

Enabling Technologies for Development and Optimization of Bi-Specific Antibodies for T Cell Redirection

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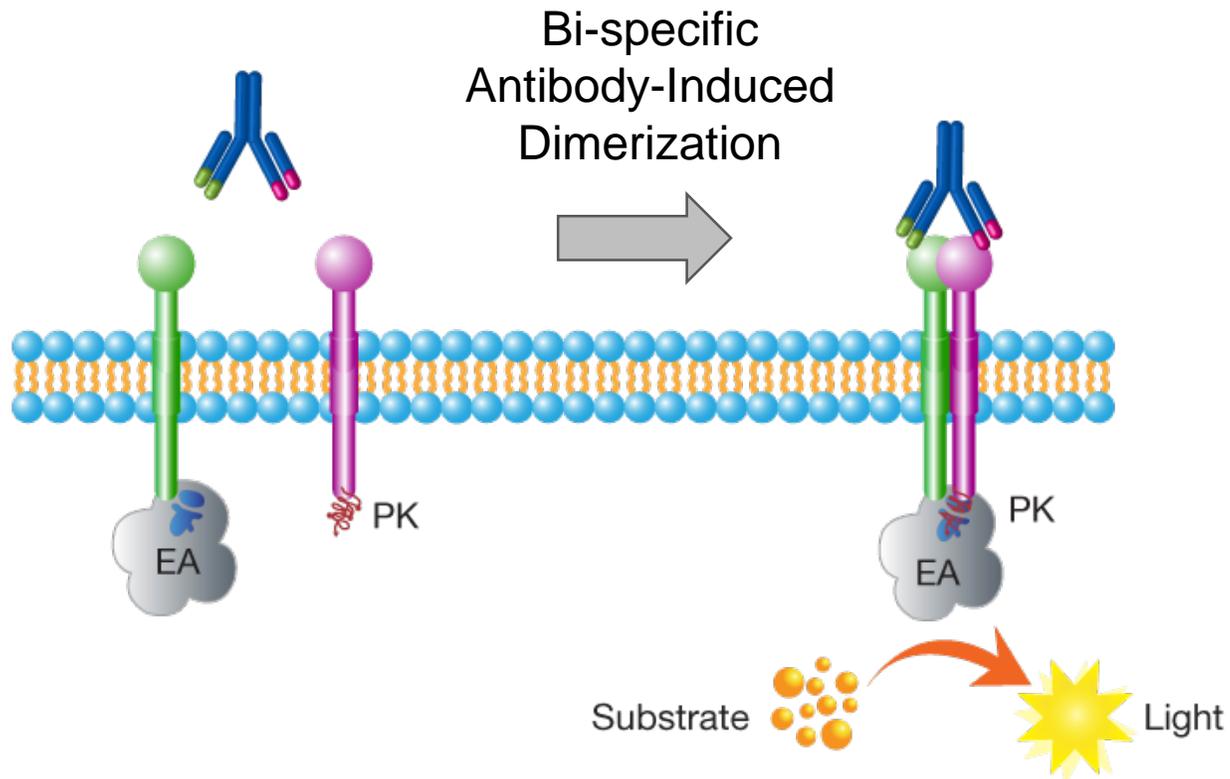
Accelerate Cancer Immunotherapy Towards Clinic

From screening to clinic & beyond!



Cell-Based Assay for Bi-Specific Engagement

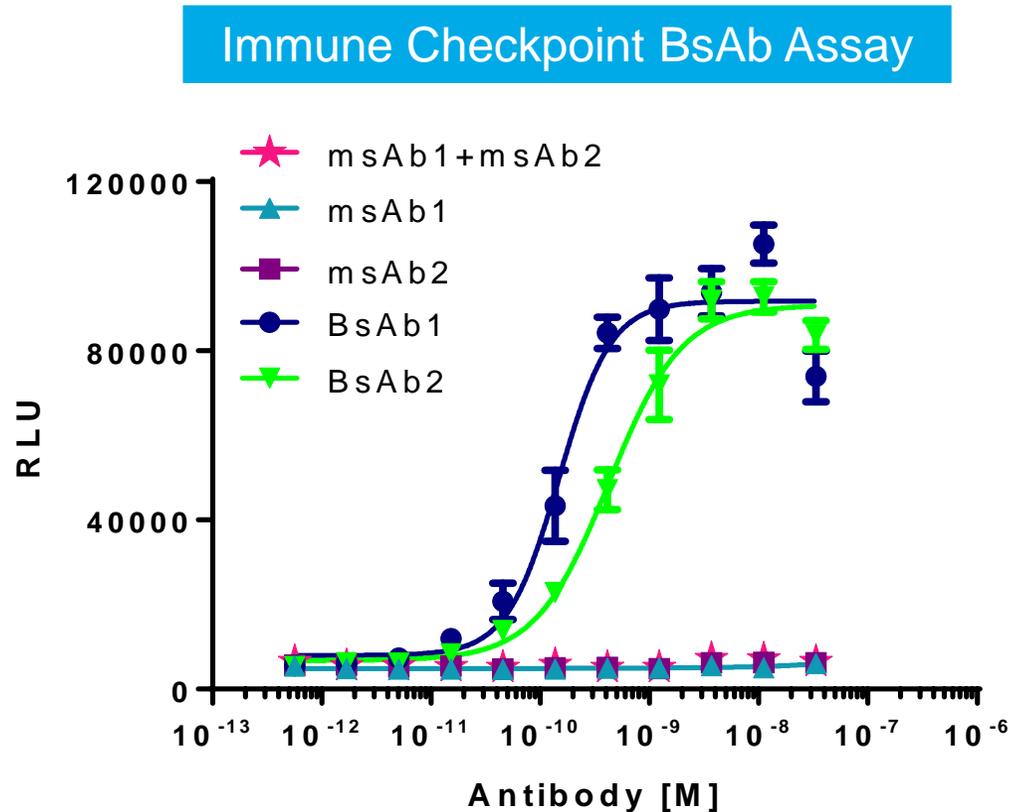
Concept for quantifying engagement of both arms of BsAb in single assay



- Quantifies BsAb-induced association of two antigens expressed on same cell (physiologically relevant context)
- Homogeneous assay amenable to high throughput (luminescence readout)
- Allows rapid evaluation of effect of different linkers or chemistries in single readout
- Suitable for early discovery through QC & lot release

BsAb Assays for Immuno-Oncology

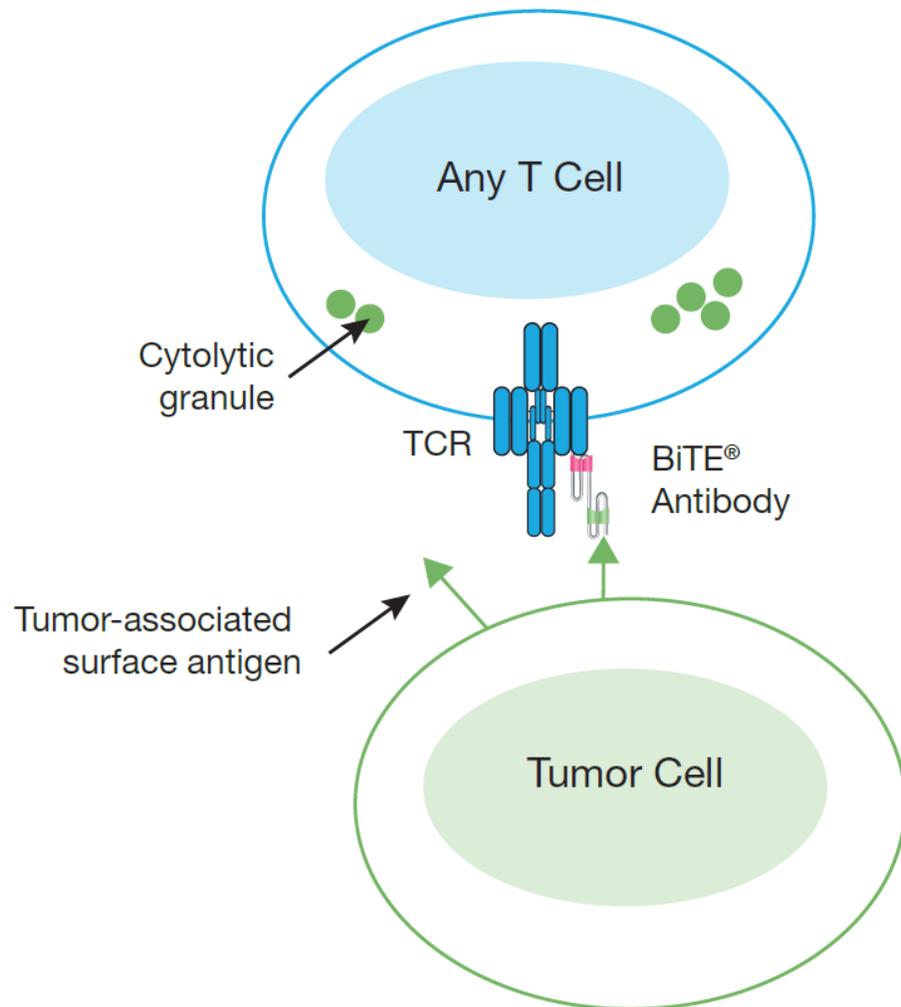
Assays for BsAbs to Immune Checkpoint Targets



- Highly specific response
- ~10 receptor combinations involving immune checkpoint targets (e.g. PD-1, LAG3, TIM3, TIGIT, etc)
- Also applicable to antibodies that mediate dual inhibition of oncogenic receptors (e.g. C-Met/EGFR)
 - Assay used to establish MOA of C-Met-x-EGFR BsAb published by Jarantow *et al* in JBC (2015)
- POC underway to evaluate suitability for BiTEs

MOA of the BiTE Molecule Blinatumomab

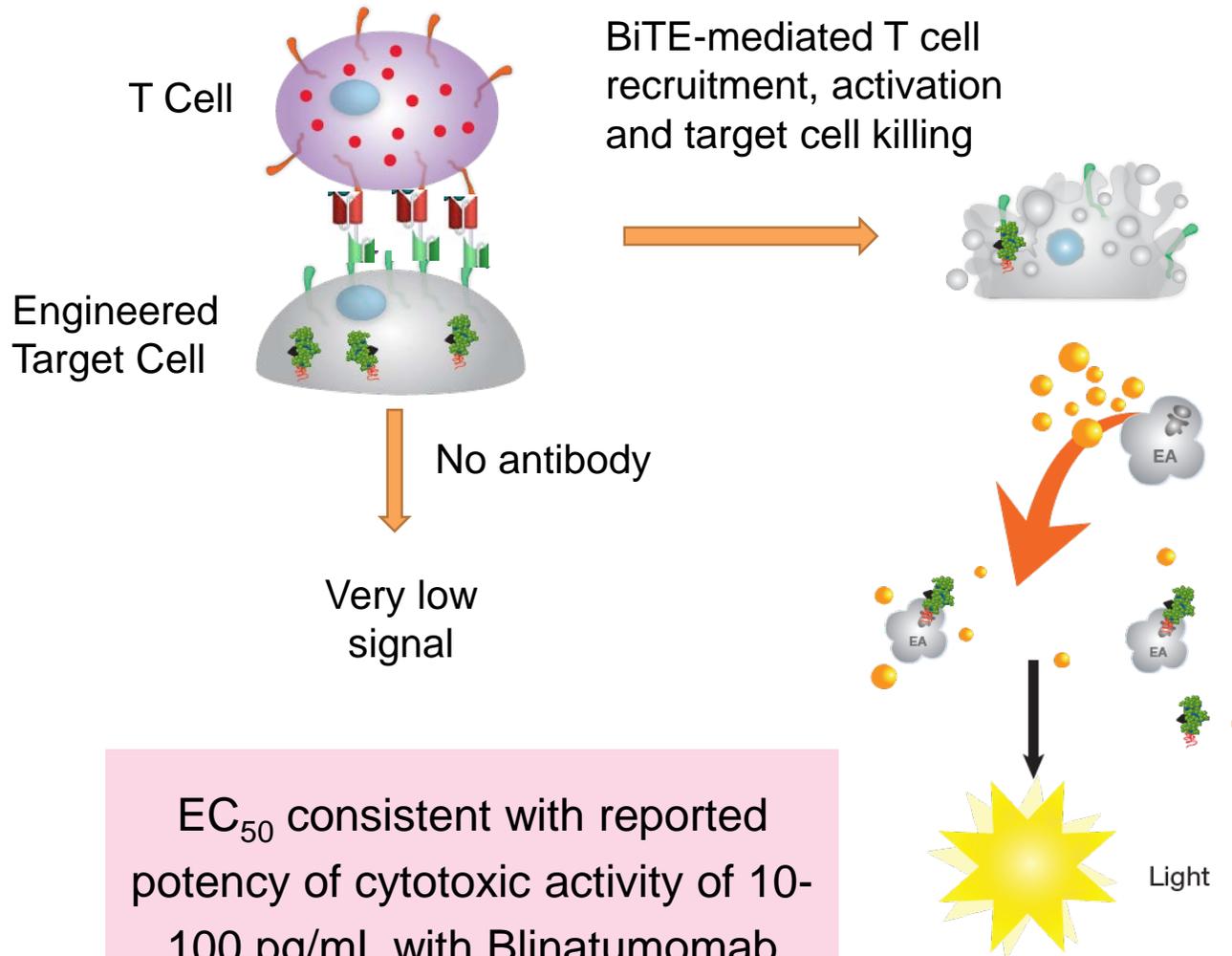
T Cell Redirecting Therapeutic



- First-in-class Bispecific T cell engaging antibody (BiTE)
- Activates unstimulated T cells (via CD3 arm) and redirects them to lyse CD19+ B cells (malignant and non-malignant)
 - Does not require MHC Class I and/or peptide antigen
- Approved for treatment of refractory ALL

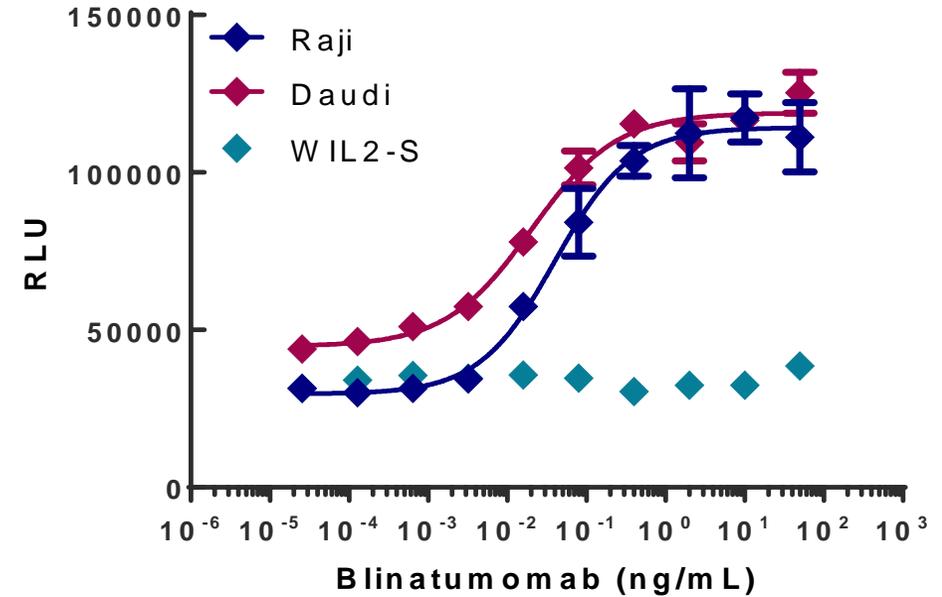
Robust Assay to Measure T Cell Redirection (TCR)

KILR[®] TCR assay with Blinatumomab



KILR Raji Cell Pool

Pan T Cells (E:T= 10:1)
24hr incubation

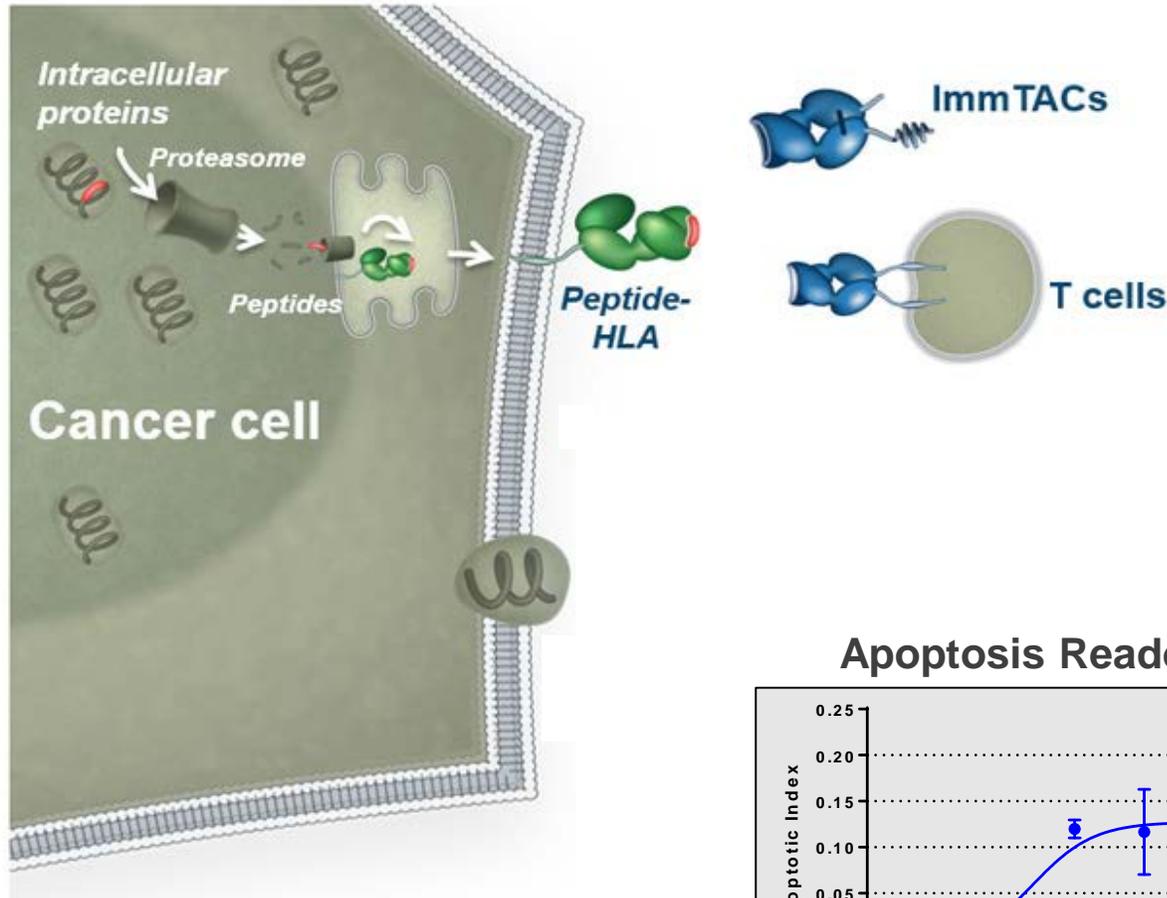


EC₅₀ consistent with reported potency of cytotoxic activity of 10-100 pg/mL with Blinatumomab

Sample	CD19 Receptor Density	% Max Cytotoxicity	EC ₅₀ (pg/ml)
Raji	7,400	59.4	40
Daudi	4,500	44.7	20
WIL2-S	2,500	--	--

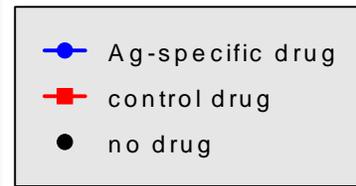
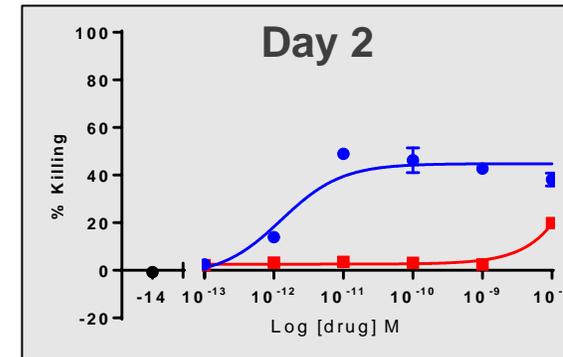
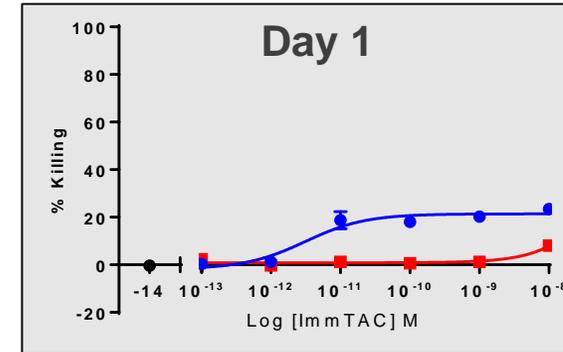
T Cell Redirection Using ImmTACs

Robust T cell redirection using KILR[®] assay format

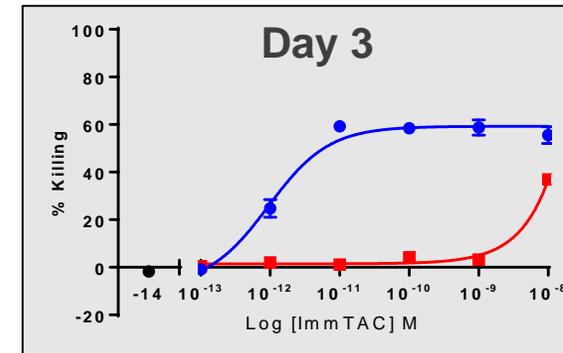
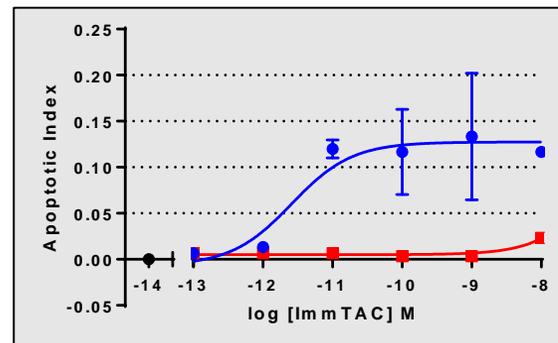


Data: Courtesy of Immunocore

KILR Assay Format



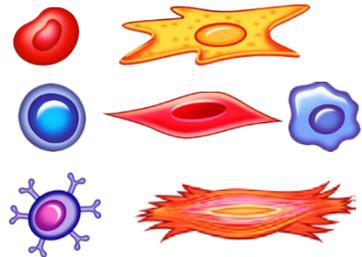
Apoptosis Readout



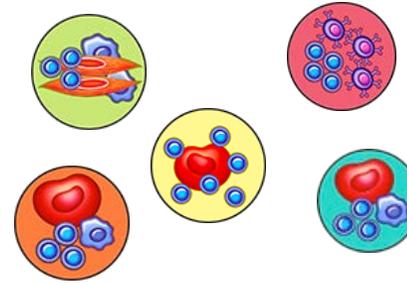
Overview of BioMAP® Phenotypic Screening Platform



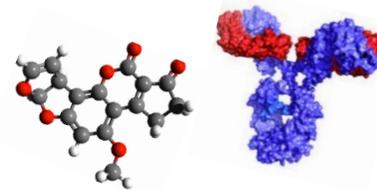
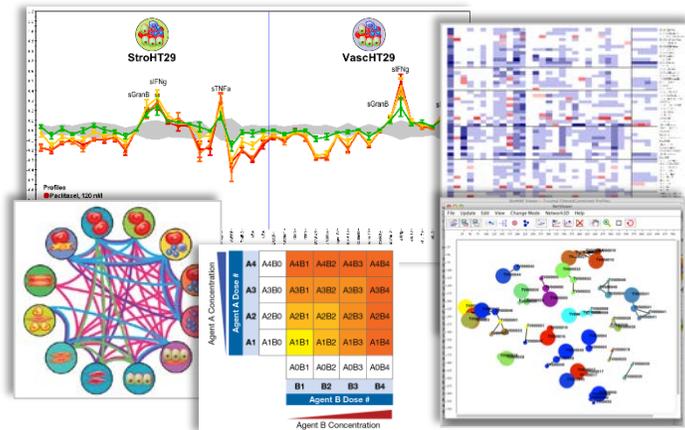
Multiple Healthy Donors
(population responses)



Human primary cell types
(physiological relevant)



56+ BioMAP co-culture systems
(human tissue/disease models)



Screen Large or Small
Molecules or Combinations

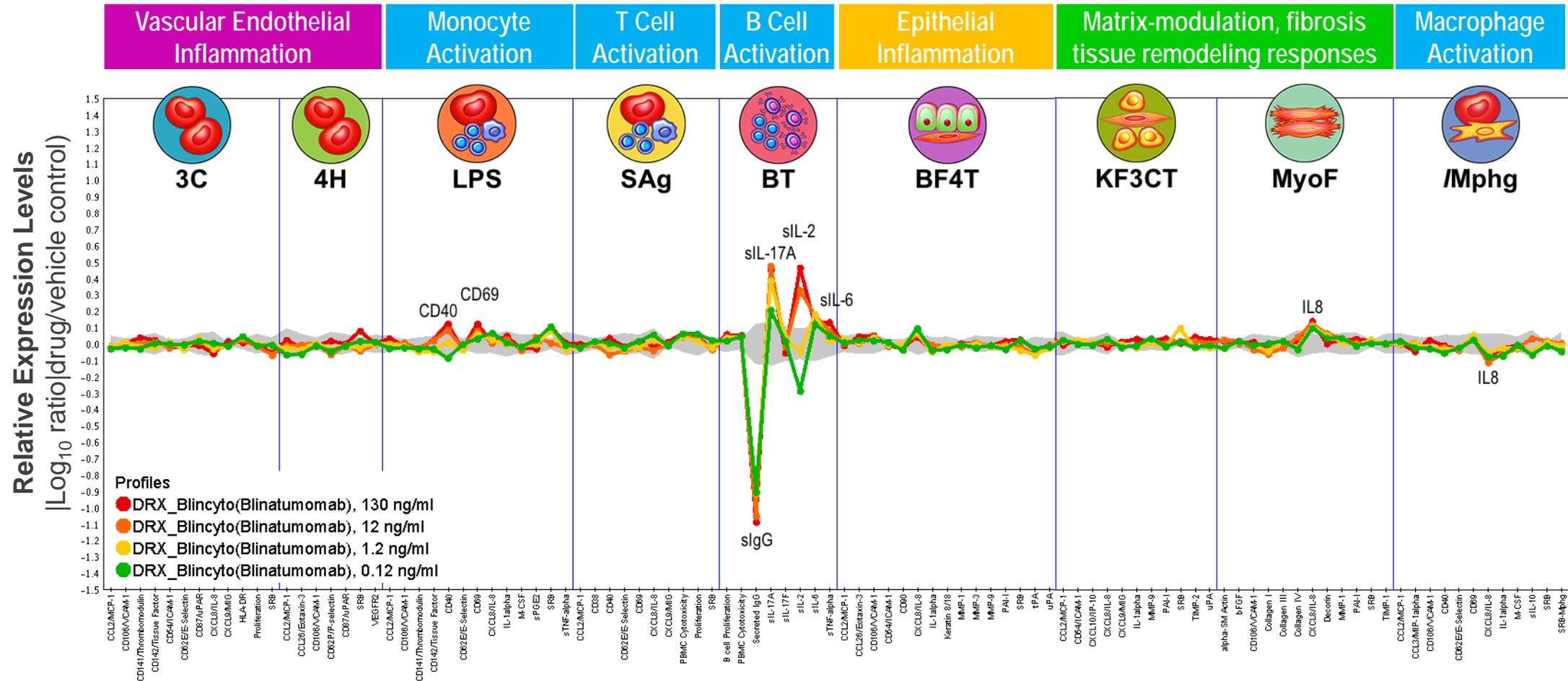


Robust and reproducible
in vitro screening assays

Expert analysis and interpretation provides actionable information to guide compound progression

Blinatumomab Signature in BioMAP® Diversity Plus™

Effects on B cell model consistent with MOA of Blinatumomab



Increase in cytokine production and inhibition of IgG secretion consistent with MOA

Questions?

www.discoverx.com/iOnc



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