isoplexis

Precision Profiling

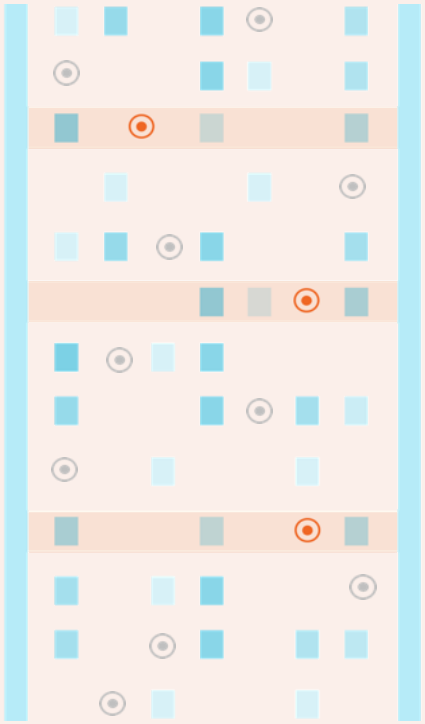
...predictive single-cell response.

November 8th, 2017

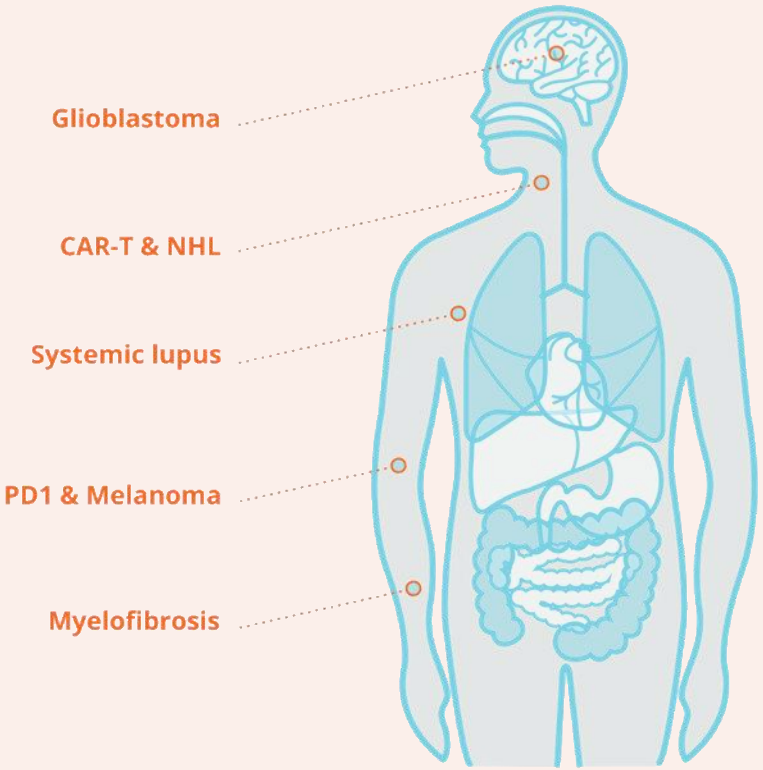
Target the right therapies, early

to highest urgency cancer patients

Predictive Single Cell Response

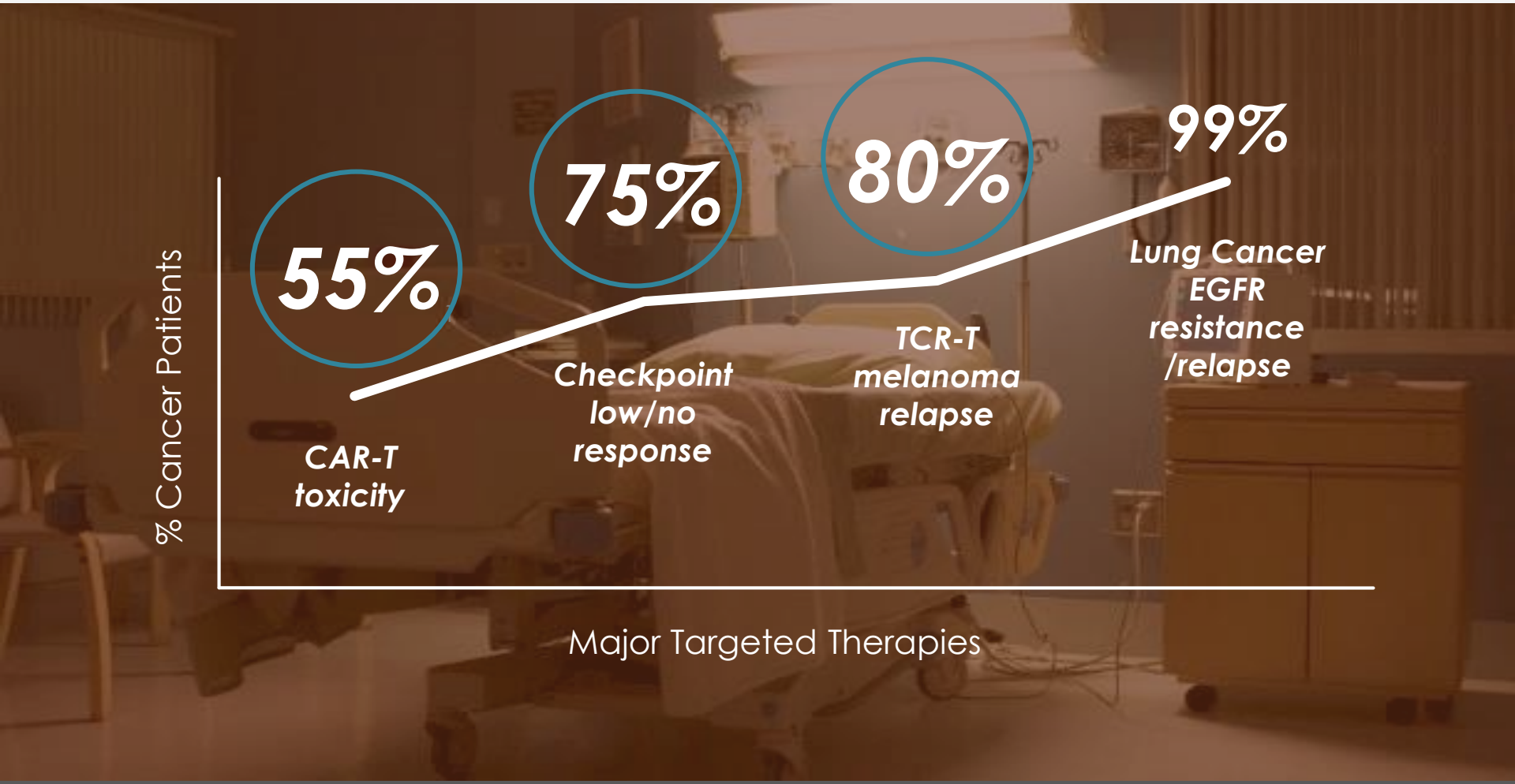


Precision Profiling



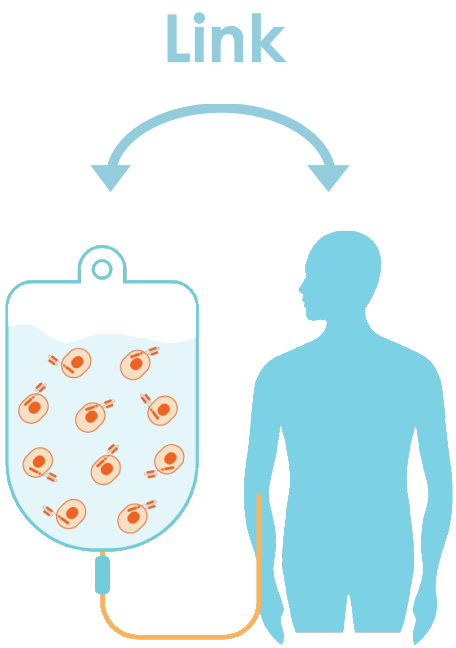
Three broader challenges in cancer immunotherapy

IsoPlexis aims to lower three major statistics in immuno-oncology



IsoPlexis uniquely addresses these challenges

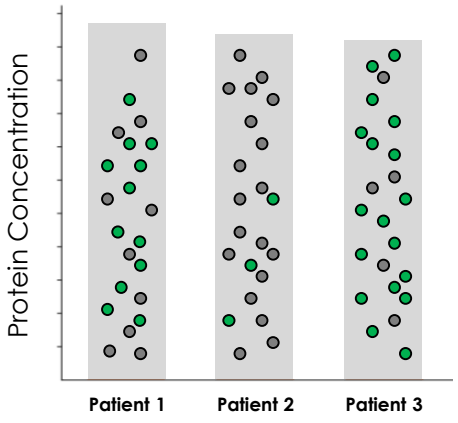
IsoCode assay links the product function to patient outcome



IsoCode's more sensitive detection can lead to

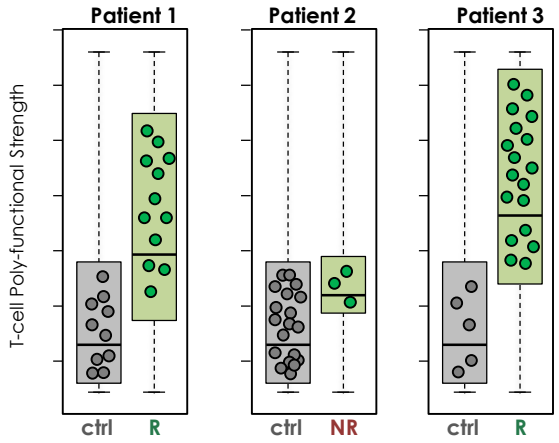
- Manufacturing feedback and excellence
- Improved development decisions
- Improvement in patient management

Bulk blood or T-cell proteins



Products look similar, despite differences in outcome

IsoPlexis single T-cell function



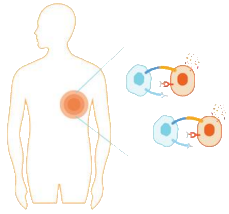
Detect patient product differences, correlated to outcome

IsoPlexis recent data: T-cell function links to outcome

Predictive single-cell response applied to I-O

ASCO-SITC Clinical Immuno-Oncology Symposium

Yale Caltech

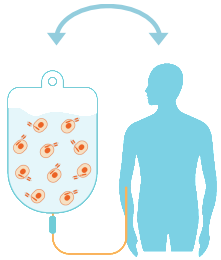


TIL function predicts response and non-response in PD1/CTLA4 treatment

AACR ANNUAL MEETING 2017 WASHINGTON, DC

Kite Pharma

National Cancer Institute

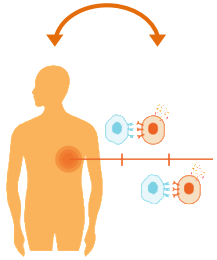


Pre-infusion product profiles predict CAR-T Patient Response

CANCER DISCOVERY

Caltech

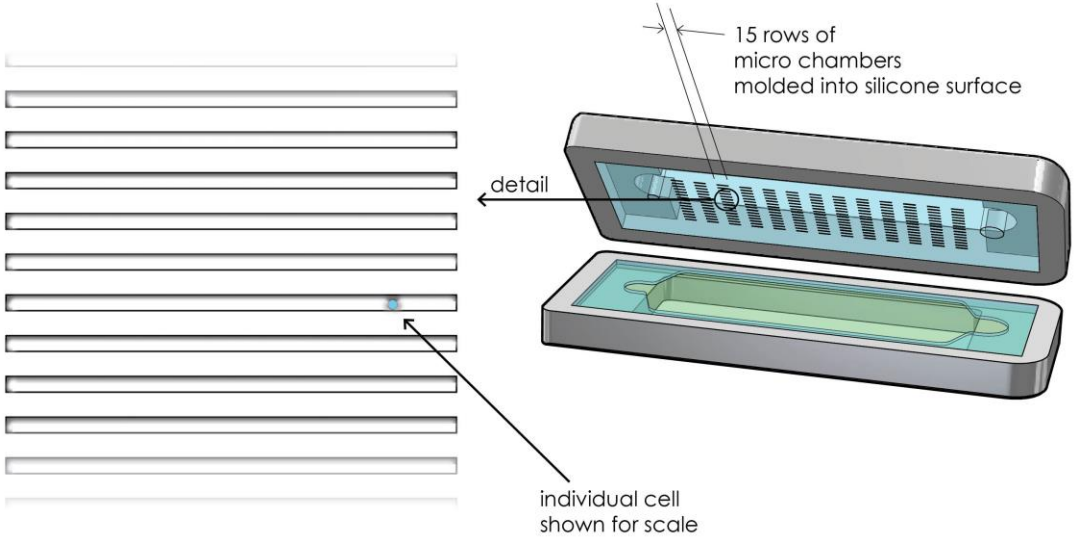
UCLA



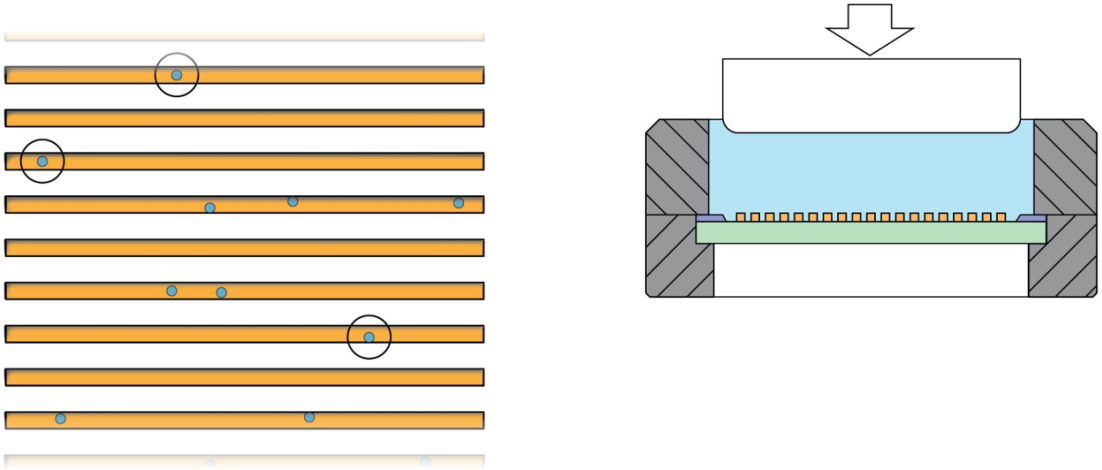
TCR-T product tracks / predicts response and relapse

IsoCode Chip: Cell Loading and Identification

Automatic cell detection and cell counting



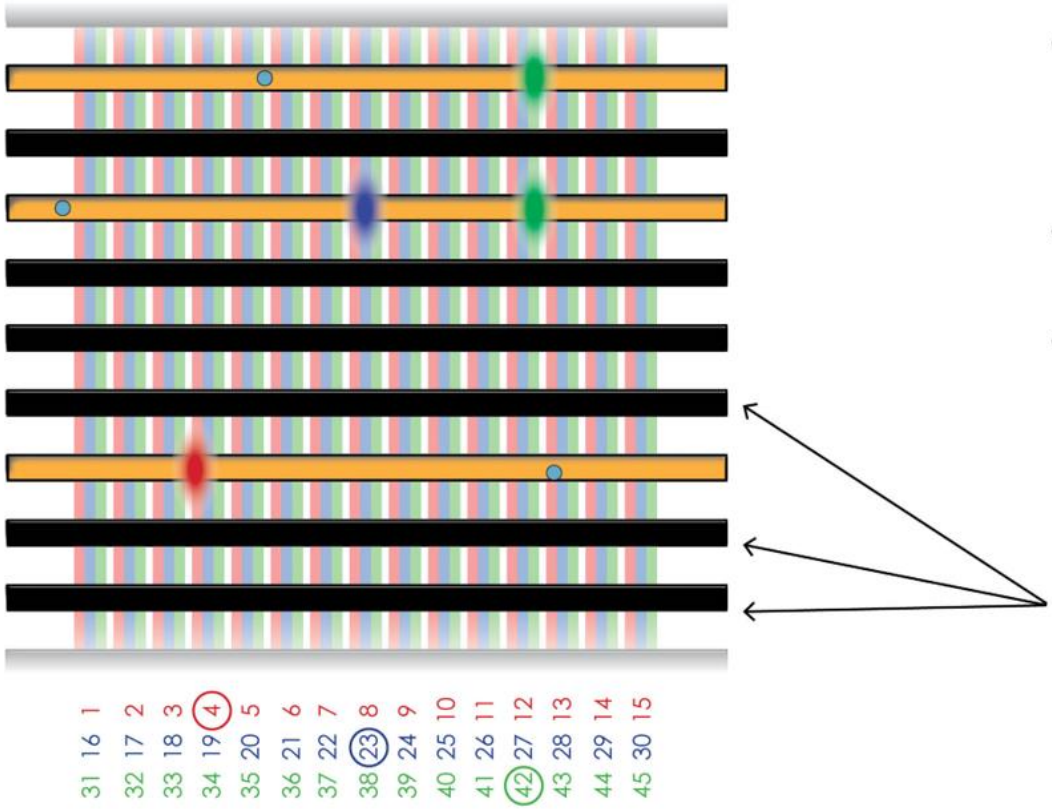
Single cells are loaded into microchambers molded into silicone top surface



Automated imaging identifies microchambers containing single cells

IsoCode Chip: Protein Quantitation – Imaging Step 2

Single cell protein profile



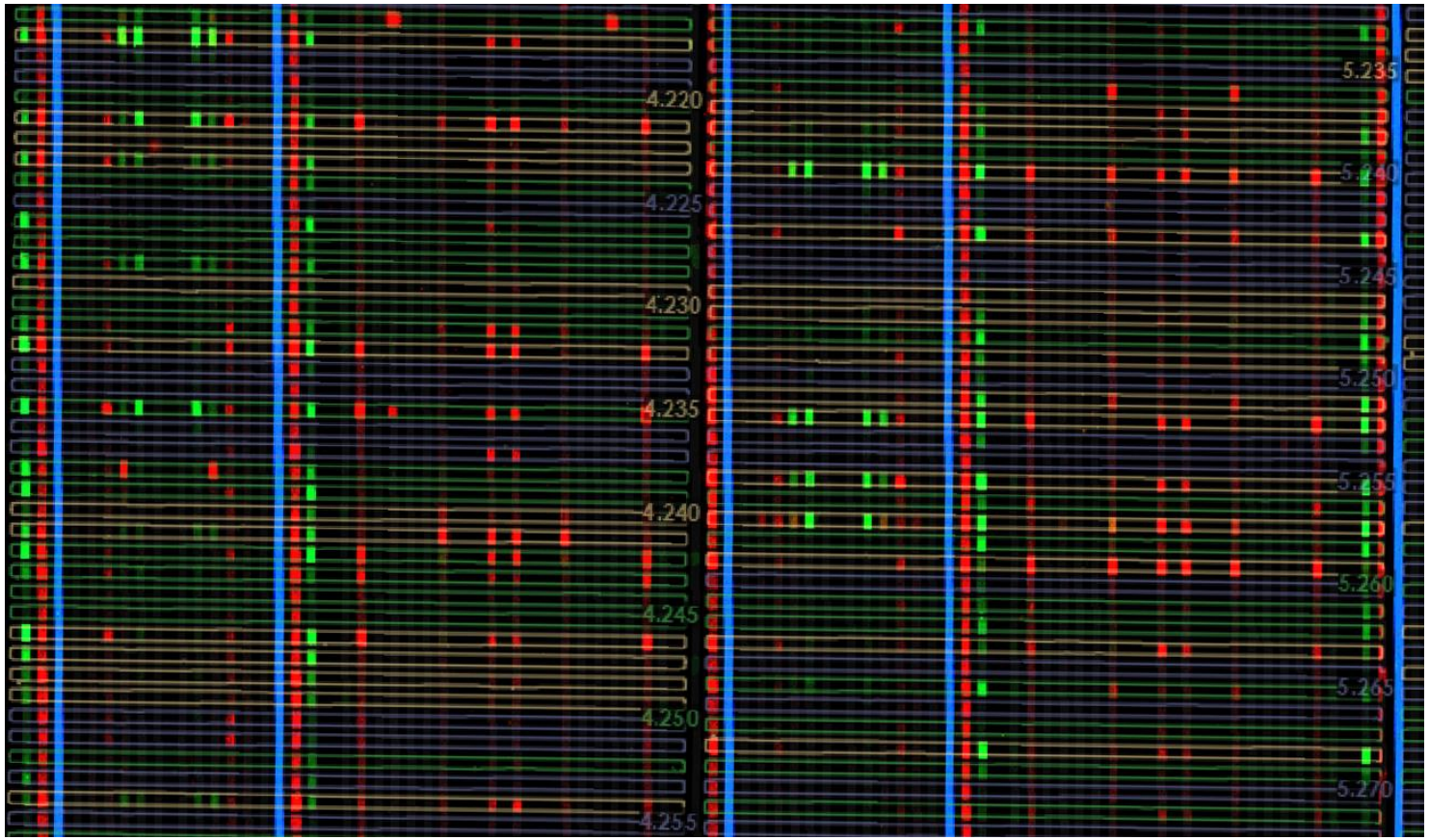
- IsoCode Chips are incubated 12 - 24 hours, causing each captured cell to secrete proteins throughout each individual micro-chamber
- each secreted protein is captured onto a corresponding antibody bar
- reagent is then introduced into the flow path, causing the captured proteins to fluoresce

scan disregards micro-chambers containing multiple or no cells

Incubated cells secrete proteins which bond to antibody bars for identification

IsoCode Chip: Actual Protein Readout, Per Chamber

Representative IsoCode Chip data

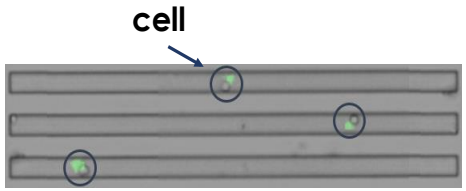


scaled detail of actual IsoCode Chip with fluorescing proteins

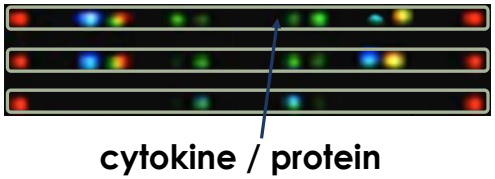
Software and Informatics pipeline

The IsoPlexis workflow enables validated analysis in larger trials

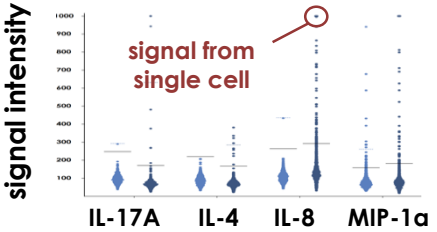
DETECT CELLS



DETECT PROTEINS

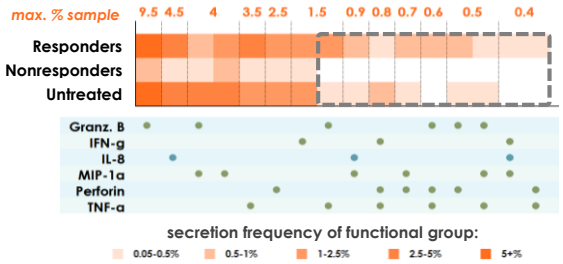


QUANTIFY READOUT



PROFILE DONORS

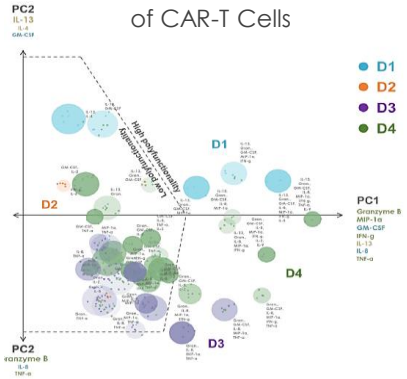
Functional Heat Map of Anti-PD-1 Treated and Untreated Patient Groups



Presented at ASCO 2017

IDENTIFY DIFFERENCES

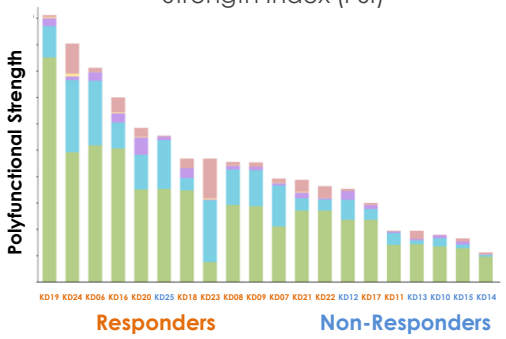
Functional Characterization of CAR-T Cells



Presented at BioMAN Workshop 2016

CORRELATE TO OUTCOME

Single-Cell CAR-T Polyfunctional Strength Index (PSI)

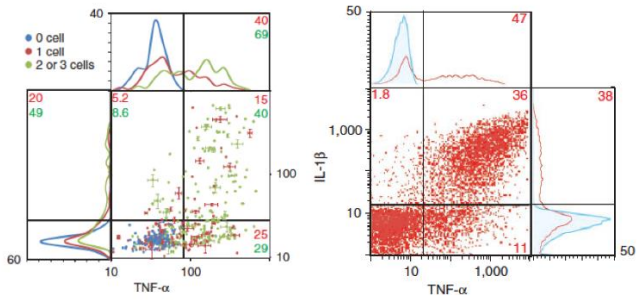


Presented at AACR 2017

IsoCode (SCBC*) compared to other immunoassays

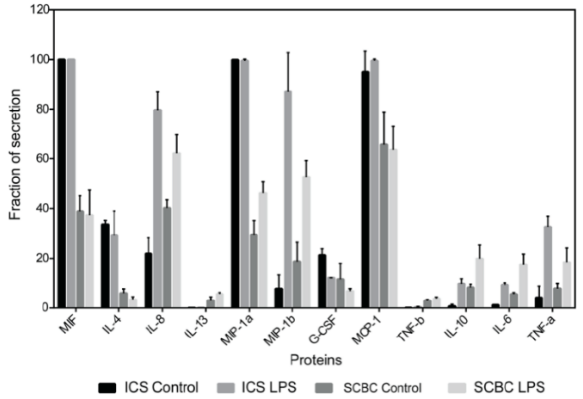
IsoCode has strong correlation with traditional low-plex single cell assays

SCBC vs Flow ICS



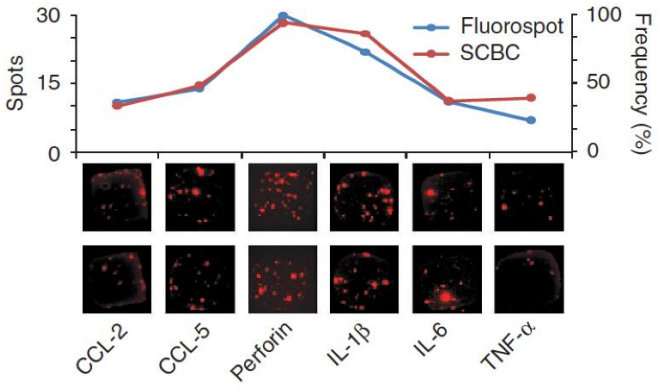
Ma, Fan, et al., ***Nature Medicine***, 17, 738-743 (2011).

SCBC vs Flow ICS



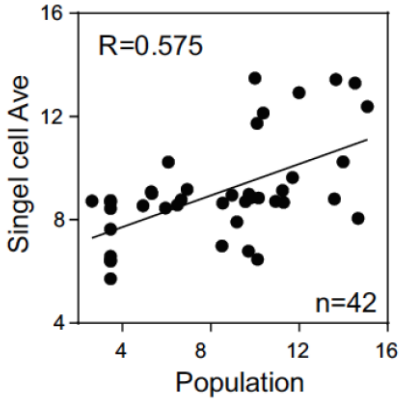
Lu, Xue, et al., ***Proc. Natl. Acad. Sci. U.S.A.***,112(7), 607-615 (2015).

SCBC vs FLUOROSpot



Ma, Fan, et al., ***Nature Medicine***, 17, 738-743 (2011).

SCBC vs Population



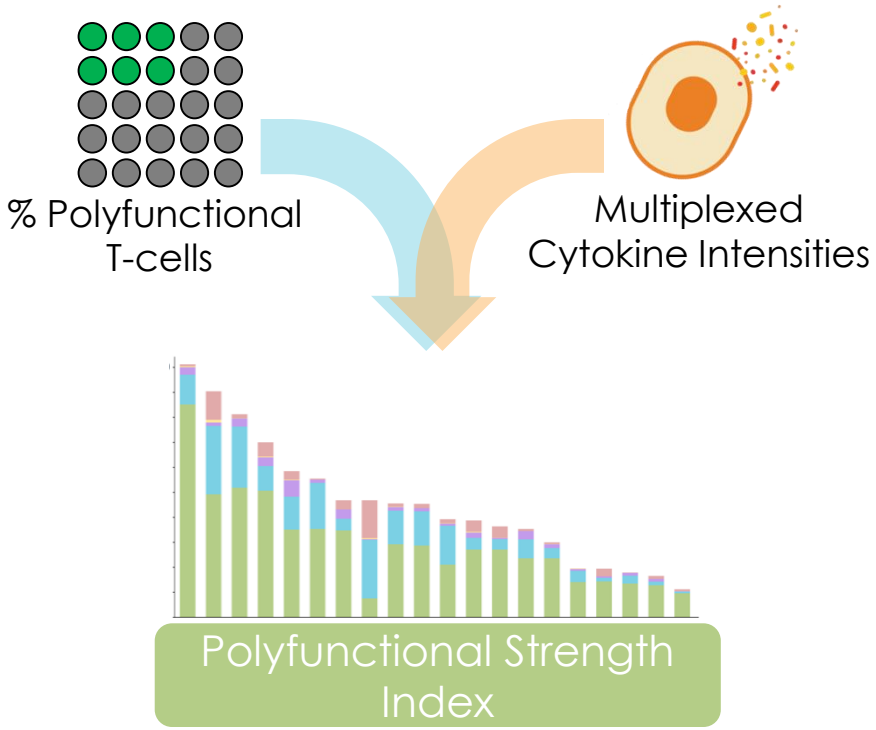
Lu, Xue, et al., ***Proc. Natl. Acad. Sci. U.S.A.***,112(7), 607-615 (2015).

* IsoCode is known as "SCBC", or Single-Cell Barcode Chip, in journal publications

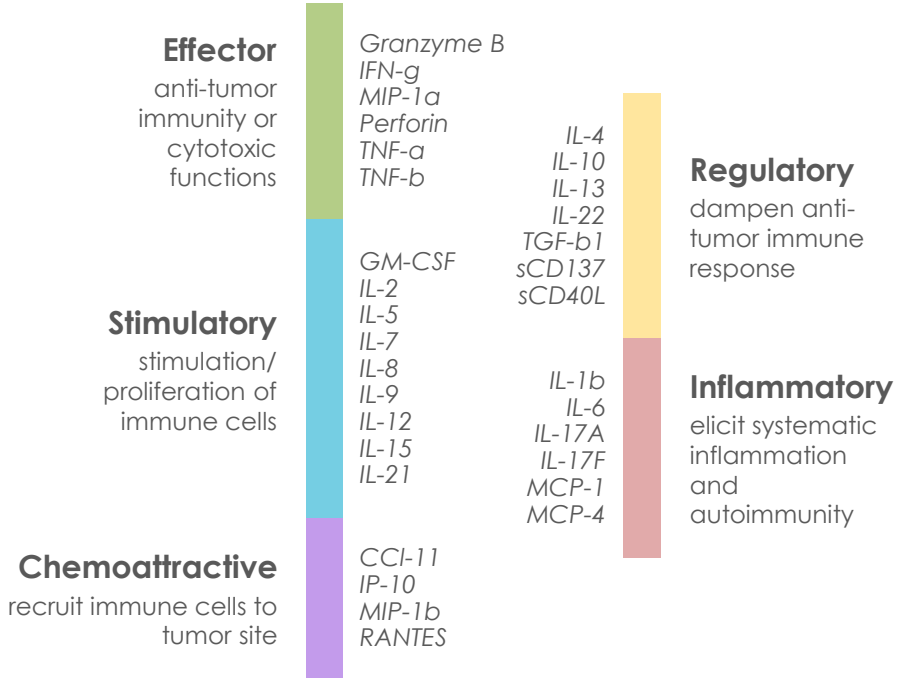
Case 1: CD19 CAR-T Polyfunctionality for Kite Product

Polyfunctional Strength Index (PSI)[1] metric links to patient outcomes

Product Metric: Requires IsoCode



IsoCode Single-Cell Panel



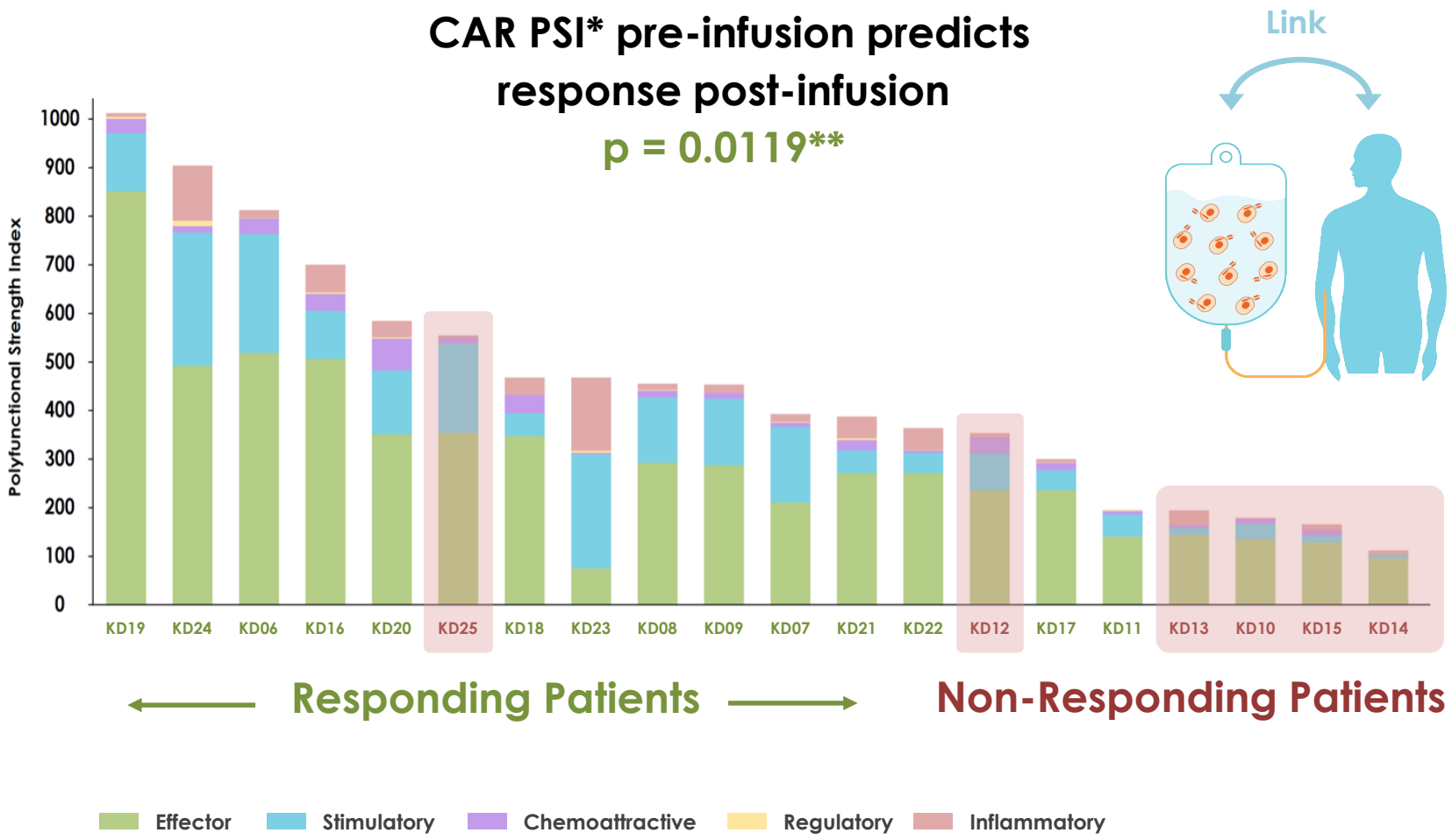
1. IsoPlexis IsoCode Technology and Ma et al 2013

CCL, chemokine ligand; GM-CSF, granulocyte macrophage colony-stimulating factor; IFN, interferon; IL., interleukin; IP, interferon-gamma-inducible protein; MCP, monocyte chemoattractant protein; MIP, macrophage inflammatory protein; PSI, polyfunctional strength index; RANTES, regulated on activation, normal T cell expressed and secreted; TGF, transforming growth factor; TNF, tumor necrosis factor.

non-functional T-cell **poly-functional T-cell** *(2+ cytokines per cell)*

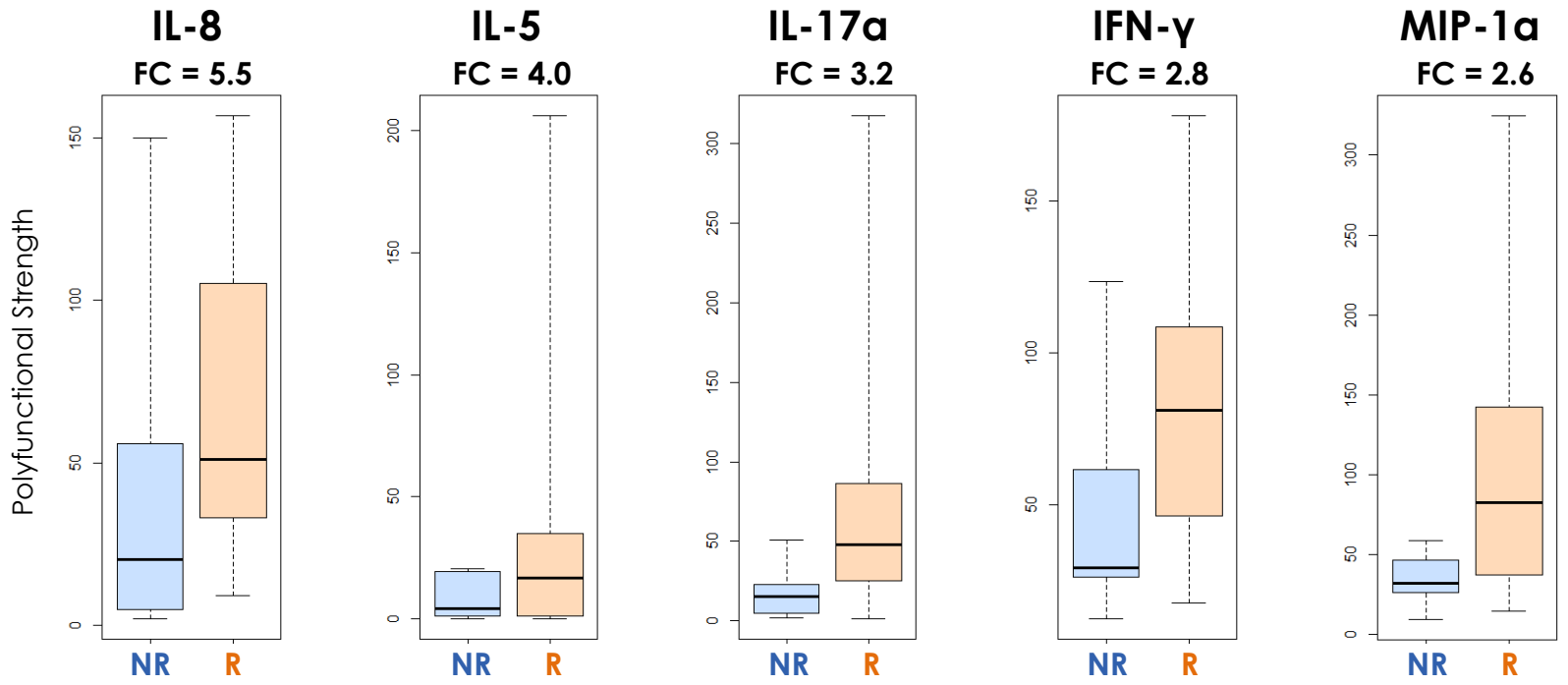
Case 1: ranking CAR-T donors by PSI

Patient pre-infusion product profiles enable early intervention



Case 1: drivers of CAR-T product potency

Further, from the readouts, non-redundant cytokines contributed to these PSI differences (CD4 ex.)

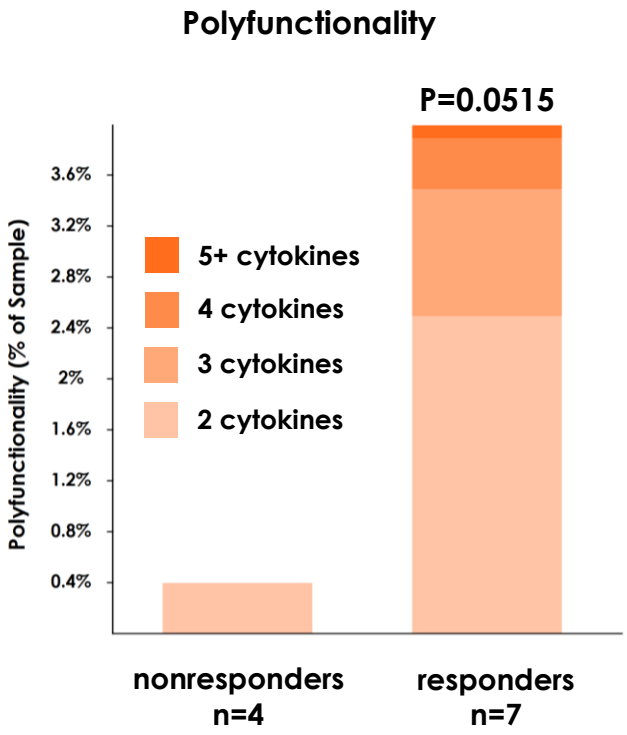


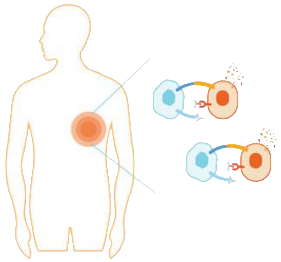
additionally, pre-infusion product is an independent variable vs. CAR-T expansion

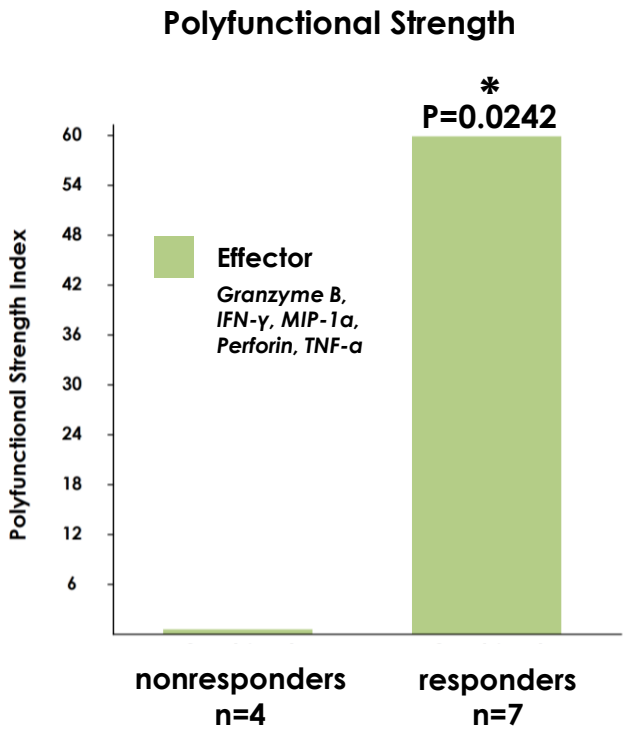
Case 2: checkpoint biomarkers

Yale Caltech

Profiling T Cells for Improved Patient Response Markers to PD-1 Tx







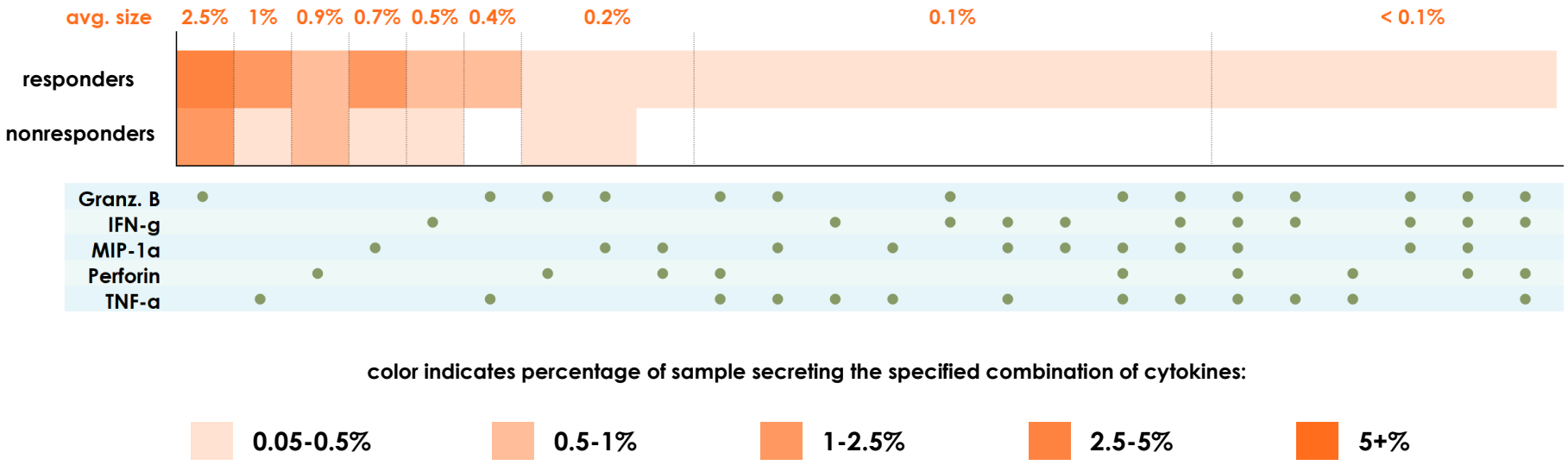
Objective: Clarity of mechanism & markers of patient selection

*P<0.05, Mann-whitney U test)

Case 2: checkpoint biomarkers

Yale Caltech

Emergence of unique polyfunctional cell subsets



Identify unique polyfunctional cell subsets in patients who responded to anti PD-1 and/or anti CTLA4 therapy

*P<0.05, Mann-whitney U test)

Deeper potency and toxicity pre-infusion clinical biomarkers

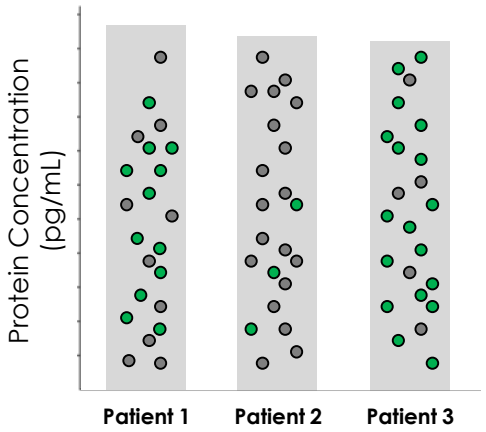
Applying improved product potency and consistency specifications

Isoplexis technology provides

data driven by & related to patient outcome

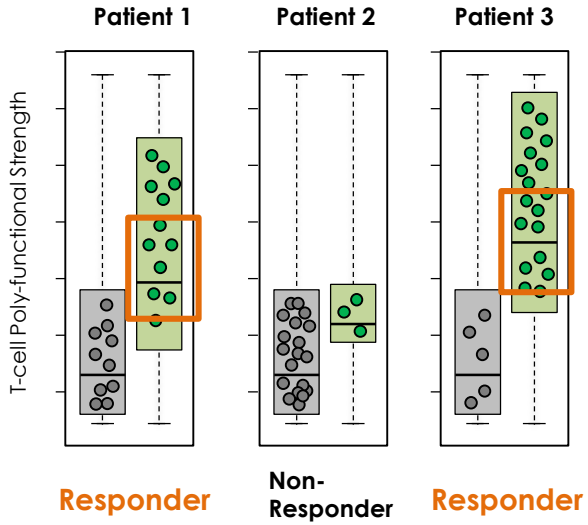
Current Methodologies

(flow cytometry / bulk assay)



- Pre-infusion biomarkers are masked in current analysis and methodologies.
- Functional differences in cellular sub-populations are unable to be differentiated.

Single T-cell Patient Response



- Improve / optimize manufacturing to achieve product poly-functional potency metrics, linked to outcome
- Improve specifications for product linked to toxicities & related management

non-functional T-cell **poly-functional T-cell** *(2+ cytokines per cell)*

Thank You & Appendix

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