OmniAb®

Opening The Barn Door To Antibody Diversity

Bill Harriman, PhD
SVP Antibody Discovery

Discovery on Target
October 18, 2022

The OmniAb Technology Suite

OmniAb®

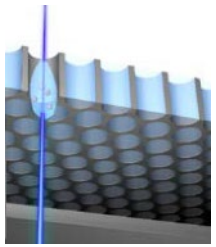
OmniRat® | OmniMouse® | OmniChicken® | OmniTaur™

OmniFlic® | OmniClic®

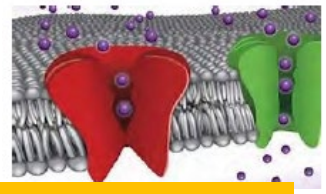
Ab Initio Biotherapeutics

See Dev's poster #51

xCella BIOSCIENCES



ICAGEN® ION CHANNEL TECHNOLOGY



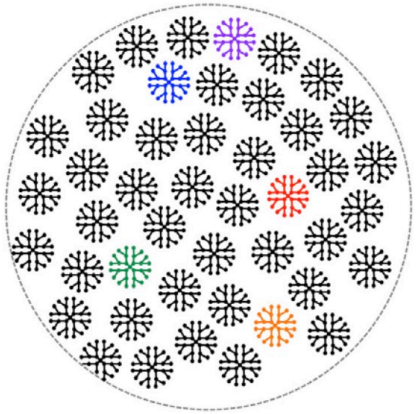
At OmniAb booth

- The only platform leveraging **four species**
- Robust solutions for **bispecific antibodies**
- Human frameworks with **ultralong CDR-H3s**
- Industry-leading **broadest offering**
- **Proven success**

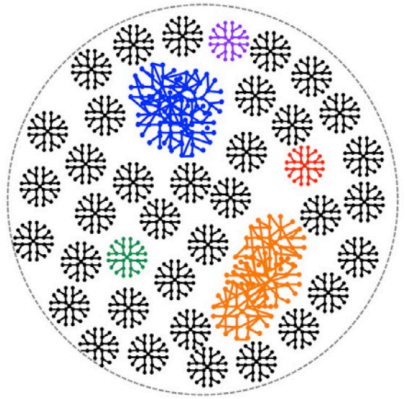
Platforms to Generate Custom Antibody Repertoires

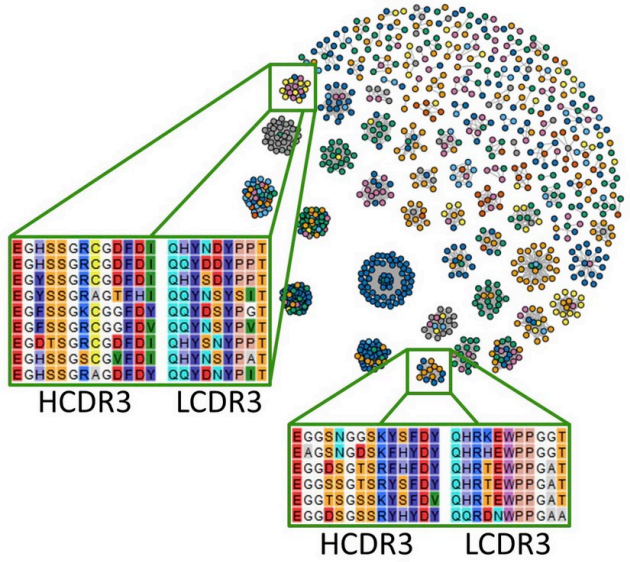
BIOLOGICAL INTELLIGENCE™: INTERPLAY BETWEEN RATIONAL GENETIC DESIGN AND POWERFUL IN VIVO PROCESSES

Naïve repertoire



Immune repertoire





Building the Animal System
V gene building blocks
Structural attributes
Diversification architecture
Transgene design
Immunological robustness

Repertoire Shaping
Antigen design
Host immune recognition
Immunization protocols
Campaign strategy
Immune response monitoring

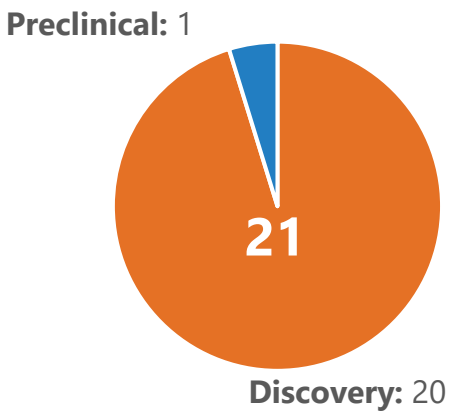
Repertoire Mining
Phenotypic screening
Clonal sampling/sequencing
Antibody characterization
Clone & Repertoire ranking
Selective "Deep Dives"
NGS hit expansion

Confidential

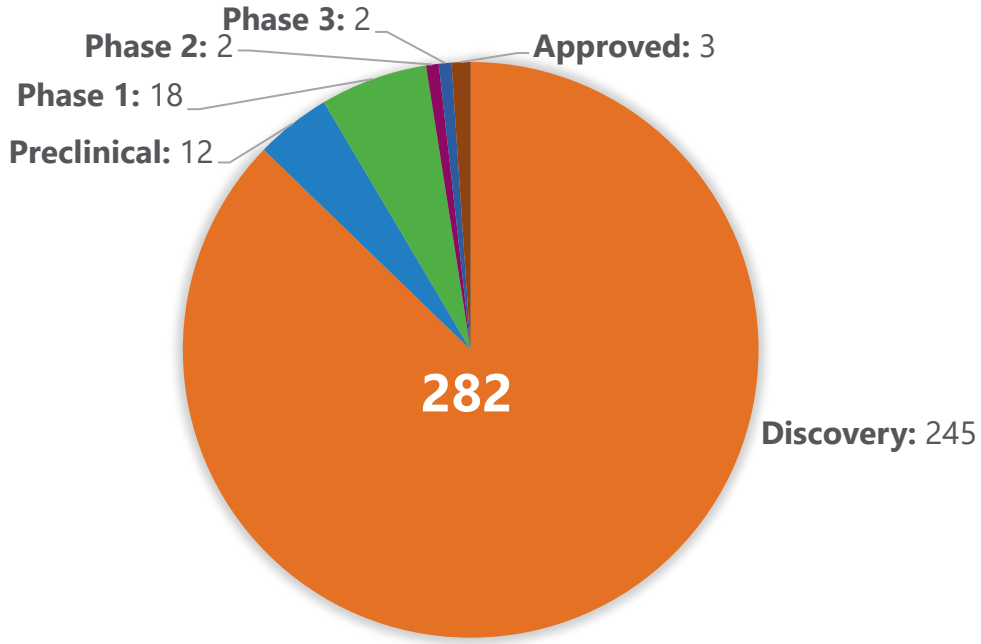
OmniAb Program Count Continues to Grow

PROGRESSION AND PERFORMANCE IN PROGRAMS BY STAGE OF DEVELOPMENT

As of 2016



As of 09/30/22



Substantial progress in all phases, increase in discovery programs expected to feed growth in new clinical programs and future approvals

OmniAb

OmniAb®

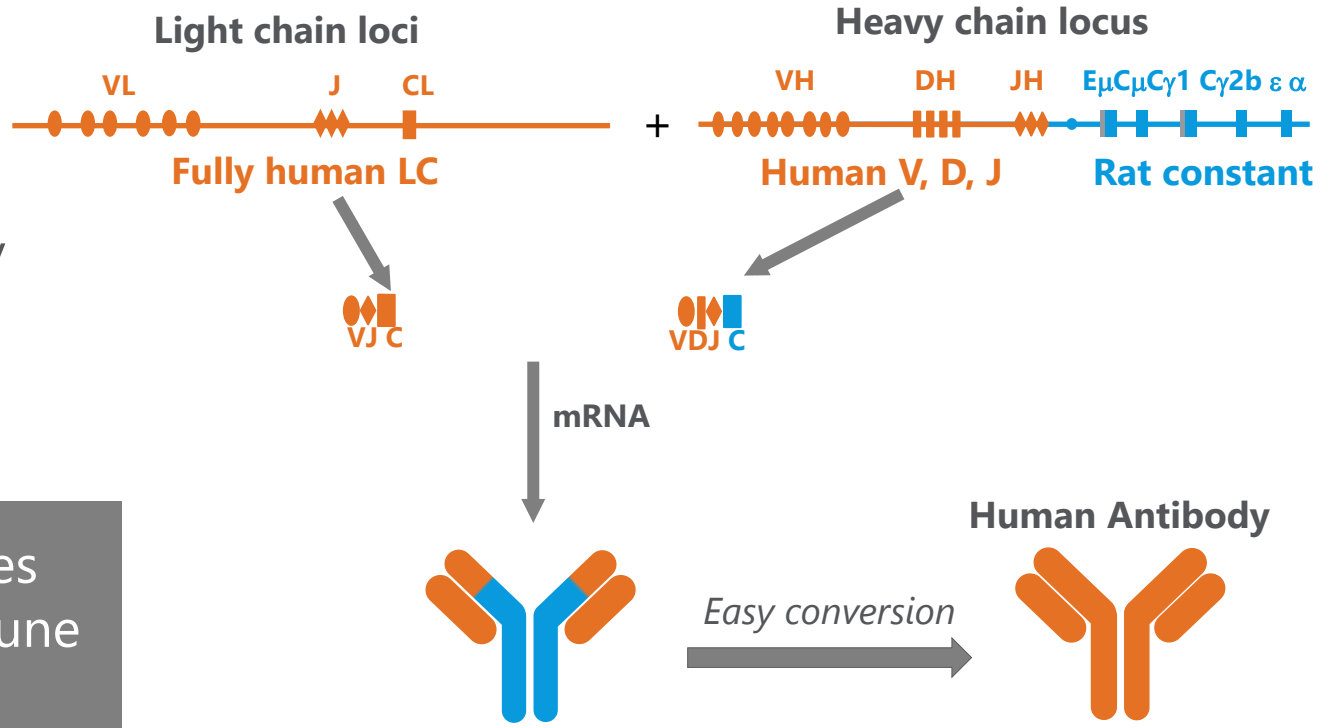
Animal Platforms

Rodent Platforms

OmniRat® OmniMouse®

- Endogenous Ig genes inactivated
- Expression of full human V gene diversity
- Streamlined conversion into fully human molecule

Well-validated transgene design utilizes rodent constant regions for robust immune responses from the B-cell repertoire

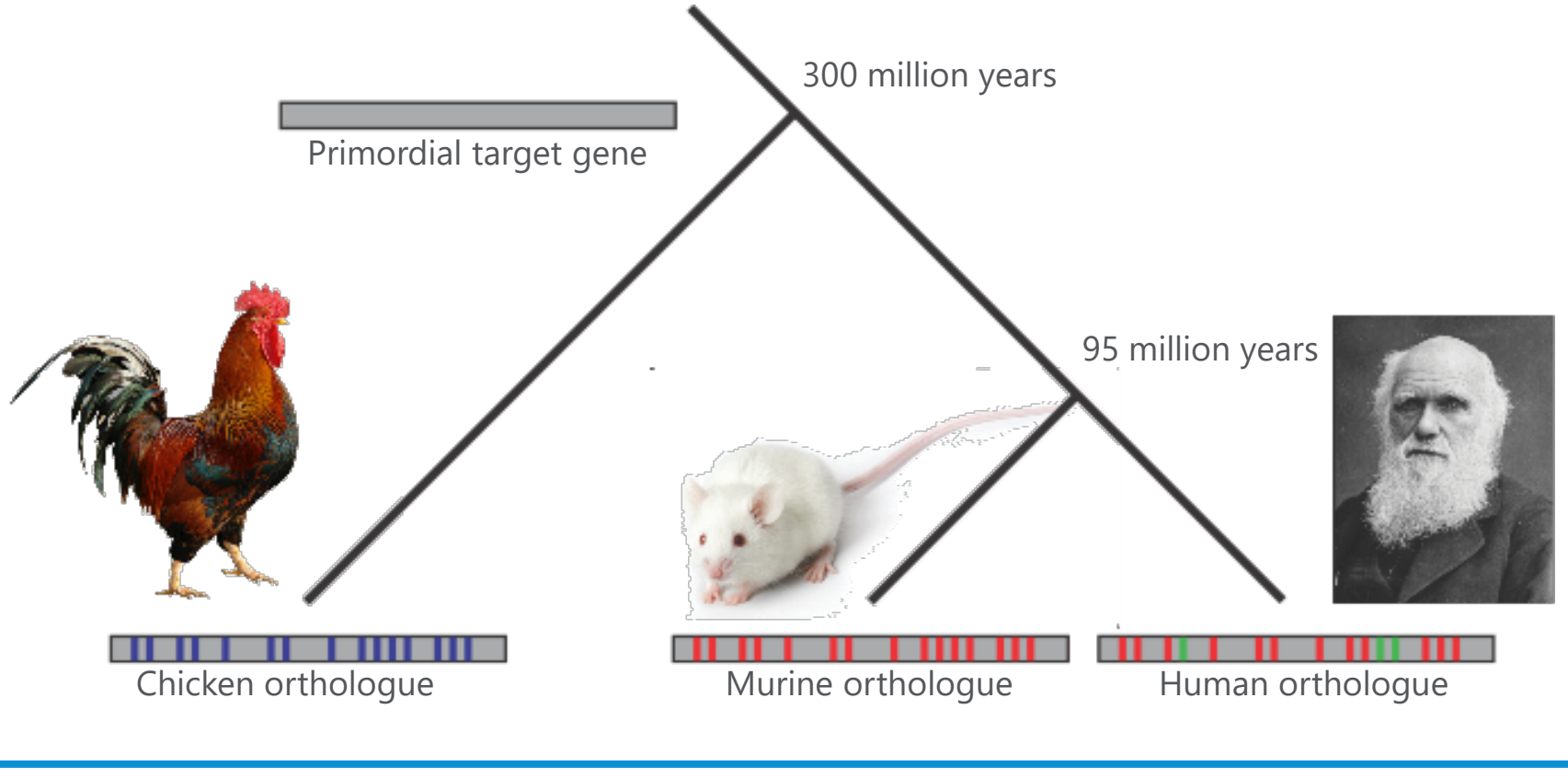


Geurts et al. Science 2009
Ménoret et al. Eur J Immunol 2010
Osborn et al. J. Immunol. 2013

OmniAb®

OmniChicken®

POWERED BY EVOLUTION



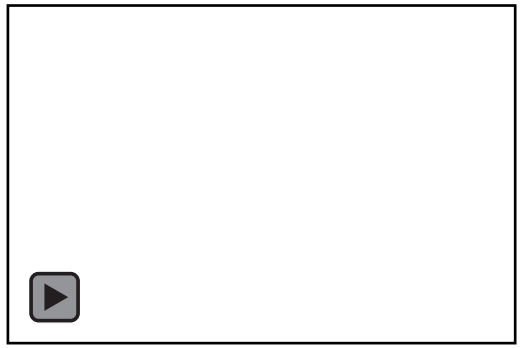
Greater evolutionary distance yields greater immunogenicity and more antibody diversity

Engineering of Ig Loci

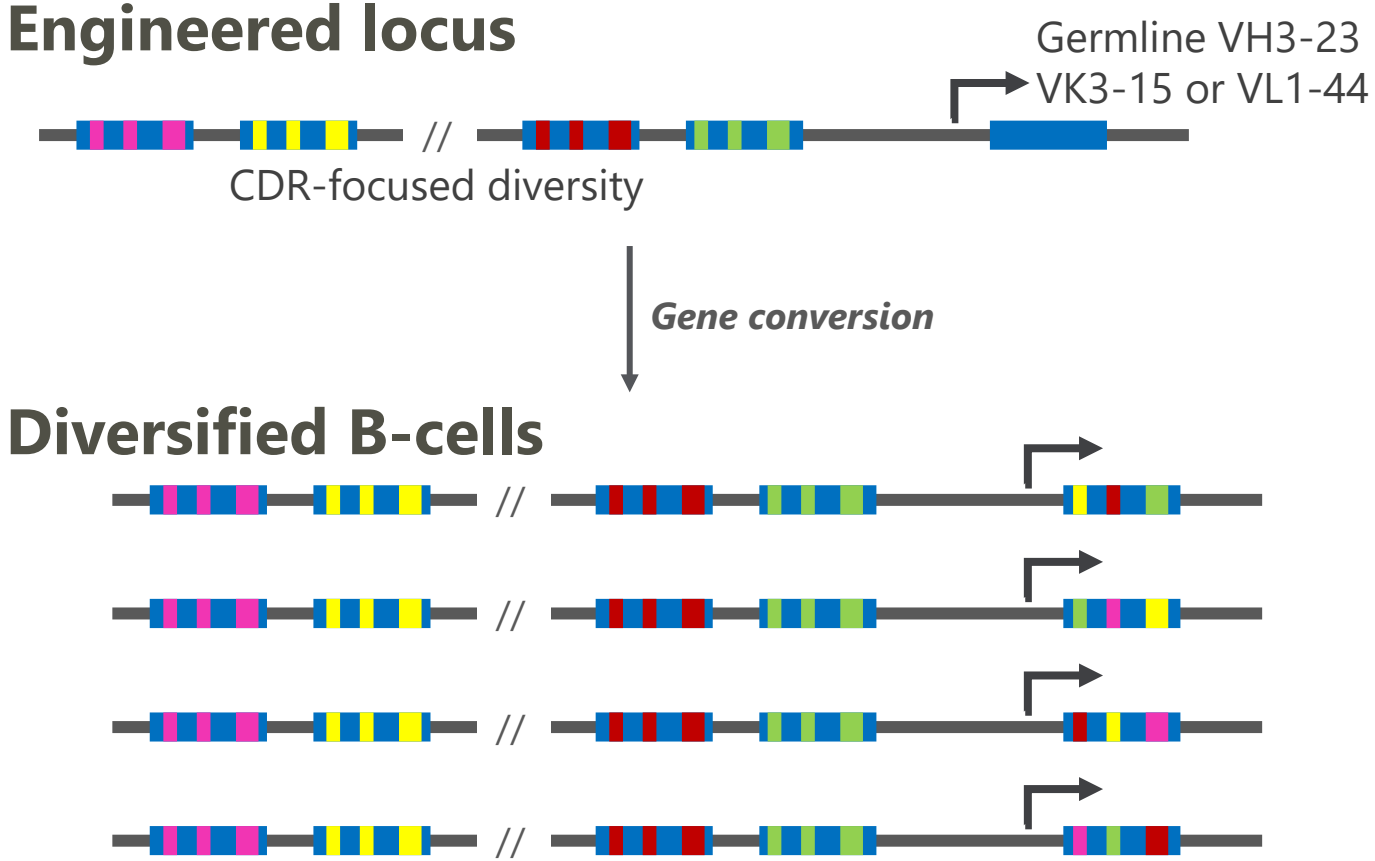
ADAPTATION TO CHICKEN GENE CONVERSION PROCESS

OmniChicken®

Gene conversion



Engineered locus



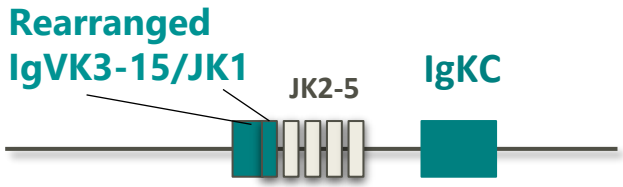
Human V's selected for:

- High expression level, stability, ubiquity
- High sequence diversity in CDRs
- Low sequence diversity in FWs

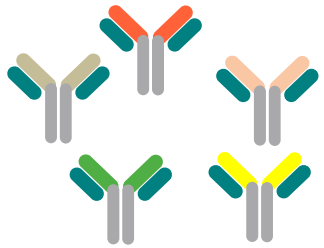
Common Light Chain Platforms

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

OmniFlic®

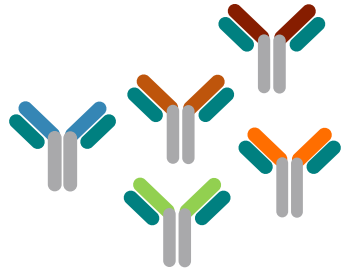


Rearranged human VK3-15 light chain combined with diversifying heavy chain



OmniClic®

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



Monospecific IgG

Simple reformatting from monospecific into bispecific for efficient production

Bispecific IgG

Common light chain for OmniFlic® and OmniClic® allows interchangeability between the platforms

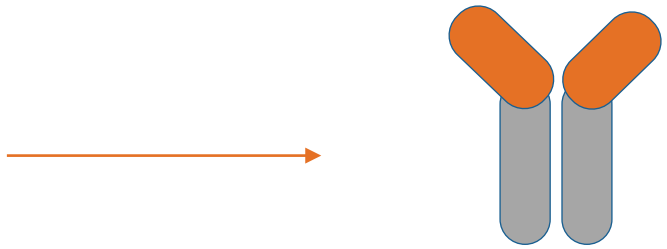
†The Evolution of Bispecifc Antibodies, Nimish Gera
https://doi.org/10.1080/14712598.2022.2040987

OmniAb®

Omni*dAb*™: Heavy Chain Only Transgenic Chickens

HCO STRATEGY USING TRUNCATED LIGHT CHAIN (TLC)

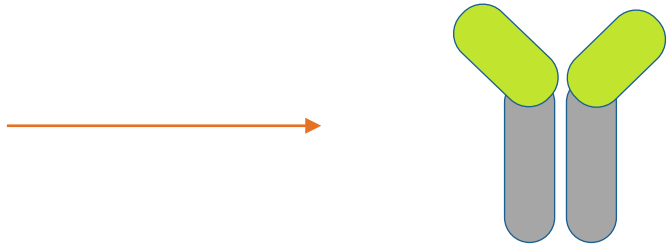
tLC transgene



Chicken VH sdAb
(hu Fc)

See Abheepsa's
poster #50

tLC transgene +
VHH transgene



human VHH sdAb
(hu Fc)

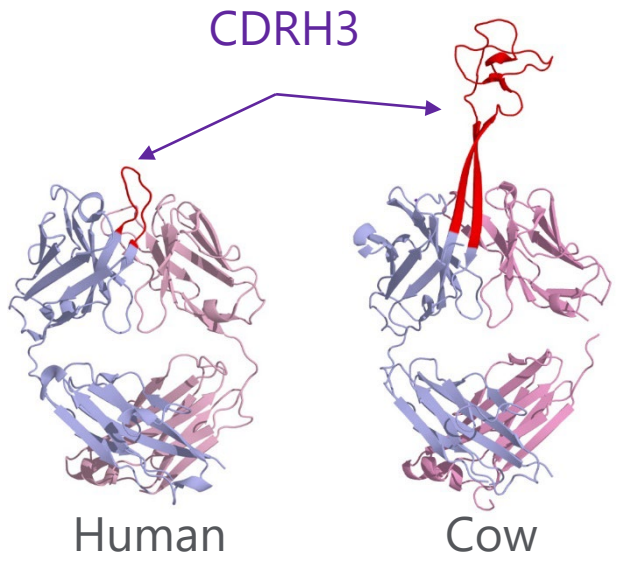
- *Normal chicken heavy chain can express as VH alone*
- *VHH transgene in development*

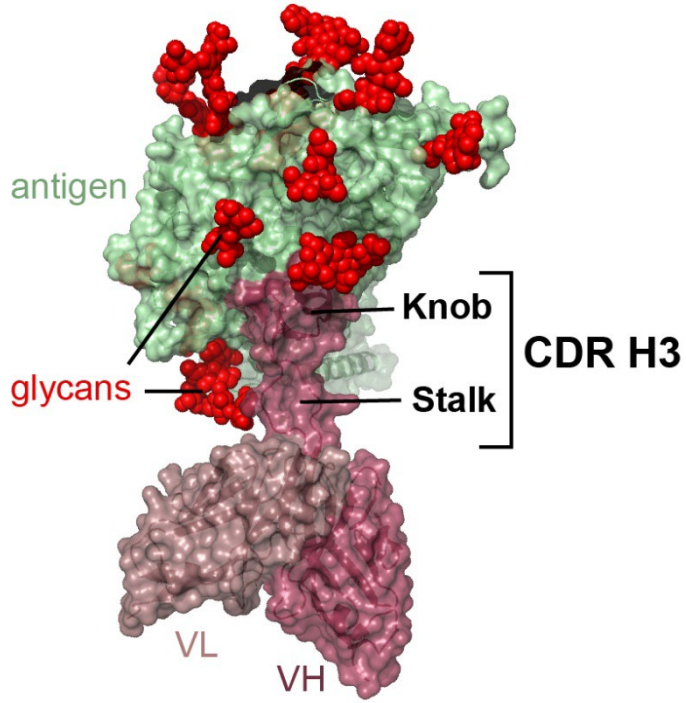
OmniAb

OmniTaur™: Ultralong CDRH3s Create Novel Binding Domains

OmniTaur™

UNIQUE STRUCTURAL FEATURES OF ULTRALONG H3 ANTIBODIES





- Novel structure may enable targeting epitopes unreachable by standard antibodies
- Long H3 domains can be expressed on human VH framework, or alone as ~5kD Picobodies™

Stanfield, et.al. *Sci Adv* (2020) 6(20): eaba0468.

OmniAb®

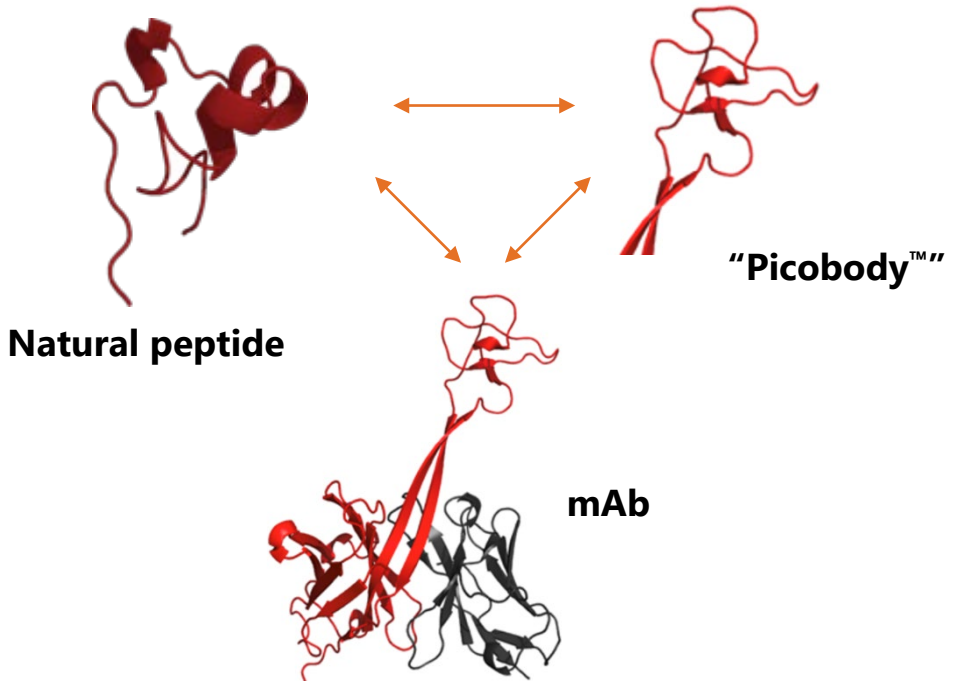
OmniTaur™ mAbs Share a Structural Theme with Bioactive Natural Peptides

Shk peptide

RSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC

Cow antibody *"knob"*

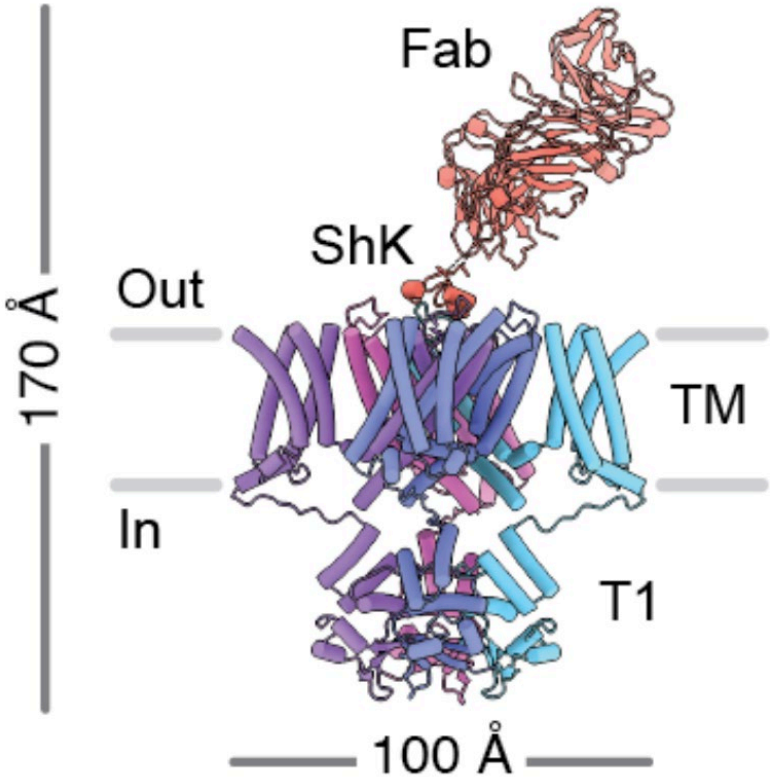
SCPDGYRERSDCSNRPACGTSDCCRVSVFGNCLTT



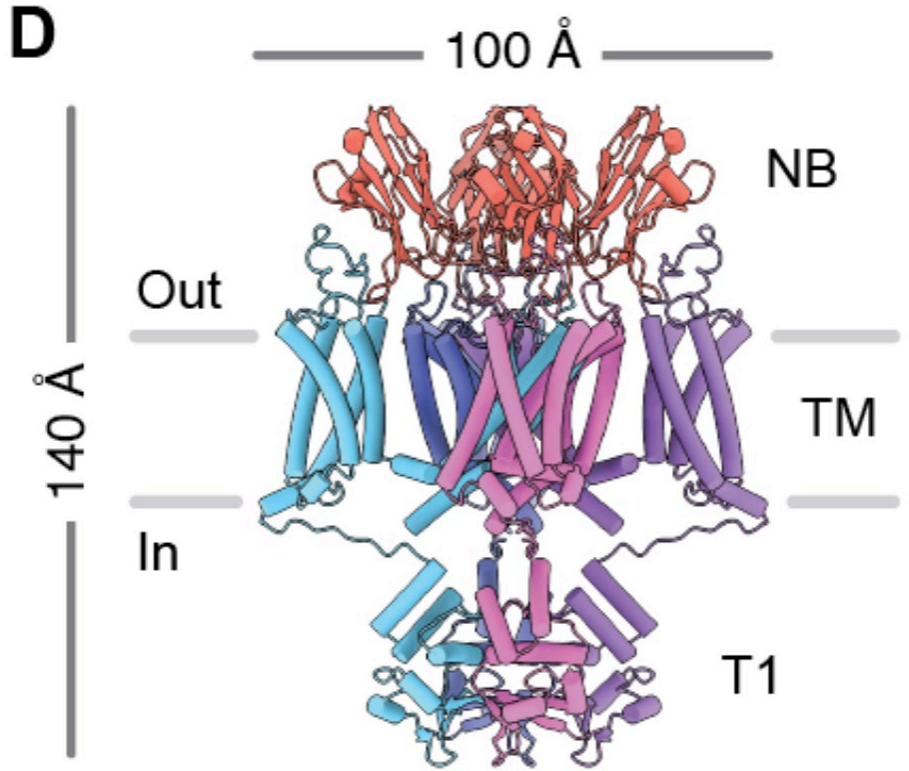
Long H3 mAbs potentially combine high biological potency with high target specificity

mAb Binding Modes to Ion Channel Kv1.3

H3 LENGTH IMPACTS TYPES OF MOLECULAR INTERACTION



Long H3 mAb binds within pore



Nanobodies (~15KD) bind turret loops

Selvakumar et al, 2022 doi: https://doi.org/10.1101/2022.04.19.488765

OmniAb

OmniAb Antibody Repertoires

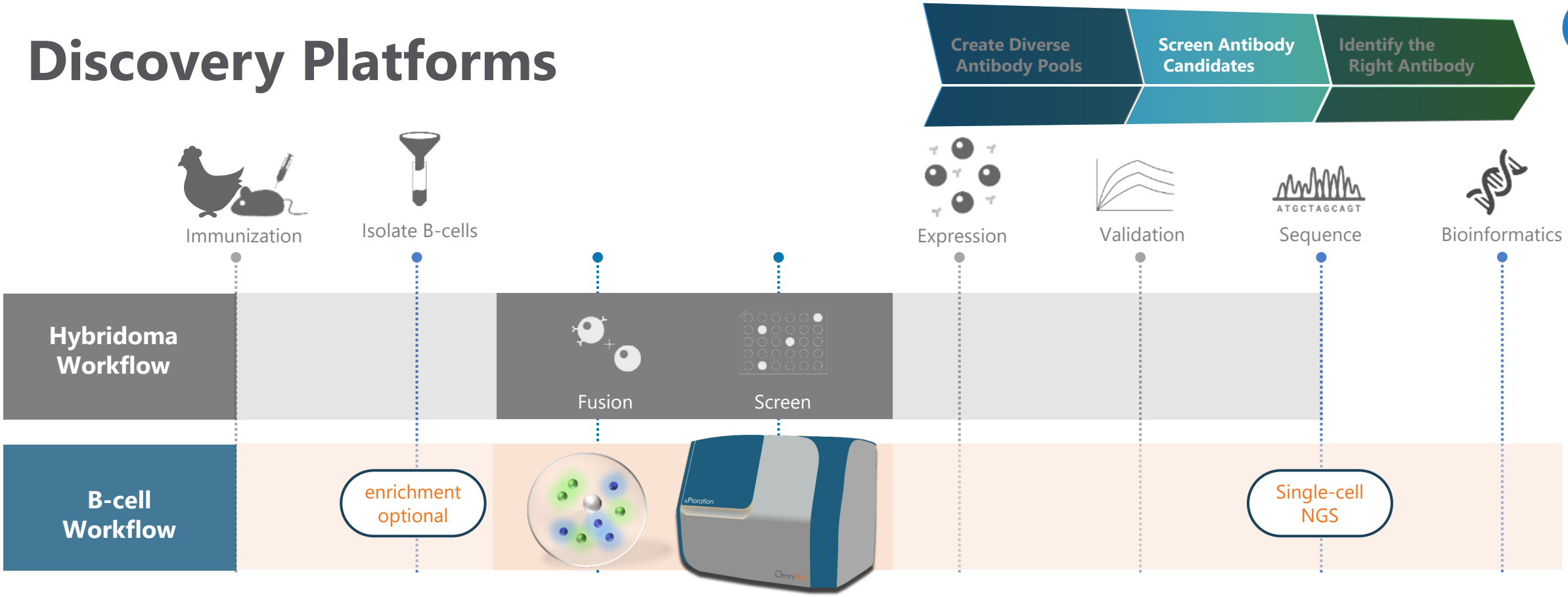
UNSURPASSED OPTIONS AVAILABLE TO ADDRESS DIVERSE PARTNER OBJECTIVES

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
Omni*dAb*™	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®

Screening Platforms

Discovery Platforms



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

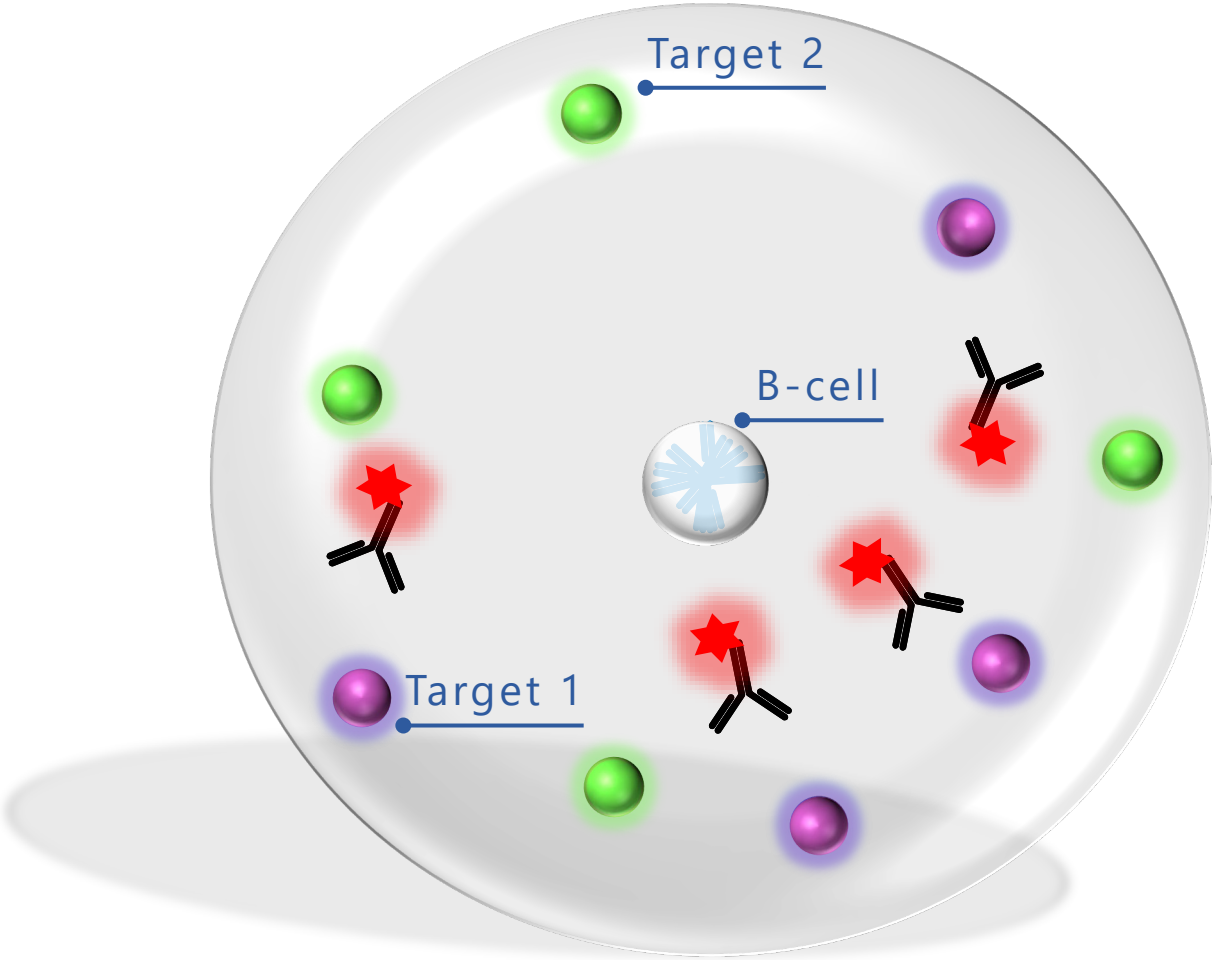
AI-driven multi-parameter screening of **tens of millions** of cells in **hours instead of weeks**

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

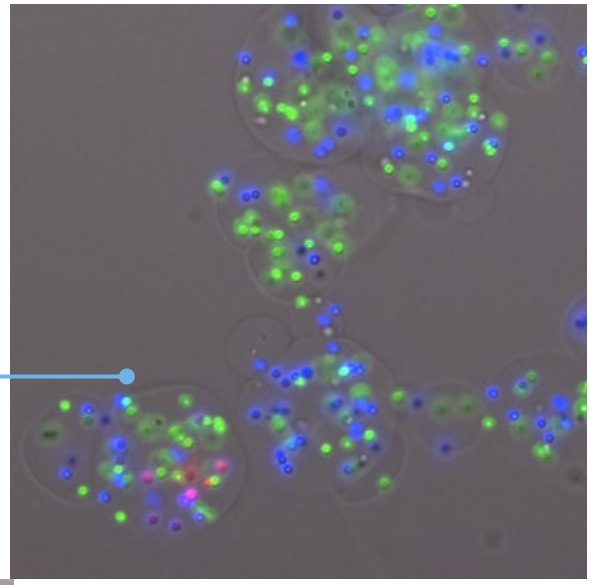
OmniAb

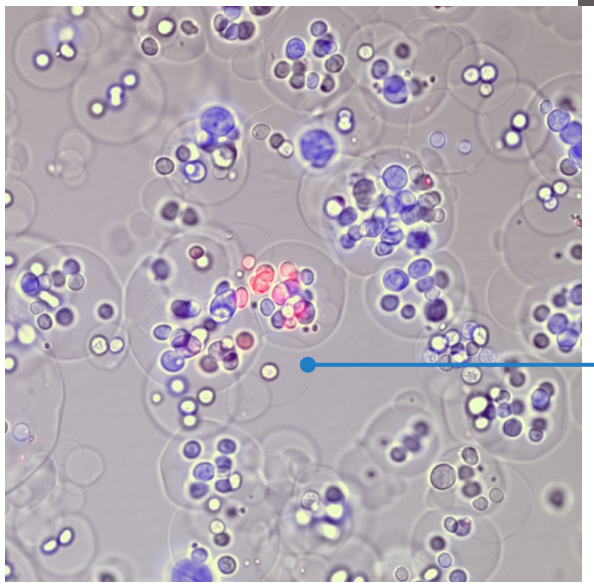
Screening Technology: GEM Assay

GEL ENCAPSULATED MICROENVIRONMENT



Dual bead GEM





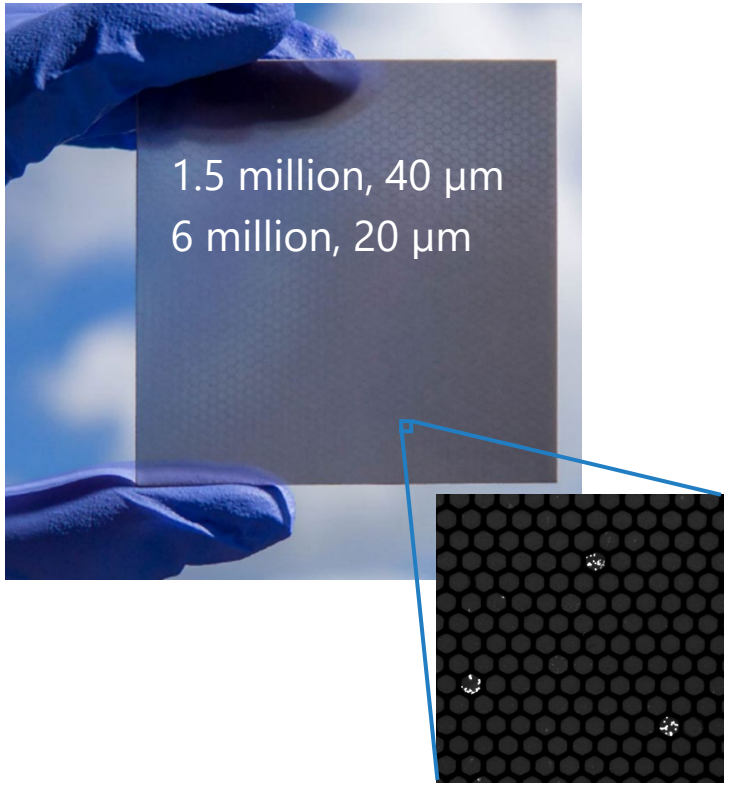
Cell-based GEM

Izquierdo et al. Microscopy, 2016, 1-12

OmniAb

Screening Technology: xPloration®

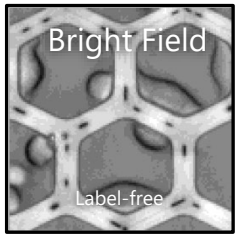
1 | Loading

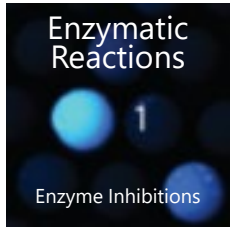


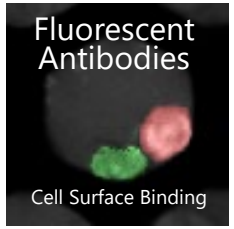
Unique through-hole format

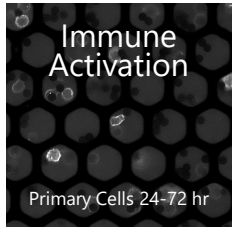
Workflows for OmniAb B-cells

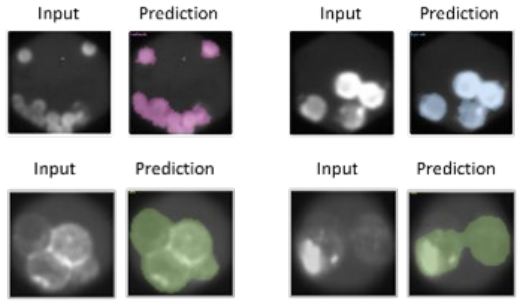
2 | Assay + Machine Vision





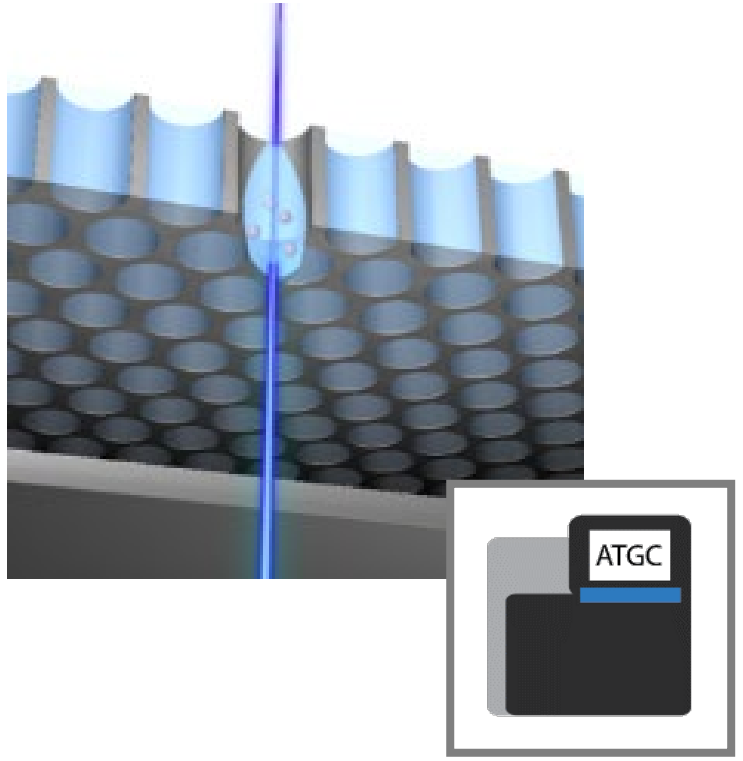






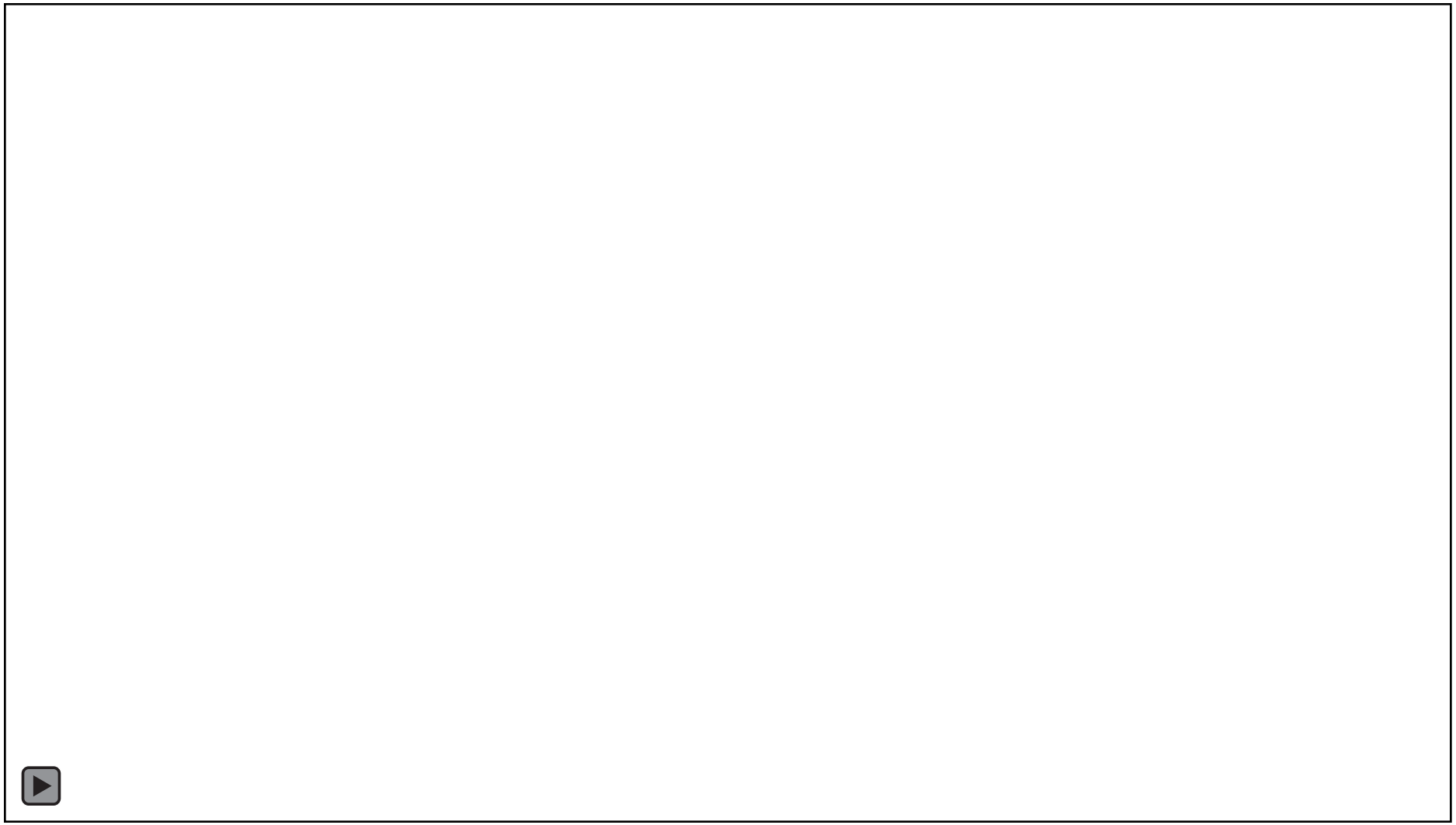
AI-driven hit detection

3 | Recovery & Single-Cell NGS

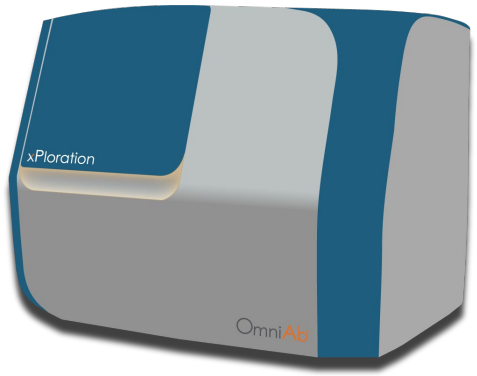


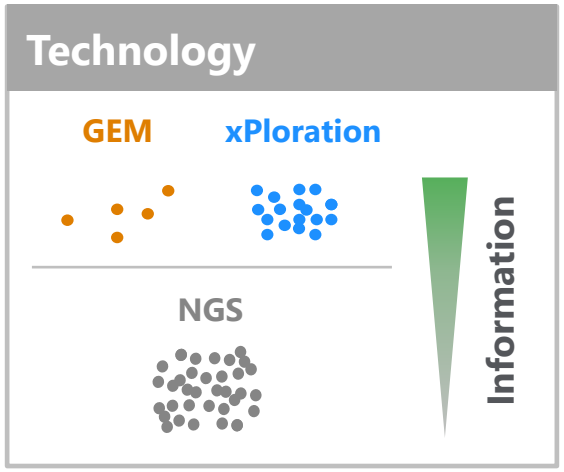
Precise laser-based recovery

1 cell/sec (single-cell mode), single-cell barcoding

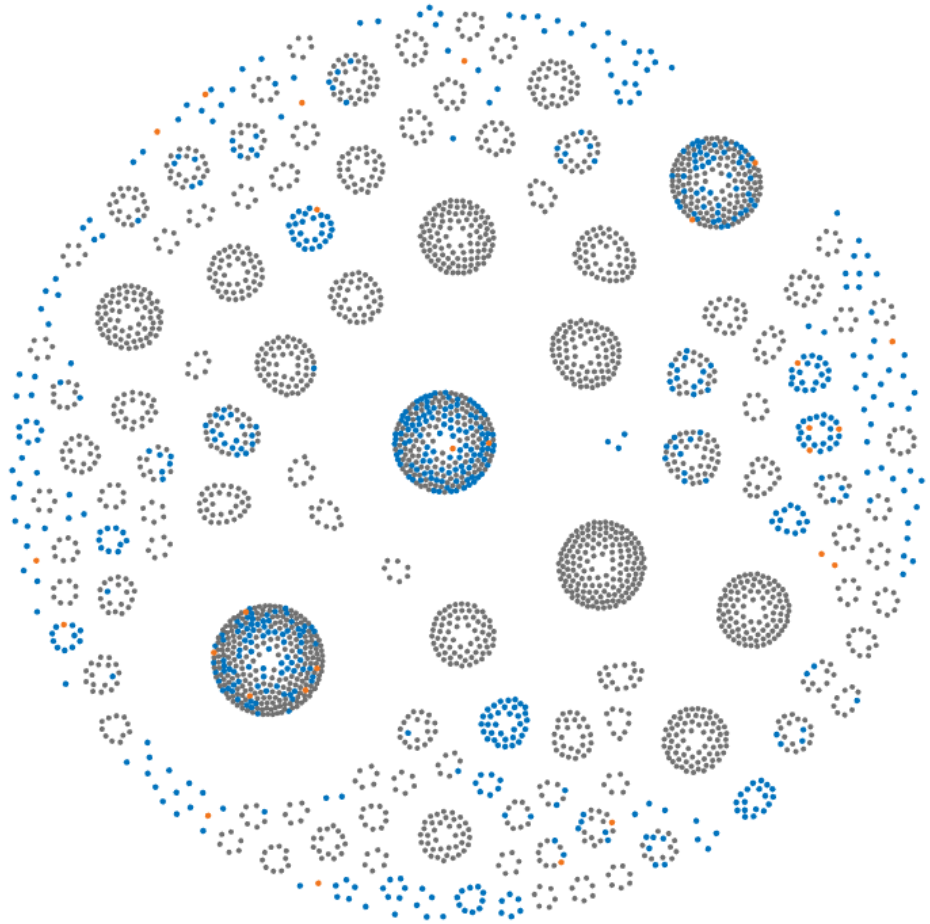


Deeper Characterization Identifies New Clonotype Families





Each dot represents an antibody



- **xPloration®** expands on majority of clonotypes identified by GEM assay
- Multiple new clonotype families identified
- Next-generation sequencing (NGS) adds support to new clusters and reveals even more diversity

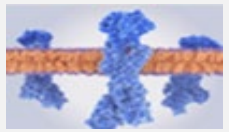
OmniAb®

The OmniAb Platform

OmniAb Technologies

Create Diverse Antibody Repertoires

Create Diverse Pools of High-Quality Naturally Optimized Antibodies



Computational Antigen Design & Proprietary Reagents

OmniRat® OmniChicken OmniMouse

Robust Antibodies for Any Target

OmniFlic

OmniClic

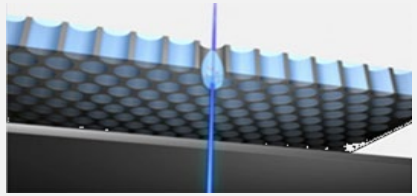
Bispecific Antibody Generation

OmniTaur

Cow-inspired Antibodies for Difficult Targets

Screen Antibody Candidates

Screen Millions of Cells to Find Potential Therapeutic Candidates



xPloration High-Throughput Single Cell Screening

Gel Encapsulated Microenvironment (GEM) Single Cell Screening

Identify the Right Antibody

Further Characterize, Select & Optimize the Right Antibody

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

- *Comprehensive Functional Characterization*
- *Proprietary Ion Channel Assays*

Technology offering addresses the most critical challenges of antibody discovery

OmniAb®