OmniAb®

Wrangling Diverse OmniAb Antibody Repertoires with OmniDeep™

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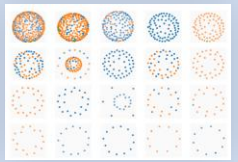
Antibody Engineering & Therapeutics US
December 15, 2023

The OmniAb Technology Offering is Expanding

TECHNOLOGY OFFERING ADDRESSES THE MOST CRITICAL CHALLENGES OF ANTIBODY DISCOVERY

Technologies

Create	Screen	Deliver
Create Diverse Repertoires of High-Quality Antibodies	***Screen Millions of Cells to Find Potential Therapeutic Candidates***	***Further Characterize, Select and Optimize the Right Antibody***
 *Computational Antigen Design & Proprietary Reagents*	xPloration®  *High-Throughput Single Cell Screening*	• *Custom Bioinformatics* • *Next Generation Sequencing (NGS) Hit Expansion* 
OmniRat® OmniChicken® OmniMouse® *Robust Antibodies for Any Target*	 *Gel Encapsulated Microenvironment (GEM) Single Cell Screening*	 • *Comprehensive Functional Characterization* ICAGEN® ION CHANNEL TECHNOLOGY • *Proprietary Ion Channel Assays*
OmniFlic® OmniClic® *Bispecific Antibody Generation*		• *STR: Fc-Silencing Technology** STR®
OmnidAb® OmniTaur® *Novel Scaffolds*		

OmniDeep™ *Suite of in silico tools for discovery and optimization that are woven throughout our various technologies and capabilities. Includes structural modeling, large multi-species antibody databases, molecular dynamics simulations, AI, and machine and deep learning sequence models, and more*

*OmniAb entered into an agreement with mAbsolve Ltd. for STR, mAbsolve's Fc-silencing platform technology, which provides OmniAb with exclusive, sublicensable right to incorporate the STR technology with antibodies that have been generated using OmniAb's antibody discovery platform.

Deep Repertoires

Deep Screening

OmniDeep™

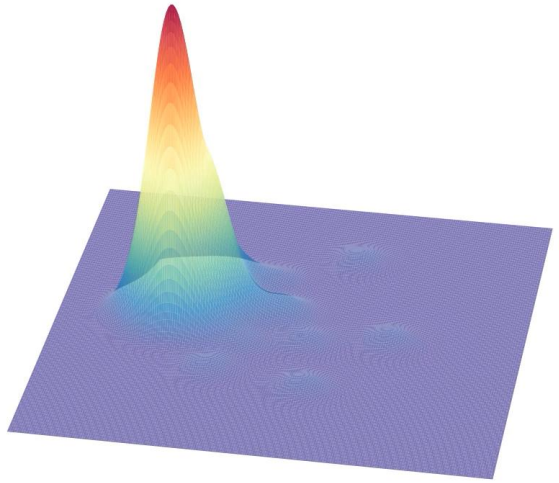
Deep Sequencing

Deep Learning

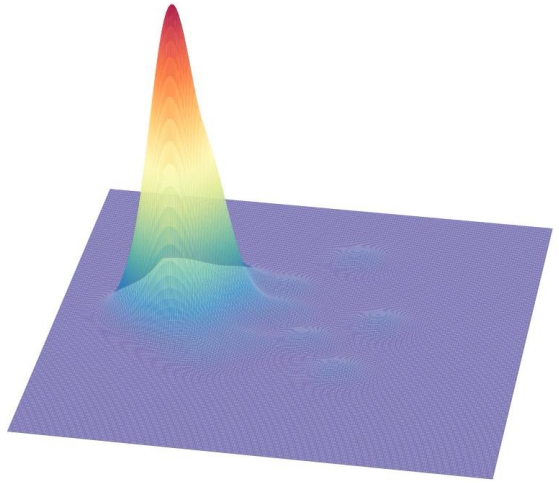
Custom Antibody Repertoires for Every Target

Biological Intelligence™: Interplay between rational genetic design and powerful *in vivo* processes

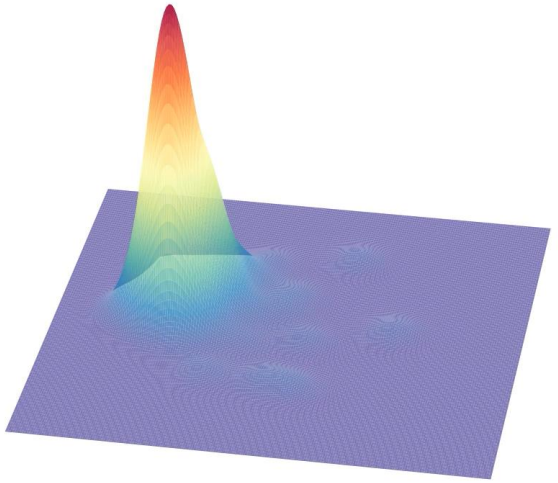
Animal 1:
Protein immunization



Animal 2:
Protein immunization



Animal 3:
Genetic immunization



Biological Intelligence can create a vast and diverse antibody repertoire within and across animals

OmniAb Antibody Repertoires

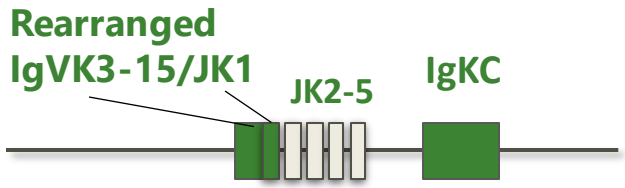
BROAD PLATFORM AVAILABLE TO ADDRESS DIVERSE PARTNER OBJECTIVES

Host	V genes	Structural and immunological features	Benefits for therapeutics discovery and development
OmniMouse®	• Full human V gene diversity • Choice of light chain isotype	• Diverse V gene usage and mixed genetic backgrounds	• Widely accessible and flexible workflows
OmniRat®	• Full human V gene diversity • Choice of light chain isotype	• Diverse V gene usage and mixed genetic backgrounds • Distinctive target recognition	• Industry standard • Widely accessible and flexible workflows • Extensive track record
OmniChicken®	• Single framework • VH3/VK3 or VH3/VL1	• Evolutionarily divergent host system for robust immune responses	• Diverse and new epitope coverage • High homology targets • Excellent physical properties
OmniFlic®	• Full human VH gene diversity with non-diversifying VK3	• Fixed light chain for bispecific applications	• Bispecific applications leveraging standard IgG format
OmniClic®	• Single framework • VH3/non-diversifying VK3	• Fixed light chain for bispecific applications	• Diverse epitope coverage • Excellent physical properties • Ease of manufacturing
OmnidAb®	• Single camelized human VH framework with truncated LC	• Domain antibody of the “VHH” type	• Diverse and new epitope coverage from human single-domain format, 12-15kD • Building blocks for multispecific molecules
OmniTaur™	• Single framework • VH4/VL1	• Ultralong CDR-H3’s for enormous structural diversity	• Access cryptic epitopes • Unique modalities (picobodies™) • Building blocks for multispecific molecules

Common Light Chain Platforms

STANDARD IGG FORMAT TO DE-RISK DOWNSTREAM DEVELOPMENT[1] OF BISPECIFIC MABS

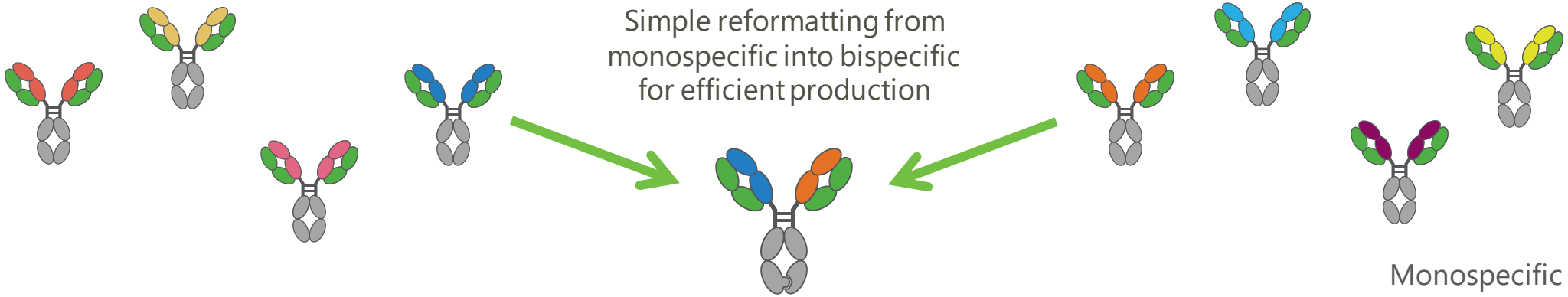
OmniFlic®



Rearranged human VK3-15 light chain combined with diversifying heavy chain

OmniClic®

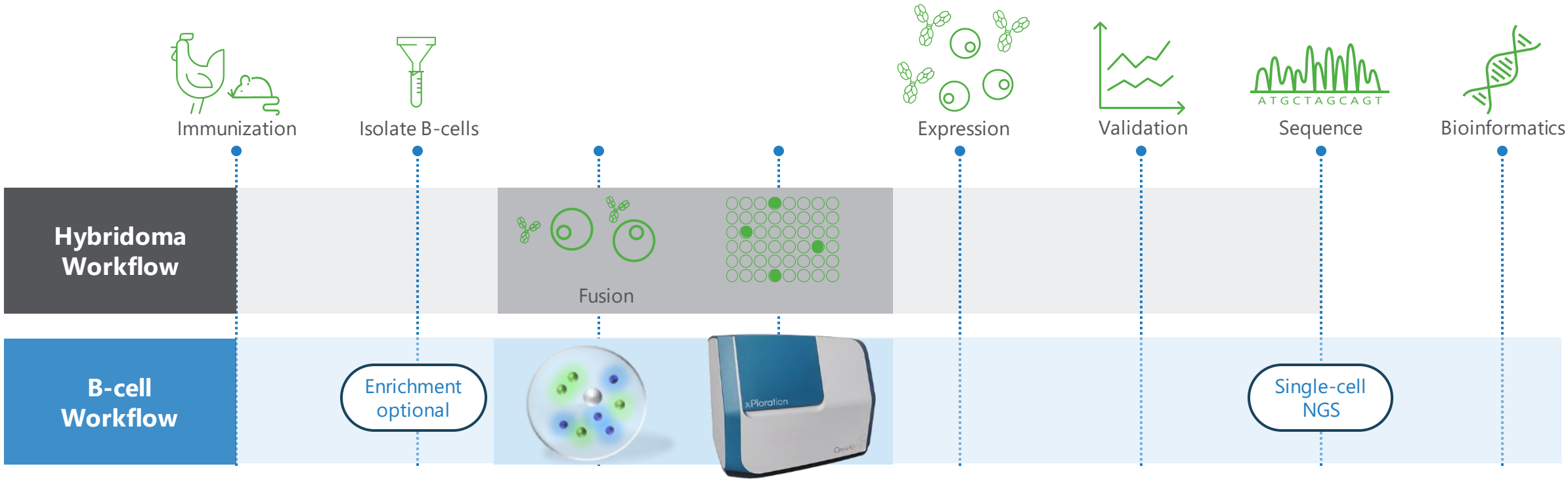
"Germlining" human VK3-15 light chain combined with diversifying heavy chain



†The Evolution of Bispecific Antibodies, Nimish Gera
https://doi.org/10.1080/14712598.2022.2040987

OmniAb®

Deep Screening Platforms



Our powerful single B-cell screening technologies, **xPloration® and GEM assay**, **bypass bottlenecks of hybridoma workflows**

AI-driven multi-parameter screening of **tens of millions** of cells in **hours instead of weeks**

Technologies enable **screening against difficult targets**: GPCRs, ion channels and surface antigens

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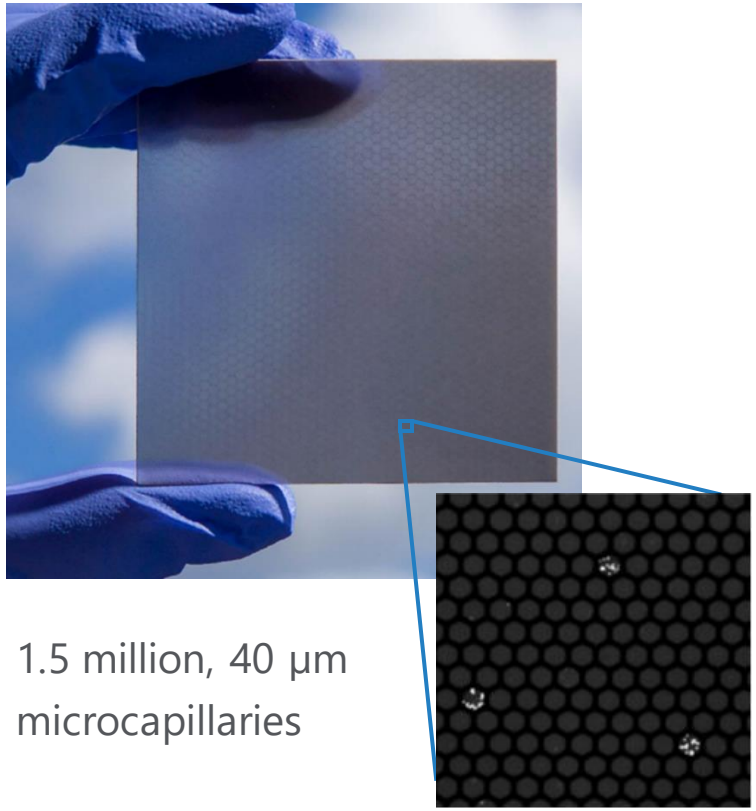
xPloration®: AI-Driven Deep Functional Screening

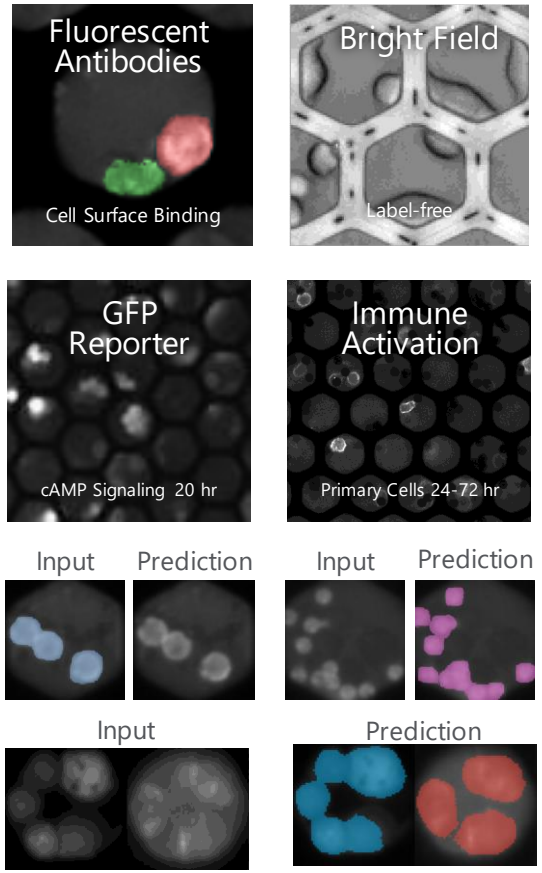
1 | Loading



1.5 million, 40 µm microcapillaries

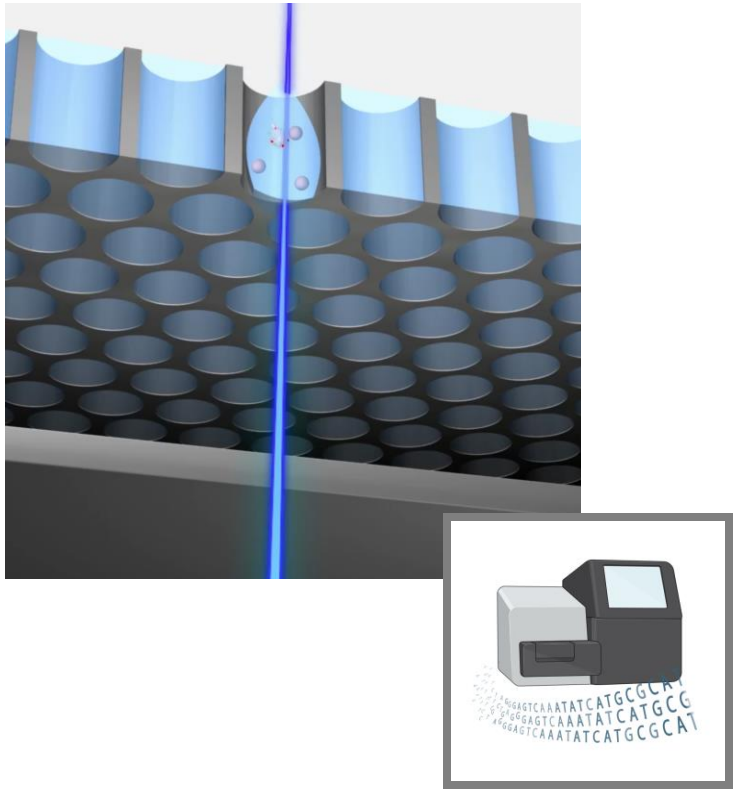
Unique through-hole format

2 | Assay + Machine Vision



Machine vision hit detection

3 | Recovery & Single-Cell NGS



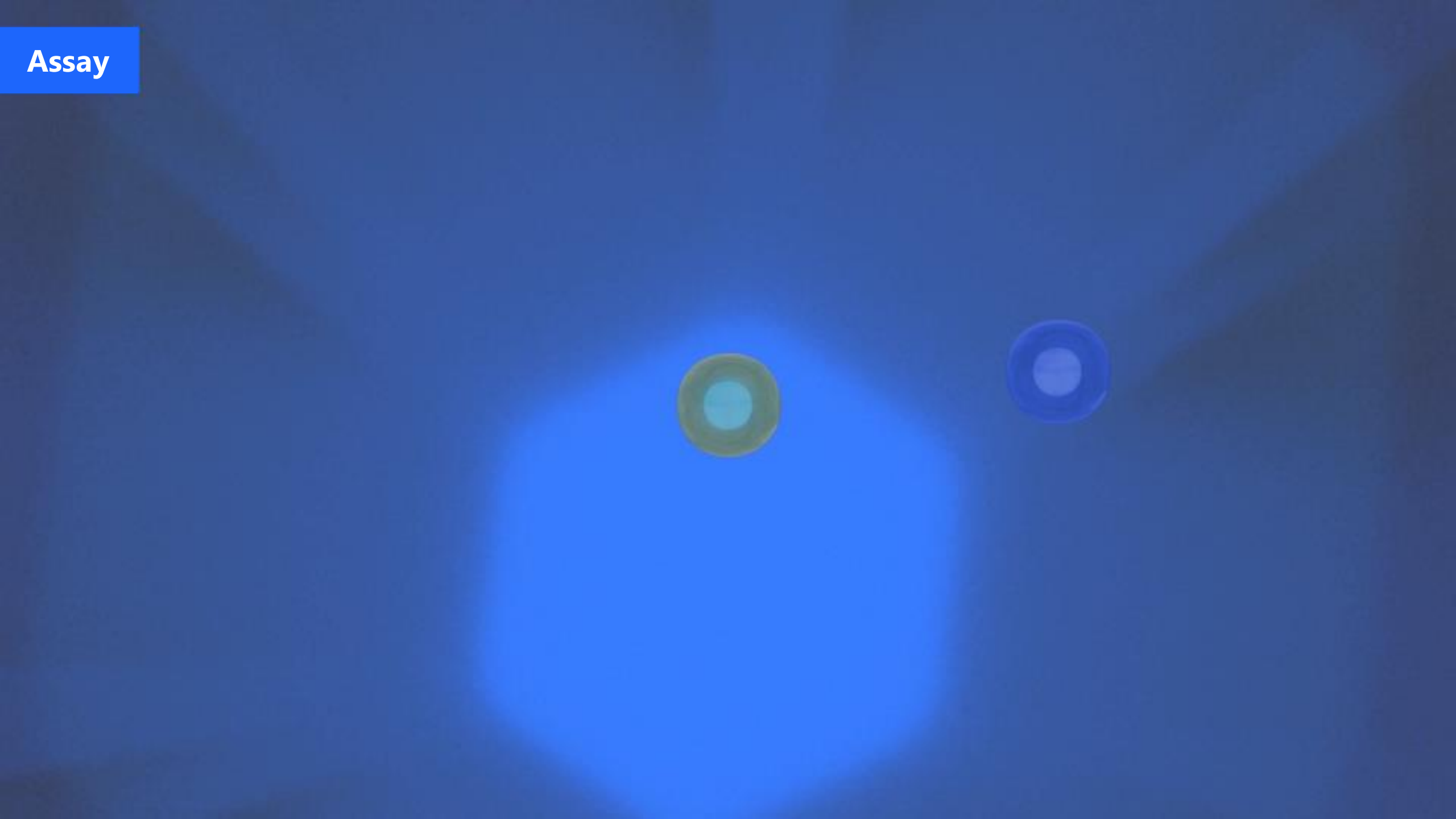
Precise laser-based recovery

Single-cell barcoding or pooled

OmniAb

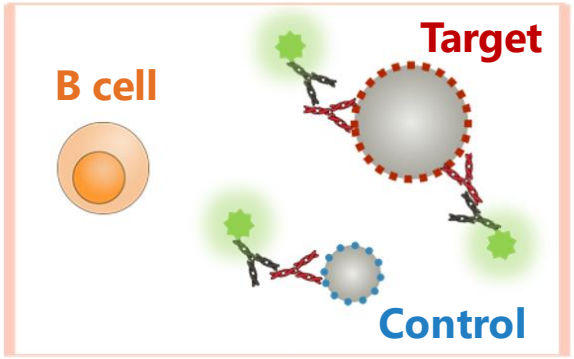
Assay

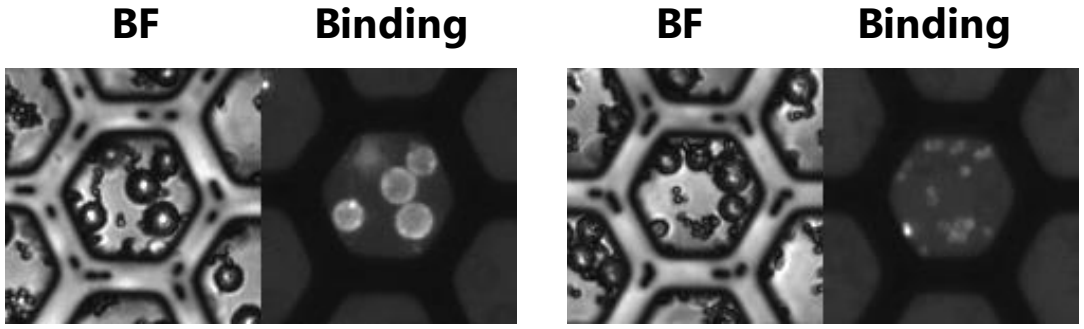
Assay


Assay

Multi-Parameter Screening: Multiplex Phenotypic Data

Selective binding of target on beads

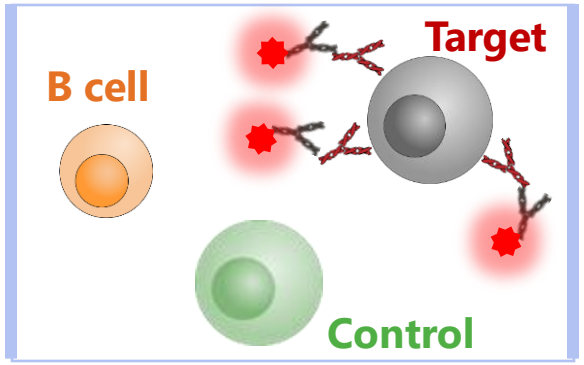


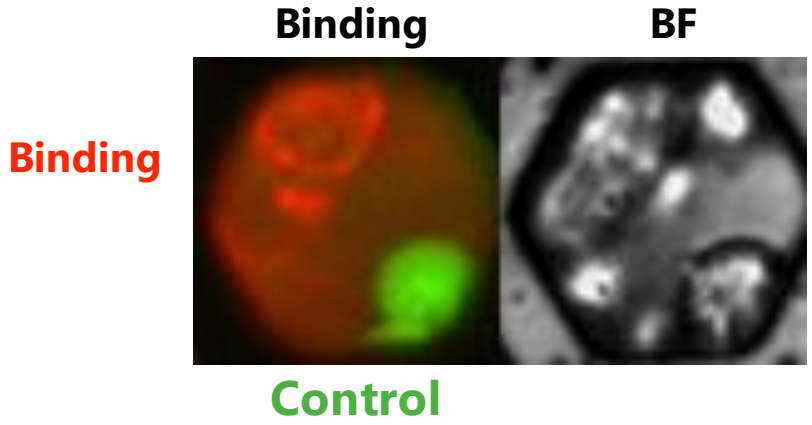


Binding to Target

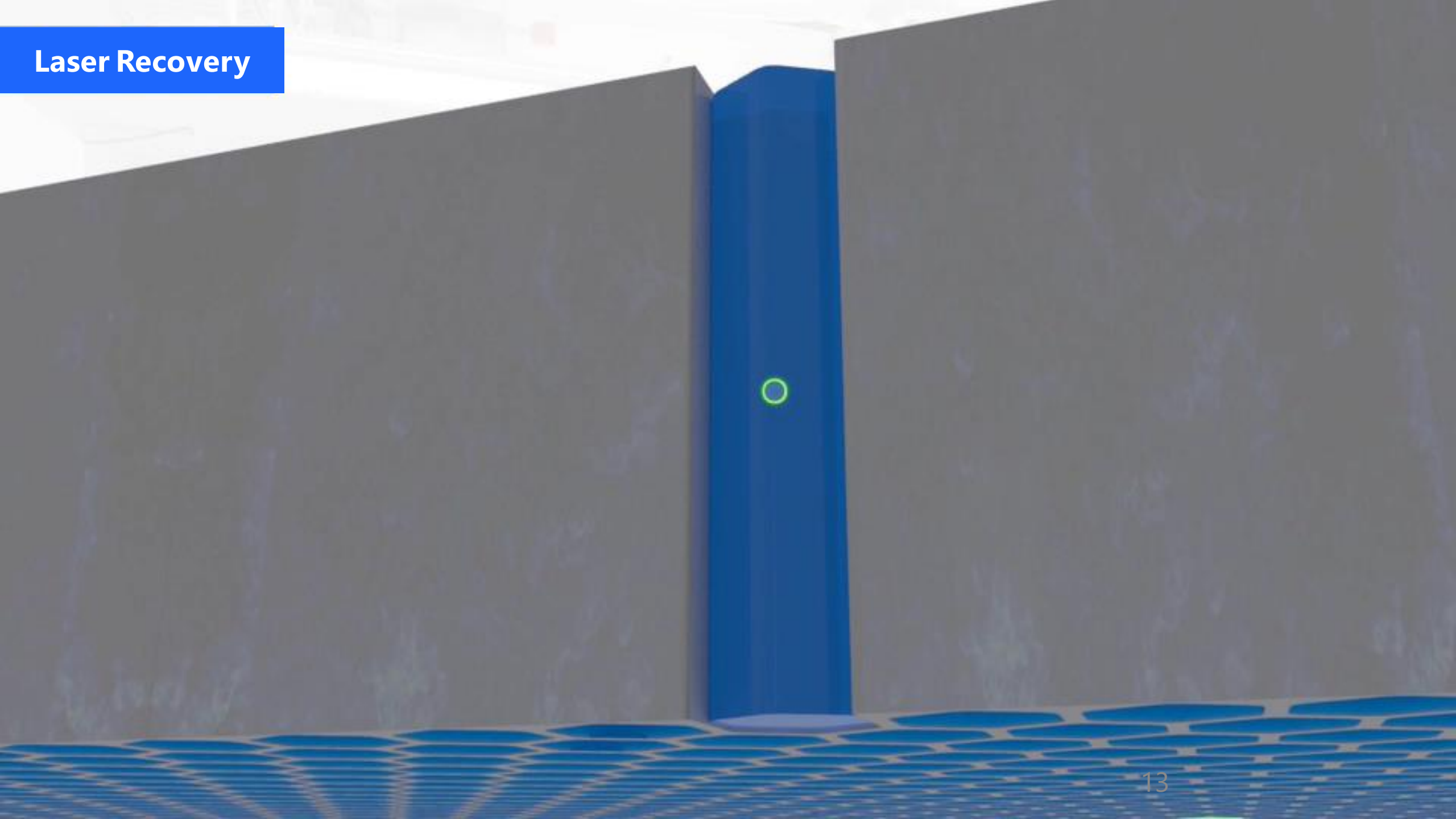
Binding to Control

Selective binding of target cell



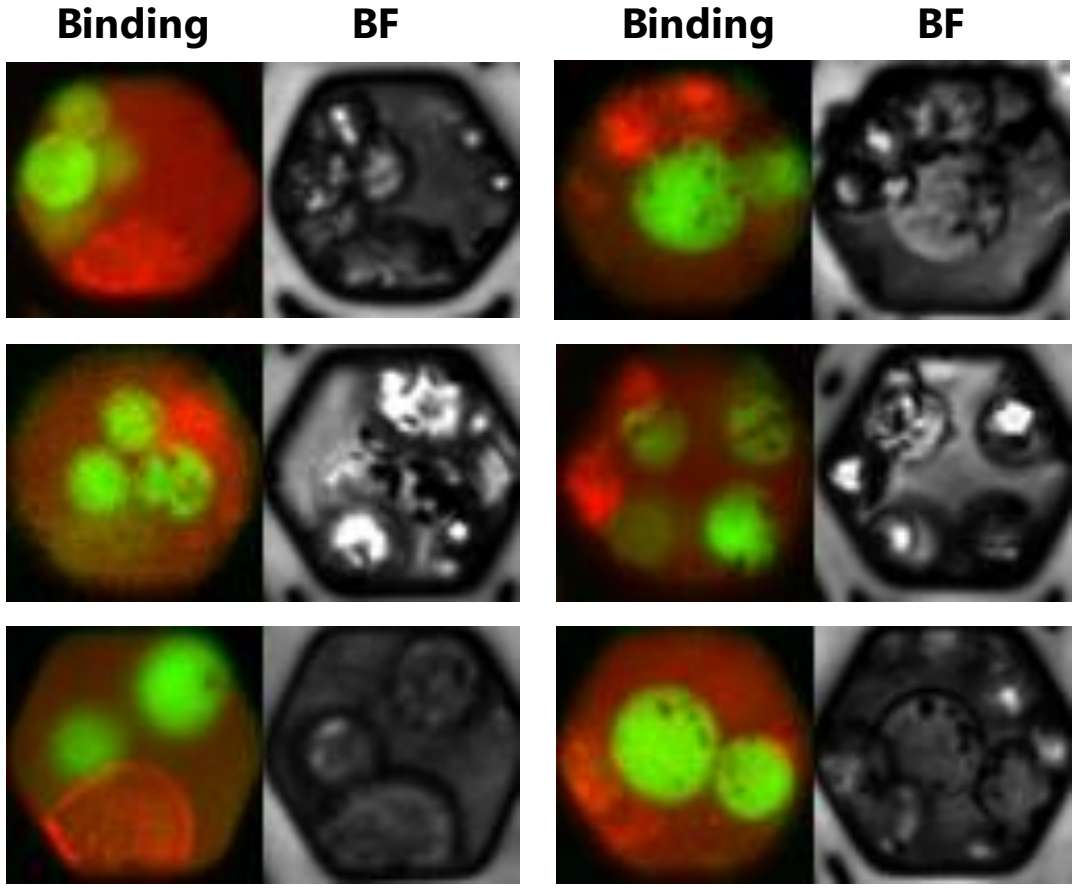


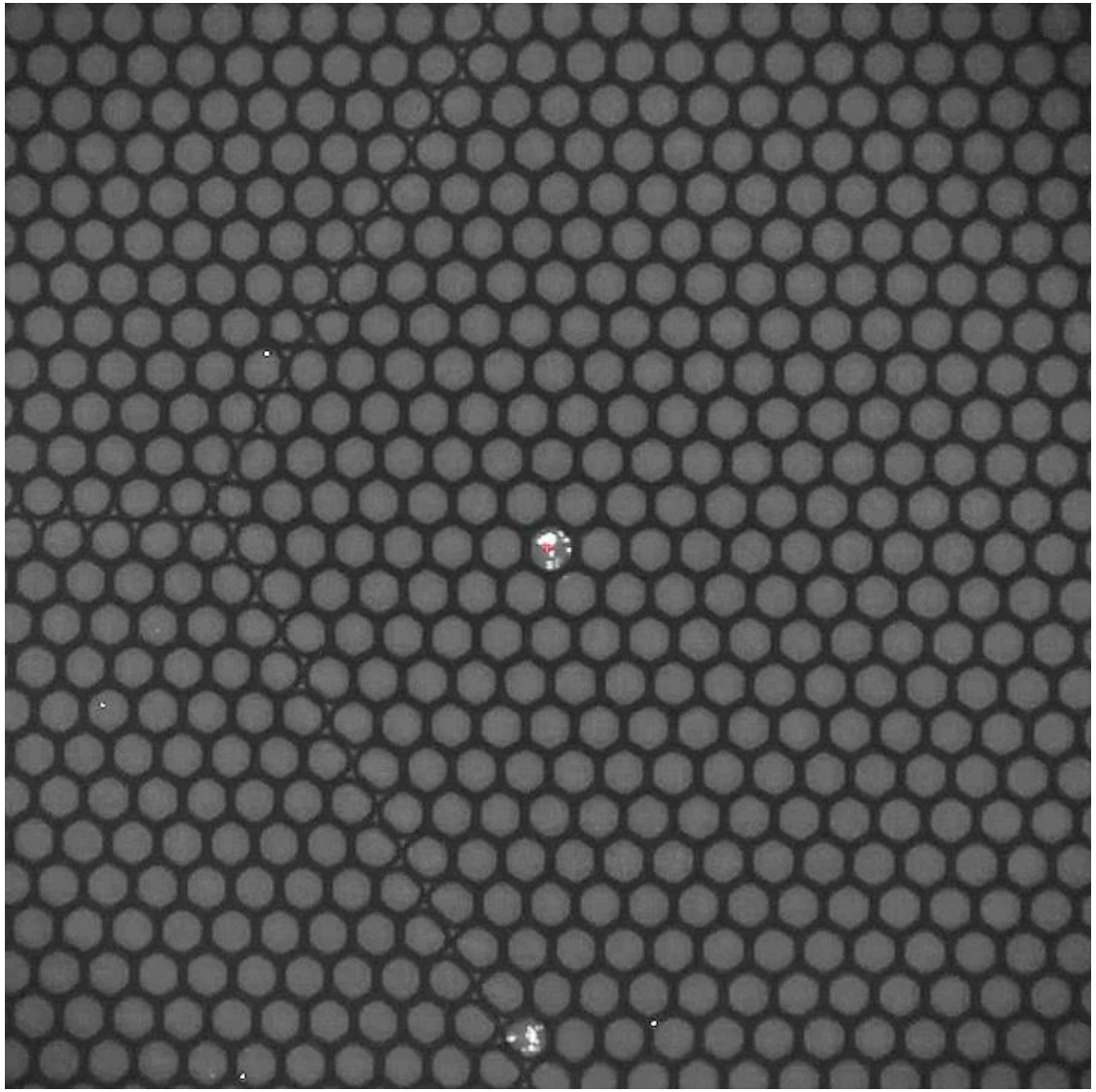
Laser Recovery



Rapid Laser Recovery of Hits

Example target cell specific hits





1x speed video of laser recovery

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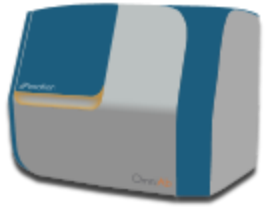
Integrating Biological Intelligence™ with AI

IN SILICO TOOLS TO BETTER MINE DIVERSE IMMUNE REPERTOIRES

Biological Intelligence

Deep Screening + Deep Sequencing



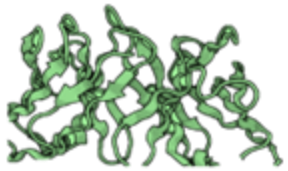
Large-scale data collection

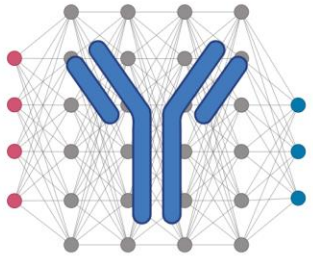
Proprietary Databases

Multi-species databases

Structure-Based Design Tools

Deep Learning Models





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OmniAb®

NKp46 Case Study:

Discovering NK cell engager arm for bispecific antibody

Project Background

Target

- NKp46 (NCR1, CD335) is a 46-kDa glycoprotein
- No statistically significant downregulation of NKp46 on both NK and T cells has been observed in many cancers

From PDB 6IAP

Discover anti-NKp46 antibodies from OmniClic for bispecific antibody (NKCE)

OmniDeep™ Empowers Large-Scale Antibody Discovery

OmniDeep™

Biological Intelligence™

\+

xPloration®

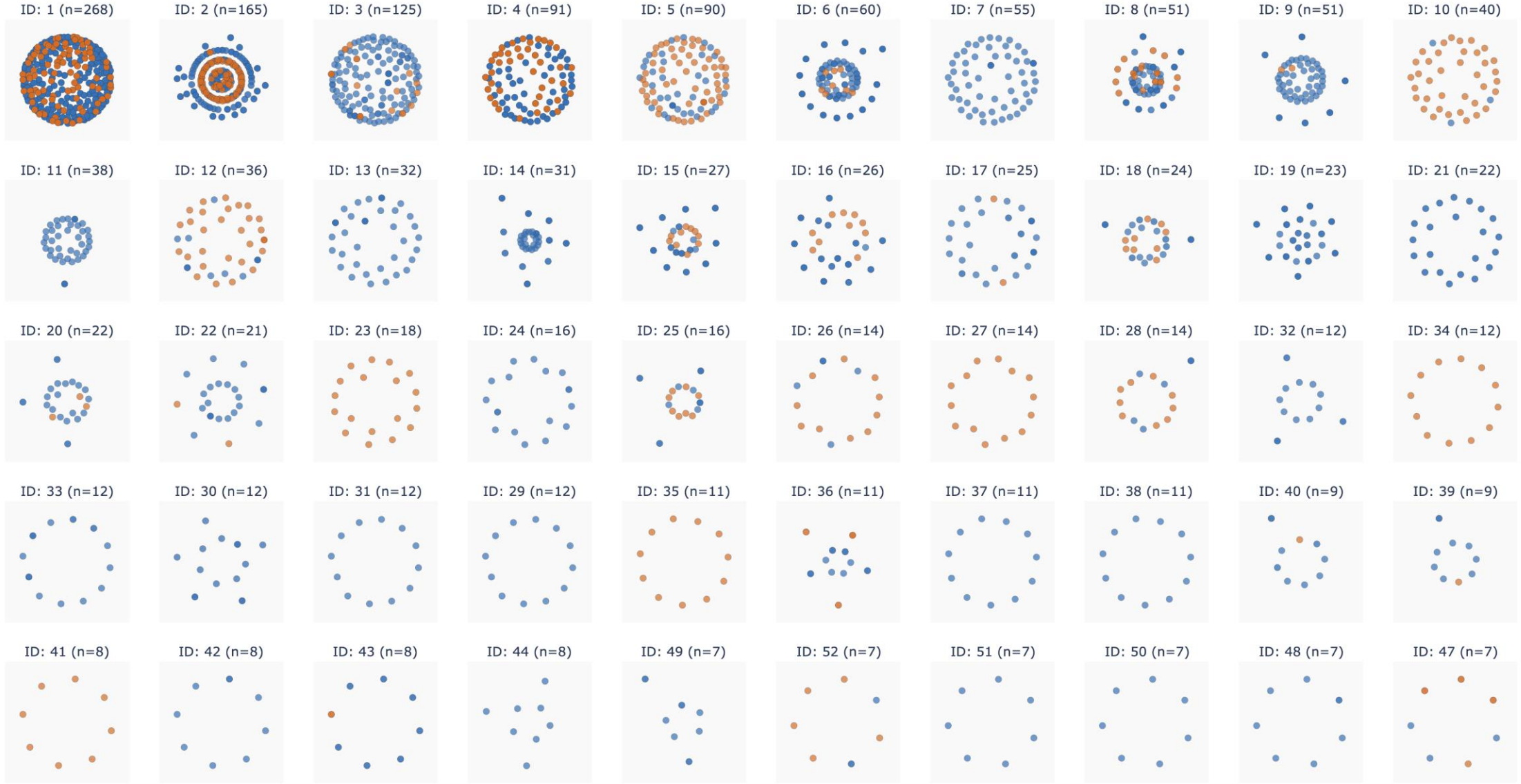
OmniClic® Screening Summary

Bird	Screen Type	# Cells Screened	# Hits
1	Antigen on beads	1.4 M	1200
	Cells	3.2 M	203
2	Antigen on beads	1.4 M	1199
	Cells	3.1 M	602
3	Antigen on beads	2.6 M	1326
	Cells	1.3 M	699
	Total	**13 M**	**5229**

- Processed with pooled NGS sequencing for **2130 unique sequences**

Synergy between OmniClic, xPloration® and NGS enables large-scale repertoire mining

OmniClic® Repertoire Space



Bead screen Cell screen

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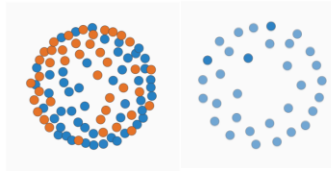
Bioinformatics-Aided Antibody Selection

Activity profile

Profile 1:
Cell + Protein binder

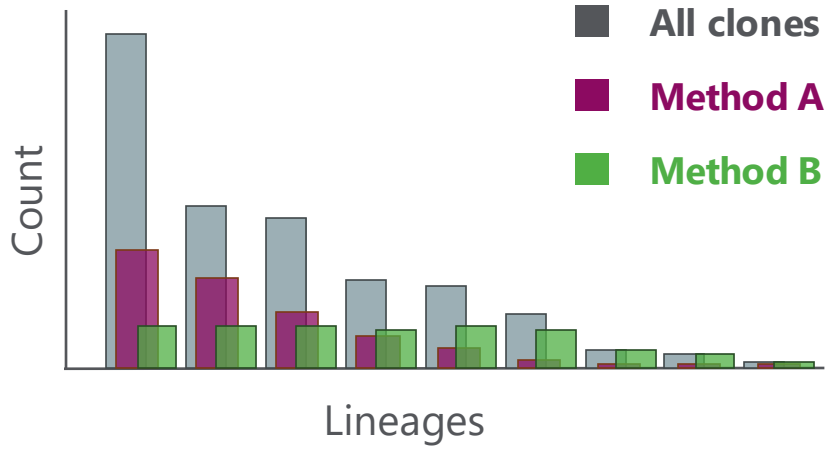
Profile 2:
All Cell binders



Profile 3:
Cell binder only

- Post-sort selection of desired functional profile
- Focused on cell and protein binders

Diversity

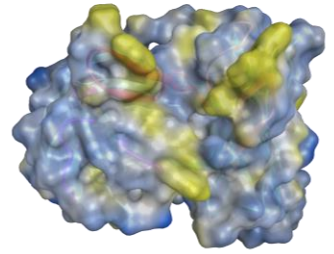


Clone selection considerations:

- Maximize coverage of sequence diversity
- Bias towards or away lineage distribution

In Silico Developability Filter

Sequences
↓
3D homology models
↓
Structure-based predictions



Hydrophobic patches near CDRs

Potential isomerization

- Structure-based method for cost and time efficient filtering for the most promising clones based on predicted properties

In silico tools guide data-driven antibody selection process

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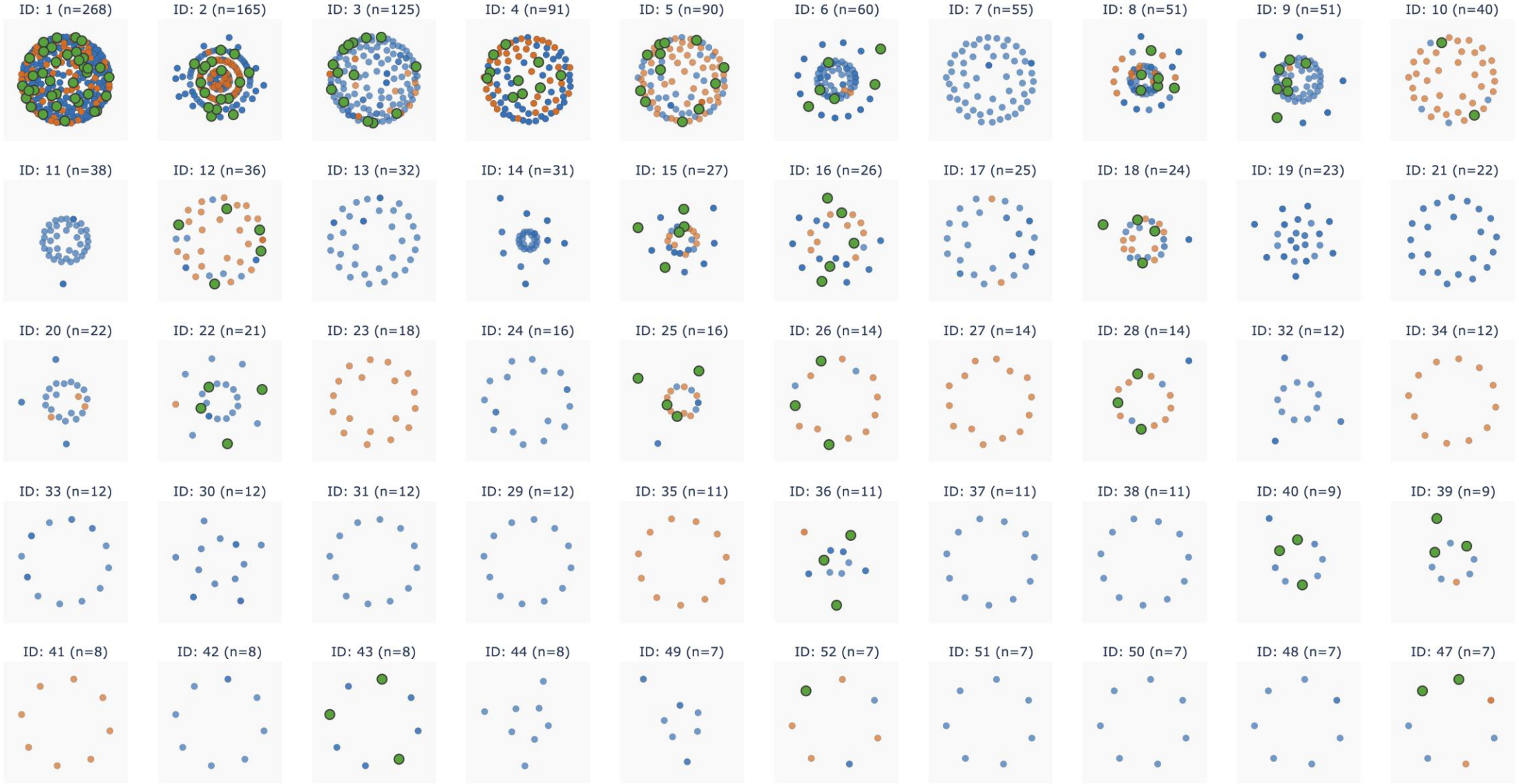
OmniClic® Repertoire Space



Selected Bead screen Cell screen

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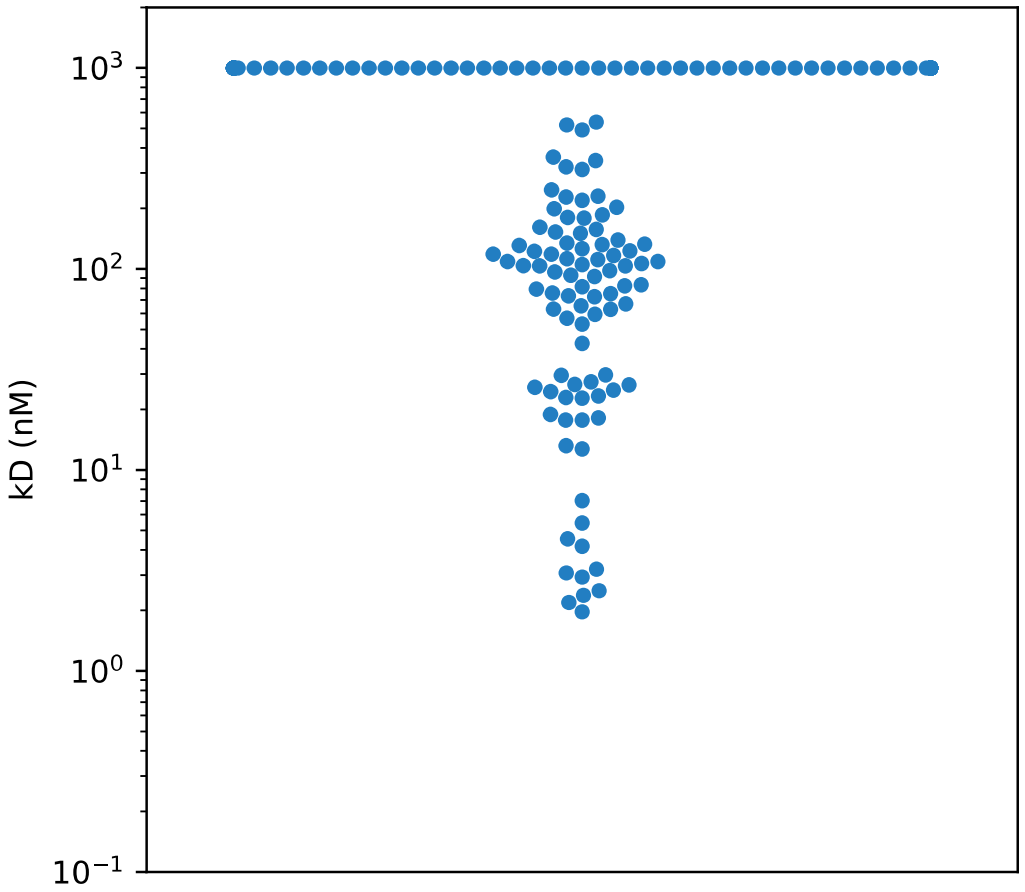
Discovery of NKp46 Binders

carterra

# Selected Clones	Binding (%)	<10 nM (%)
178	49	6%

- Expressed clones with common light chain
- 88 confirmed binders
  - Average affinity ~100 nM



Can we employ deep learning to increase yield and affinity?

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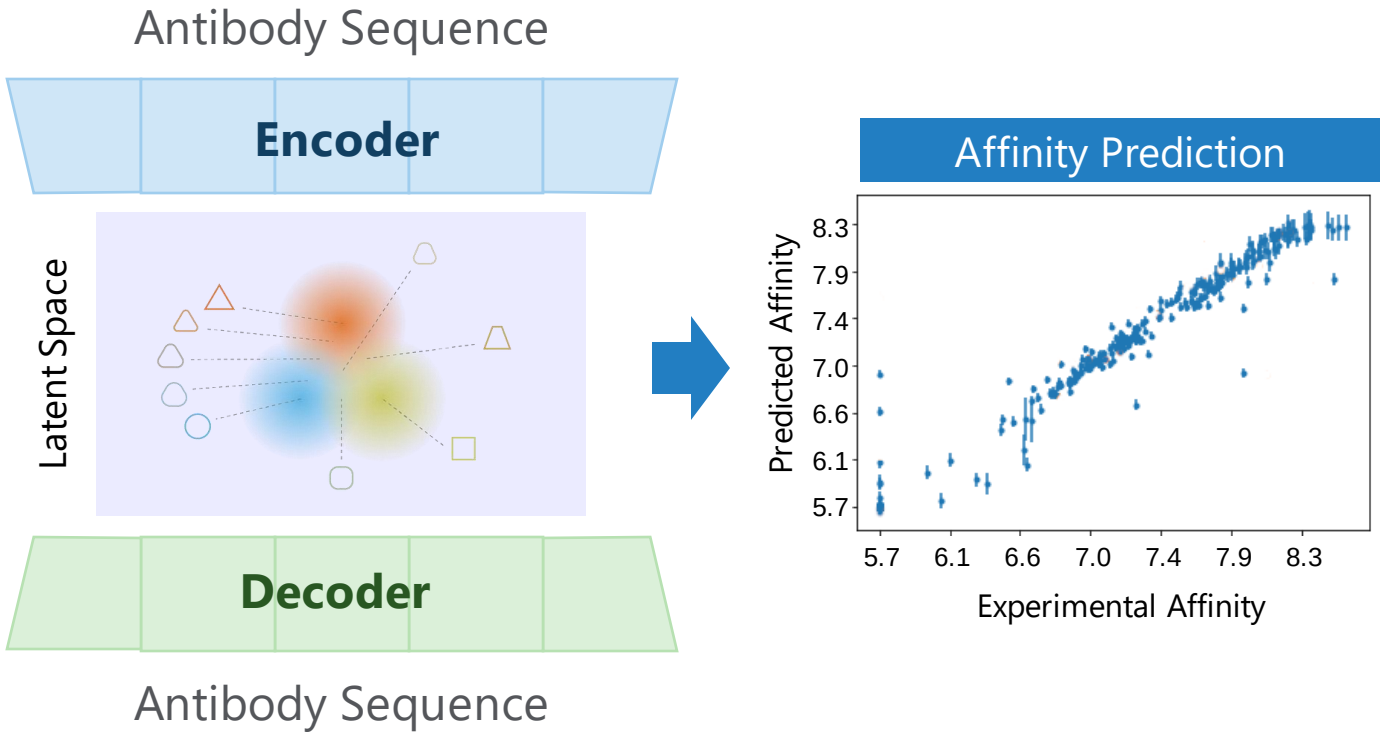
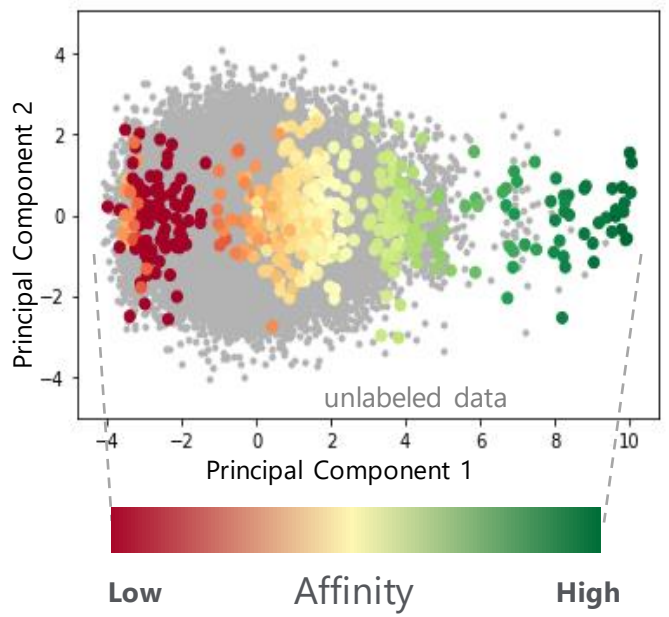
Encoding Sequence Space with Deep Learning

Variational Autoencoder (VAE) Model



Encoded Antibody Space



Property prediction organizes model space according to affinity

- **Input data:** xPloration® sorted sequences, affinity data, and bulk NGS
- Organization is purely data-driven both by the provided sequence and given affinity data

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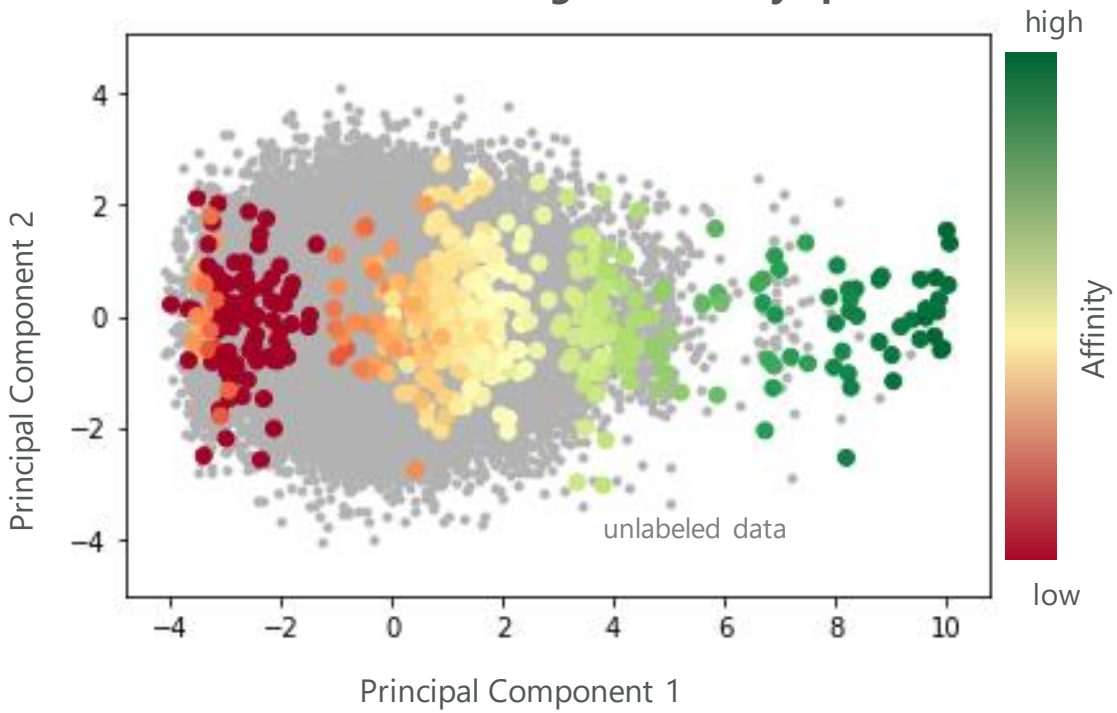
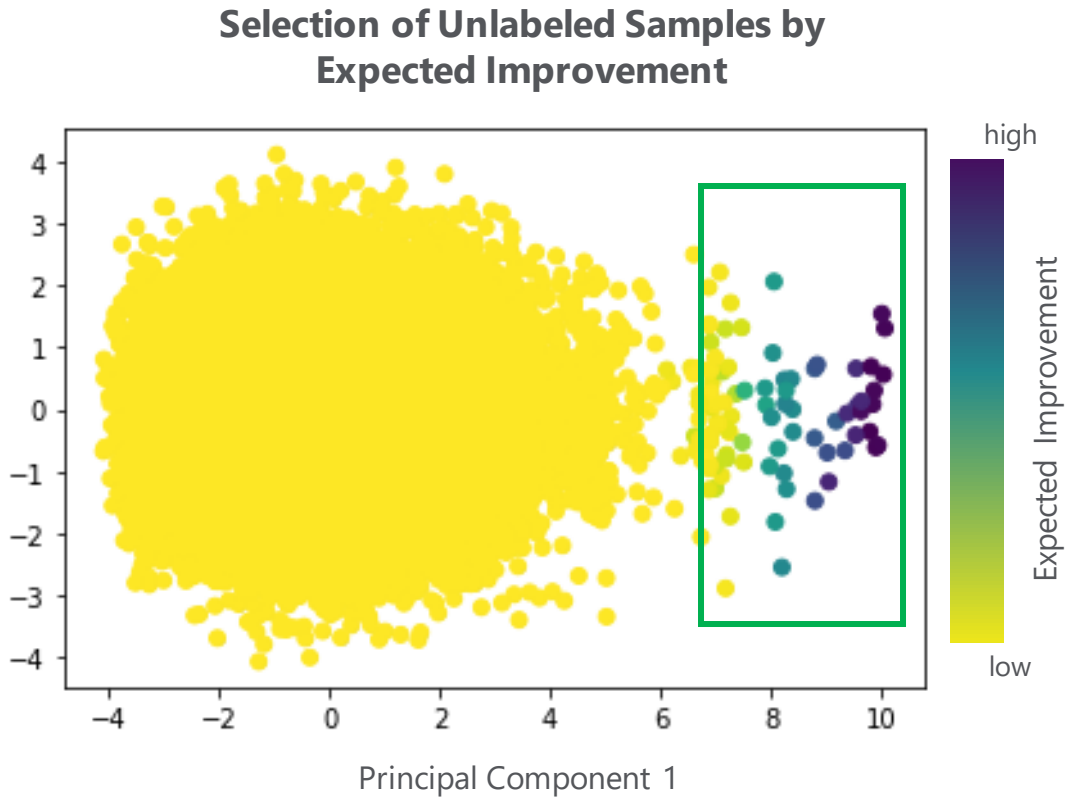
Identifying Higher Affinity Antibody Sequences

SELECTION FROM UNLABELED POOL OF DATA

- **Expected Improvement (EI)** of the entire unlabeled data set can be calculated and sequences with highest values are selected





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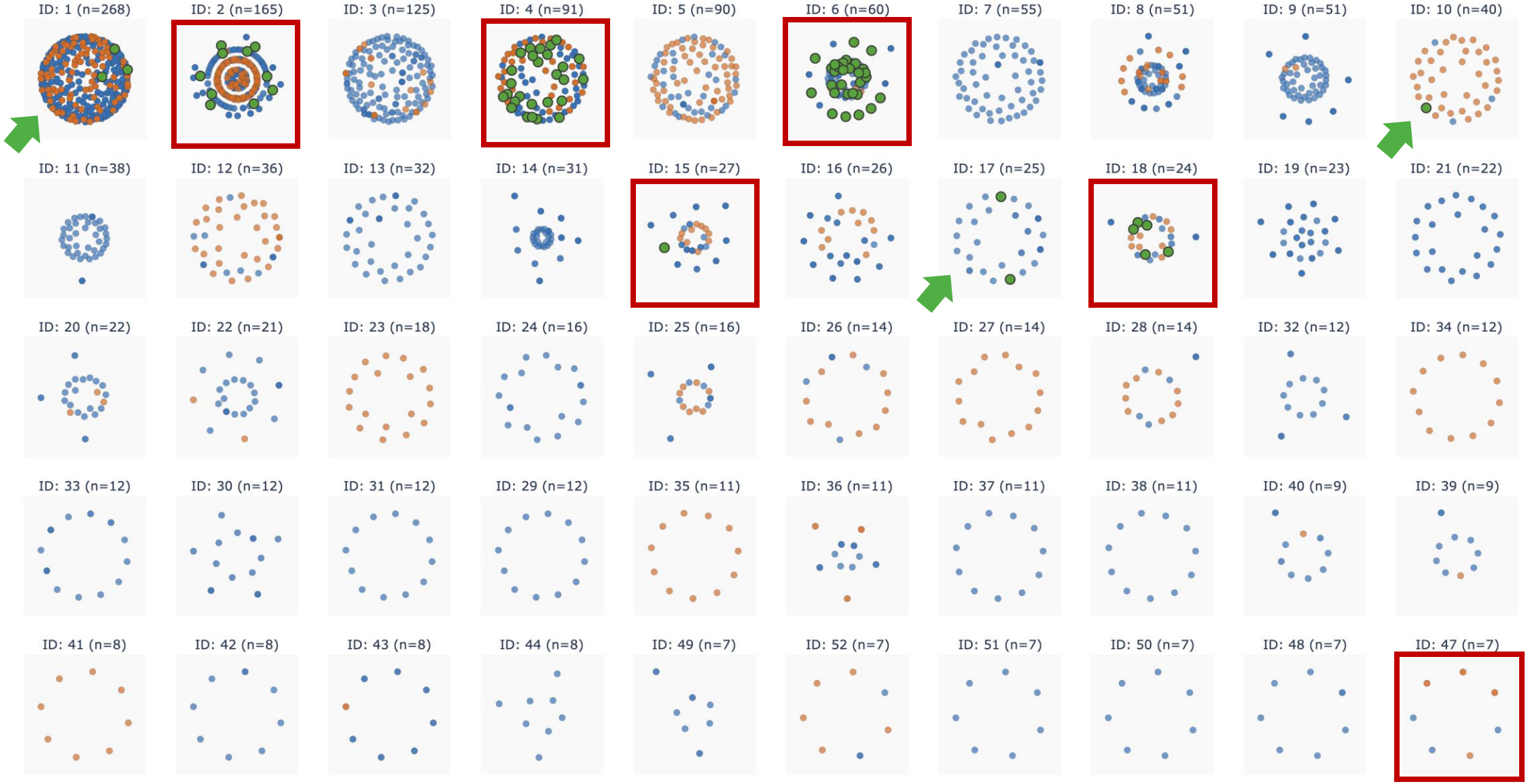
VAE Highlight New Clusters to Prioritize



VAE Selected Seed Bead screen Cell screen

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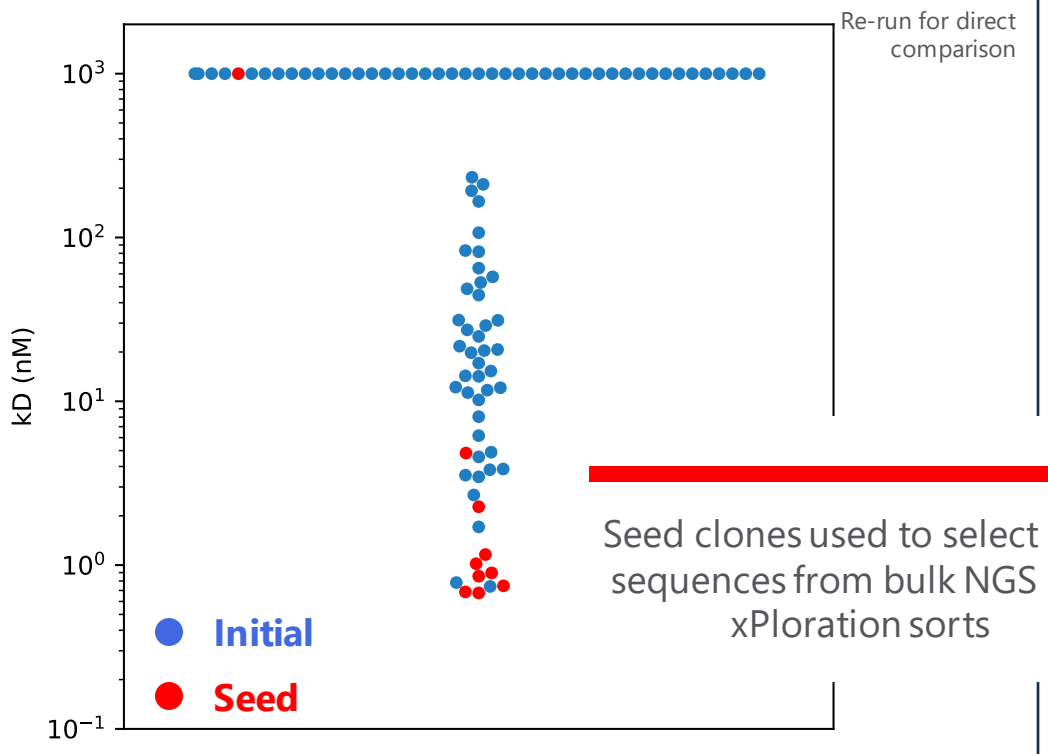
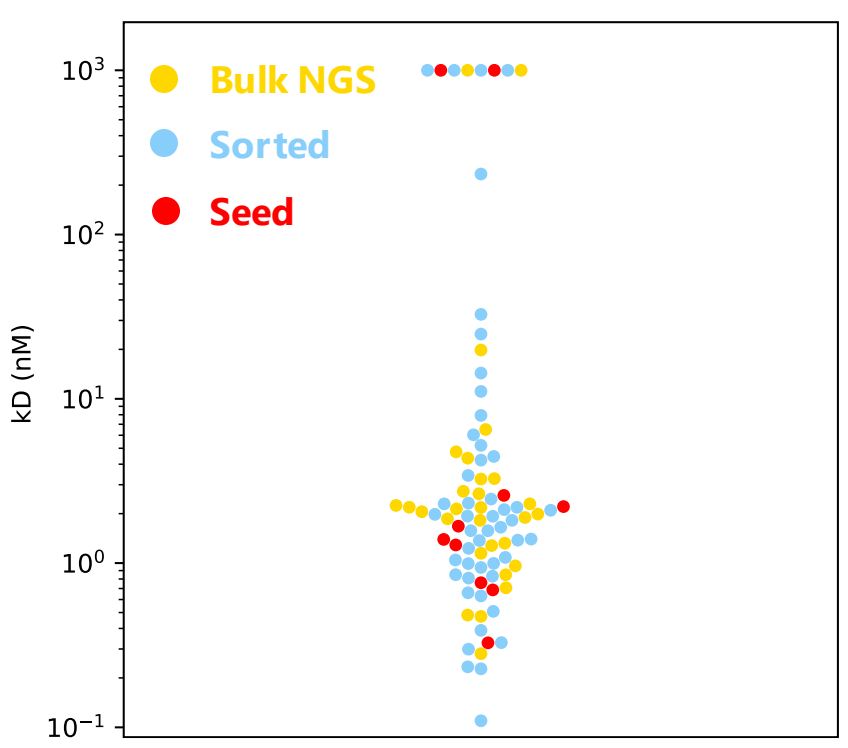
OmniDeep™ Successfully Selected High Affinity Clones

Initial selection



Seed clones used to select new sequences from bulk NGS and xPloration sorts

AI selection



Successfully found additional unique clones at 91% rate with ~10x improvement in mean affinity

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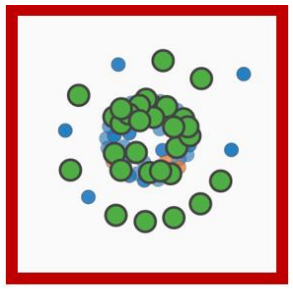
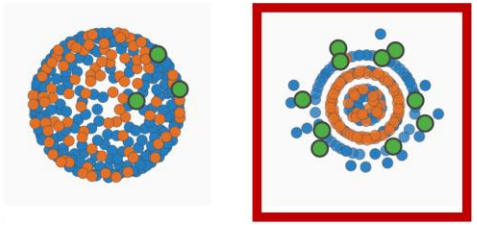
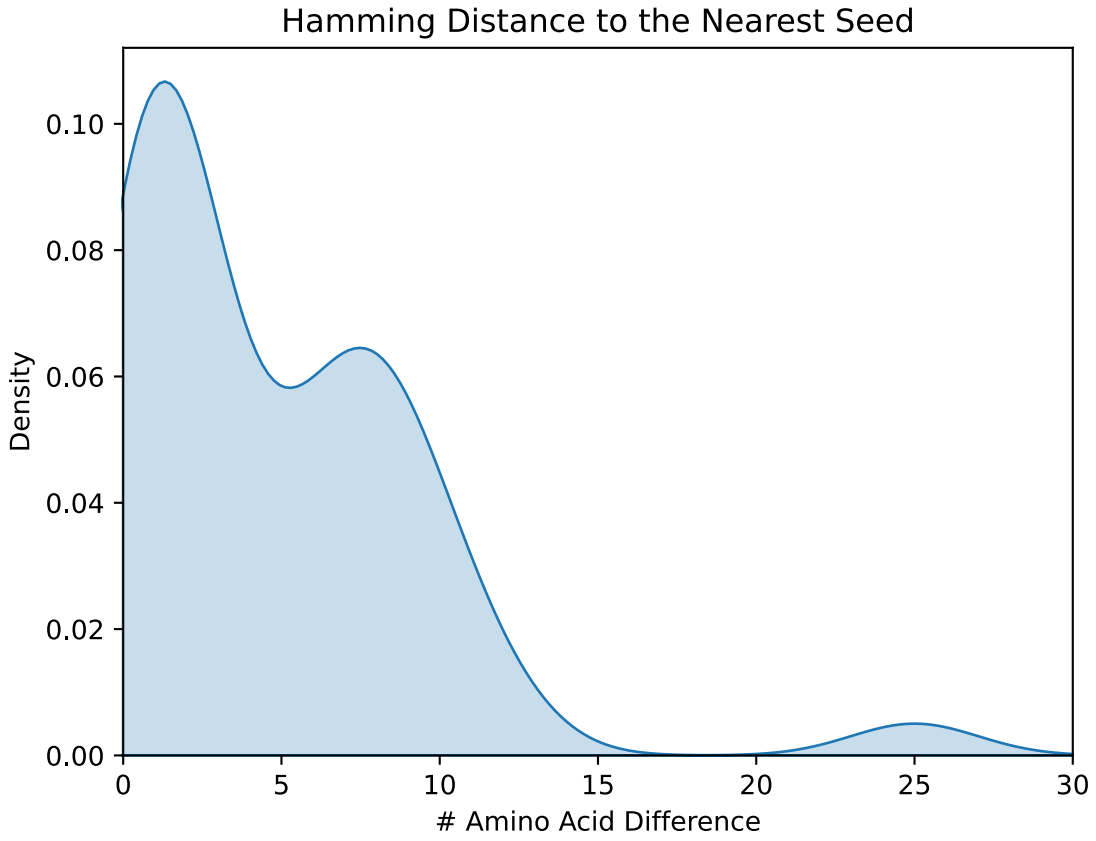
New Insights from OmniDeep™



- Prioritize clones within standard lineage definitions
- Found 70 pM clone (10x seed affinity)



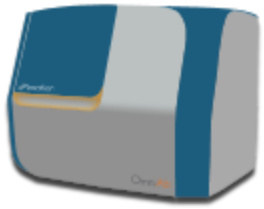
- Identifies new non-obvious clones in other lineages



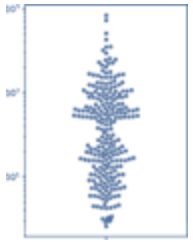
Deep learning provides new non-obvious insights for partners

OmniDeep™ Leverages Deep Learning

High-Quality Input Data



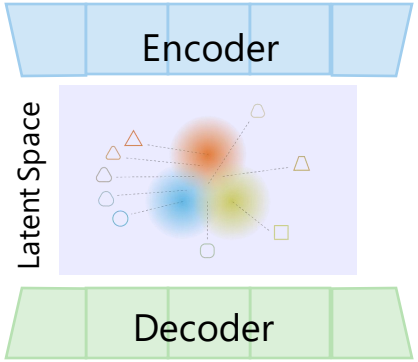
xPloration hits



Assay data

Animal NGS data

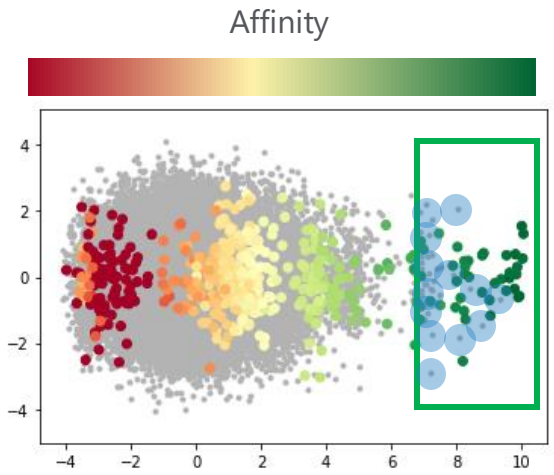
Deep Learning Model



Variational Autoencoder (VAE) :

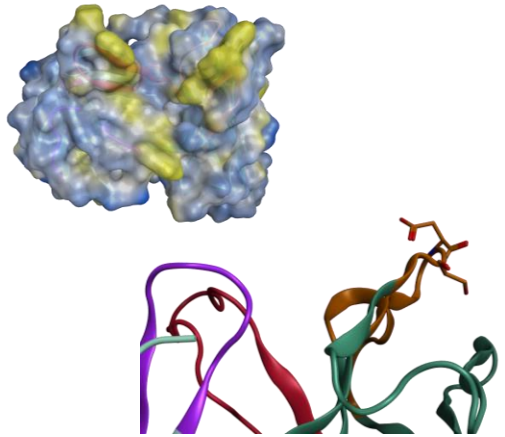
- Extends insights from confirmed hits to infer function of untested clones

New Suggested Hits



Suggested antibodies highlighted in light blue

in Silico Developability Filter



Structure-based method:

- Provides cost and time efficient filtering for the most promising clones based on predicted properties

AI suggests additional high affinity and developable antibody sequences

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The OmniAb Technology Offering is Expanding

TECHNOLOGY OFFERING ADDRESSES THE MOST CRITICAL CHALLENGES OF ANTIBODY DISCOVERY

Technologies

Create

Create Diverse Repertoires of High-Quality Antibodies

Computational Antigen Design & Proprietary Reagents

OmniRat® OmniChicken® OmniMouse®

Robust Antibodies for Any Target

OmniFlic® OmniClic®

Bispecific Antibody Generation

OmnidAb® OmniTaur®

Novel Scaffolds

Screen

Screen Millions of Cells to Find Potential Therapeutic Candidates

xPloration®

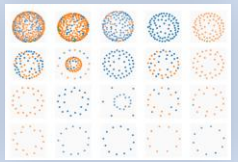
High-Throughput Single Cell Screening

Gel Encapsulated Microenvironment (GEM) Single Cell Screening

Deliver

Further Characterize, Select and Optimize the Right Antibody

- *Custom Bioinformatics*
- *Next Generation Sequencing (NGS) Hit Expansion*



- *Comprehensive Functional Characterization*

ICAGEN® ION CHANNEL TECHNOLOGY

- *Proprietary Ion Channel Assays*

- *STR: Fc-Silencing Technology**

STR

OmniDeep™ *Suite of in silico tools for discovery and optimization that are woven throughout our various technologies and capabilities. Includes structural modeling, large multi-species antibody databases, molecular dynamics simulations, AI, and machine and deep learning sequence models, and more*

*OmniAb entered into an agreement with mAbsolve Ltd. for STR, mAbsolve's Fc-silencing platform technology, which provides OmniAb with exclusive, sublicensable right to incorporate the STR technology with antibodies that have been generated using OmniAb's antibody discovery platform.

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