The OmniAb Technology Suite

OmniAb®

OmniRat | OmniMouse | OmniChicken | OmniTaur

OmniFlic | OmniClic

Ab Initic
Biotherapeutics

xCella
Biosciences

ICAGEN
ImmunoAb Technology

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

- 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
Greater evolutionary distance yields greater immunogenicity and more antibody diversity.
Engineering of Ig Loci

ADAPTATION TO CHICKEN GENE CONVERSION PROCESS

Gene conversion

Engineered locus

Diversified B-cells

Germline VH3-23
VK3-15 or VL1-44

Human V’s selected for:

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

CDR-focused diversity

Gene conversion
Common Light Chain Platforms

STANDARD IGG FORMAT TO DE-RISK DOWNSTREAM DEVELOPMENT\(^1\) OF BISPECIFIC MABS

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

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

Simple reformatting from monospecific into bispecific for efficient production

Common light chain for OmniFlic\(^{\circledR}\) and OmniClic\(^{\circledR}\) allows interchangeability between the platforms
**OmnidAb™: Heavy Chain Only Transgenic Chickens**

HCO STRATEGY USING TRUNCATED LIGHT CHAIN (TLC)

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

Diagram:
- tLC transgene
- tLC transgene + VHH transgene
- Chicken VH sdAb (hu Fc)
- human VHH sdAb (hu Fc)
OmniTaur™: Ultralong CDRH3s Create Novel Binding Domains

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™

OmniTaur™ mAbs Share a Structural Theme with Bioactive Natural Peptides

Shk peptide

RSCIDTIPKSRCTAFQCKHSMKYRLSFCKRKTGC

Cow antibody “knob”

SCPDGYRERSDCNRPCA\GTSDCCRVSVFGNCLTT

Natural peptide

“Picobody™”

mAb

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
CRYO-EM ~3.5Å

Long H3 mAb binds within pore
Nanobodies (~15KD) bind turret loops

OmniAb Antibody Repertoires

**UNSURPASSED OPTIONS AVAILABLE TO ADDRESS DIVERSE PARTNER OBJECTIVES**

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

GEL ENCAPSULATED MICROENVIRONMENT

Target 1

Target 2

B-cell

Dual bead GEM

Cell-based GEM

Izquierdo et al. Microscopy, 2016, 1-12
1 | Loading

Unique through-hole format

1.5 million, 40 µm
6 million, 20 µm

Workflows for OmniAb B-cells

2 | Assay + Machine Vision

Bright Field
Label-free
Enzymatic Reactions
Fluorescent Antibodies

GFP Reporter
Immune Activation

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

- **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
Leveraging Biological Intelligence with Computational Tools

**Biological Intelligence**
- OmniRat
- OmniChicken
- OmniMouse
- OmniTaur
- OmniFlic
- OmniClic

**Differentiated sources of antibody sequences**

**Model-aided optimization**
- Antibody homology modeling
- Computational antibody optimization

**In silico developability**
- Sequence liability assessment
- Comparison to clinical antibodies
- Structure-based calculations

**Sequence databases and Bioinformatics**
- Customized cloud-based antibody sequence databases
- Large-scale repertoire analysis

See posters #67 & 68
Technology offering addresses the most critical challenges of antibody discovery

## The OmniAb Platform

<table>
<thead>
<tr>
<th>OmniAb Technologies</th>
<th>Create Diverse Antibody Repertoires</th>
<th>Screen Antibody Candidates</th>
<th>Identify the Right Antibody</th>
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<tr>
<td>Create Diverse Pools of High-Quality Naturally Optimized Antibodies</td>
<td>Computational Antigen Design &amp; Proprietary Reagents</td>
<td>Screen Millions of Cells to Find Potential Therapeutic Candidates</td>
<td>Further Characterize, Select &amp; Optimize the Right Antibody</td>
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<td>OmniRat, OmniChicken, OmniMouse</td>
<td>Robust Antibodies for Any Target</td>
<td>xPloration High-Throughput Single Cell Screening</td>
<td>• Custom Bioinformatics</td>
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<td>OmniFlic, OmniClic, OmniTaur</td>
<td>Bispecific Antibody Generation</td>
<td>Gel Encapsulated Microenvironment (GEM) Single Cell Screening</td>
<td>• Next Generation Sequencing (NGS) Hit Expansion</td>
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<td>Cow-inspired Antibodies for Difficult Targets</td>
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<td>• Comprehensive Functional Characterization</td>
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- Gel Encapsulated Microenvironment (GEM) Single Cell Screening
- xPloration High-Throughput Single Cell Screening
- Computational Antigen Design & Proprietary Reagents
- Robust Antibodies for Any Target
- OmniRat, OmniChicken, OmniMouse
- OmniFlic, OmniClic, OmniTaur
- Bispecific Antibody Generation
- Cow-inspired Antibodies for Difficult Targets
- Custom Bioinformatics
- Next Generation Sequencing (NGS) Hit Expansion
- Comprehensive Functional Characterization
- Proprietary Ion Channel Assays
THANK YOU TO THE OMNIAB TEAM!

www.OmniAb.com