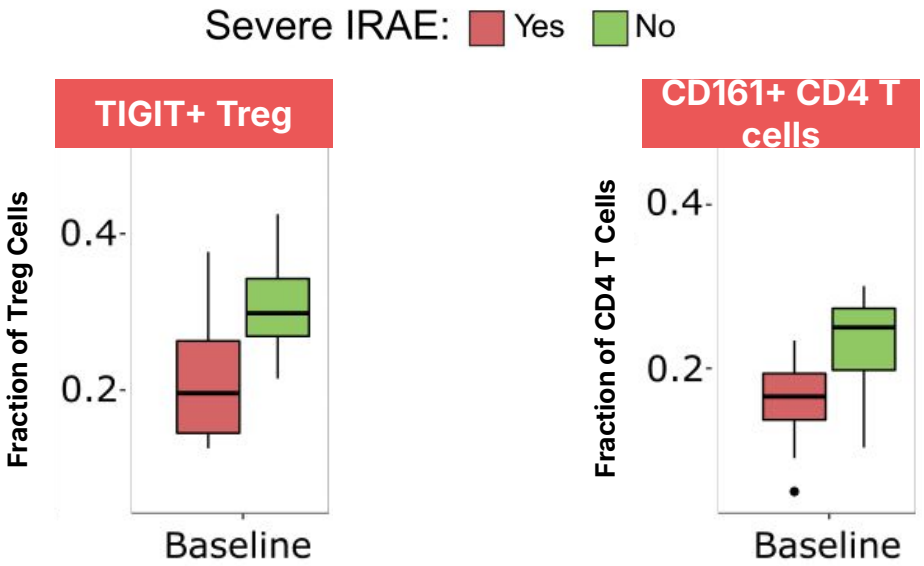
⬆ $CD62L^{low}$ in total populations of $CD4^+$, $CD8^+$ T cells

⬆ $CD25^+FOXP3^+$ $CD4^+$ T cells [P = 0.034]

Sensitivity of 92.9%, specificity of 72.1%
n=40 patient prediction cohort
n=86 patient validation cohort

Teiko has shown that baseline levels of peripheral T cells are associated with adverse events (irAE)

n=29 patients with metastatic melanoma



Data presented as a poster at SITC 2022. In collaboration with Dr. Siwen Hu-Lieskovan from the Huntsman Cancer Institute
Adjusted p-values for all comparisons p<0.01

Want to learn more?
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