OmniAb®

Deep Screening in Harmony with AI for Bispecific Antibody Discovery

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Sr. Director, Discovery Systems

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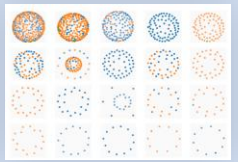
The OmniAb Technology Offering is Expanding

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* • *Proprietary Ion Channel Assays* ICAGEN® ION CHANNEL TECHNOLOGY
OmniFlic® OmniClic® *Bispecific Antibody Generation*		• *STR: Fc-Silencing Technology** STR®
OmnidAb® OmniTaur® *Novel Scaffolds*		

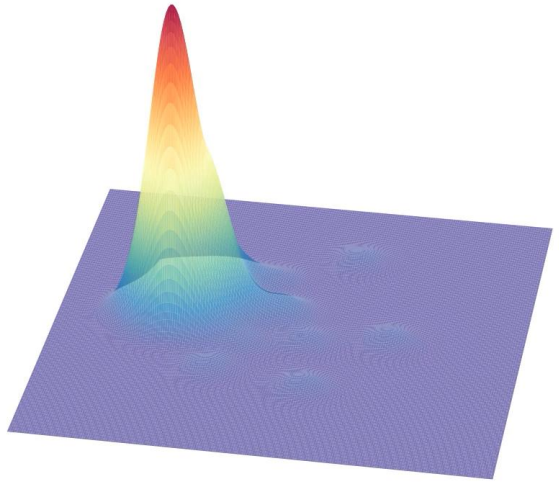
OmniDeep® *Suite of in silico tools for discovery and optimization that are woven throughout our various technologies and capabilities. Includes structural modeling, large multi-species antibody databases, molecular dynamics simulations, AI, and machine and deep learning sequence models, and more*

*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.

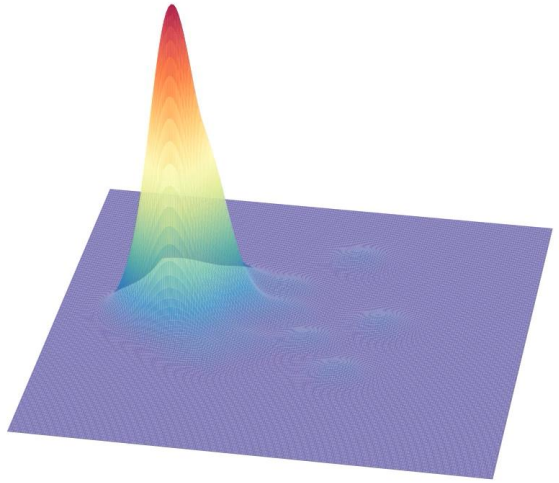
Custom Antibody Repertoires for Every Target

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

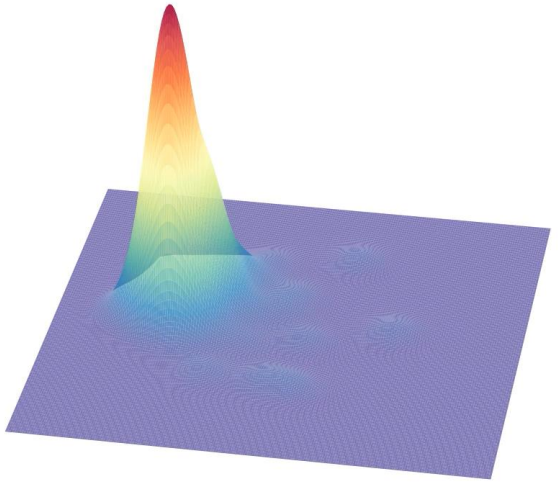
Animal 1:
Protein
immunization



Animal 2:
Peptide
immunization



Animal 3:
mRNA
immunization



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

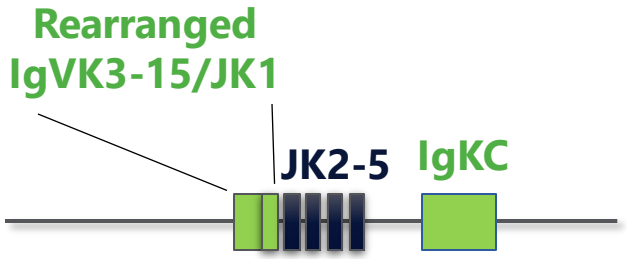
OmniAb Antibody Repertoires

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

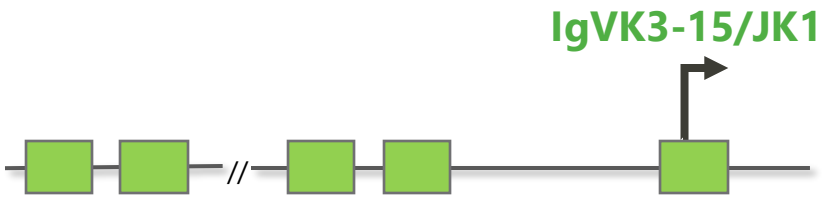
OmniAb's Common Light Chain Platforms

OmniFlic™

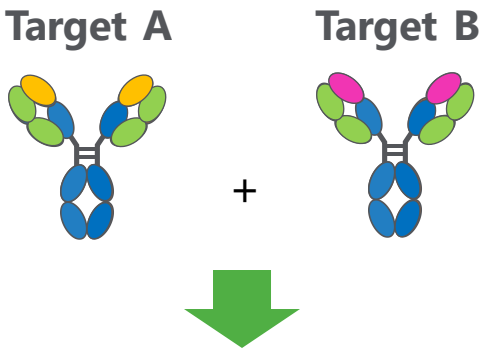


Fixed human VK3-15 light chain expressed with diversifying heavy chain from *any* human germline (44 VHs)

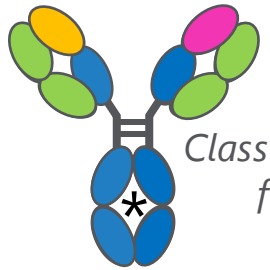
OmniClic®



Fixed human VK3-15 light chain combined with diversifying heavy chain on single scaffold (VH3-23) for superior developability



Facile reformatting via Knob-in-Hole or other Fc-mutations that drive Fc heterodimerization



*Classical IgG-like format**

Bispecific

Classical IgG format may de-risk downstream development of bispecifics
Gera, Expert Opin Biol Ther. 2022

OmniFlic® & OmniClic® enable IgG-like asymmetric formats

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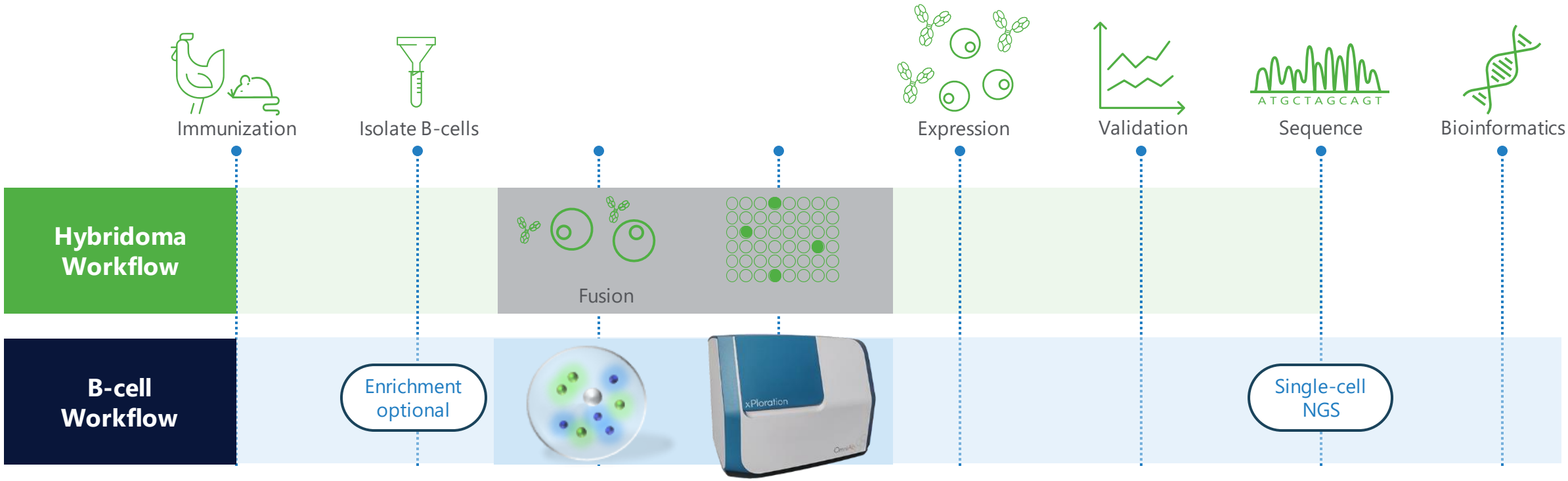
Deep Screening Platforms



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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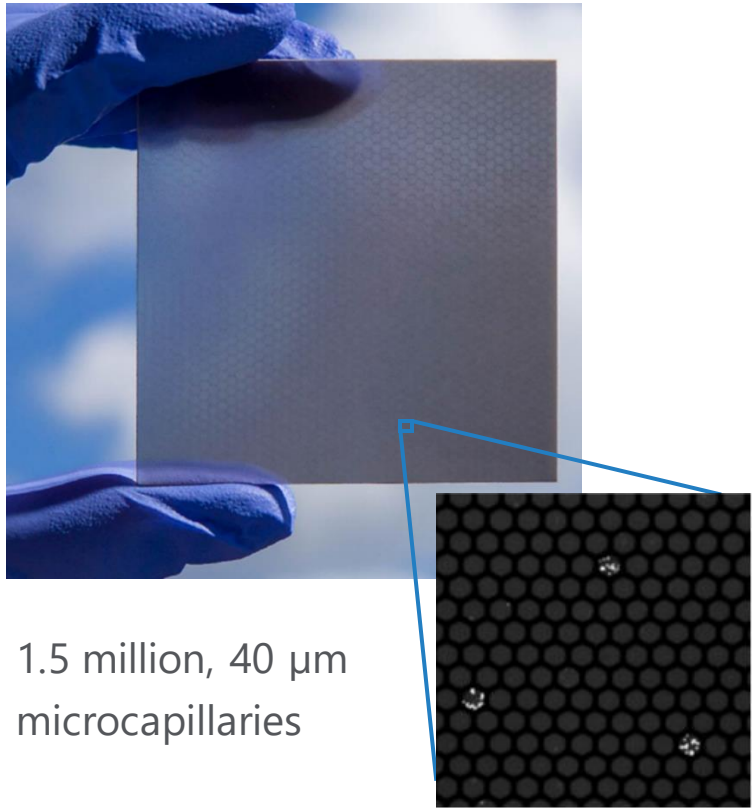
xPloration®: AI-Driven Deep Functional Screening

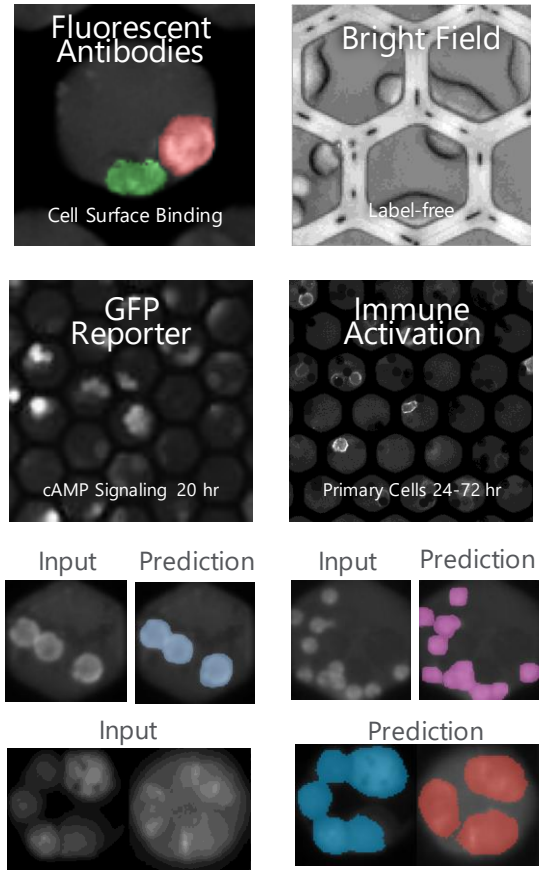
1 | Loading



1.5 million, 40 µm microcapillaries

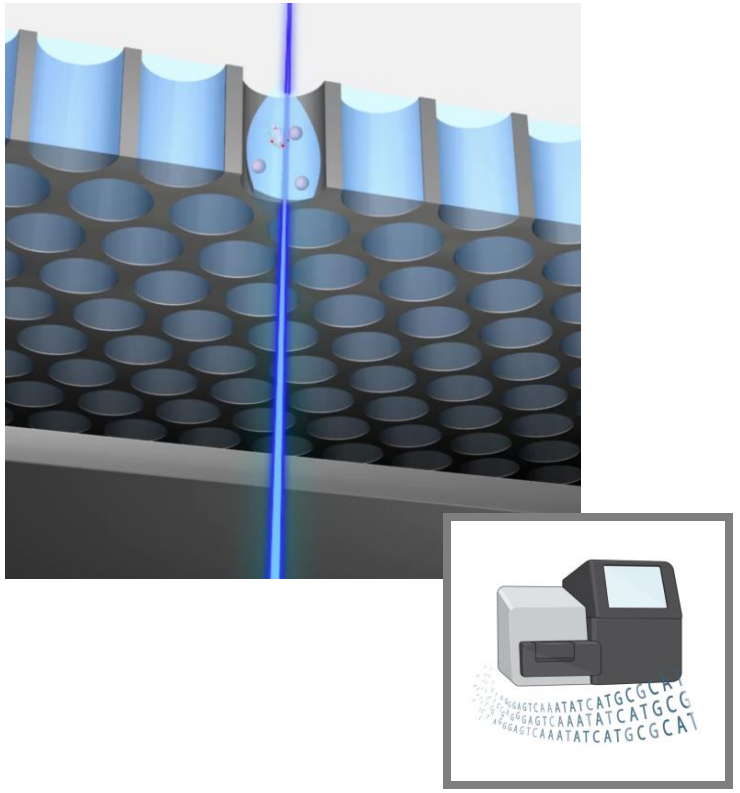
Unique through-hole format

2 | Assay + Machine Vision



Machine vision hit detection

3 | Recovery & Single-Cell NGS



Precise laser-based recovery

Single-cell barcoding or pooled

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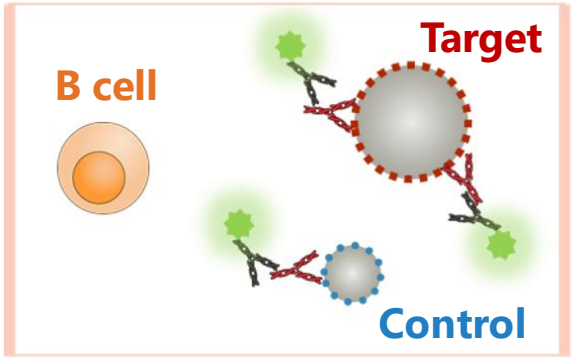
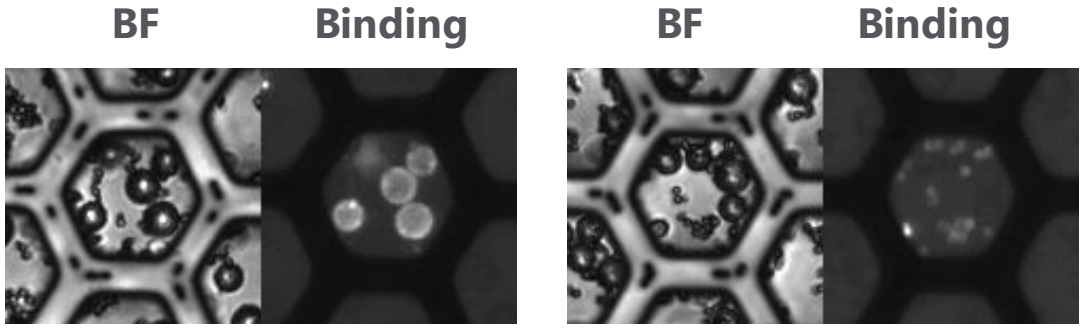
Multi-Parameter Screening: Multiplex Phenotypic Data

Selective binding of target on beads

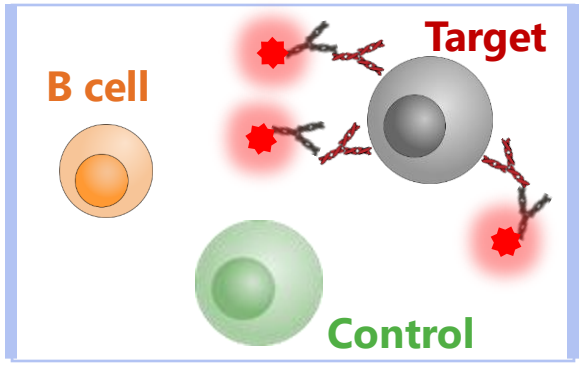


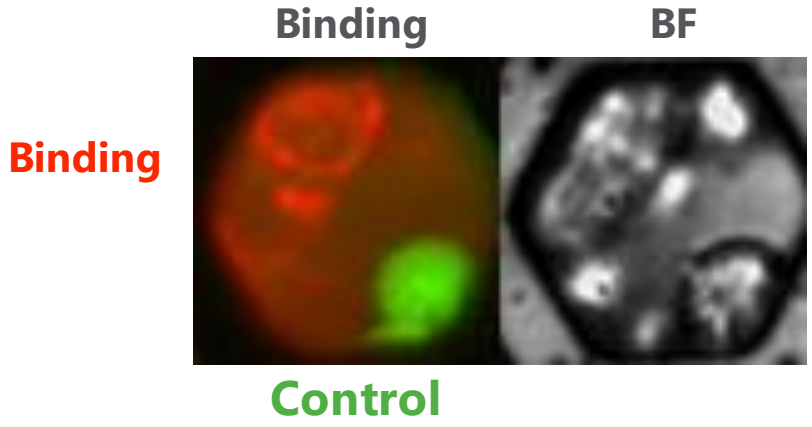


Binding to Target

Binding to Control

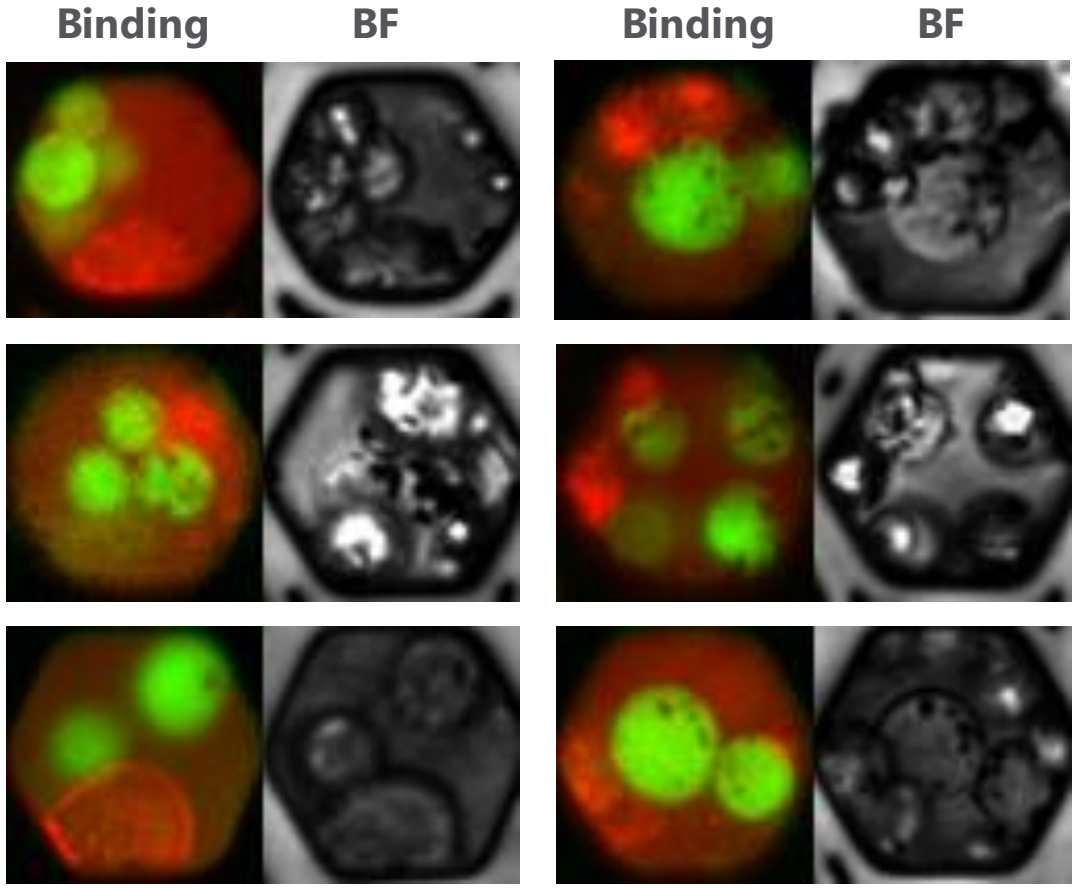
Selective binding of target cell

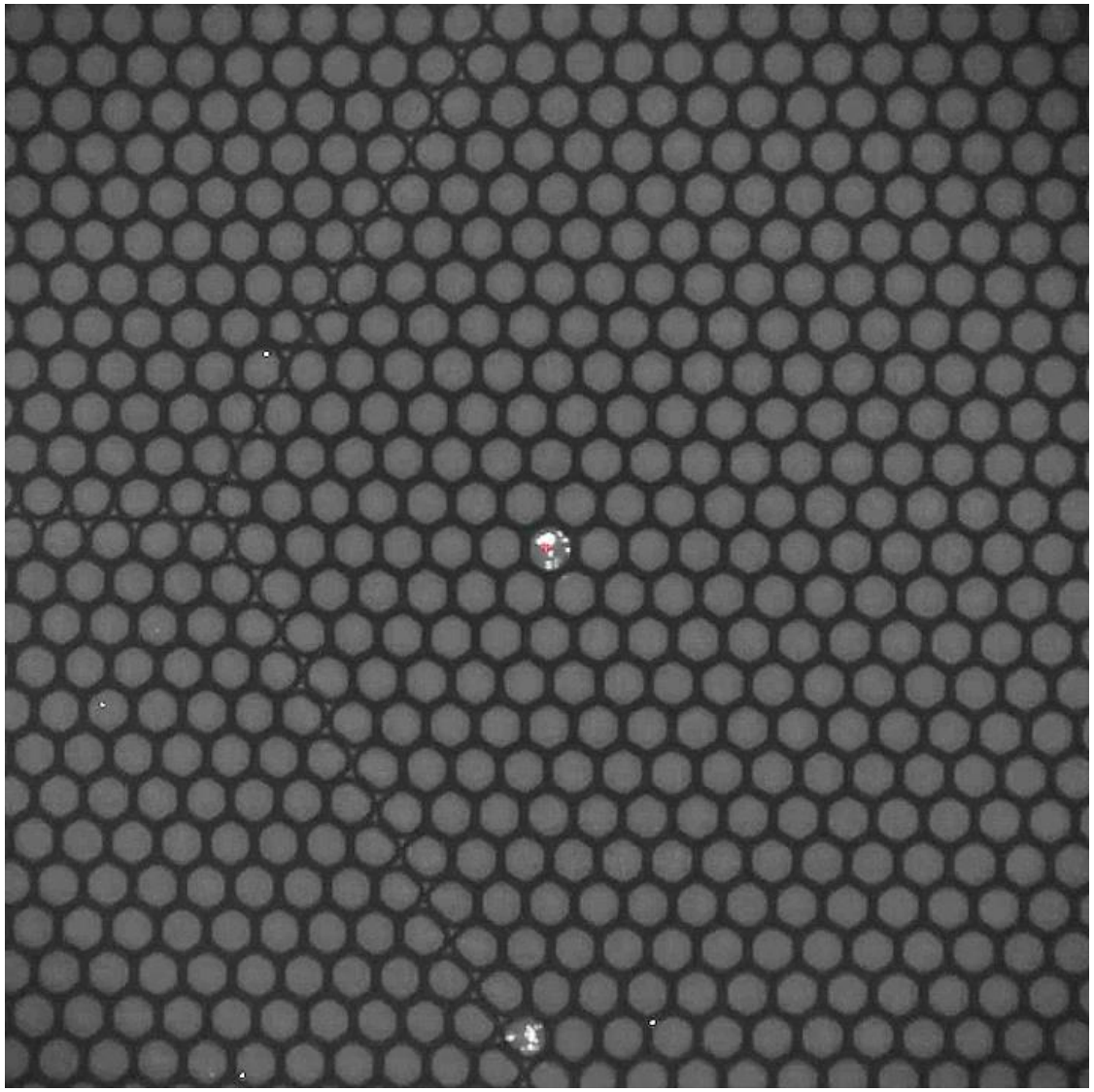




Rapid Laser Recovery of Hits

Example target cell specific hits





1x speed video of laser recovery

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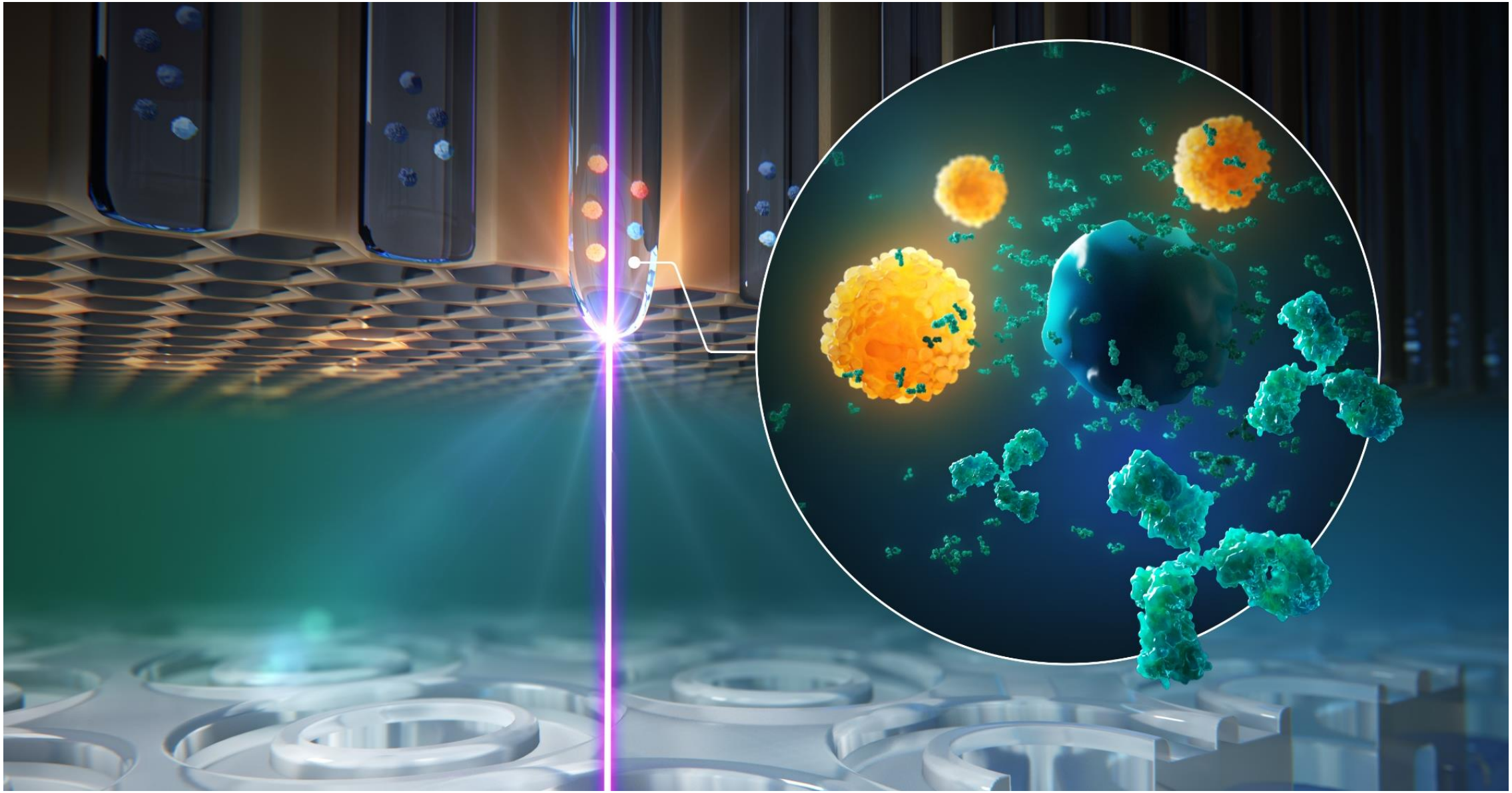


OmniAb®

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
- Potential target for a NK cell engager

From PDB 6IAP

Discover anti-NKp46 antibodies using OmniFlic and OmniClic for bispecific antibody

OmniDeep® Empowers Large-Scale Antibody Discovery

OmniDeep®

Biological Intelligence™

\+

xPloration®

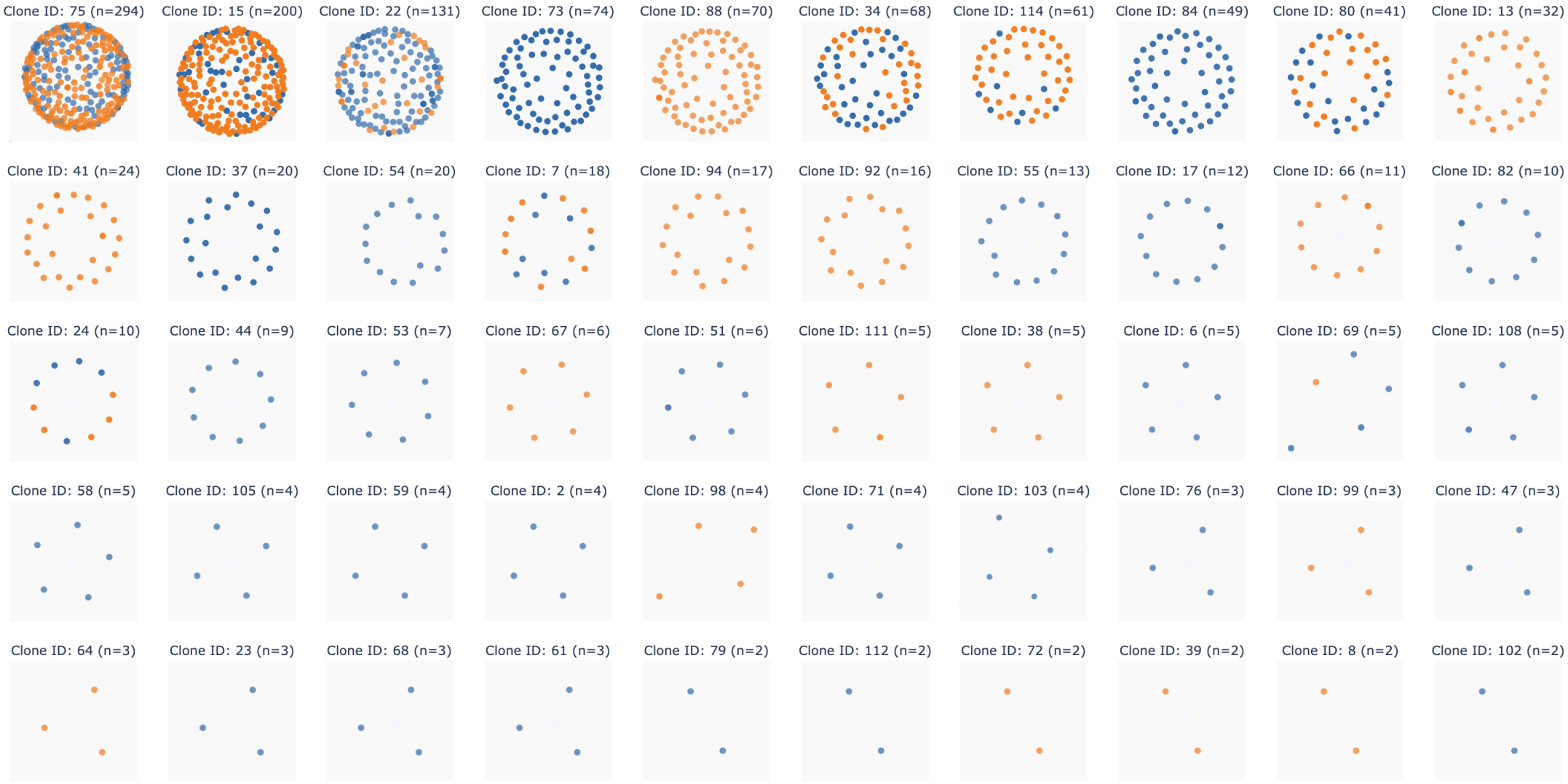
OmniFlic® Screening Summary

	Screen Type	# Cells Screened	# Hits
1	Antigen on beads	5 M	1429
	Cells	7.7 M	345
2	Antigen on beads	3.7 M	751
	Cells	3.7 M	158
3	Antigen on beads	3.7 M	308
	Cells	3.7 M	33
	Total	**27.5 M**	**3024**

Processed with pooled NGS sequencing for **1375 unique sequences**

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

OmniFlic® Repertoire Space



● Bead screen ● Cell screen

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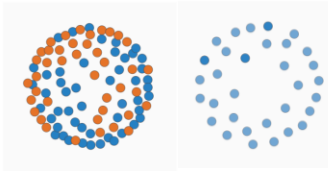
Bioinformatics-Aided Antibody Selection

Activity profile

Profile 1:
Cell + Protein binder

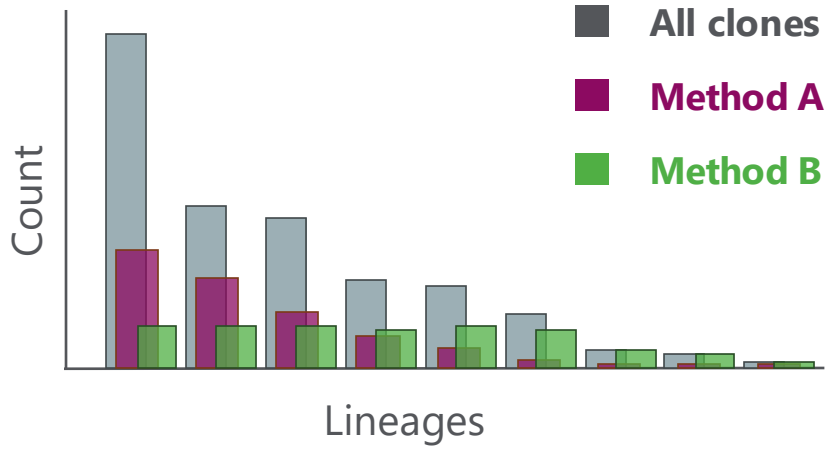
Profile 2:
All Cell binders



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

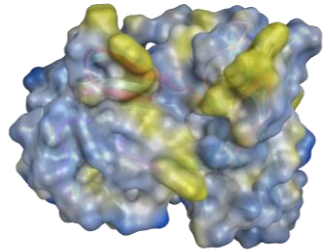
Sequences

↓

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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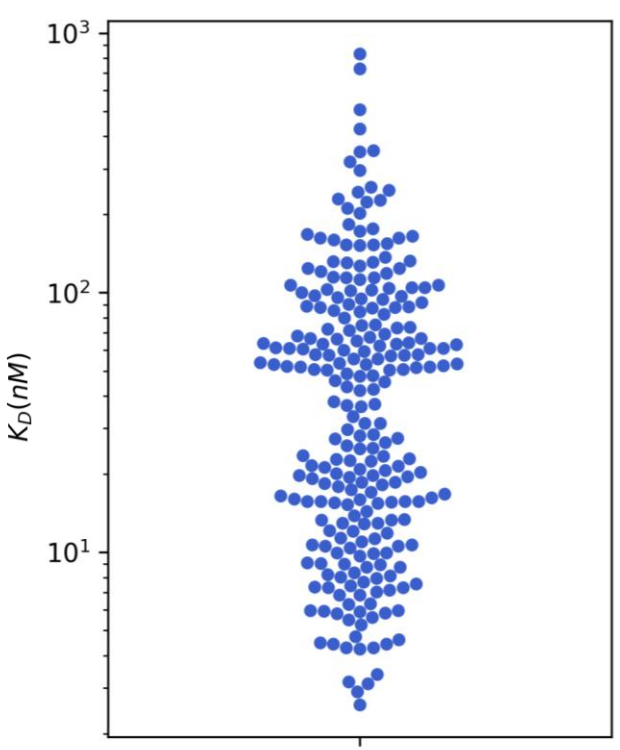
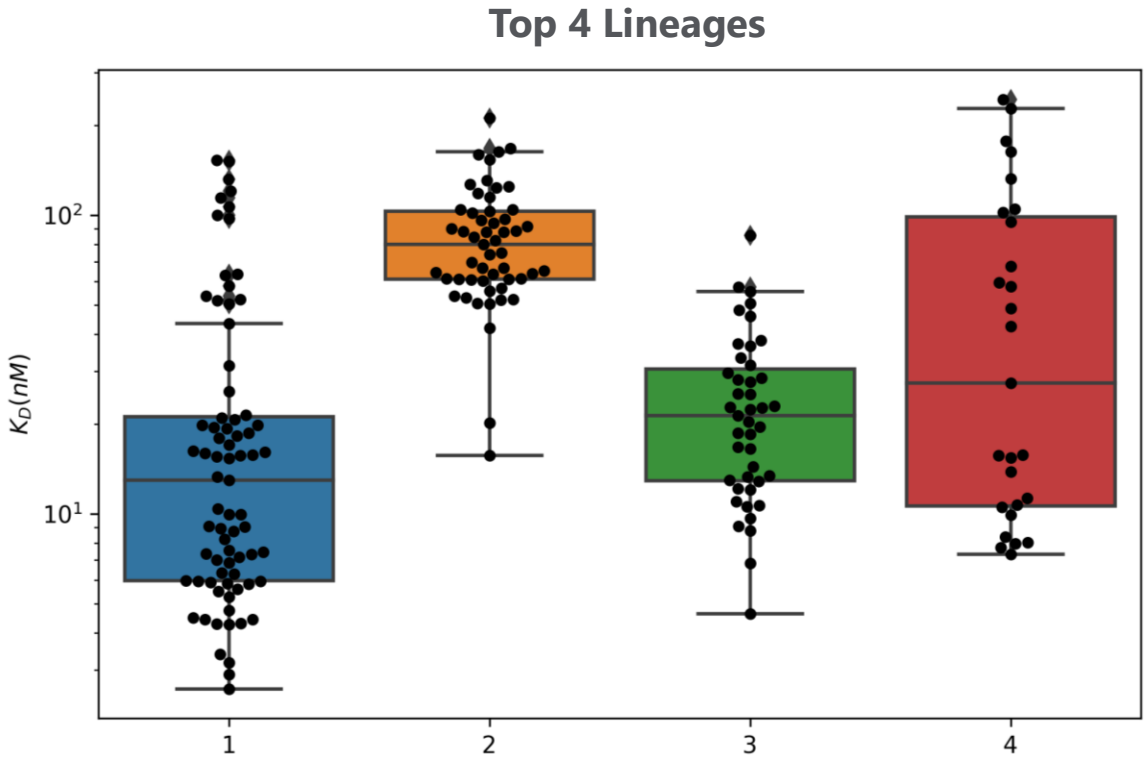
Discovery of High Affinity NKp46 Binders

# Selected Clones	Expression (%)	Binding (%)	<10 nM (%)
301	95.7	84.7	20.1





xPloration® OmniFlic campaigns are available to partners

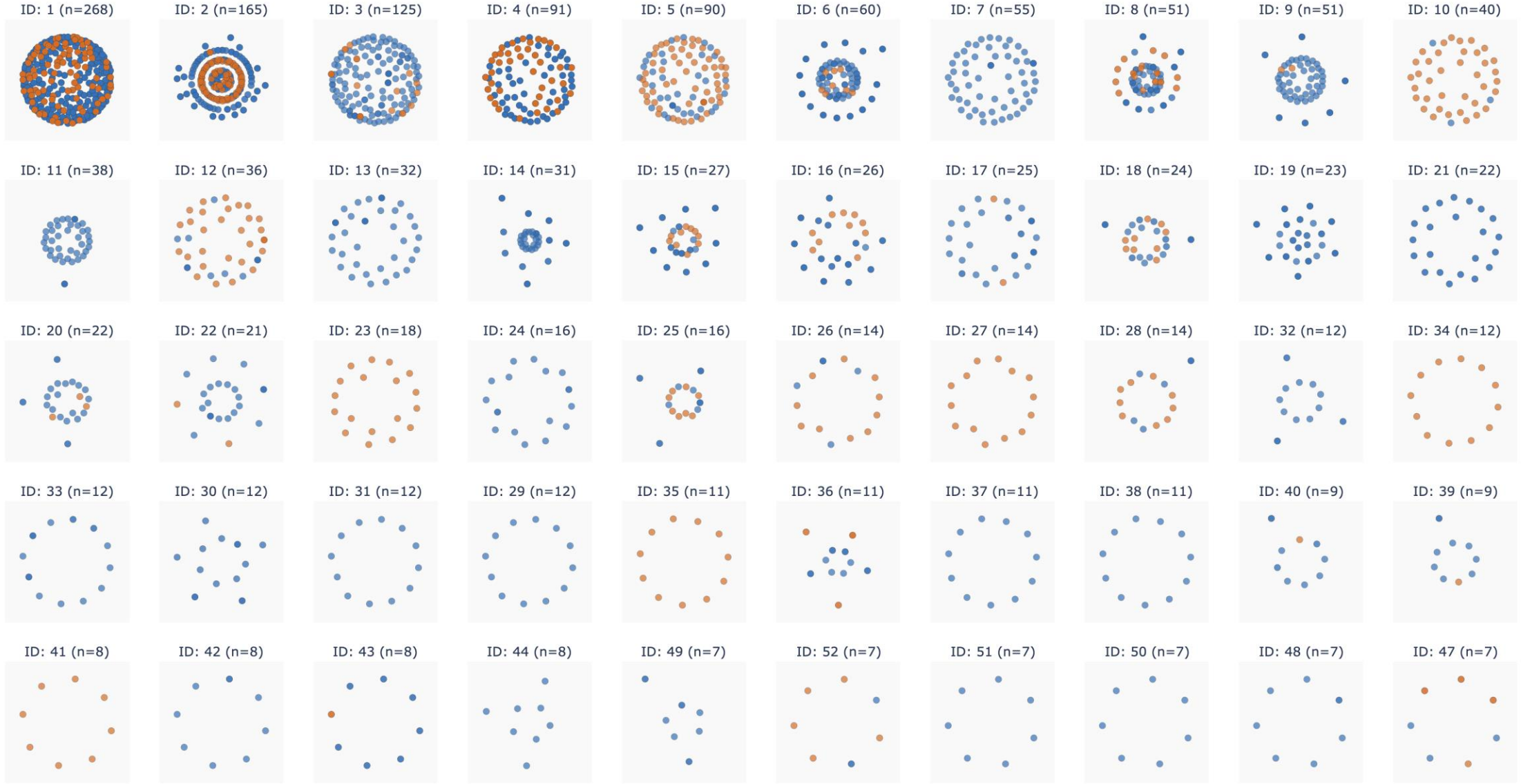
OmniClic® Screening Summary

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



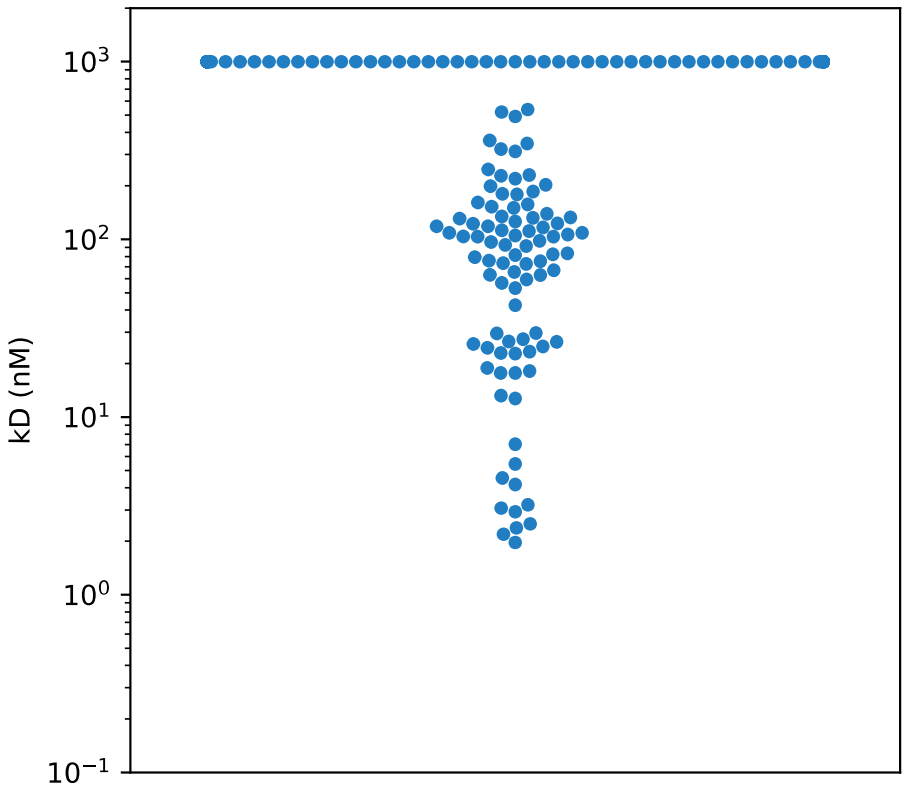
● Bead screen ● Cell screen

OmniAb

Discovery of NKp46 Binders

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

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



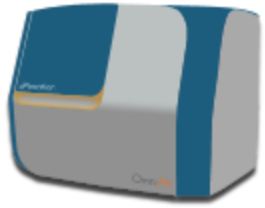
Can we employ deep learning to increase yield and affinity?

Integrating Biological Intelligence™ with AI

IN SILICO TOOLS TO BETTER MINE DIVERSE IMMUNE REPERTOIRES

Biological Intelligence™

Deep Screening + Deep Sequencing

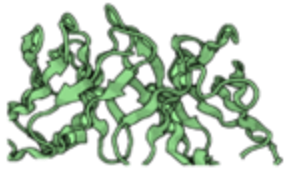


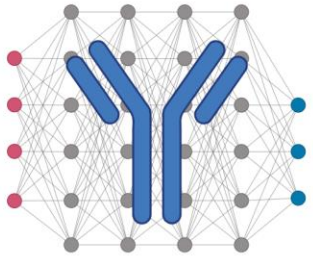
Large-scale data collection

Proprietary Databases

Multi-species databases

Deep Learning Models





Structure-Based Design Tools

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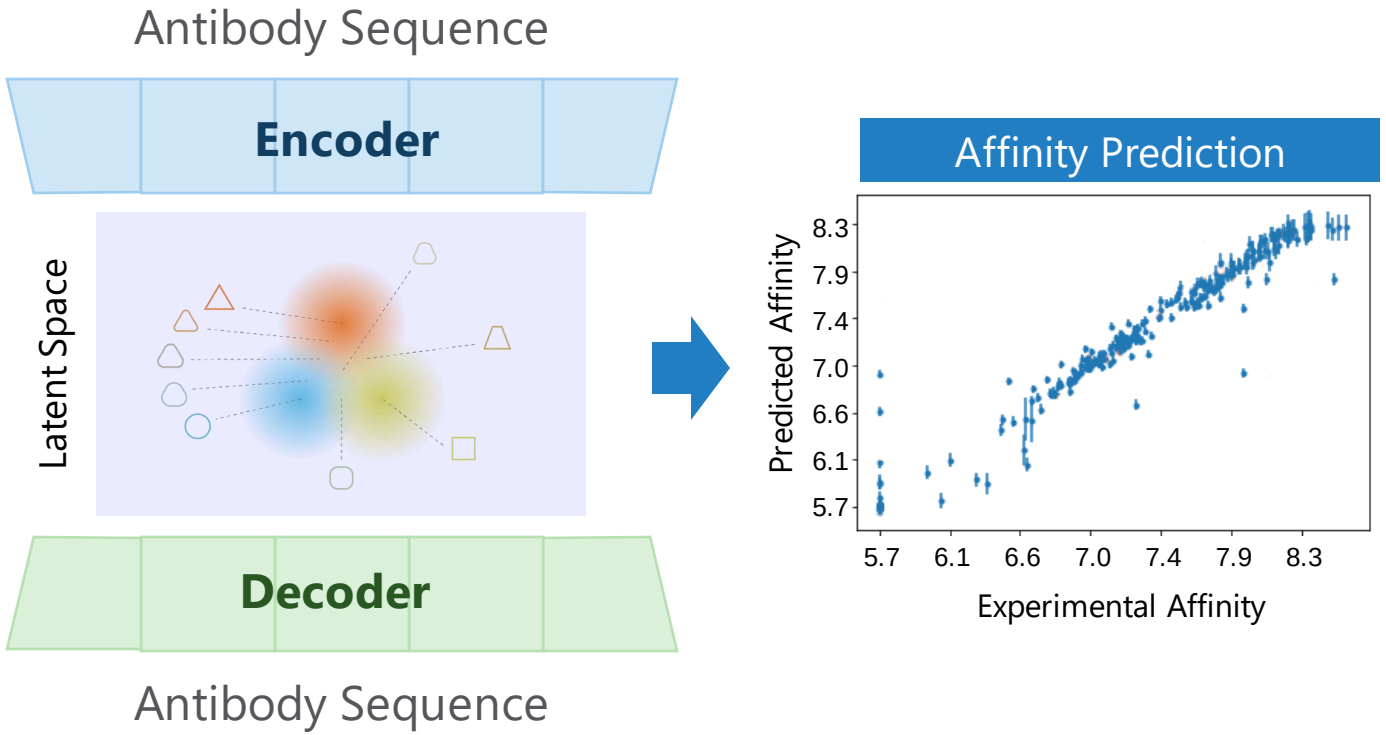
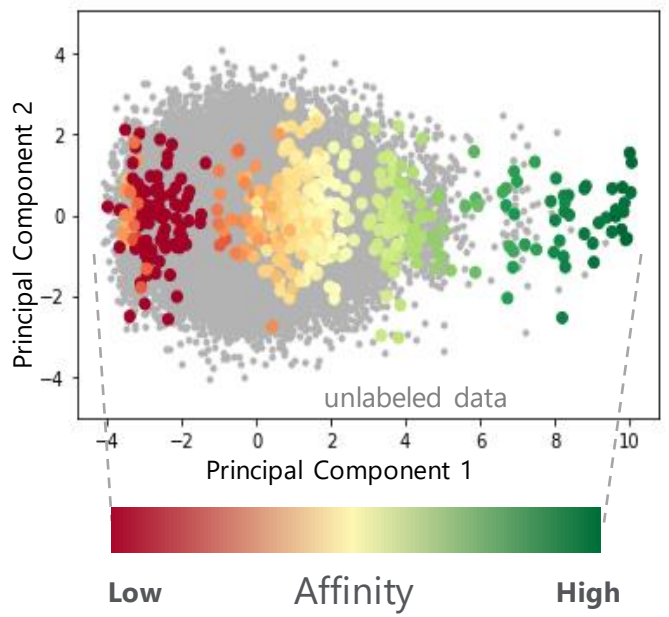
Encoding Sequence Space with Deep Learning

Variational Autoencoder (VAE) Model



Encoded Antibody Space



Property prediction organizes model space according to affinity

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

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Active Learning for Clone Selection

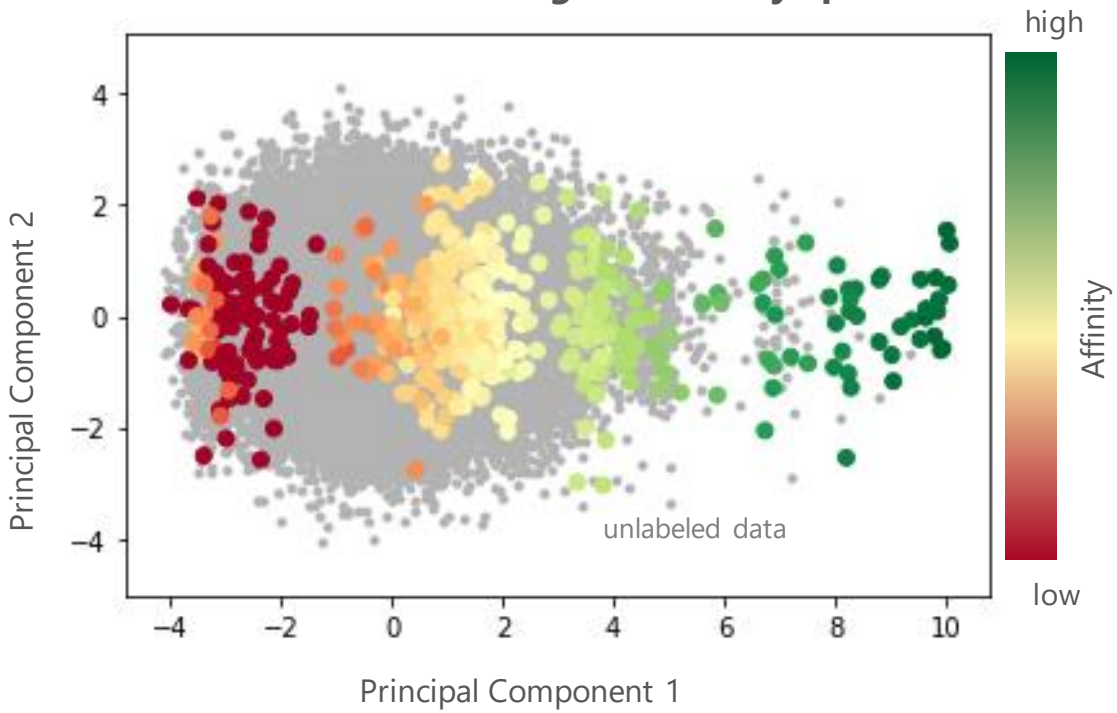
- **Active Learning**
  - Uncertainty estimates drive novel region exploration
  - Most efficient learning of predictive models
  - Statistically driven exploration of sequence space

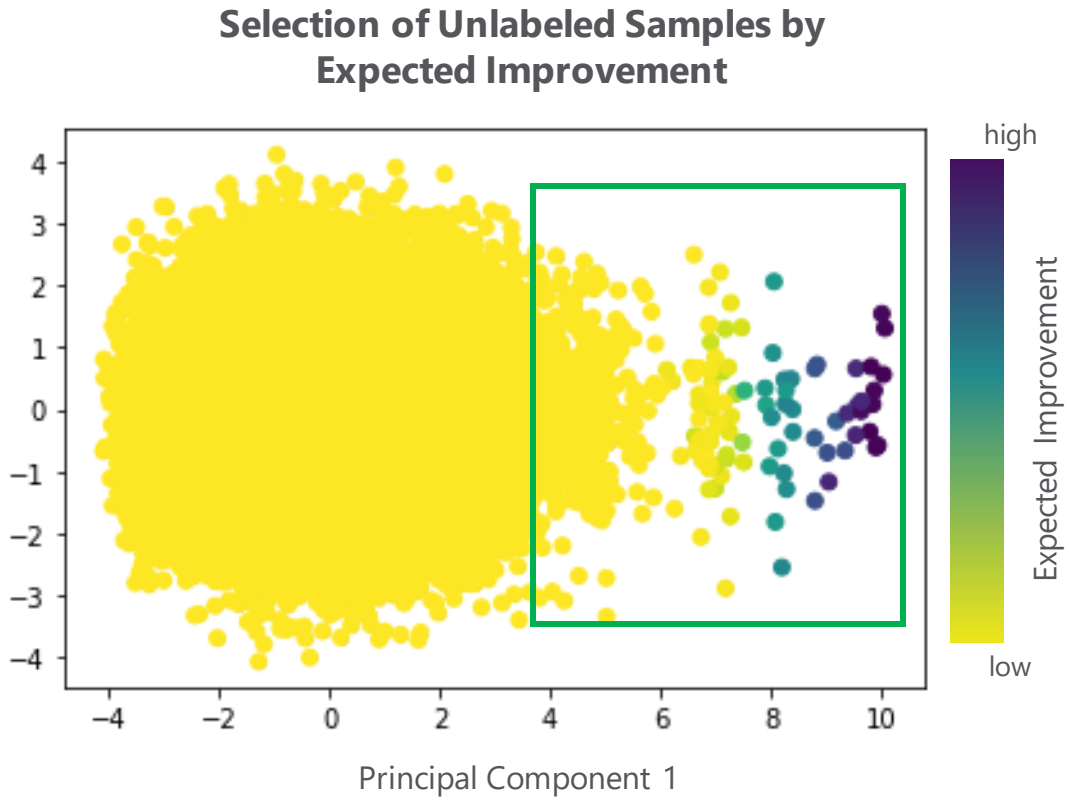
- Iterations between deep learning and experiment
- Expected Improvement
  - Bayesian optimization acquisition function
    - Mathematical formulation guiding the selection of new samples
  - Function that has inputs of
    - Estimated mean (μ)
    - Estimated standard deviation (σ)
    - Current observed maximum (s_{max})

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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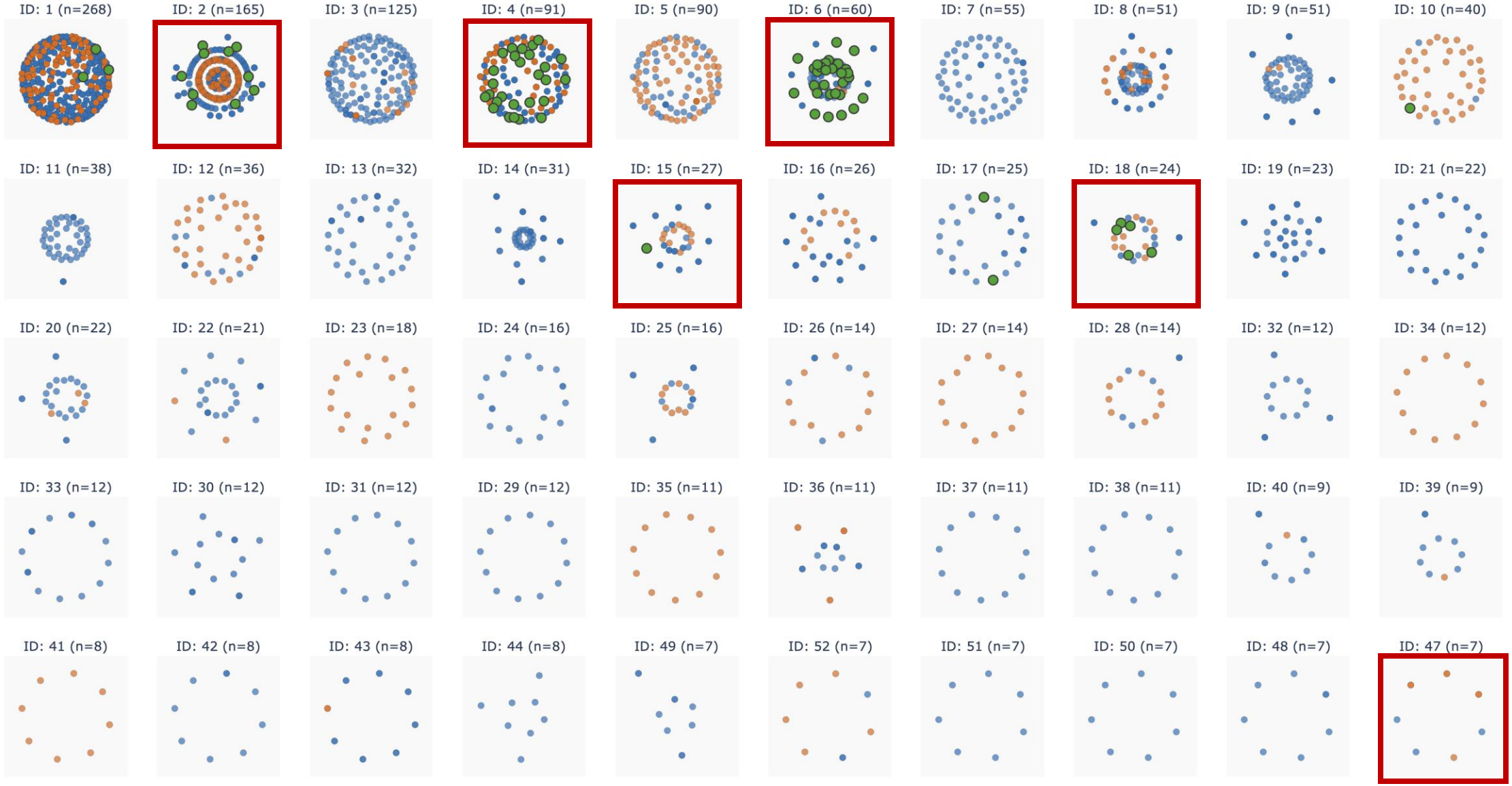
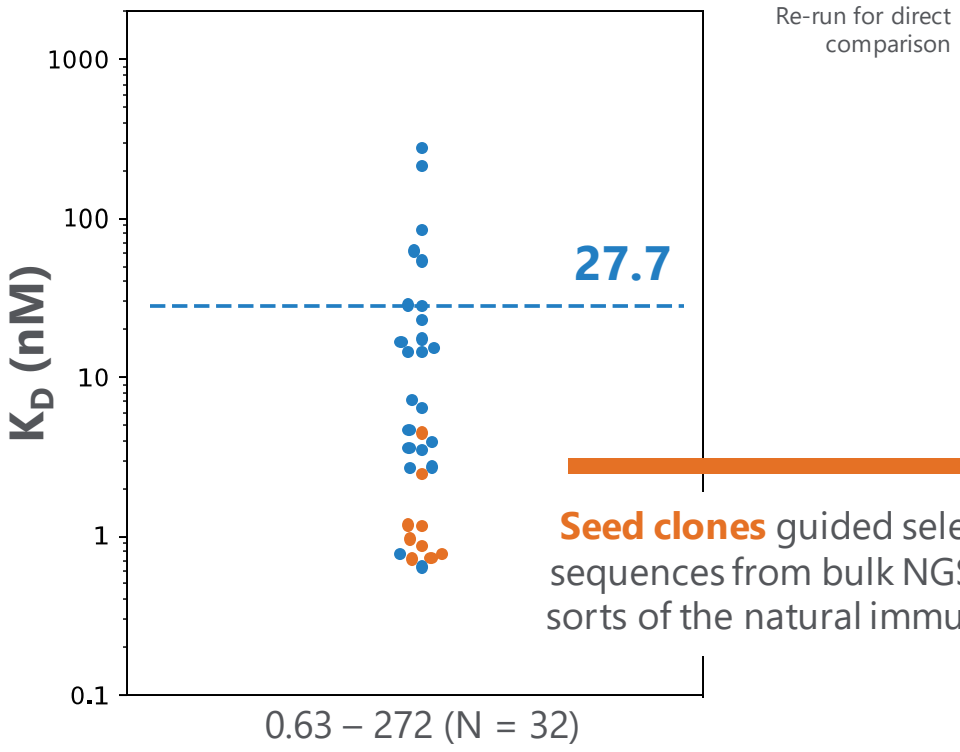
VAE Highlight New Clones to Characterize



● VAE Selected ☐ Seed ● Bead screen ● Cell screen

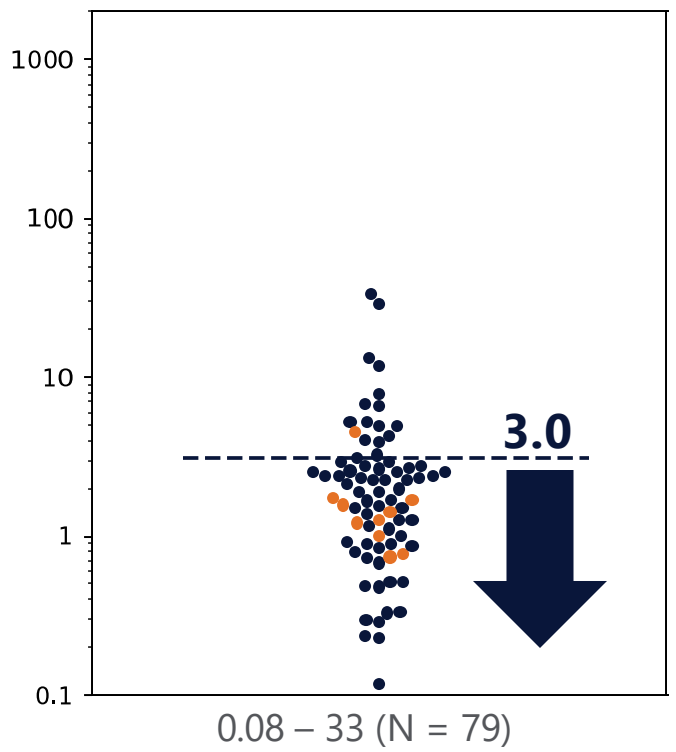
OmniDeep® Successfully Selected High Affinity Clones

Initial selection



Seed clones guided selections of new sequences from bulk NGS & xPloration sorts of the natural immune repertoires

OmniDeep selection

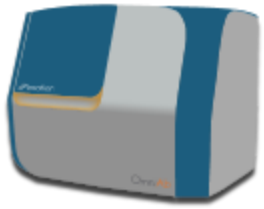


Successfully found additional unique clones at 91% rate with ~10x improvement in mean affinity

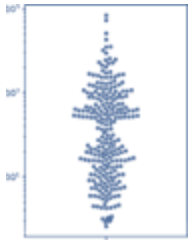
OmniAb

OmniDeep® Leverages Deep Learning

High-Quality Input Data



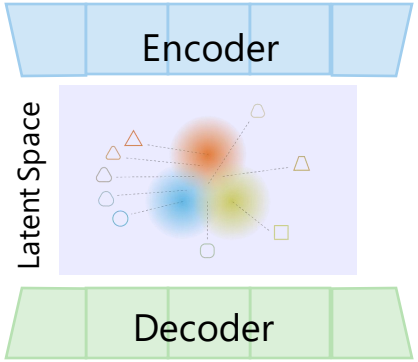
xPloration hits



Assay data

Animal NGS data

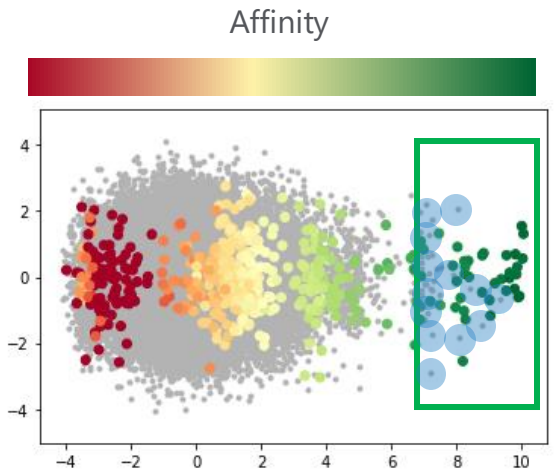
Deep Learning Model



Variational Autoencoder (VAE) :

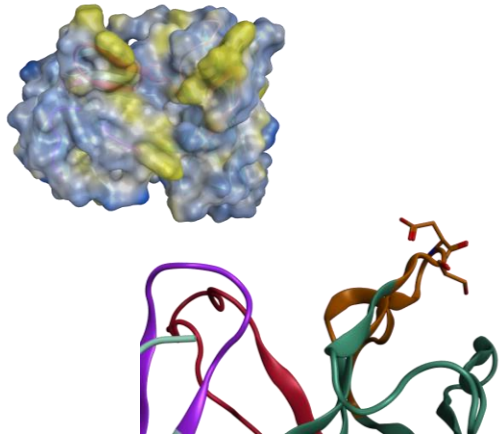
- Extends insights from confirmed hits to infer function of untested clones

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

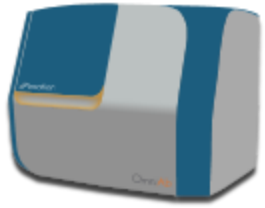
OmniAb

Integrating Biological Intelligence™ with AI

IN SILICO TOOLS TO BETTER MINE DIVERSE IMMUNE REPERTOIRES

Biological Intelligence™

Deep Screening + Deep Sequencing



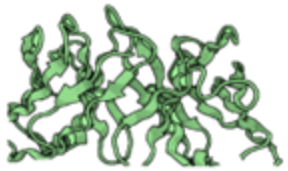
Large-scale data collection

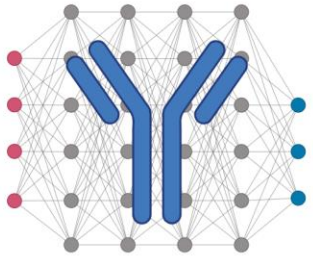
Proprietary Databases

Multi-species databases

Structure-Based Design Tools

Deep Learning Models





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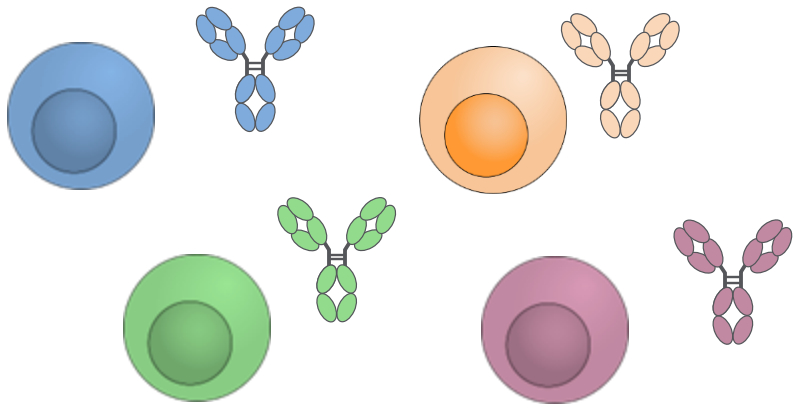
Mammalian Secretion Libraries and xPloration®

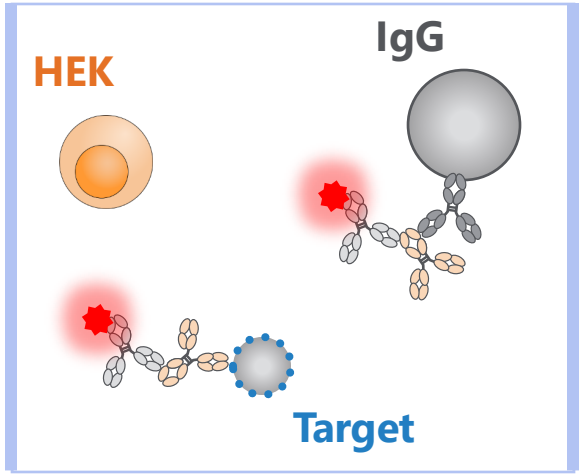
EMPOWERING LARGE-SCALE HIGH-QUALITY EVALUATION OF SEQUENCES

Library Design



- One library variant per cell: phenotype/genotype linkage
- Secretion rate comparable to native B cells

Selection Assay



- Assay detects secretion of IgG and binding of target
- Enables sorting of binding sequences and non-binding sequences

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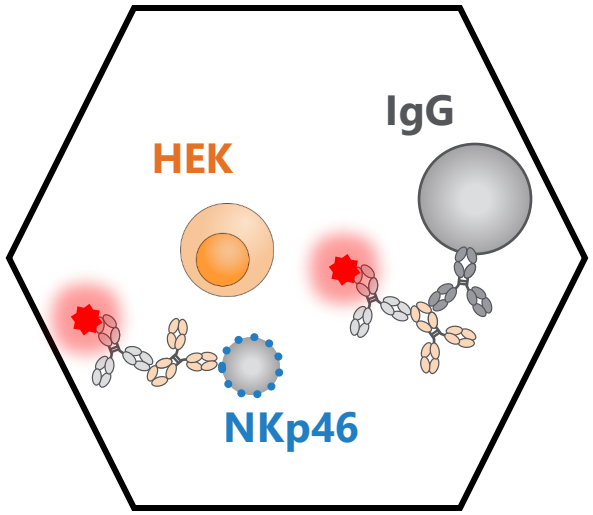
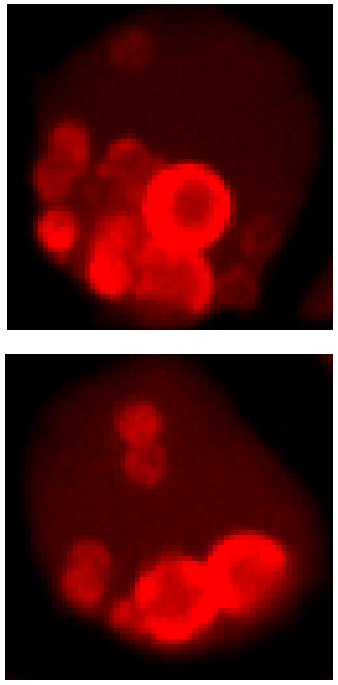
Mammalian Library Sort

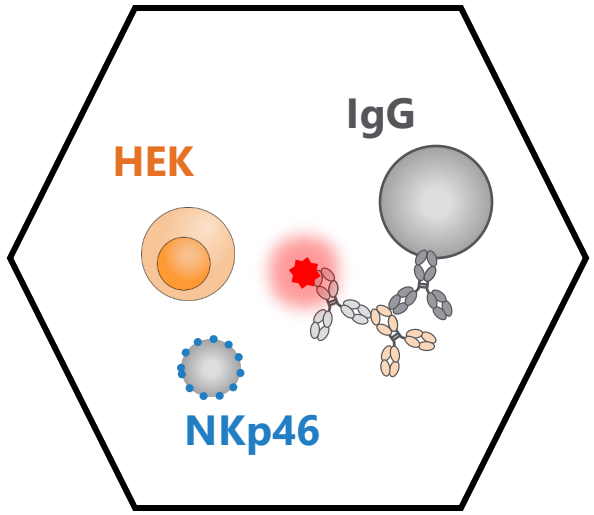
POSITIVE AND NEGATIVE DATA FOR ML MODELS

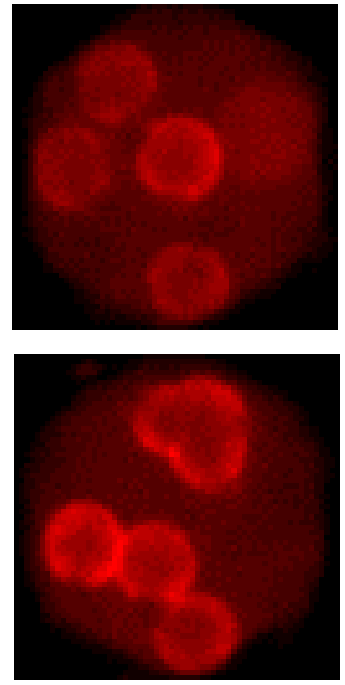
NKp46 Positive





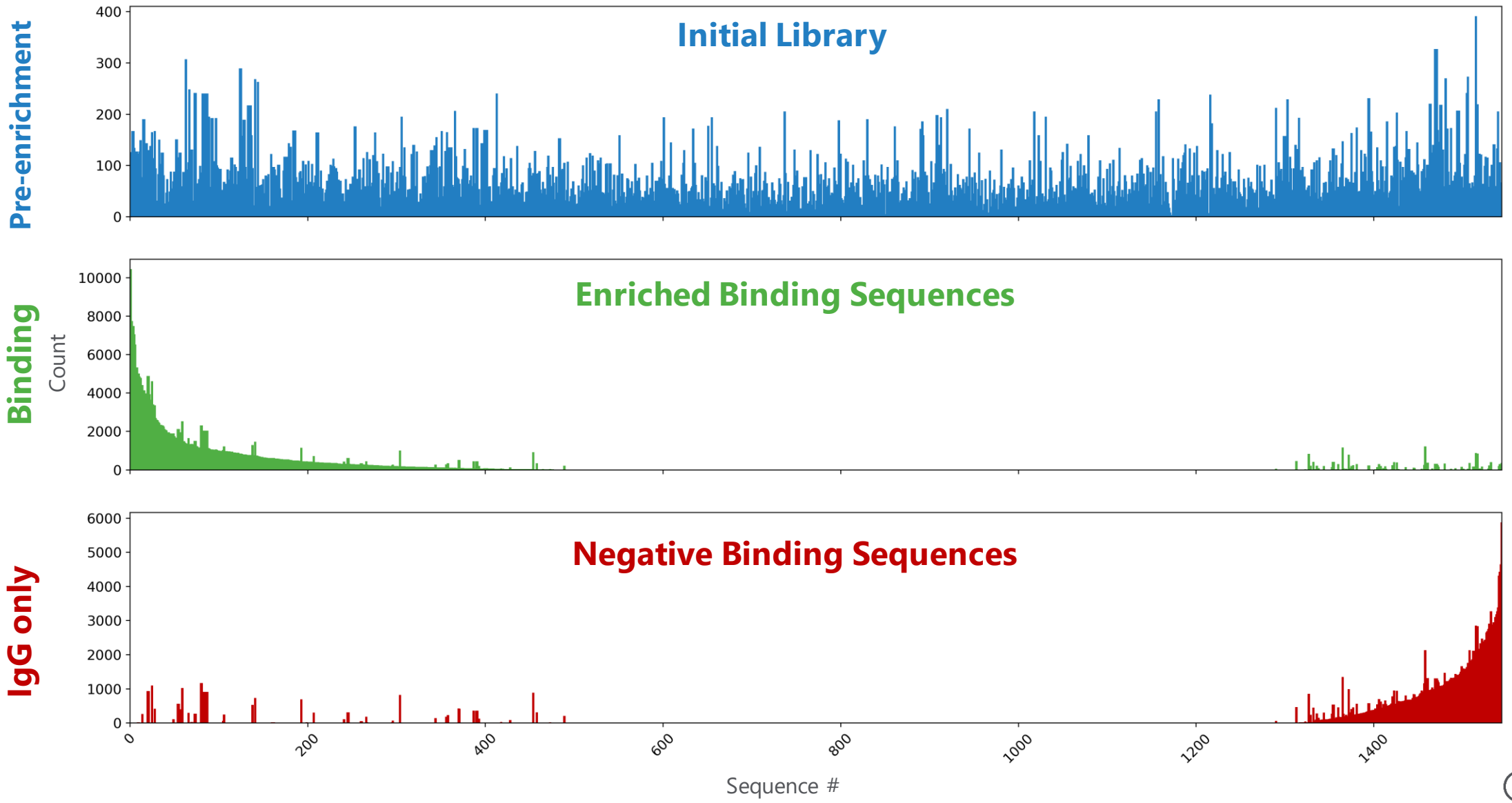
NKp46 Negative





Successfully evaluated ~1500 selections and sorted for positive and negative binding sequences

xPloration® Sorting Enriches Binders/Non-binders



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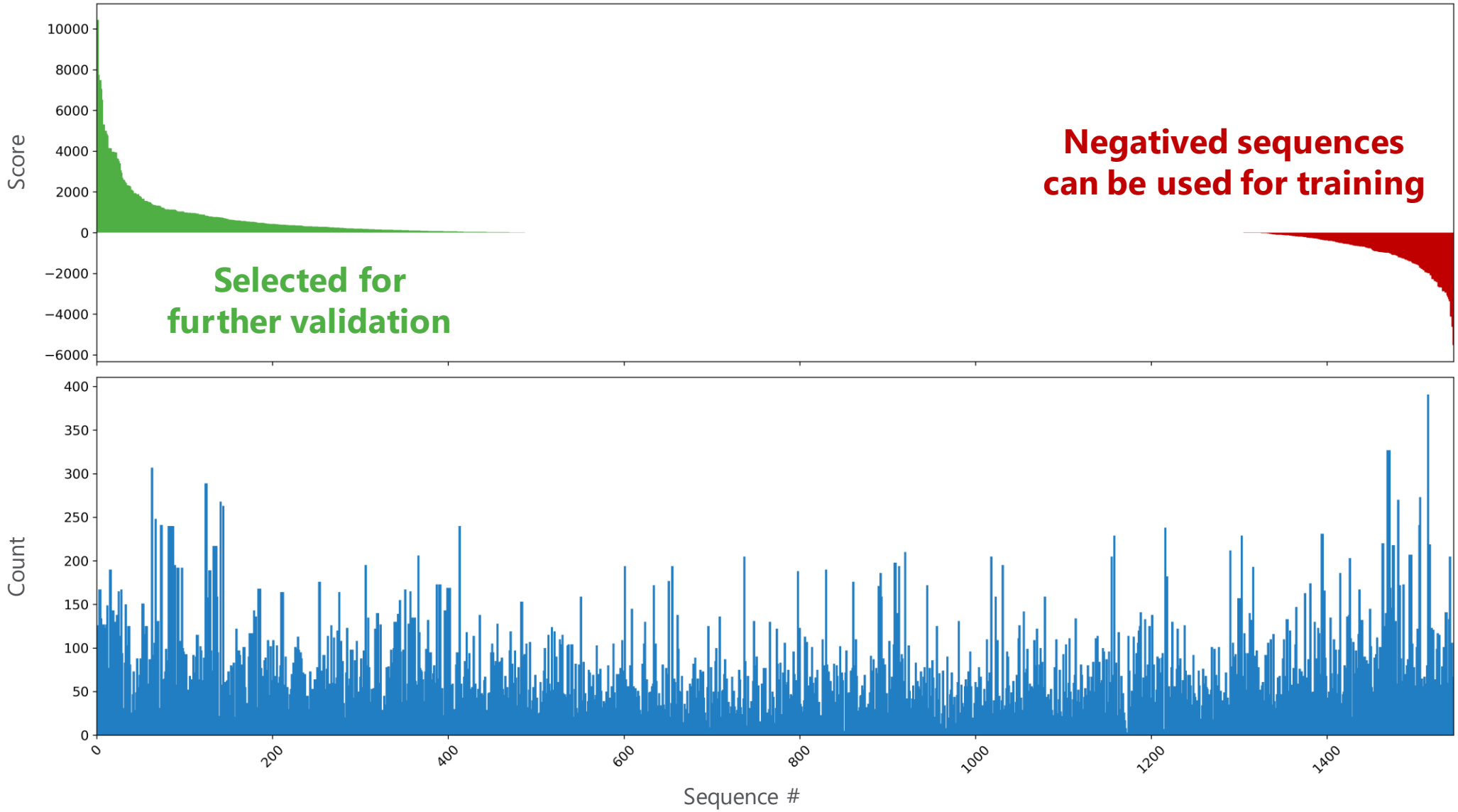
Scoring Sequences for Selection and Model Training

SCORE = POSITIVE COUNTS – NEGATIVE COUNTS



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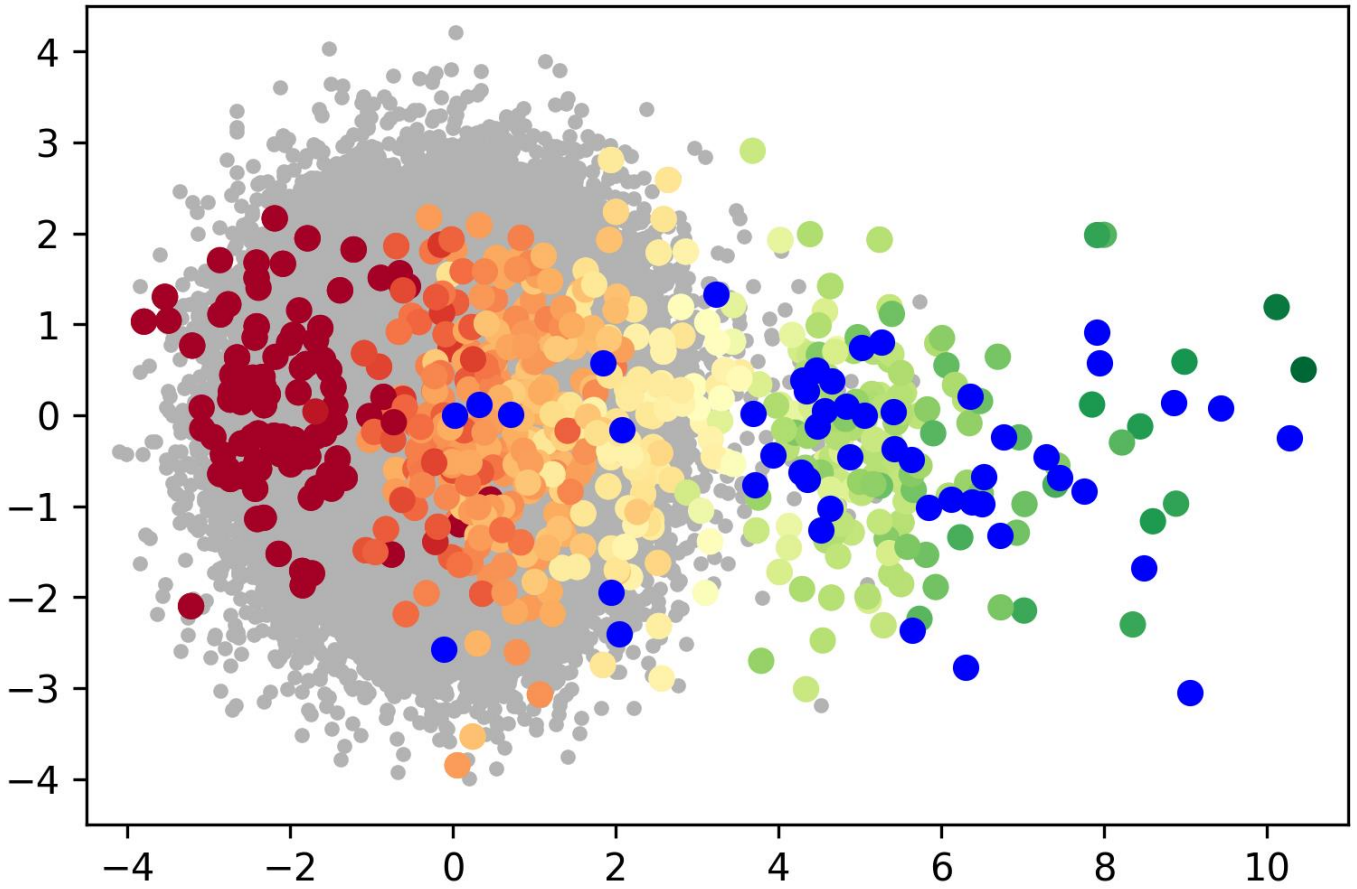
Next Active Learning Cycle Empowered by xPloration®

Round 2 Selection



Efficient guided evaluation of repertoire space for high affinity sequences

Deep Screening in Harmony with AI

xPloration® enables large-scale data collection from Biological Intelligence for training OmniDeep™ models

xPloration facilitates efficient evaluation of AI selections from OmniAb immune repertoires

Synergy between OmniFlic® and OmniClic®, xPloration, and OmniDeep enables new bispecific antibody discovery workflows for partners

OmniDeep®

xPloration®

OmniAb®

Advanced Antigen Design Strategies for Shaping Human Antibody Repertoires in OmniAb Animals

June 12, 2024 | 9 AM PT | 12 PM ET

Devendra Srivastava, PhD

Director, Protein Sciences

OmniAb, Inc.

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THANK YOU!

Visit us at Booth #504

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