

RNA VACCINES FOR PANCREATIC CANCER

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IMMUNO-ONCOLOGY PROGRAM

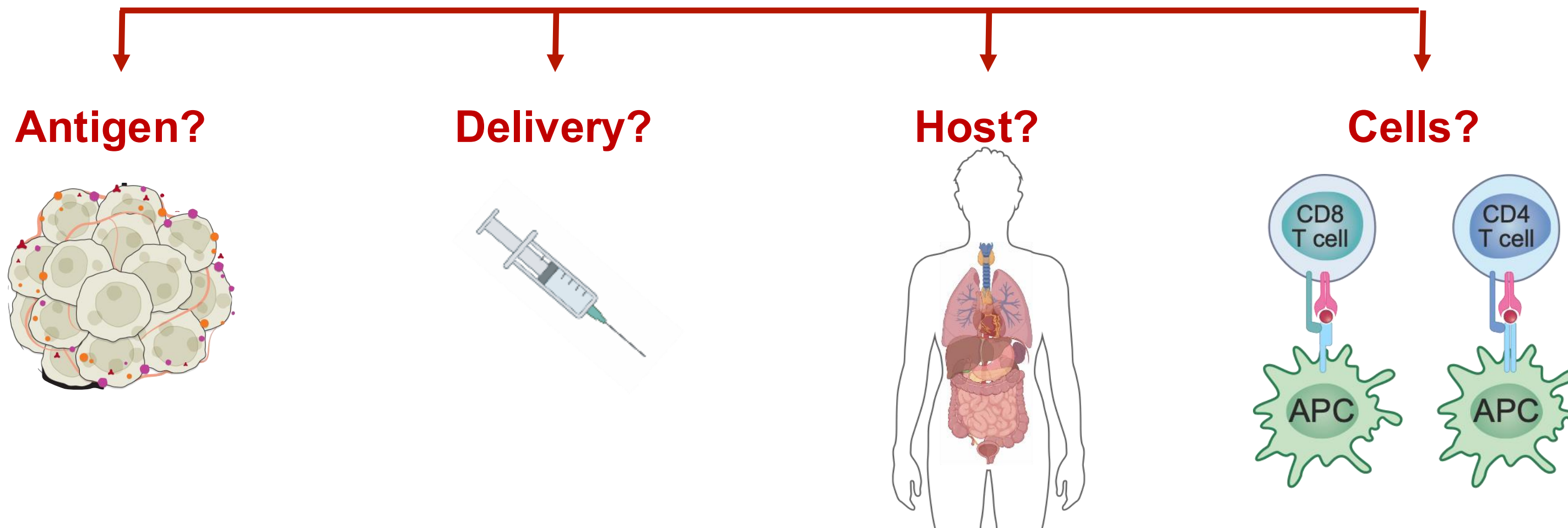
DEPARTMENT OF SURGERY

MEMORIAL SLOAN KETTERING CANCER CENTER

Cancer Vaccines: Fundamental Challenge

How DO You Teach The Immune System to Recognize CANCER?

Strong, Specific, Functional, Durable T cells in Diseased Hosts



REQUIREMENTS:

Pancreatic Ductal Adenocarcinoma (PDAC) - Vaccine Unsuitable?

Pancreatic Ductal Adenocarcinoma (PDAC)

Immunologically Invisible?

PDAC



Few neoantigens (~ 35/tumor)

Few T cells

~ 0% RR to checkpoint blockade

~ 80% of cancers



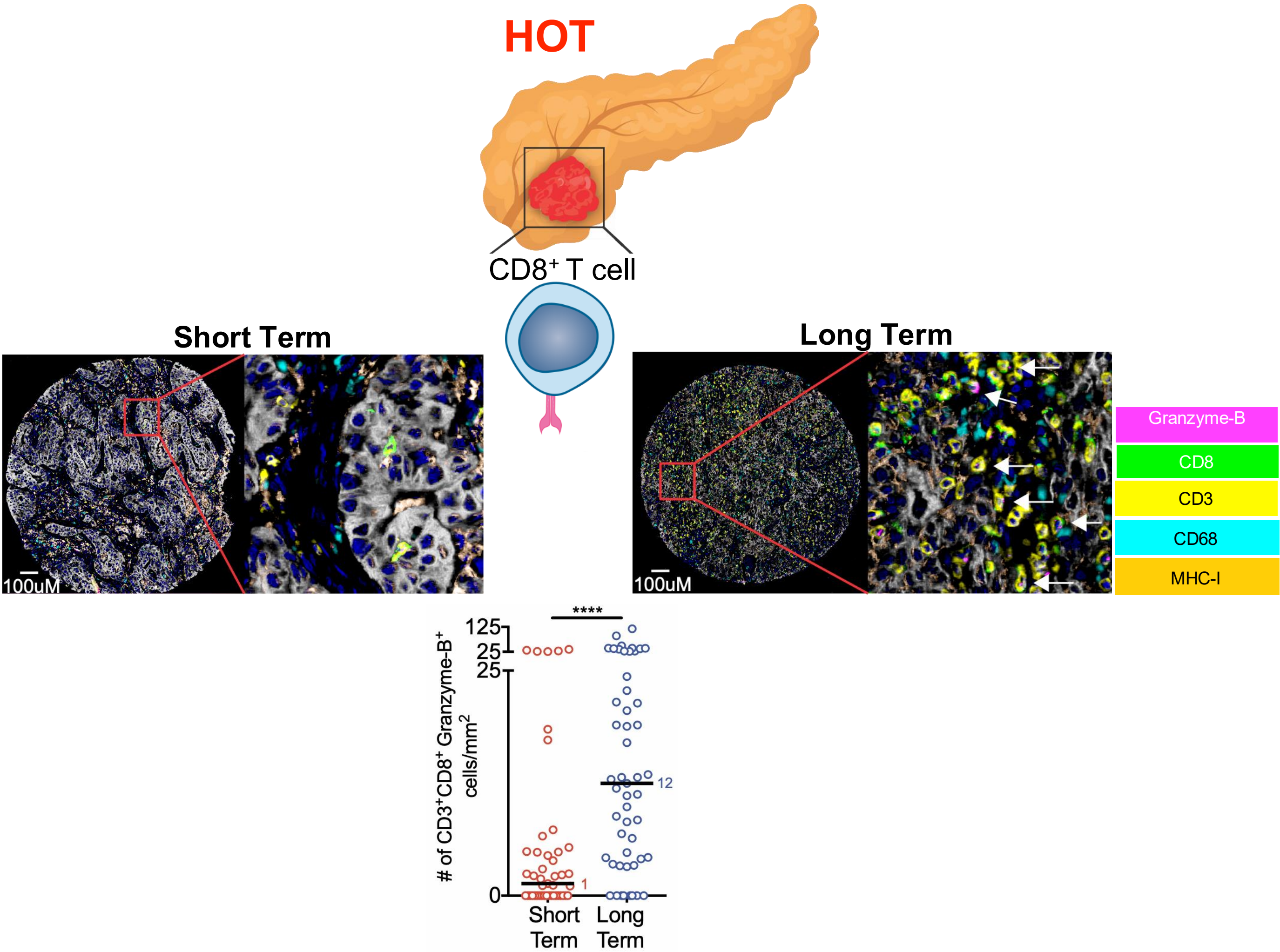
Cold

Immunotherapy
Insensitive

High unmet need: Second deadliest cancer, ~10% survival

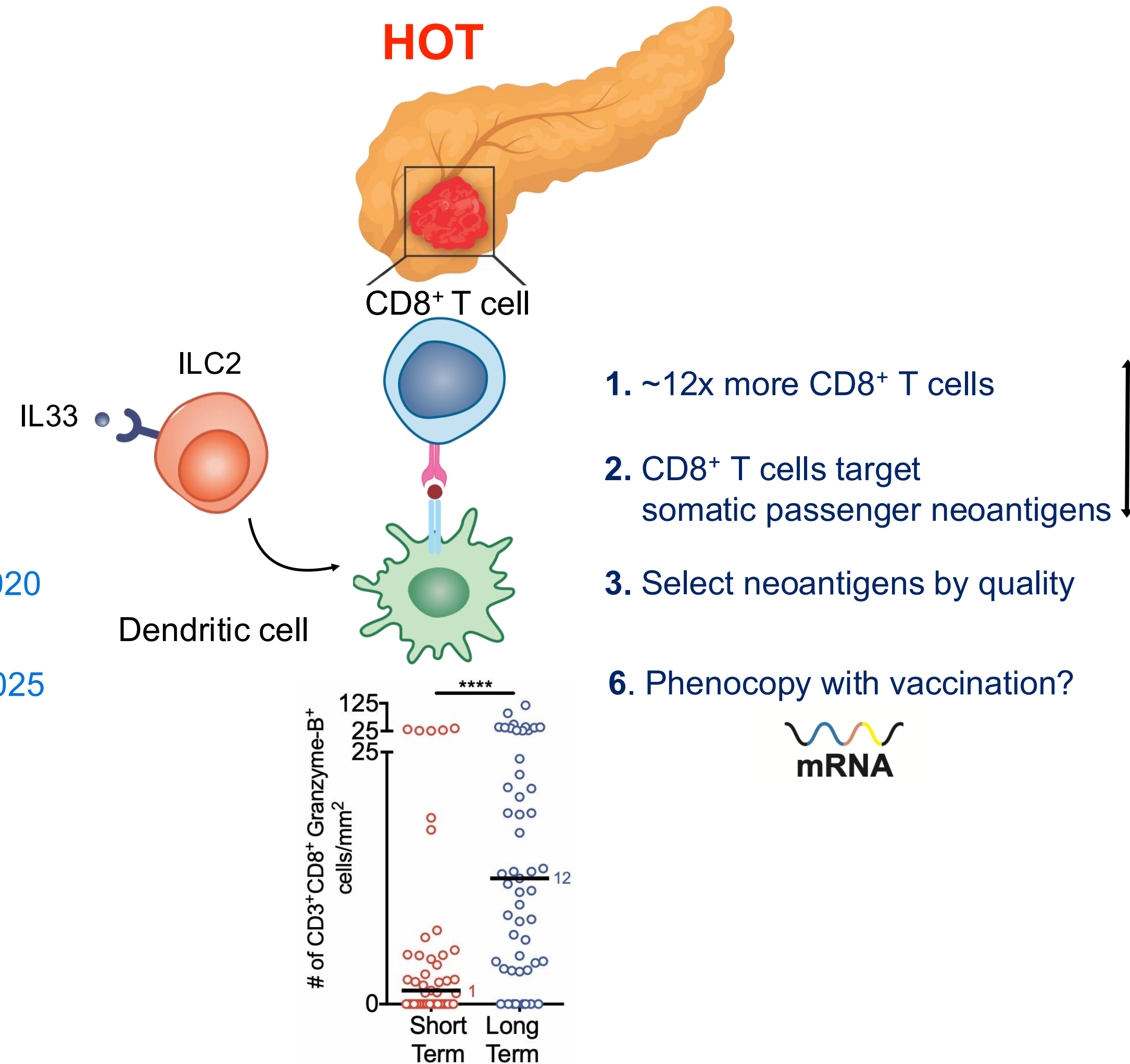
Long-term PDAC survivors

Natural T cell Immunity



Long-term PDAC survivors

Natural T cell Immunity



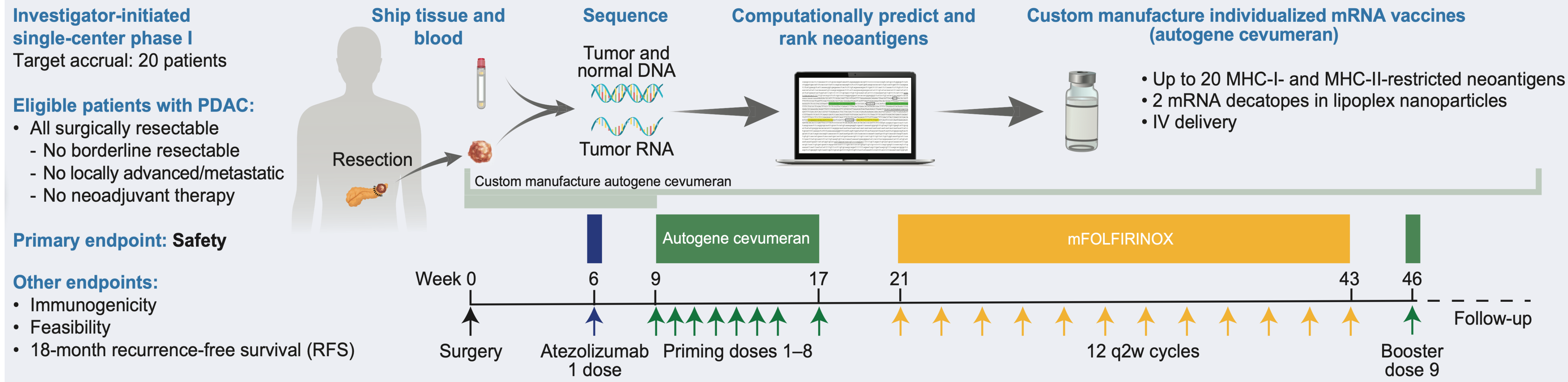
Balachandran, *Nature*, 2017

Luksza, *Nature*, 2022

Rojas, *Nature*, 2023

Personalized RNA Neoantigen Vaccine in Pancreatic Cancer

HYPOTHESIS: Individualized mRNA neoantigen vaccines expand neoantigen-specific T cells → delay recurrence



Memorial Sloan Kettering
Cancer Center™

BIONTECH

Genentech

A Member of the Roche Group

PDAC Survivor Program
Begins



2015



2017 Collaboration
begins

Trial opens
1st patient
treated

2019

PANDEMIC!

Teams
accelerate trial

2021

Teams complete trial 1 year
ahead of schedule



Rojas, Sethna, *Nature*, 2023
Sethna, Guasp, *Nature*, 2025

Vaccine Immunogenicity

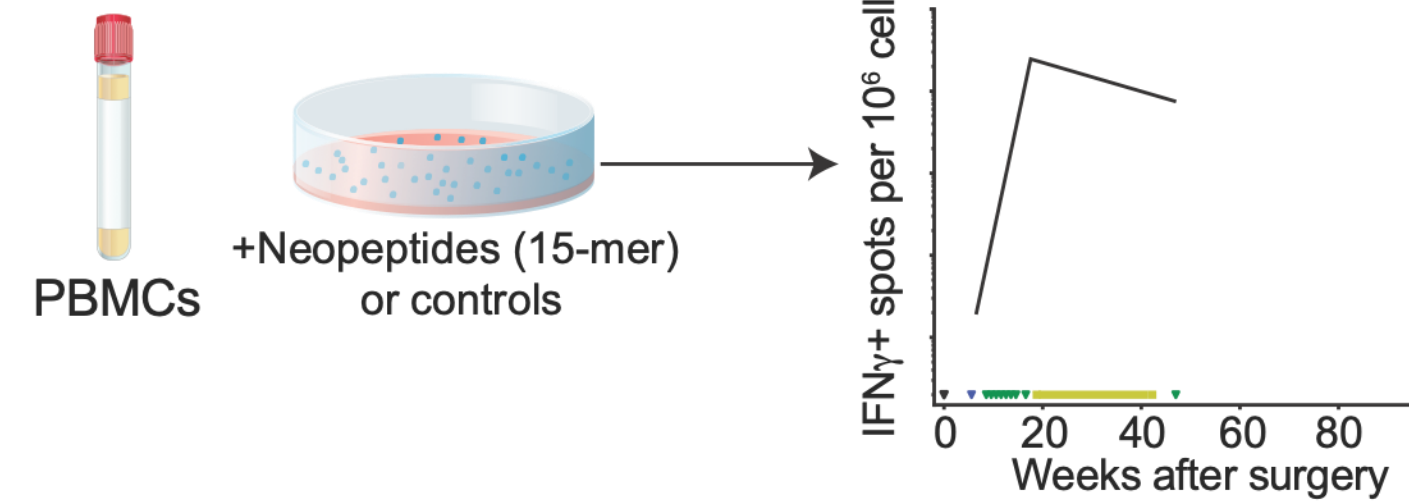
Vaccine Induced Neoantigen Specific T cells



Primary Test

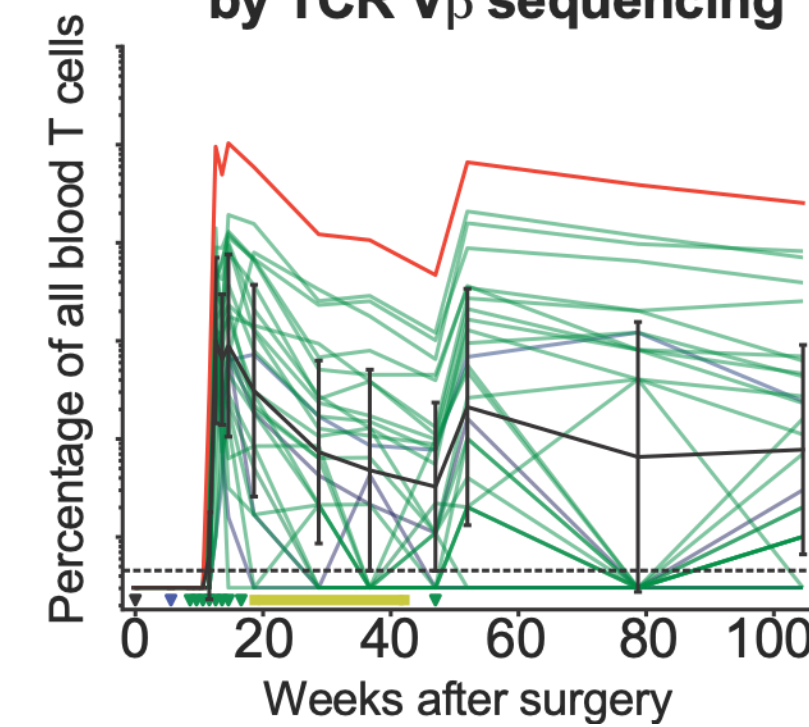
Confirmatory Test

T cell specificity to vaccine neoantigens
by ex vivo IFN γ ELISPOT

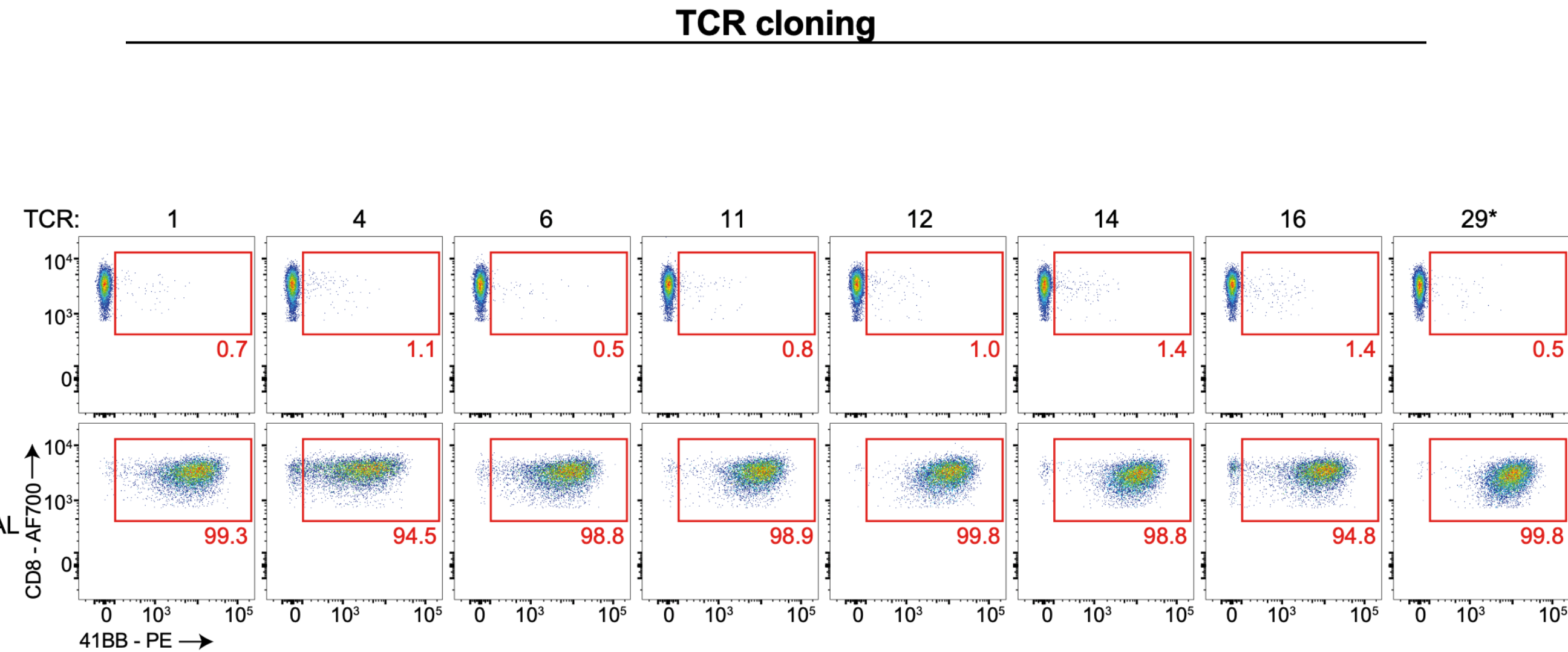
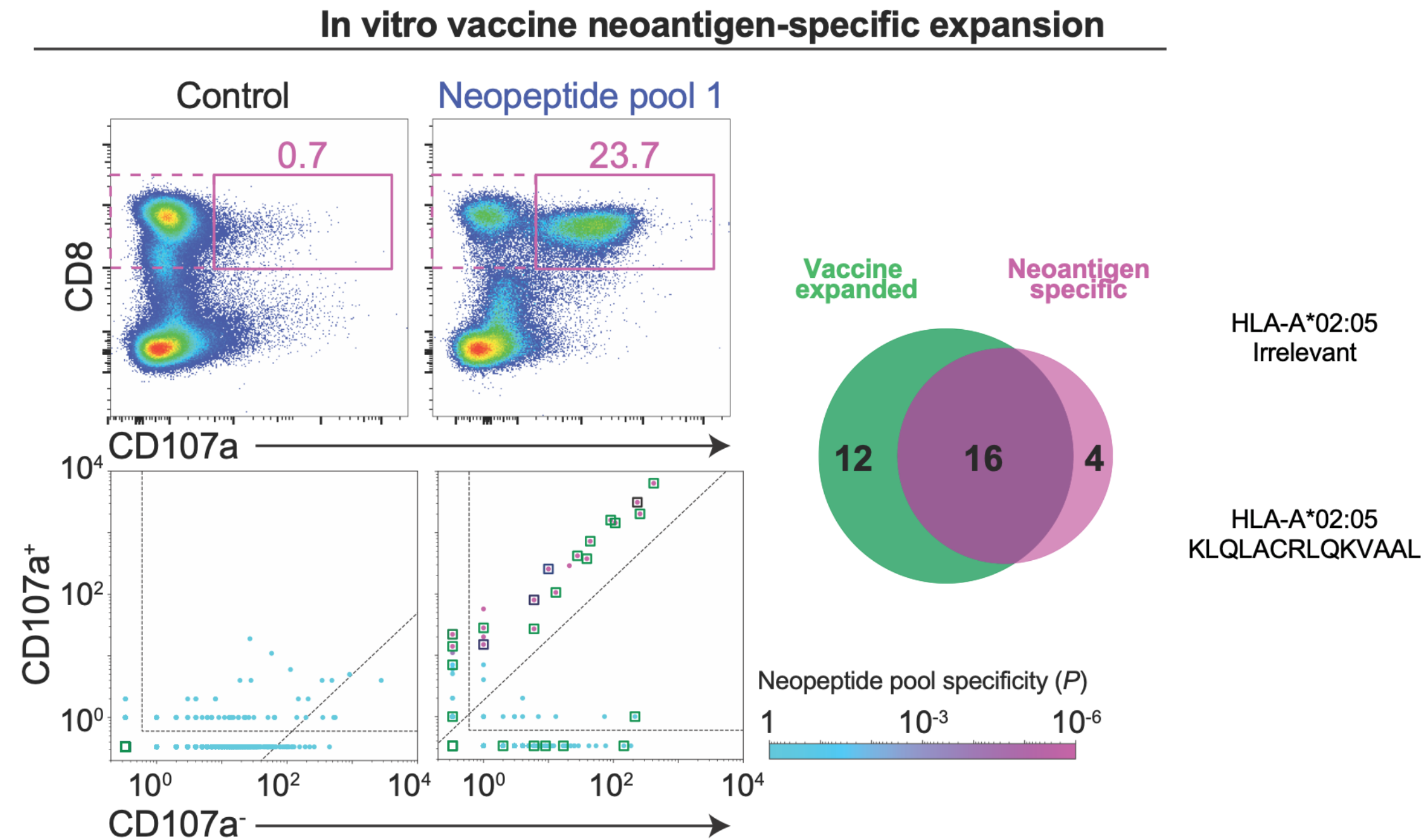
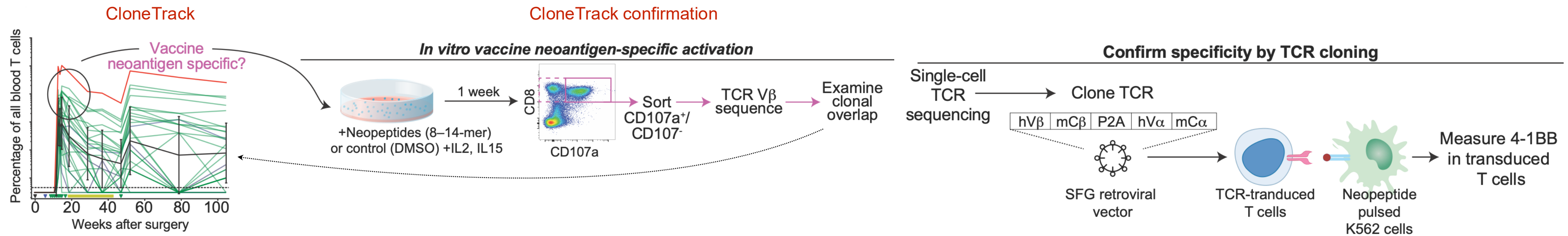


CloneTrack

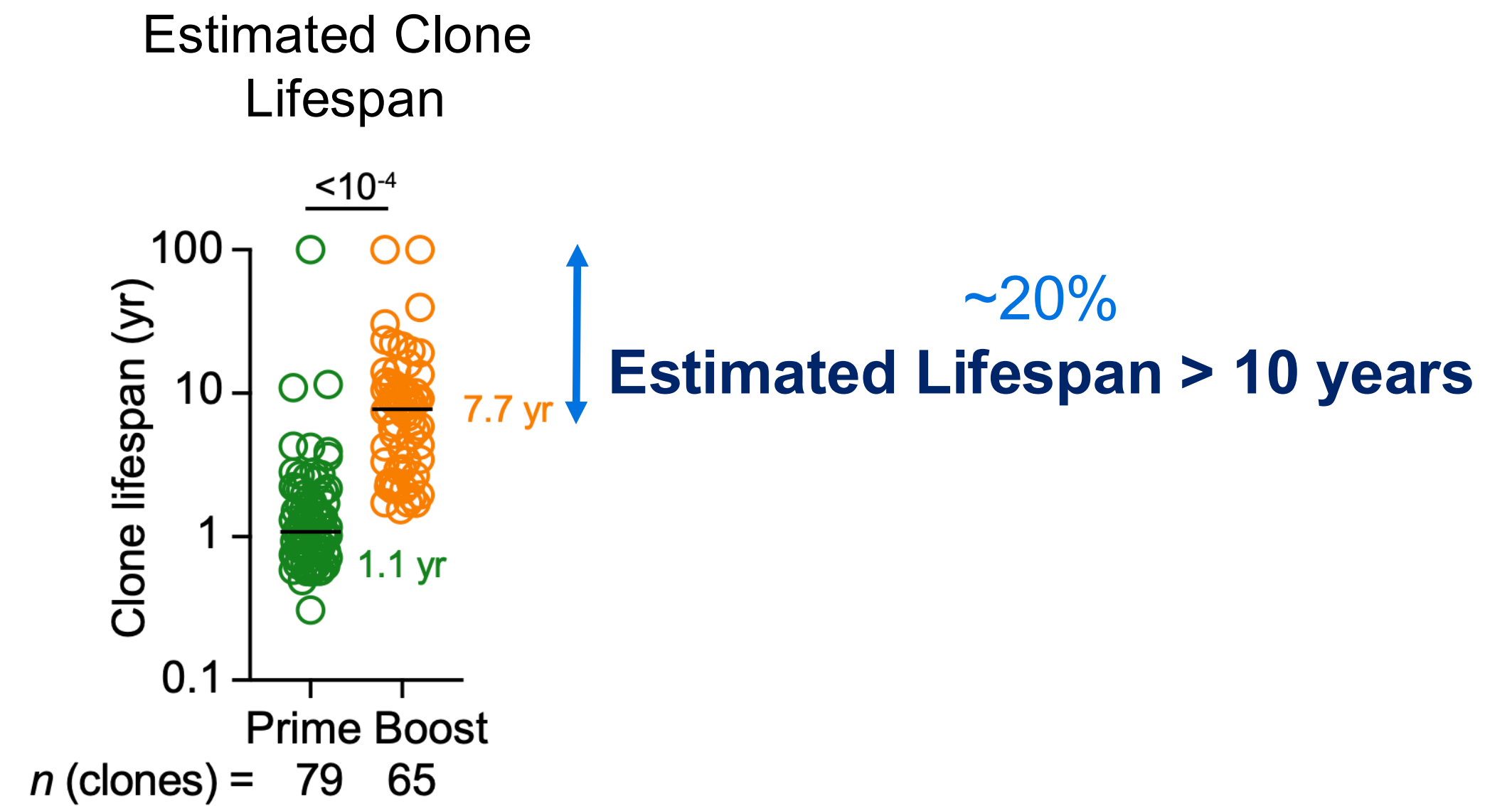
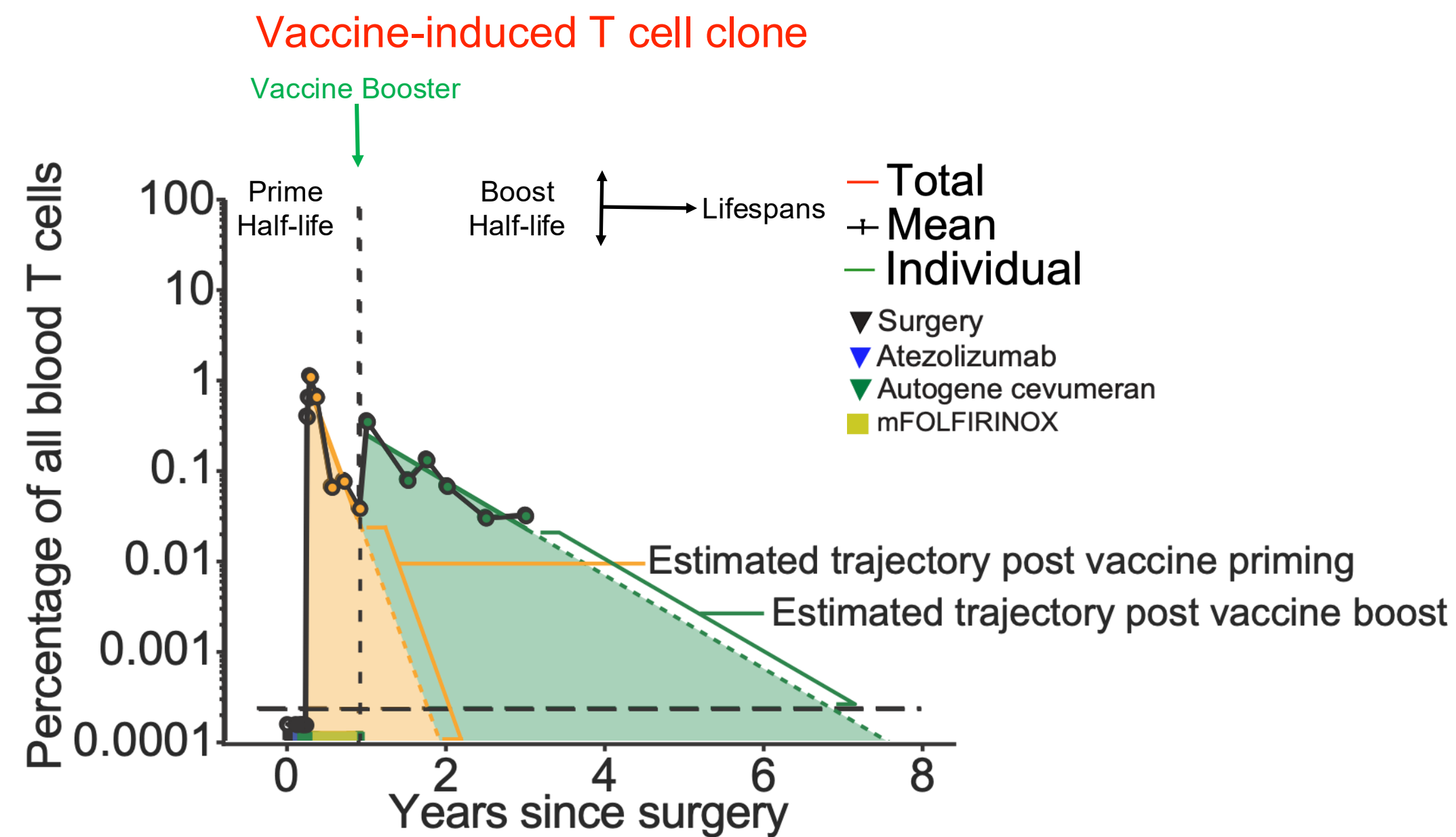
T cell clonal expansion
by TCR V β sequencing



Vaccine Induced T cells Recognize Neoantigens



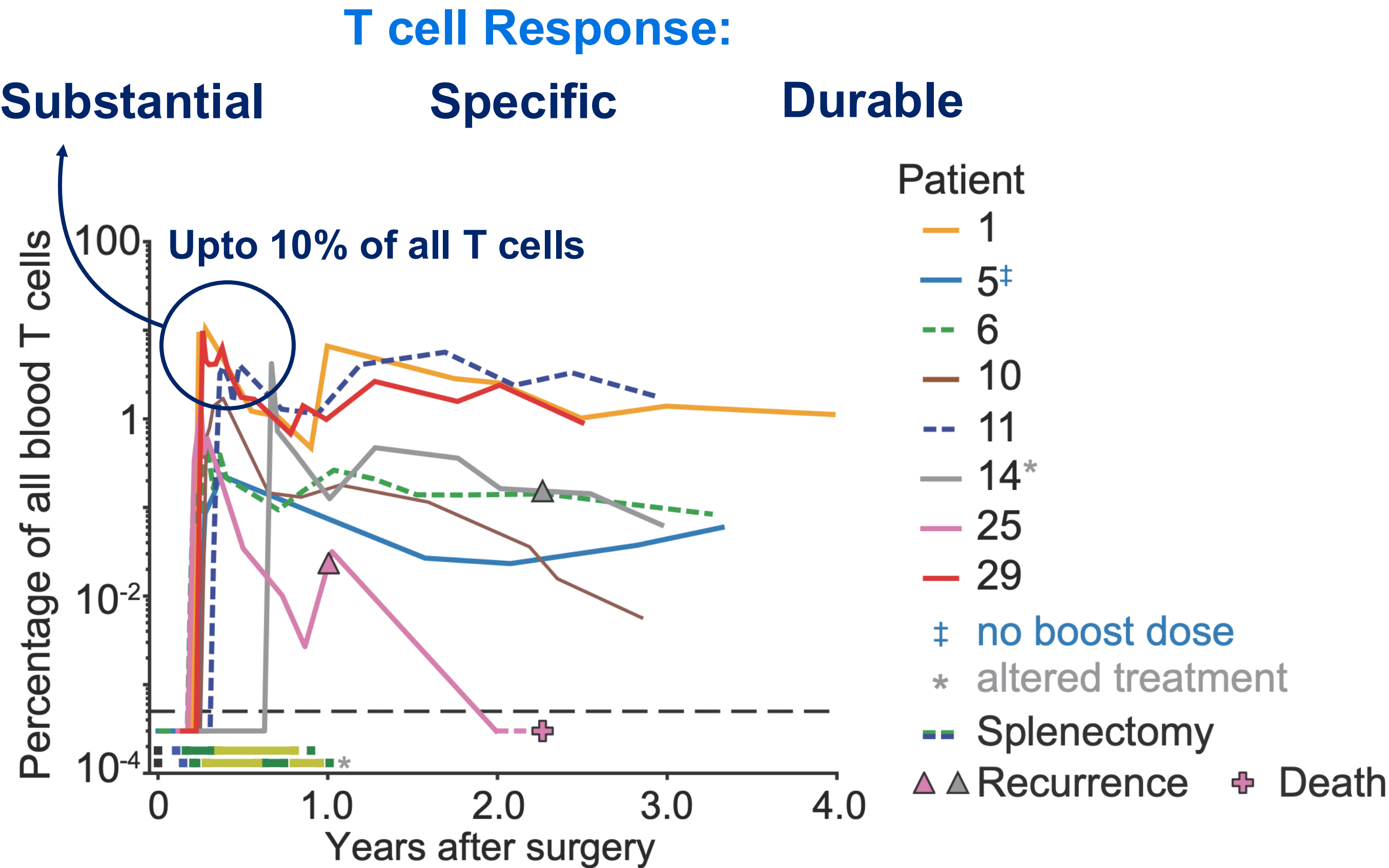
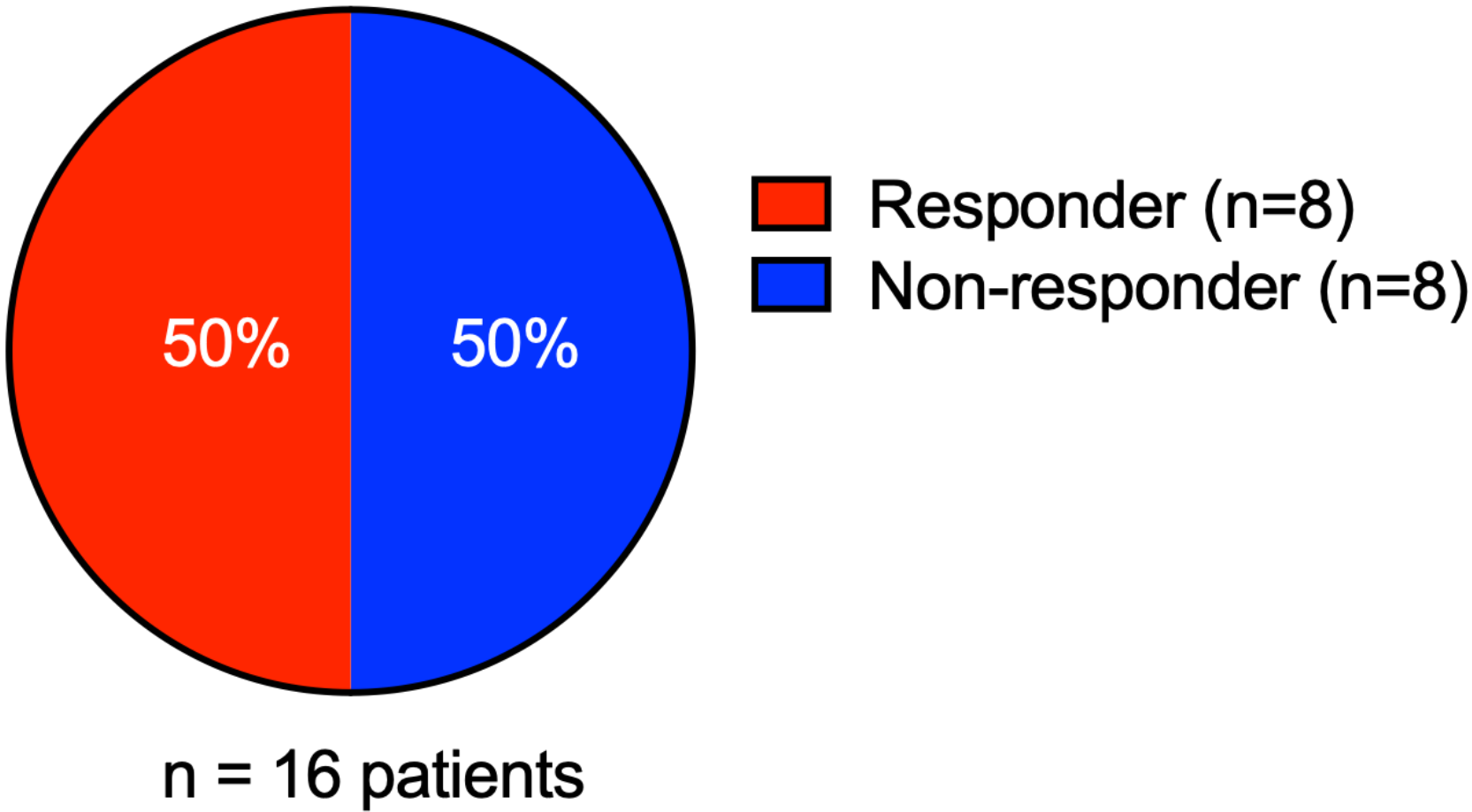
Vaccines Induce T cells in Pancreatic Cancer That May Persist For Decades



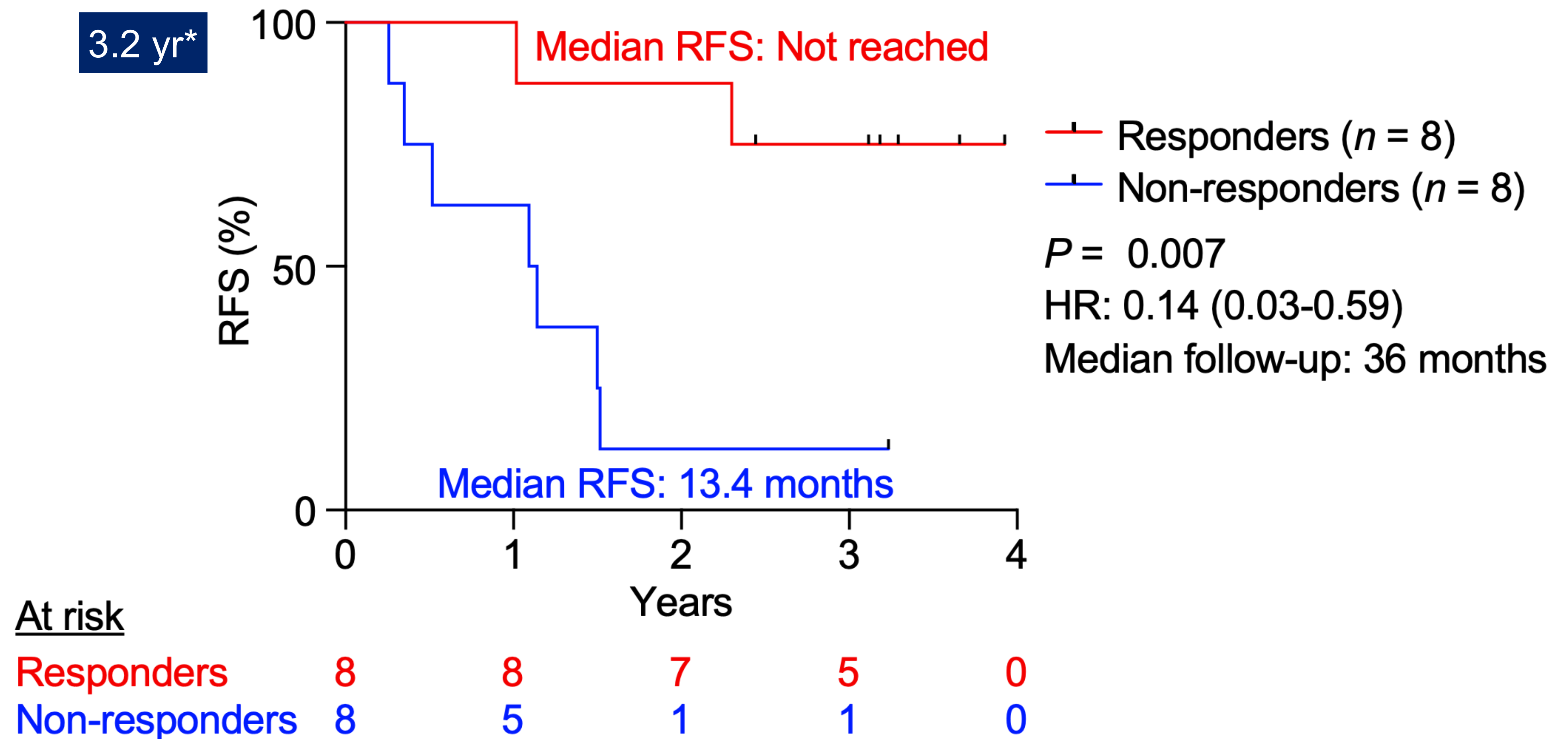
T cell Response Appears To Have Exquisite Longevity!

Vaccines Induce Robust T cells in 50% of Pancreatic Cancer Patients

50% Vaccine Response

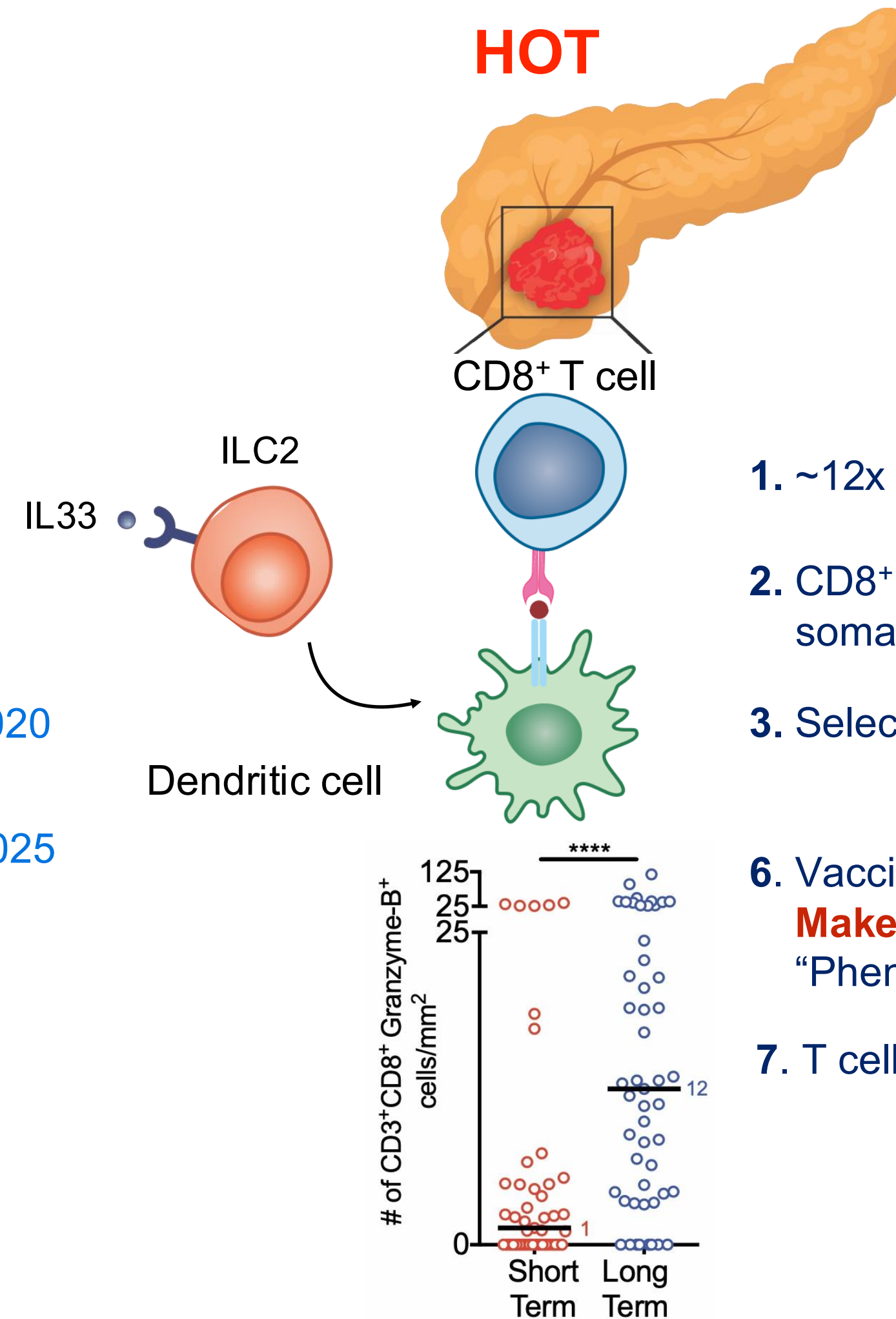


Vaccine Response Correlates with Delayed Pancreatic Cancer Recurrence



Long-term PDAC survivors

Natural T cell Immunity



4. Amplify with innate immunity [Moral, *Nature*, 2020](#)

5. Via lymphoneogenesis
“Engineerable” [Amisaki, *Nature*, 2025](#)

1. ~12x more CD8⁺ T cells

2. CD8⁺ T cells target
somatic passenger neoantigens

3. Select neoantigens by quality

6. Vaccinate with neoantigens with RNA
Make MANY T cells
“Phenocopy” survivor state

7. T cells = exceptional longevity, function

[Balachandran, *Nature*, 2017](#)

[Luksza, *Nature*, 2022](#)

[Rojas, *Nature*, 2023](#)

[Sethna, *Nature*, 2025](#)

Summary

In Pancreatic Cancer Personalized mRNA Neoantigen Vaccines induce T cells

Substantial Estimated Longevity + Durable function

Desirable Features for Cancer Vaccines

De Novo

Not restricting vaccine response to patients with pre-existing immunity

Expands Vaccine Eligible Cancer Pool beyond pancreatic cancer

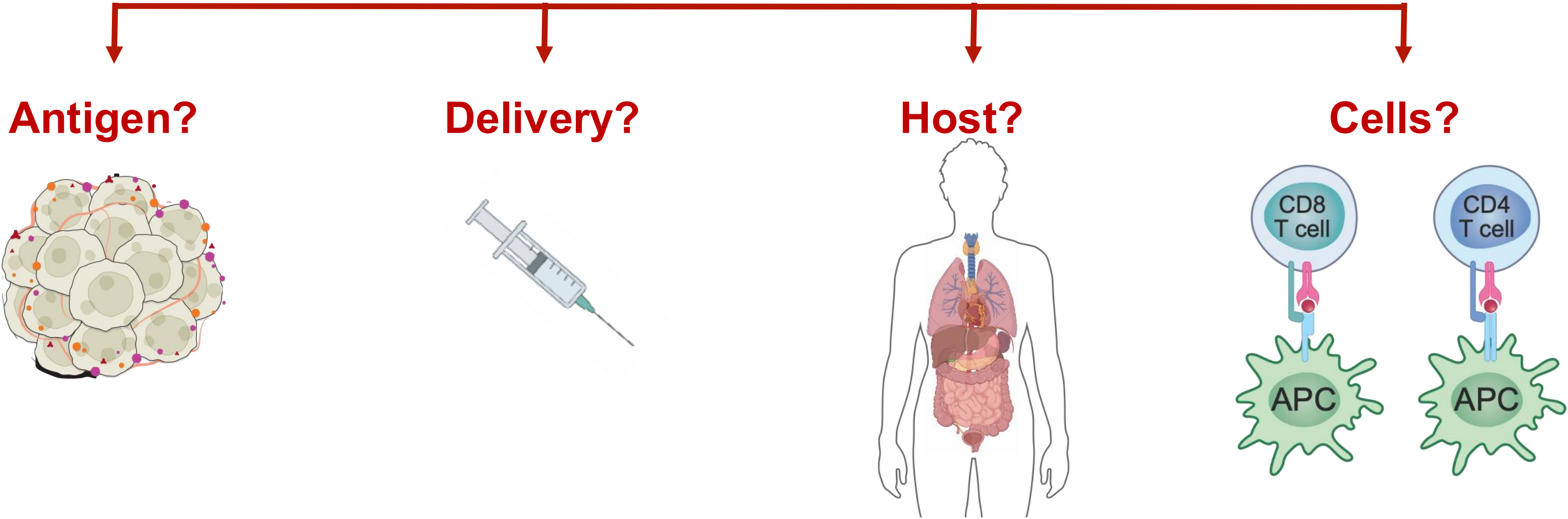
Correlates with Delayed Recurrence at 3-year follow-up

Global Randomized Ph-2 in Progress

Implication....

Cancer Vaccines: Next Promising Cancer Immunotherapy

Strong, Specific, Functional, Durable T cells in Diseased Hosts



REQUIREMENTS:

Passenger Neoantigens

mRNA

Minimal Disease

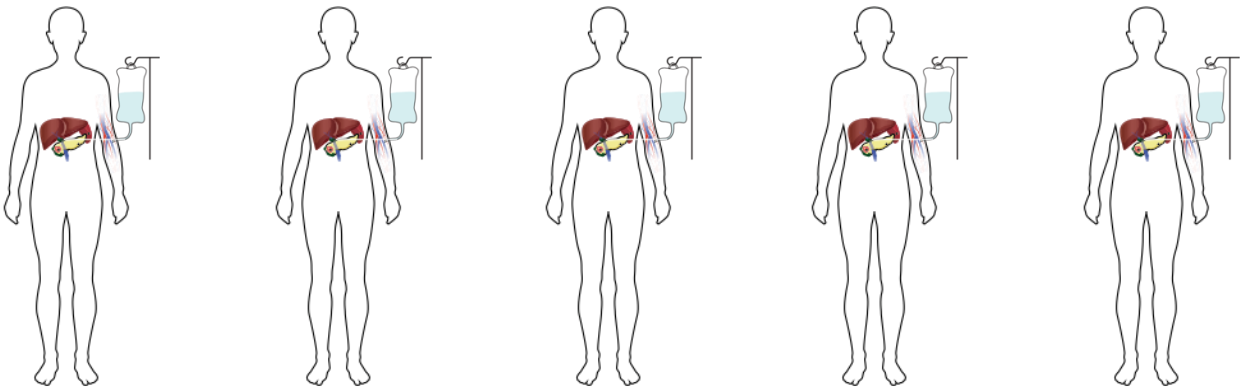
CD8

Ideal Combination



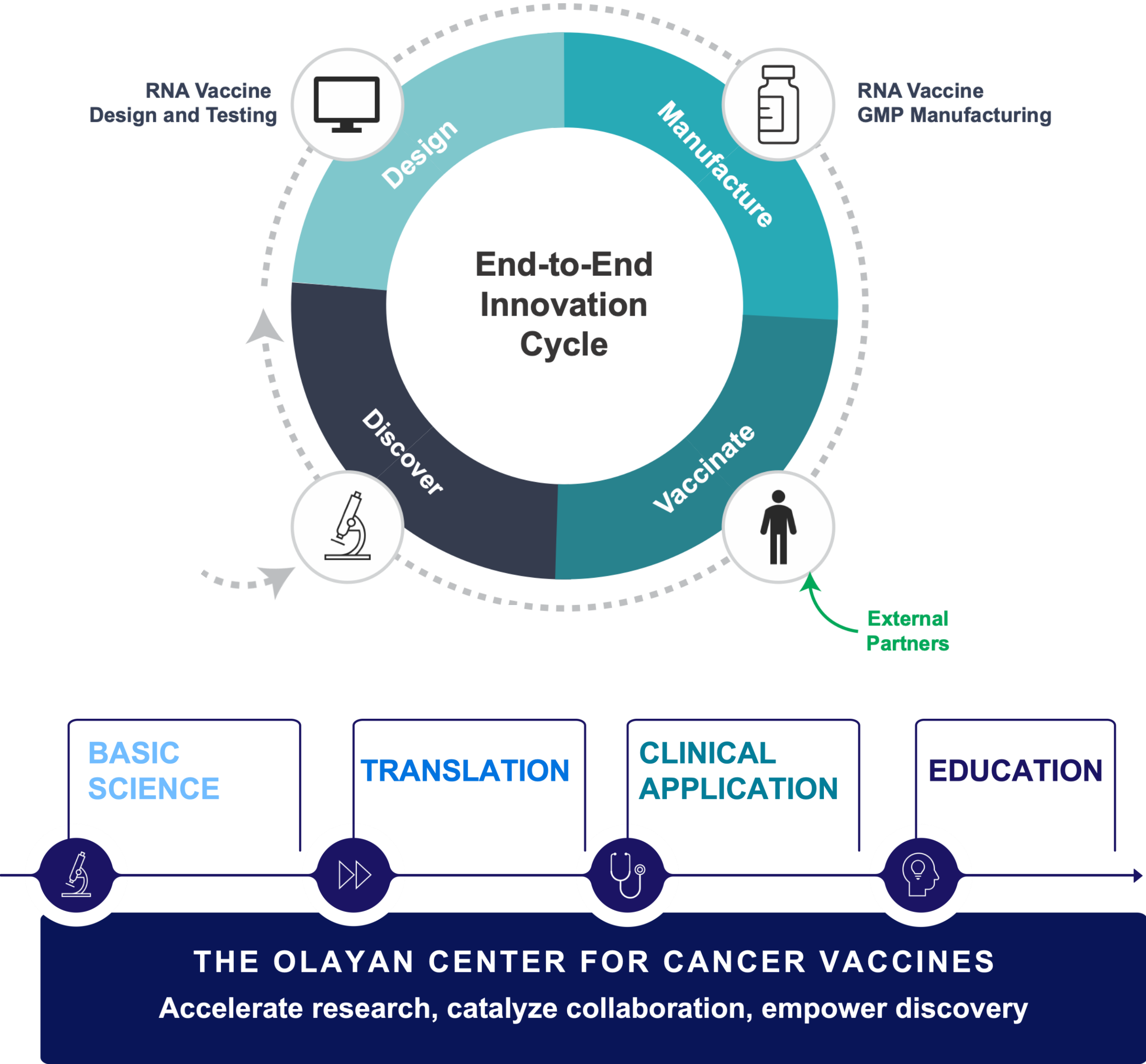
Pancreatic Cancer

Adjuvant RNA Neoantigen Vaccines



The Olayan Center for Cancer Vaccines
Launched in September 2024

Cement Principles & Practice of *Next-Gen Vaccines* and *Precision ImmunoOncology*



Our laboratory team

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Yuval Elhanati
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many others

Patients!



The Olayan Center for Cancer Vaccines
Memorial Sloan Kettering Cancer Center



MSK Pancreas Clinical Team

O'Reilly



Drebin



Soares

