Teiko.bio

Why measure the immune state in blood in solid tumors?

Focus on colorectal cancer

High-parameter cytometry for clinical trials made simple

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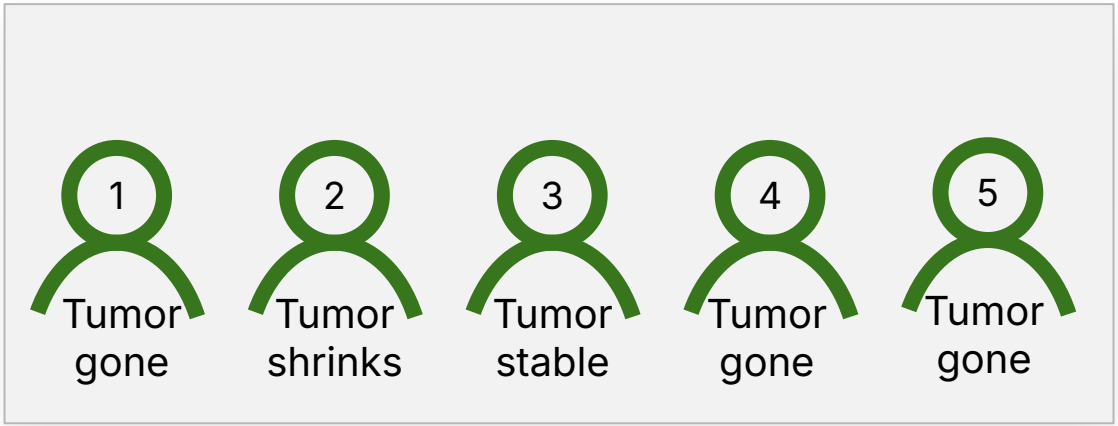
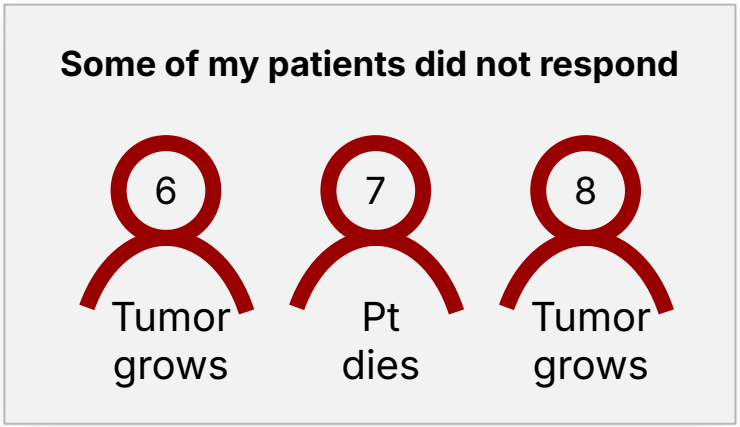
Teiko CEO

Who cares about this question?

Drug developers who want to reproducibly cure cancer.

Assume $5M spent on a 12 month drug program with 8 enrolled patients...





Do you roll the dice again for a Phase 2 for $20M?

Claim:
Measuring the immune cells in blood can lead to reproducible cures.

Why blood?

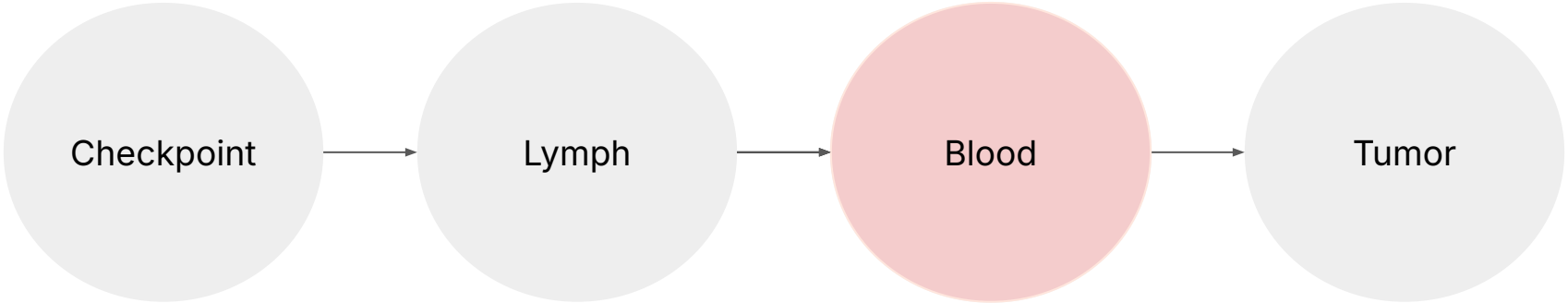
Easy to collect

Perfect for tracking

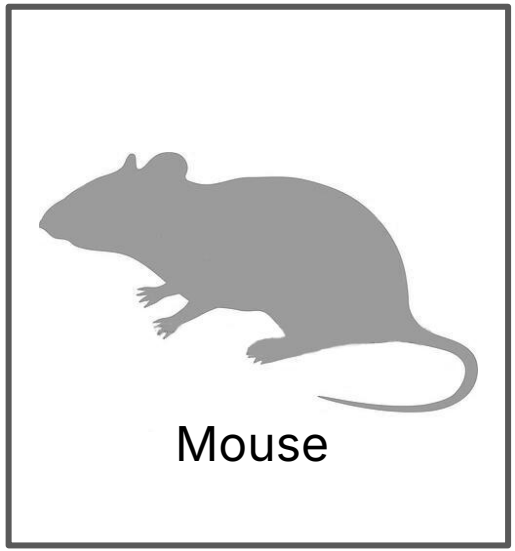
Where the action is

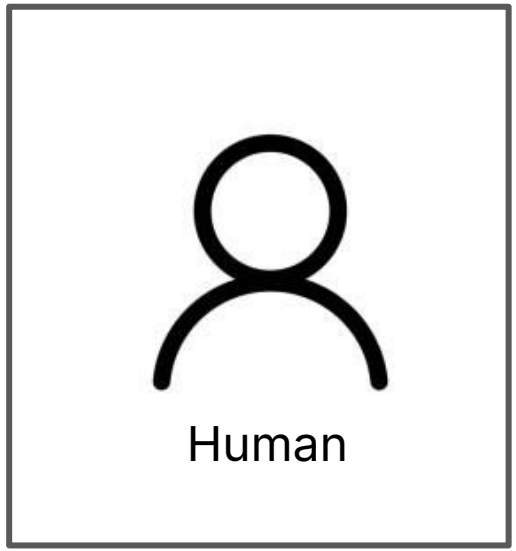
Are you sure there is action in the blood?

Pretty sure: emerging view of how immunotherapy works

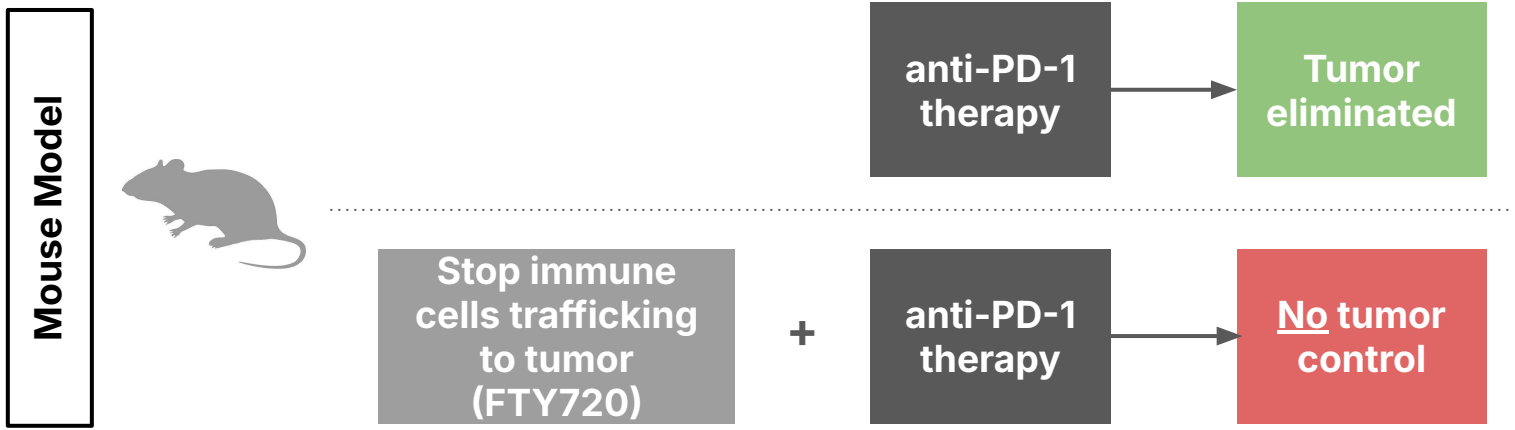


Immune cells broadly follow this flow: Spitzer et al, Cell 2023.


Mouse


Human

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



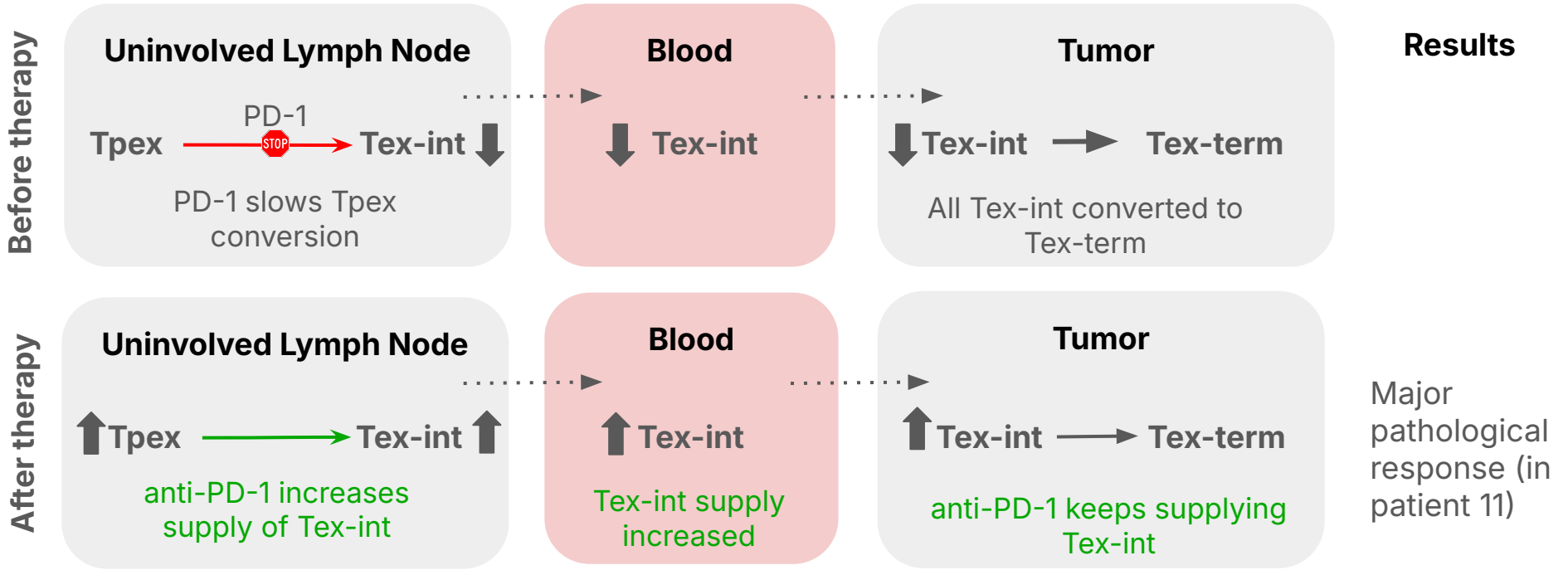
Other studies have replicated these findings in different mouse models

Chamoto et al. PNAS 2017 PNAS

Fransen et al. JCI Insight 2018 JCI insight

Dammeijer et al. Cancer Cell 2020 Cancer Cell

Immune cell traffic through blood allows for sustained tumor response



Tpex: Progenitor Exhausted T Cell (PD-1+ TCF-1+)
Tex-int: Exhausted Intermediate T Cell (PD-1+ TCF-1- CD69-)
Tex-term: Terminally Exhausted T Cell (PD-1+ TCF-1- CD69+)

Spitzer et al 2023

OK, blood it is, but how to measure?

Cytometry: a tool to measure hundreds of immune populations

Attribute	Before Treatment	After Treatment
T cells proportion of live cells	9%	96%
B cells proportion of live cells	83%	55%
NK cells proportion of live cells	57%	68%
Number of T cells	73,322	782,101
Number of B cells	676,192	448,079
Number of NK cells	464,373	553,989
Live Cells	814,689	901,259

Paper tour

Blood-based markers of immune response for colorectal cancer found via cytometry

Study	Title	Population Studied	Key Peripheral Blood Findings	Techniques Used
Krijgsman et al. (2019)	Characterization of Circulating T-, NK-, and NKT Cell Subsets in Patients with Colorectal Cancer: The Peripheral Blood Immune Cell Profile	71 CRC patients and 19 healthy donors	Reduced natural cytotoxicity receptors (NKp44, NKp46) on NK and NKT-like cells; high % of $CD16^{+}$ NKT-like cells correlated with worse survival.	Flow Cytometry
Zhang et al (2024)	Changes in subset distribution and impaired function of circulating natural killer cells in patients with colorectal cancer	107 CRC patients and 182 healthy controls	"This is shown by the decreased frequency and absolute count of $CD56^{dim}CD16^{+}$ NK cells with antitumor effects, contrary to the increased frequency of $CD56^{bright}$ NK and $CD56^{dim}CD16^{-}$ NK cells with poor or ineffective antitumor effects."	Flow Cytometry
Shinko et al. (2019)	Mass Cytometry Reveals a Sustained Reduction in CD16+ Natural Killer Cells Following Chemotherapy in Colorectal Cancer Patients	10 patients	Decrease in $CD56^{dim}$ $CD16^{+}$ NK cells; increase in $CD56^{bright}$ NK cells and $CD56^{dim}$ $CD16^{-}$ NK cells.	Mass Cytometry

Characterization of Circulating T-, NK-, and NKT Cell Subsets in Patients with Colorectal Cancer: The Peripheral Blood Immune Cell Profile

Number of Patients	71 CRC patients; 19 healthy donors
Tissue Type	PBMC
Number of timepoints	Single pretreatment time point
Number of markers	9

Healthy

Normal levels of **regulatory T cells (Tregs)**, helps maintain immune balance.

NK cells and NKT-like cells had ⬆ **of natural cytotoxicity receptors** (NKp44, NKp46) → efficiently detect and attack abnormal cells.

CRC

⬆ Higher Tregs ($CD127^{low}$ $CD25^{+}$).

⬇️ NK cells and NKT-like cells (low NKp44 and NKp46) limiting their ability to kill cancer cells effectively.

For CRC patients, immune system had an increased number of “bad” suppressive cells and a reduced ability of “good” NK and NKT-like cells to kill cancer cells.

Krijgsman et al. (2019)

Changes in subset distribution and impaired function of circulating natural killer cells in patients with colorectal cancer

Number of Patients	Tissue Type	Method of Analysis	Number of Markers	Number of Timepoints
289	Peripheral Blood	Flow Cytometry	10 + 13	1

Before	After	Impact
Overall frequency of NK cells in CRC patients were reduced compared to healthy controls.	⬇️in secretion of IFN-γ by NK cells. Worse NK cell functionality correlates with disease getting worse.	As the tumor gets worse, there is a corresponding change in NK cell expression.

Zhang et al. (2024)

Mass Cytometry Reveals a Sustained Reduction in CD16+ Natural Killer Cells Following Chemotherapy in Colorectal Cancer Patients

Number of Patients	Tissue Type	Method of Analysis	Number of Markers	Number of Timepoints
10	PBMCs	Mass Cytometry	35	3

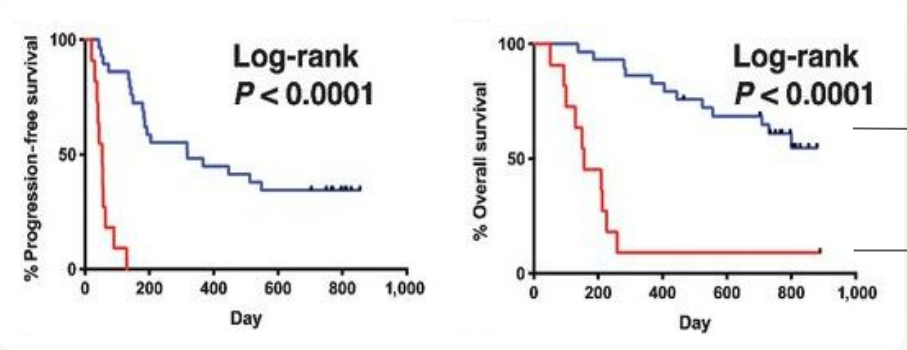
Before	After	Impact
⬆levels of $CD16^{+}$NK cells. ⬆in frequency of $CD56^{dim}$ $CD16^{-}$ NK cells.	⬇️ in $CD16^{+}$ NK cells. ⬆in less mature NK cell subsets.	Drug gets NK cells in the “right” subtype to attack tumor.

Shinko et al. (2019)

Outside CRC

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

Non-Small Cell Lung Cancer



+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]

Number of Patients	126
Sensitivity	92.90%
Specificity	72.10%
Patient Prediction Cohort	40
Patient validation Cohort	86

Kagamu, et. al. 2020

Wrapping up

Claim:
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Where the action is

Learn more about immune measurement at teiko.bio

Appendix