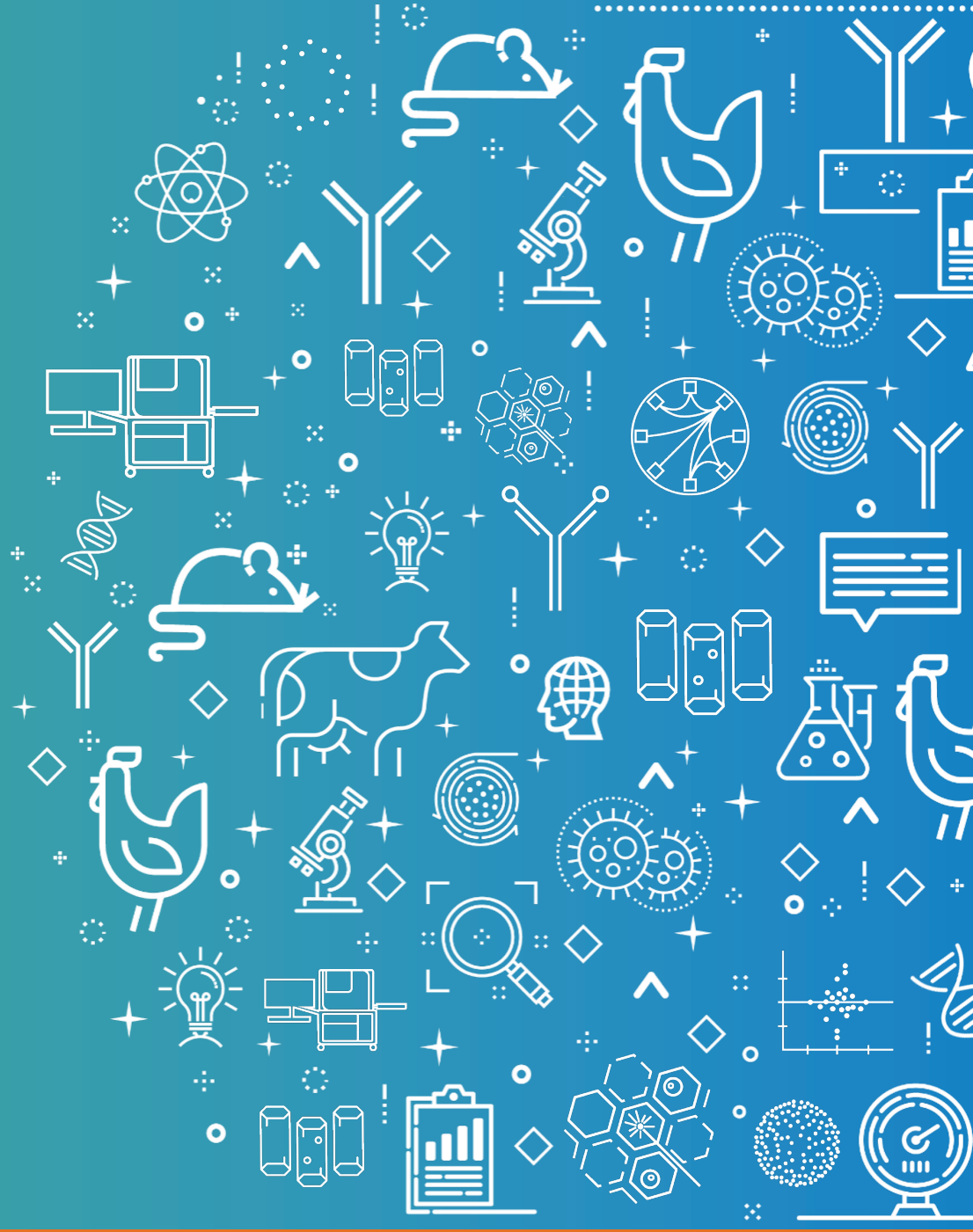
OmniAb®

OmniUltra™

Leveraging Evolutionary Distance for the Discovery of Ultralong CDRH3 Antibodies with Broad Epitope Coverage

AETC: Tuesday, December 16, 2025

Scientific Briefing #5: 12:35-1:05pm



OmniAb Enables Innovative Antibody Therapeutics

AS OF 9/30/2025

Overview

104
Active Partners

399
Active Programs

43
Total Clinical Programs and Approved Products

Clinical and Commercial-Stage Partner Pipeline(1)

Phase 1	Phase 1	1/1b	1/2	Phase 2	Phase 3	Registration	Approved
Zhikang Hongyi **BC3195** CDH3	*Cessation* **CSX1004** Fentanyl	*Zhikang Hongyi* **BC3425** 4-1BB	*Gloria* **GLS-012** LAG3	*Merck KGaA* **M6223** TIGIT	*Genmab* **Acasunlimab** PD-L1 x 4-1BB	*Hanall, Harbour, Immunovant,* **Batoclimab** FcRn	*CStone, Pfizer, EwoPharma* **Sugemalimab** PD-L1
Genmab **GEN1057** FAPα x DR4	*Innolake* **ILB2101** CD40	*Boehringer Ingelheim* **BI 765179** CD137 x FAP	*Merck KGaA* **M9140**(5) CEACAM-5	*Teva* **TEV-53408** IL-15	*Astra Zeneca* **AZ0486** CD19 x CD3	*Salubris* **SAL003** PCSK9	*J&J Innovative Med* **Teclistamab** BCMA x CD3
J&J Innovative Med **JNJ-70218902** TMEFF2 x CD3	*J&J Innovative Med* **JNJ-87562761** Undisclosed	*J&J Innovative Med* **JNJ-79635322**(4) BCMAxGPRC5DxCD3	*Servier* **S095018** TIM-3		*Abbvie* **Etentamig** BCMA x CD3		*Gloria, Arcus,Gilead* **Zimberelimab**(2) PD-1
Merck KGaA **M5542**(4) CTLA4-OX40L	*Pfizer* **PF-08046049**(3) CD228 x 4-1BB	*Aptevo* **Mipletamig** CD123 x CD3	*Servier* **S095024** CD73		*Immunovant, Hanall* **IMVT-1402**(6) FcRn		
Seismic **S-4321** PD-1 and FcγRIIb	*Teva* **TEV-56278** PD-1 (with IL-2)	*CTTQ* **TQB2223** LAG-3	*Servier* **S095029** NKG2A		*Genentech* **Tiragolumab** TIGIT		

(1) Program placement is based on most advanced status in any geography/market/indication
(2) Arcus Biosciences and Gilead Sciences are conducting multiple studies using zimberelimab in various oncology therapeutic settings and combinations in the US (see www.arcus.com)
(3) Indicates a trial is active-not recruiting or suspended and/or patients remain on study in follow-up
(4) JNJ-79635322 is also referred to as Ramantamig by Johnson and Johnson Innovative Medicines
(5) M9140 is also referred to as Precemtabart tocentecan by Merck KGaA
(6) IMVT-1402 is also referred to as Imeroprubart by Hanall Biopharma

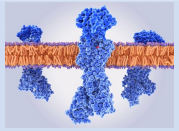
OmniAb®

OmniAb Technologies

TECHNOLOGY OFFERINGS ADDRESSES THE MOST CRITICAL CHALLENGES OF ANTIBODY DISCOVERY

Create

Create Diverse Repertoires of High-Quality Antibodies



Antigen Design & Proprietary Reagents

OmniRat™ OmniChicken™ OmniMouse™

Robust Antibodies for Any Target

OmniFlic™ OmniClic™

Bispecific Antibody Generation

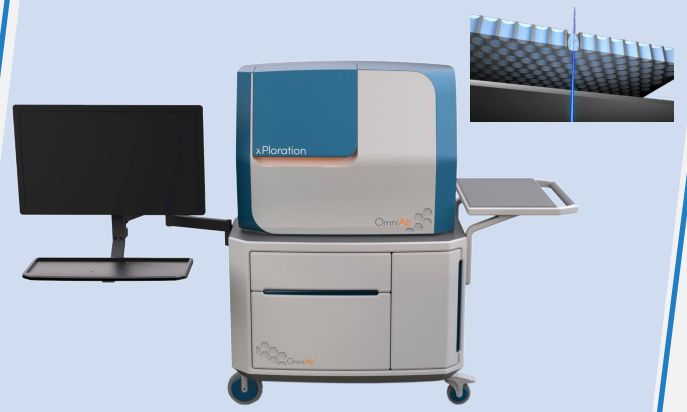
OmnidAb™ OmniTaur™ OmniUltra™

Novel Scaffolds

Screen

Screen Millions of Cells to Find Potential Therapeutic Candidates

xPloration®

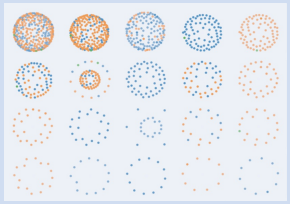


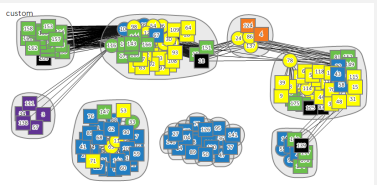
High-Throughput Single Cell Screening

Deliver

Further Characterize, Select and Optimize the Right Therapeutic Candidate

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





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

- *Fc-Silencing Technology (STR)**

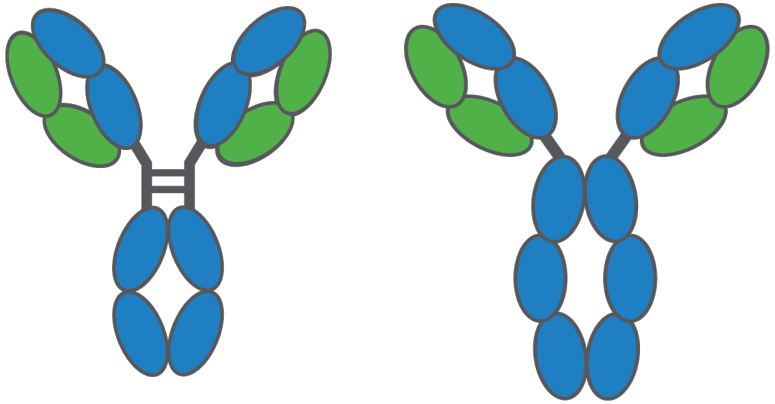
OmniDeep® *Suite of in silico tools for discovery and optimization that are woven throughout our various technologies and capabilities. Includes structural modeling, large multi-species antibody databases, molecular dynamics simulations, AI, and machine and deep learning sequence models, and more*

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

Alternative Antibody Formats are Found in Nature

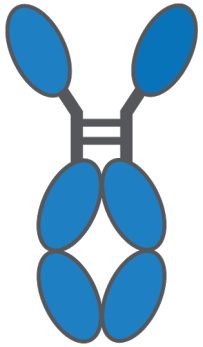
AROSE INDEPENDENTLY DURING EVOLUTION

Human **Chicken**



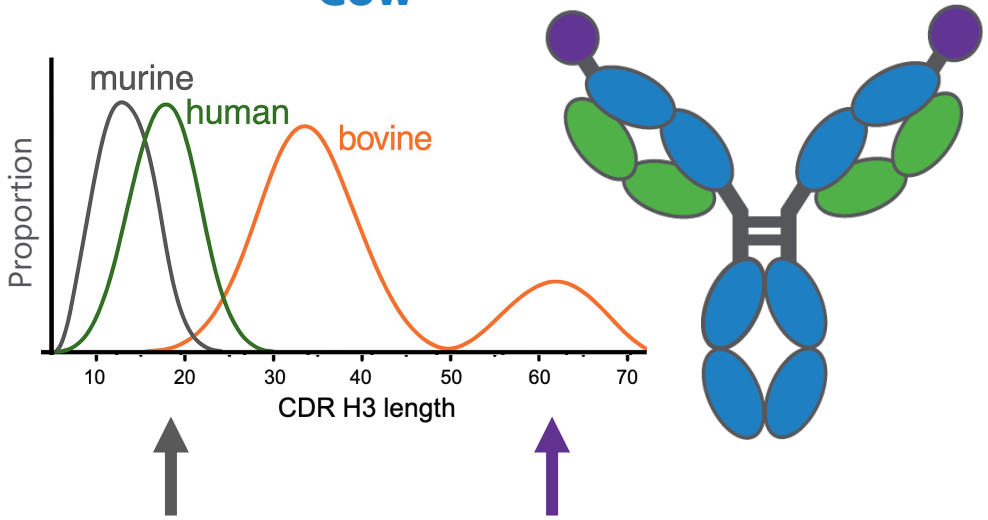
Conventional Antibody
(Heavy x Light)

Camelid



Heavy-Chain Only
(no light chain)

Cow



Standard CDRH3

***Ultralong (UL)* CDRH3**

Flajnik et al. PLOS Biology 2011

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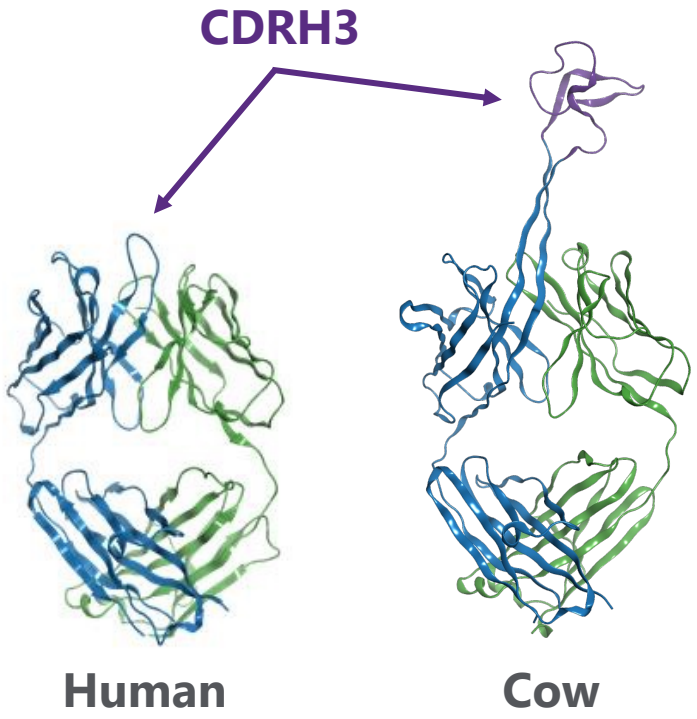
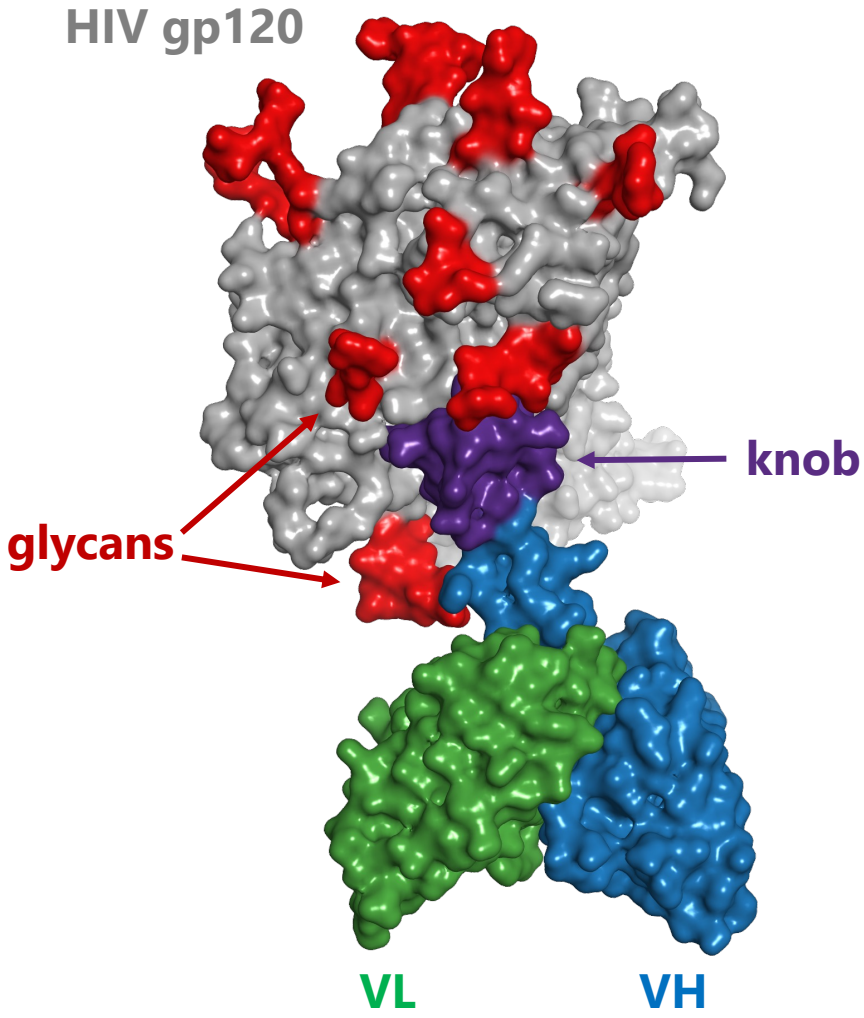
Ultralong CDRH3s Create Novel Binding Domains





Novel structure may enable targeting epitopes unreachable by standard antibodies

Stanfield et al, Sci Adv 2020

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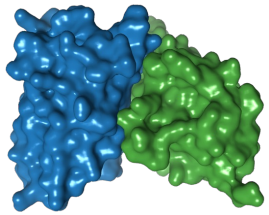
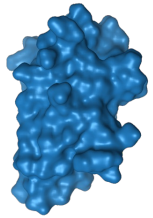
Binding Domains of Antibody-Based Biologics



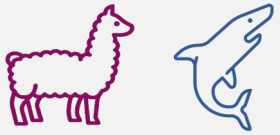
Fv
25 kDa



V_HH, V_{NAR}
15 kDa

Ultralong CDRH3
4-6 kDa

Species



OmniAb Platforms

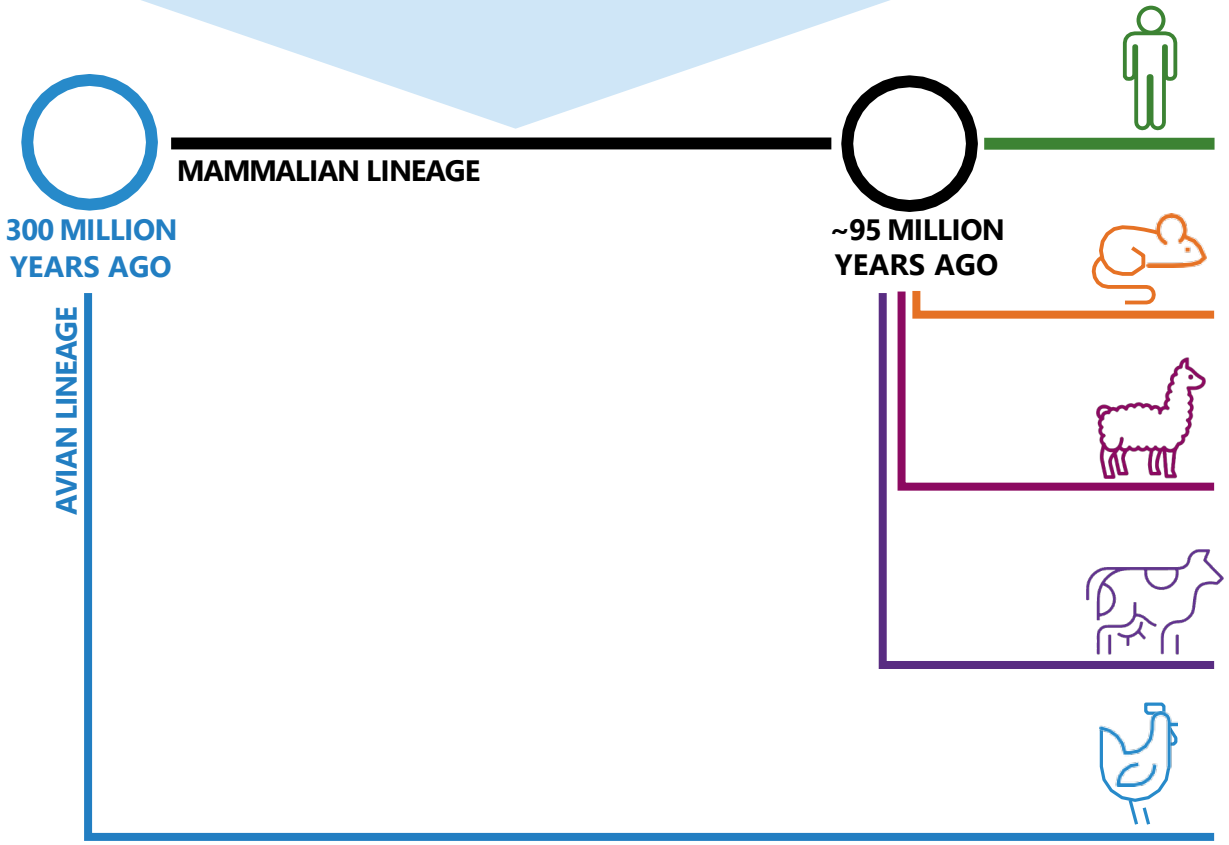
OmniRat®
OmniFlic™
OmniMouse®
OmniClic™
OmniChicken™
OmnidAb™
OmniUltra™
OmniTaur™

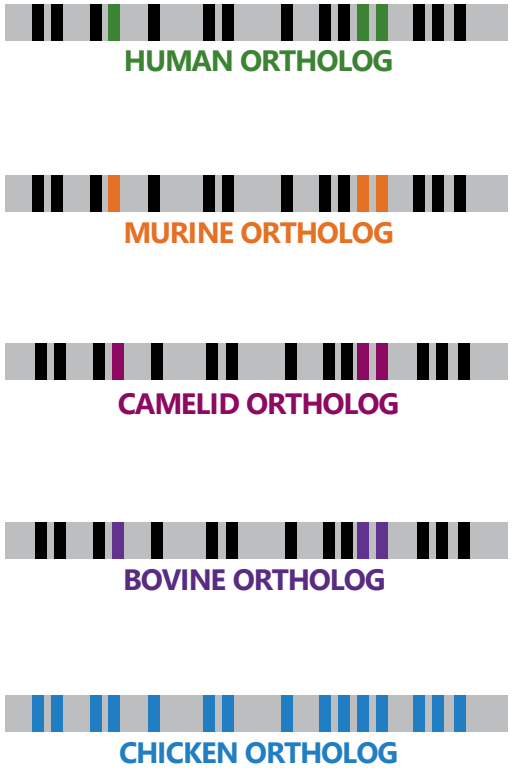
Cow antibody “knob” or "picobody™" is the smallest independent antigen binding domain

Chicken Platforms - Powered by Evolution

GREATER EVOLUTIONARY DISTANCE YIELDS
GREATER IMMUNOGENICITY AND MORE ANTIBODY DIVERSITY

PRIMORDIAL TARGET GENE
Early form of gene prior to avian/mammalian evolutionary split





Ching et al. MAbs 2018

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The Chicken Advantage - Chickens Can "See More"

DIFFERENTIAL RECOGNITION: CHICKEN ORTHOLOGS ARE MORE DISPARATE THAN MAMMALIAN

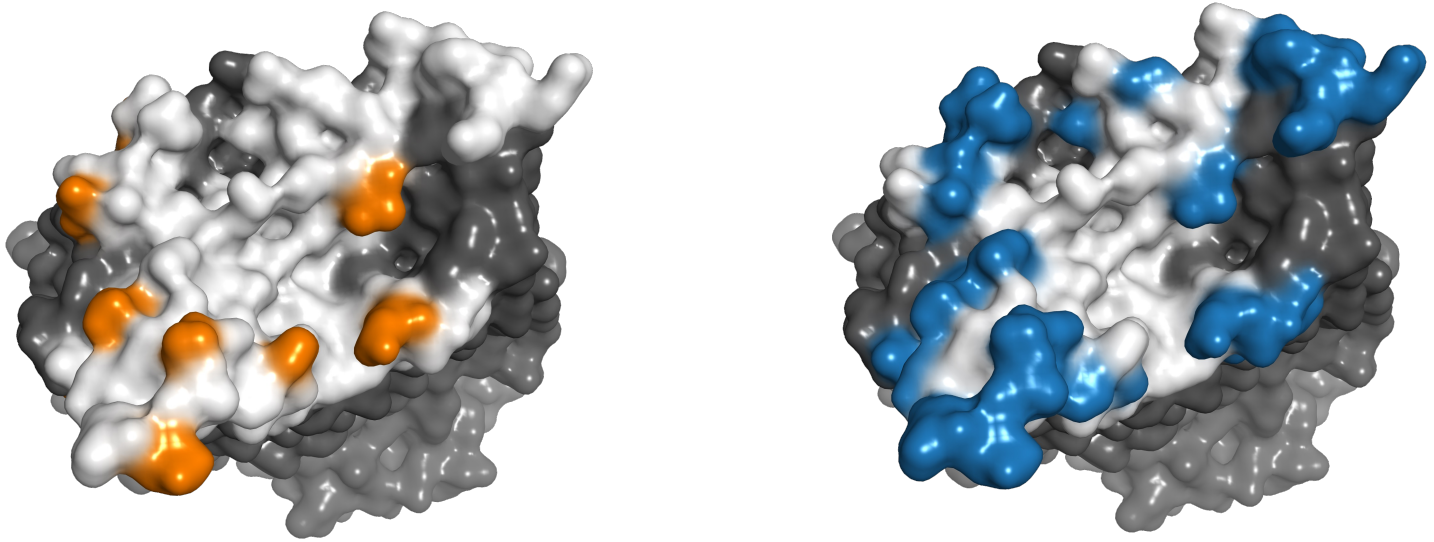
95% identity

vs.

65% identity

vs.

Example of a highly conserved multi-spanning transmembrane protein (SLC2A4)



Amino acid differences relative to human are highlighted

Chickens allow for more robust and diverse immune responses to human targets

Modified figure from Banik et al. MAbs 2023

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Why Use a Transgenic Chicken to Produce UL CDRH3s?

EVOLUTIONARY DISTANCE, PRACTICAL EFFICIENCIES, AND WORKFLOW OPTIONALITY

OmniTaur™ (Cow)

- Mammalian host
- Bovine framework
- Large animal; limited immunization cohort size, possible per-animal bias
- Display screening only

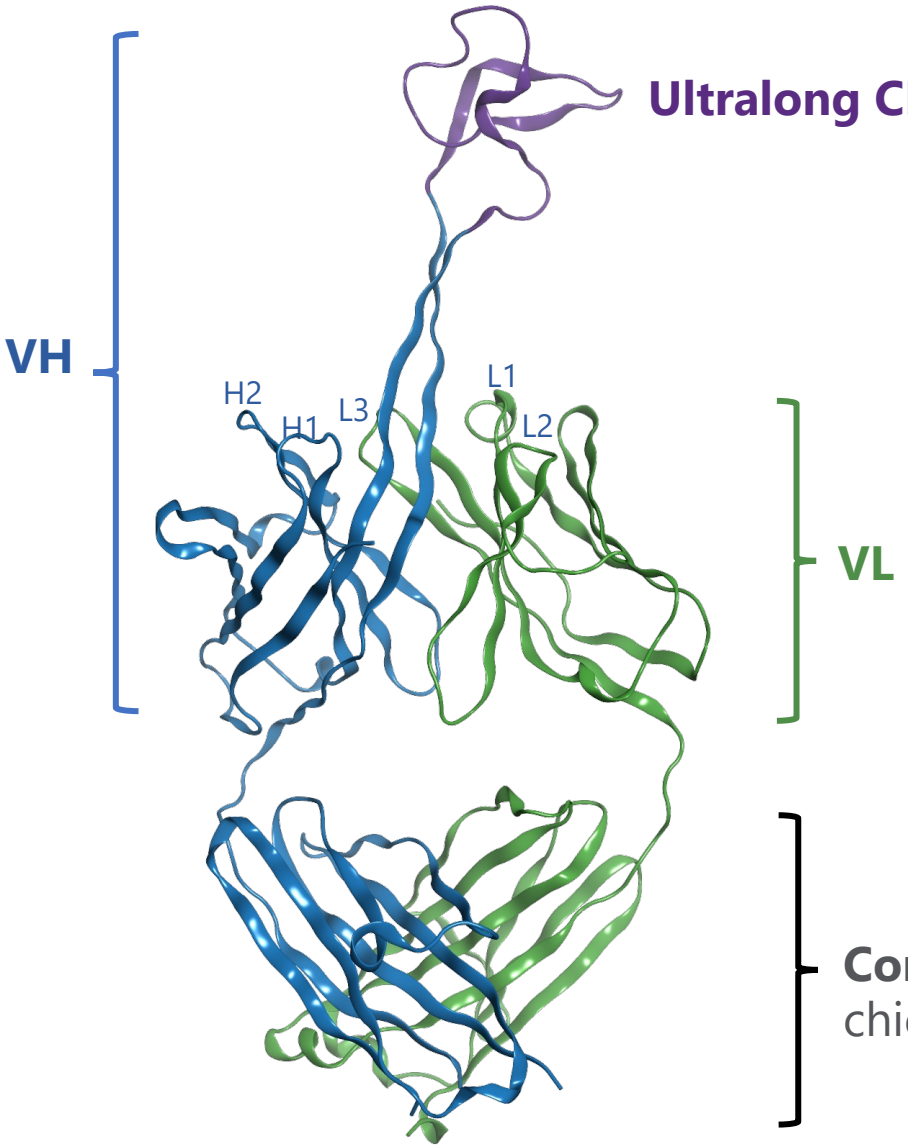
OmniUltra™ (Chicken)

- Evolutionarily distant host
- Human framework
- Established laboratory-based animal; well validated handling and immunization protocols; larger cohorts
- Phenotypic or display screening

OmniUltra™ - The Ultralong CDRH3 Transgenic Chicken

VL AND ULTRALONG VH TRANSGENES DESIGNED WITH HUMAN V FRAMEWORKS

Stabilized human VH/VL framework to support stalk-knob



Ultralong CDRH3 (knob): antigen-binding

Constant Regions:
chicken CH, human CL

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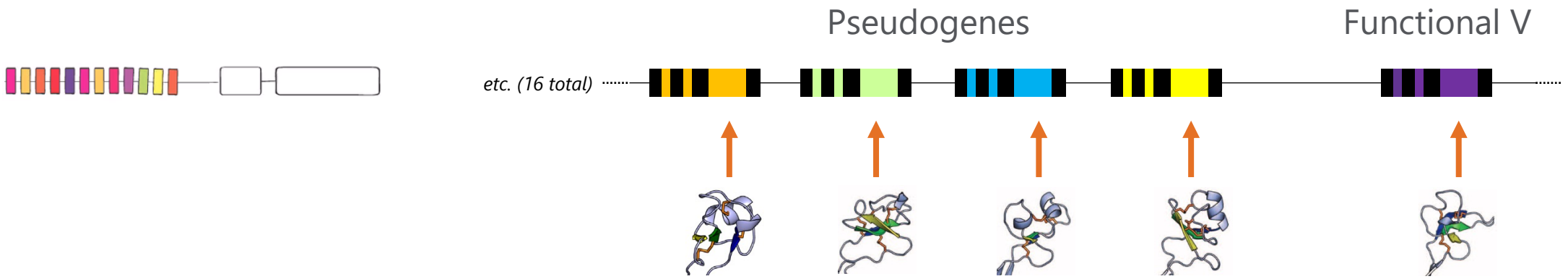
OmniUltra™ Transgene Design

CHICKENS ENGINEERED FOR GENE CONVERSION OF ULTRALONG SEQUENCES



Stanfield, et al. (2016) Science Immunology: 1(1)
Stanfield, et al. (2020) Sci Adv: 6

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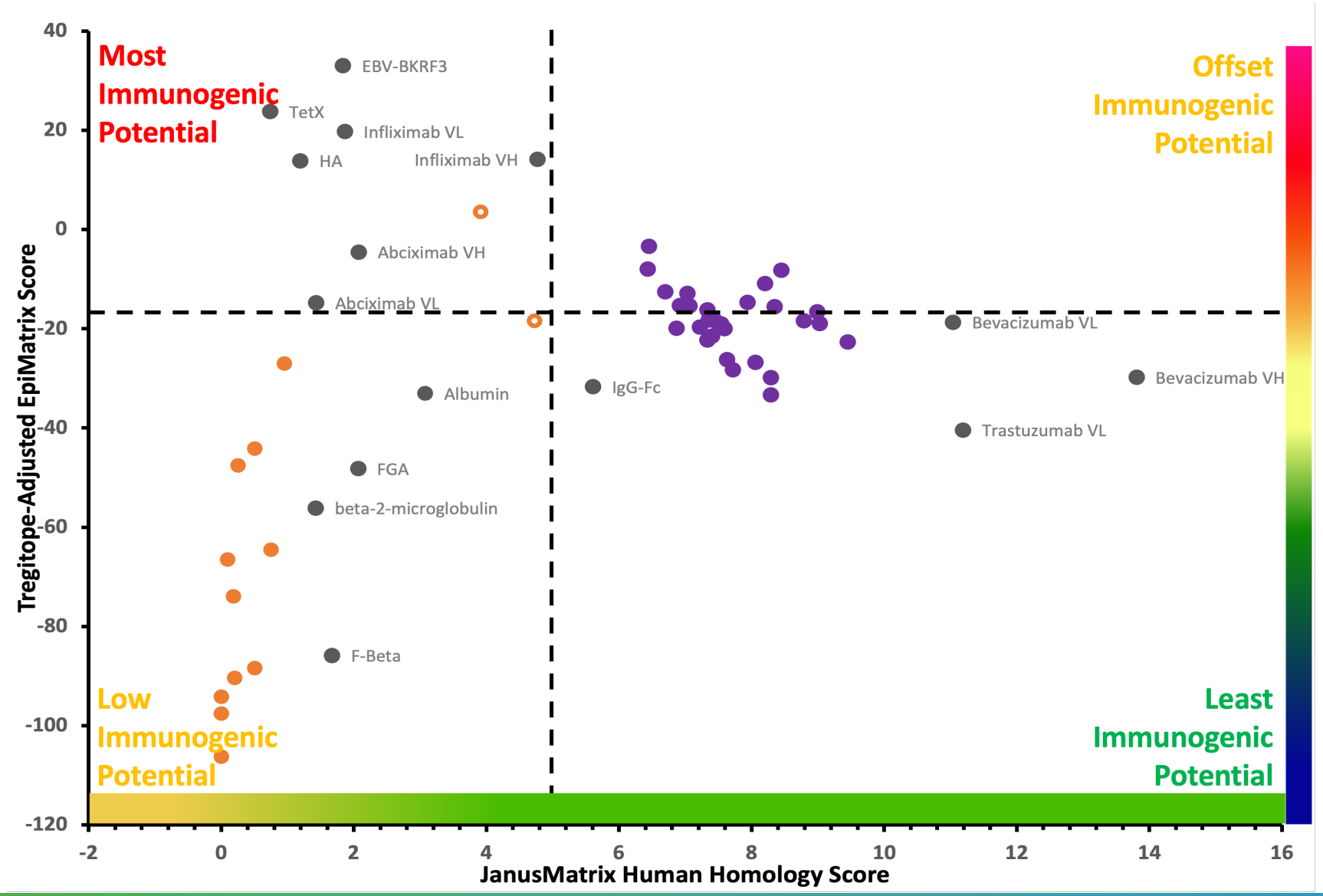
Immunogenicity Assessment of Transgene Design

EPIVAX ANALYSIS OF POTENTIAL PSEUDOGENES



- Benchmarks
- OmniUltra
- WT Cow stalk-knob
- WT Cow VH

OmniUltra™ pseudogenes predicted to have low immunogenic potential

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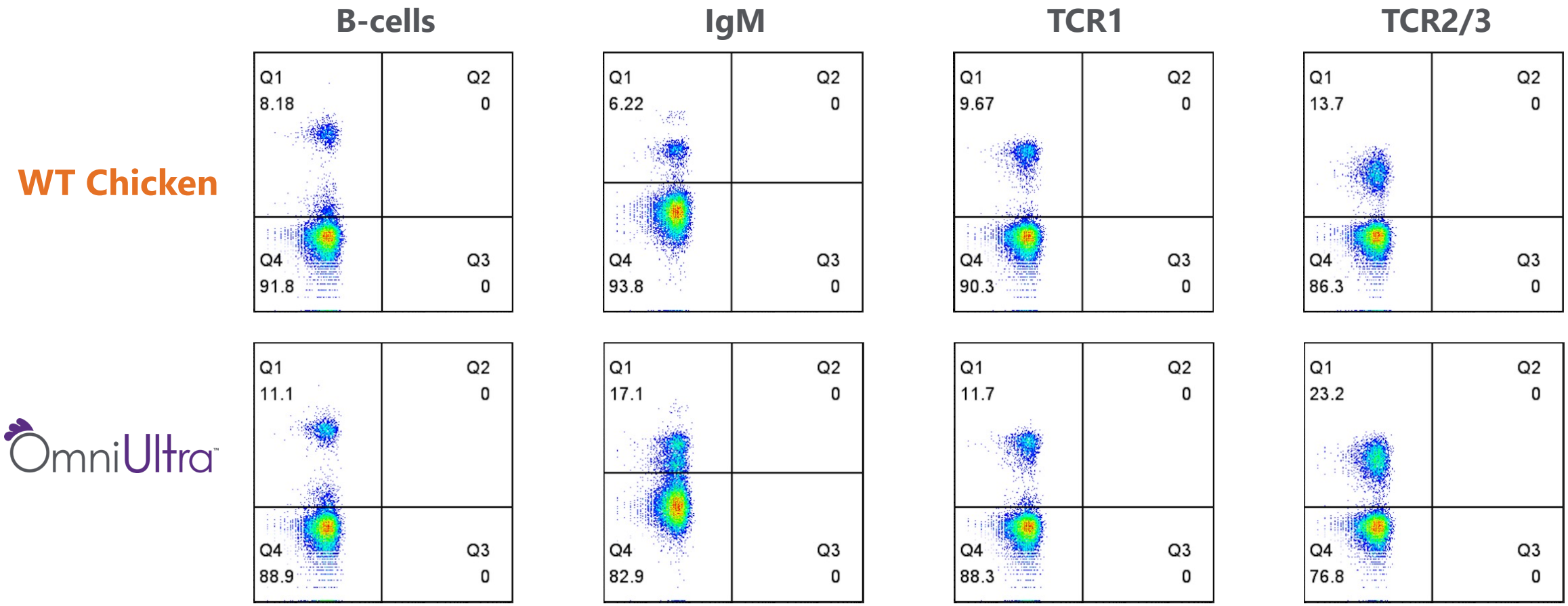
B Cell Development is Robust in OmniUltra

NORMAL B AND T CELL FREQUENCIES IN PBMC



Robust B cell populations are produced in OmniUltra™ transgenic birds

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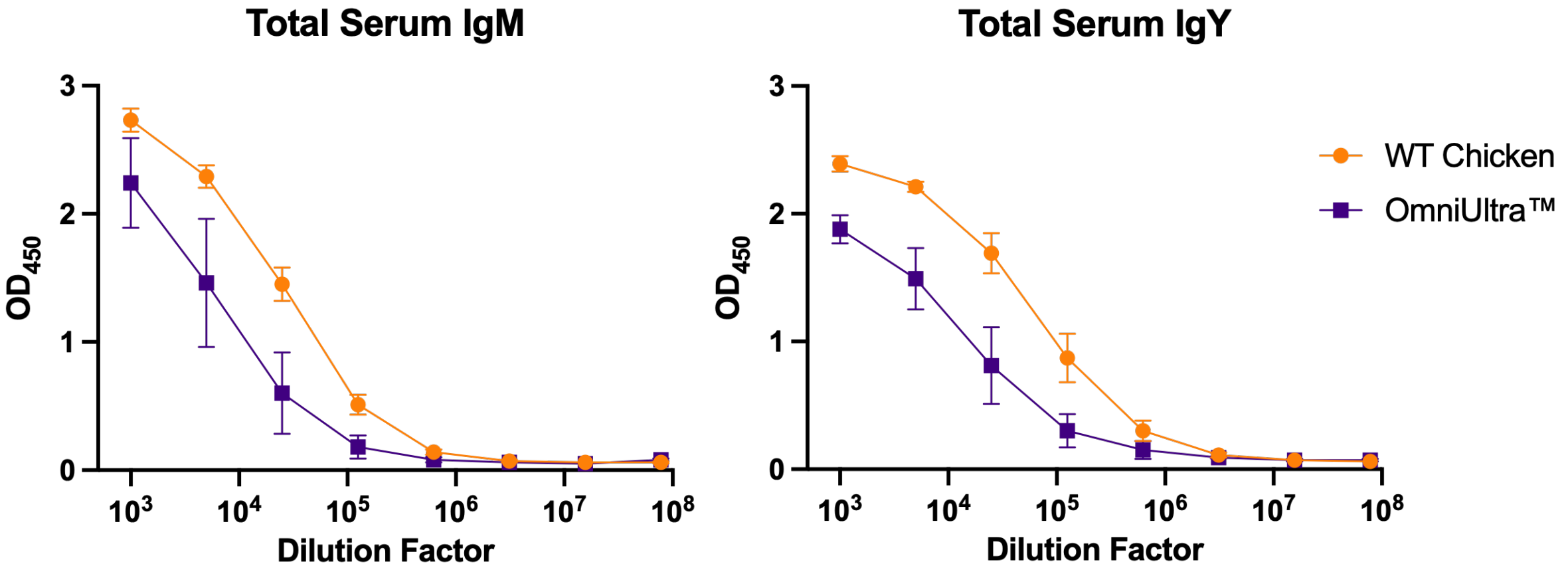
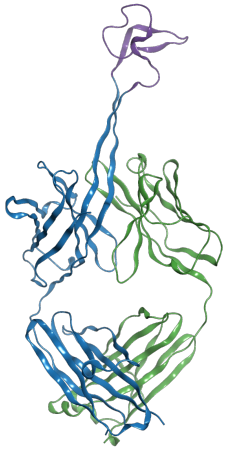
Total Serum Antibody Titers



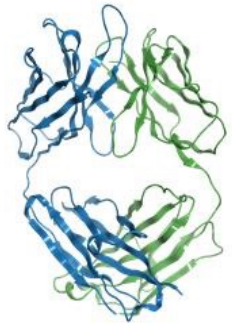
OmniUltra™ chickens express IgM and IgY antibodies

Ultralong CDRH3 Produced in OmniUltra

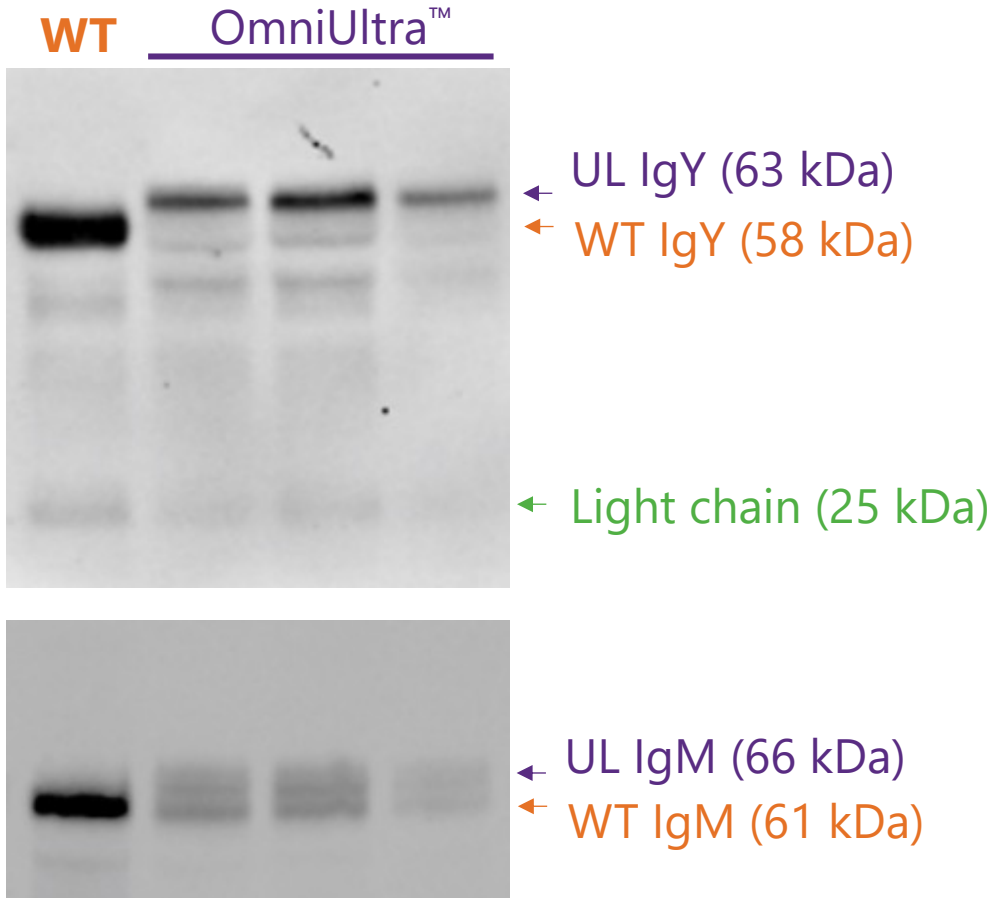
WESTERN BLOT OF SERUM IMMUNOGLOBULIN



UL CDRH3:
~4-6 kDa



WT

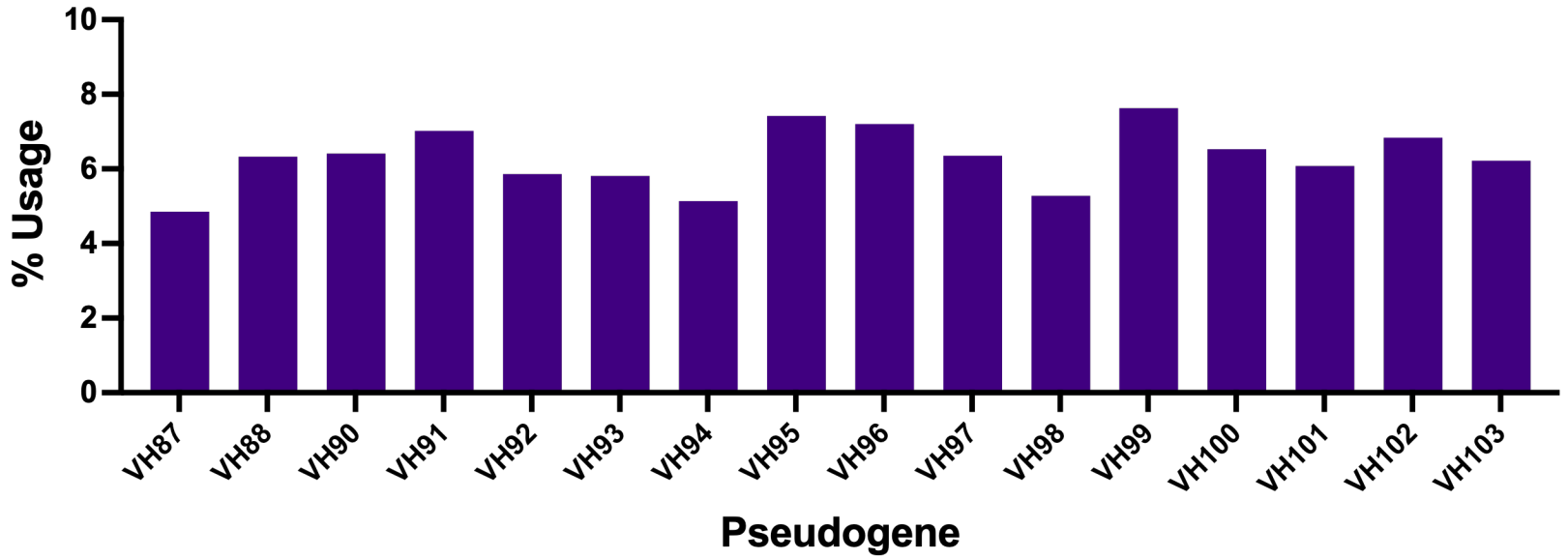


Ultralong CDRH3 is produced in class-switched serum immunoglobulin

Naïve Repertoire Diversified by Gene Conversion

NGS ANALYSIS OF NAÏVE REPERTOIRE

# Total CDRH3	# CDRH3 w/ germline seq	# CDRH3 w/ gene conversion	# CDRH3 w/ pseudogene ID
346,458	20,790 (6%)	325,668 (94%)	320,167 (92%)

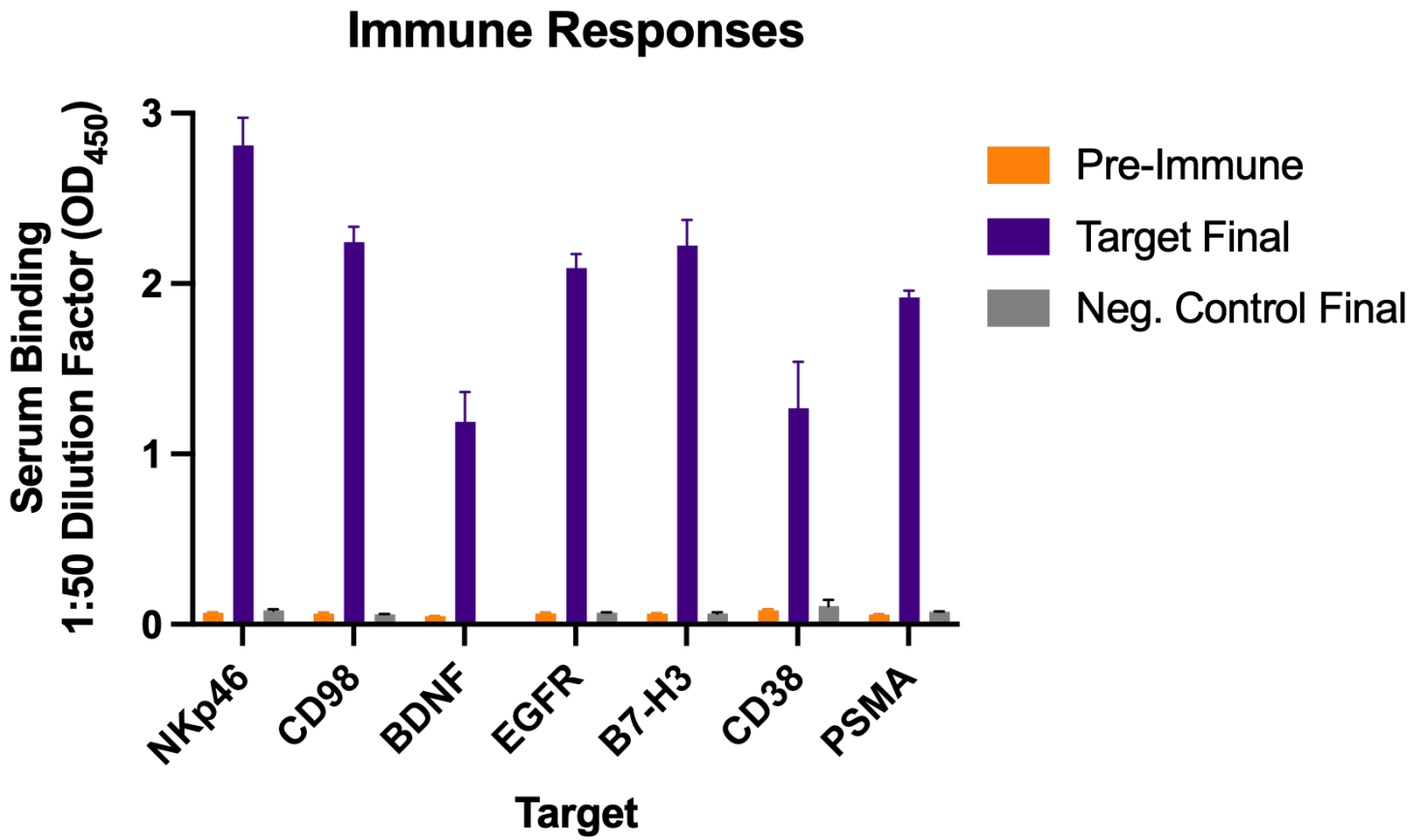


All pseudogenes participate in gene conversion of ultralong CDRH3 repertoire

OmniUltra Immune Response

BROAD ARRAY OF TARGETS ASSESSED

Target	Target Type
NKp46	Immune Engager
CD98	Brain Delivery
BDNF	Pain Modulator
EGFR	Tumor Target
B7-H3	
CD38	
PSMA	
OmniAb Partner Target 1	Confidential
OmniAb Partner Target 2	Confidential
OmniAb Partner Target 3	Confidential



OmniUltra chickens are immunoresponsive to a variety of antigen targets

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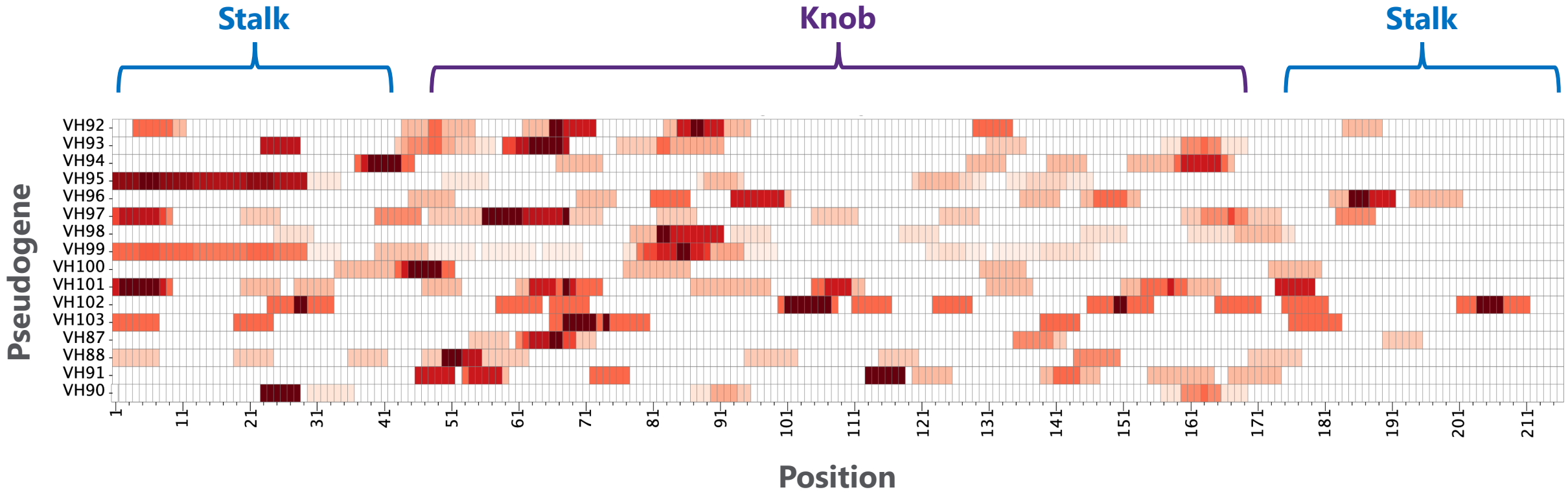
Ultralong CDRH3s Are Diversified by Gene Conversion

SEQUENCE ANALYSIS OF ANTIGEN-SELECTED CLONES



Gene conversion mainly focused on knob region in antigen-specific ultralong antibodies

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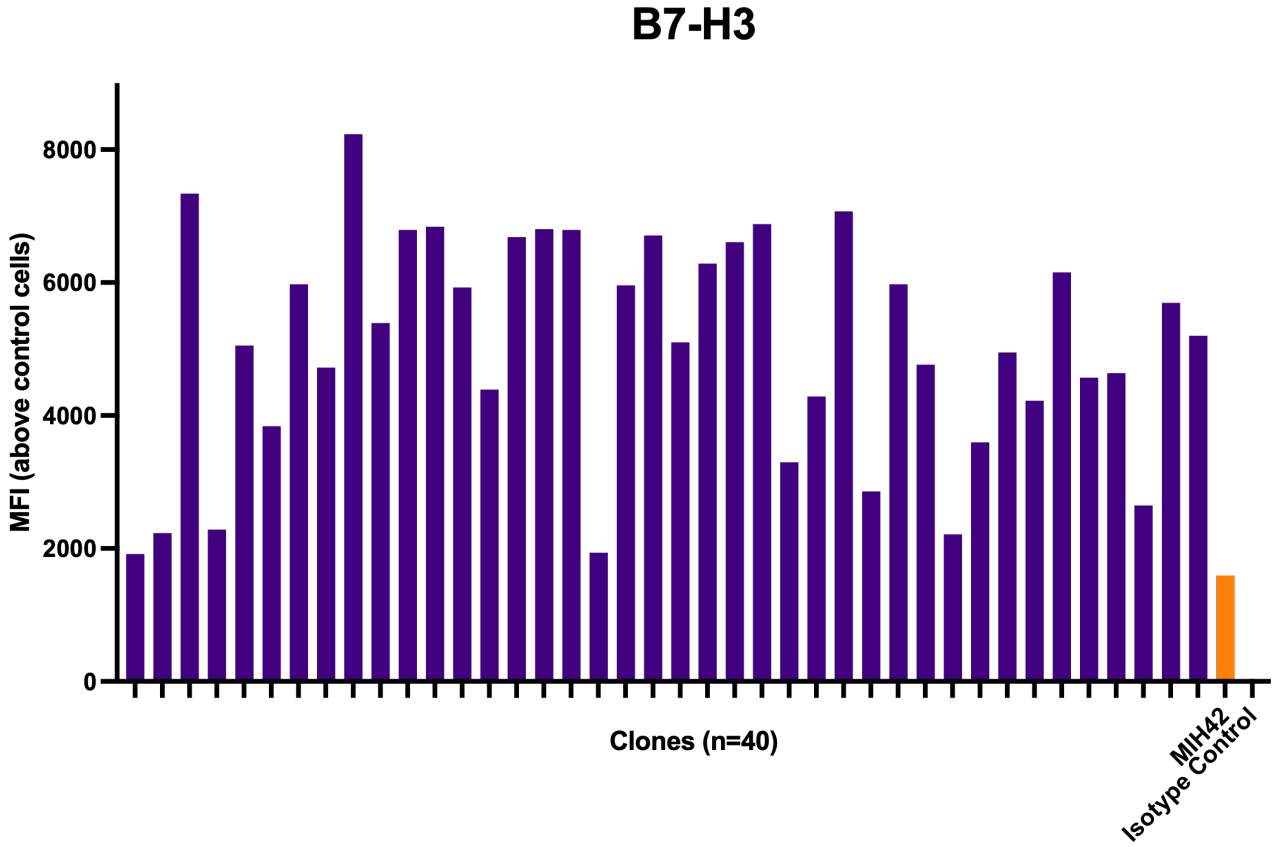
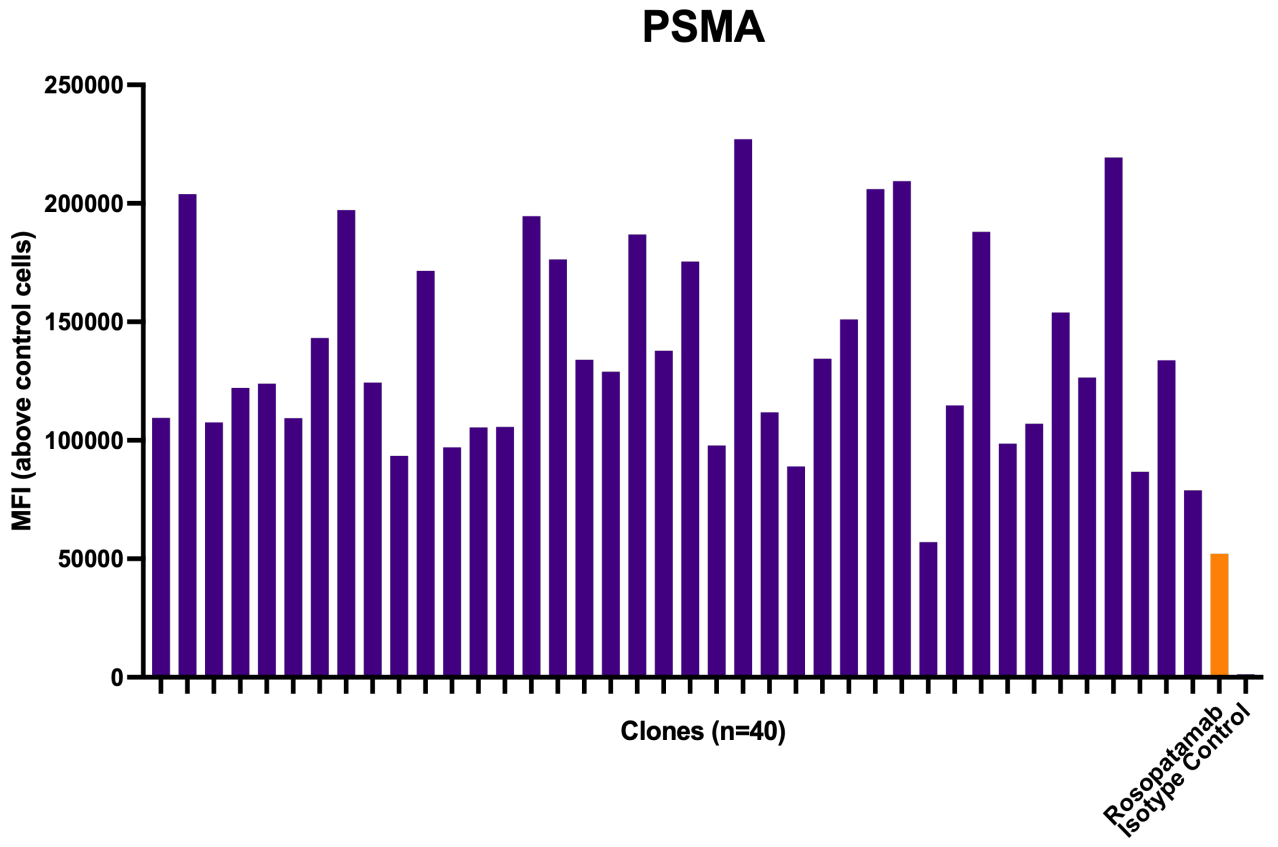
Ultralong CDRH3 Bind to Therapeutic Targets on Cells

FLOW CYTOMETRY OF ANTIGEN-SPECIFIC CLONES

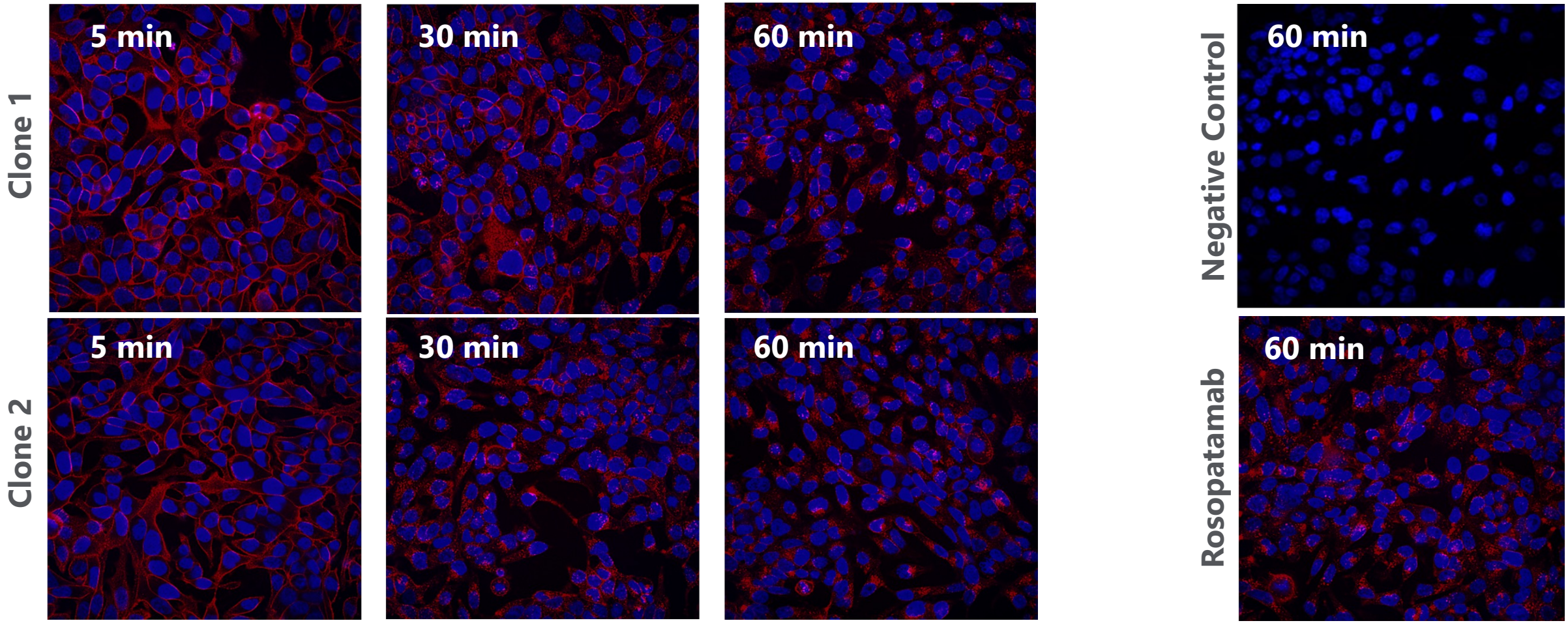




Ultralong CDRH3 IgG antibodies bind to native protein structure

Ultralong CDRH3 Can Internalize

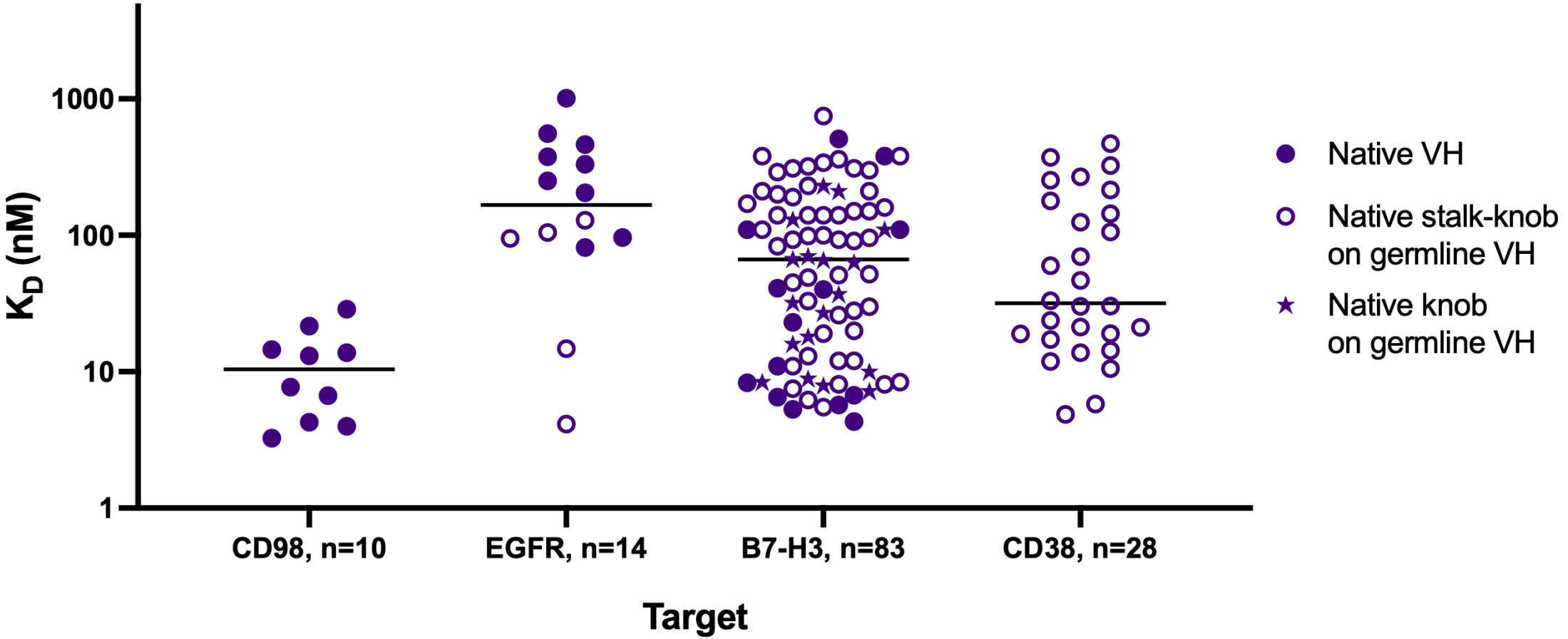
PSMA CLONES INTERNALIZE IN LNCaP CELLS



Ultralong CDRH3 IgG antibodies have potential application for ADCs

Ultralong CDRH3 Binding Affinity

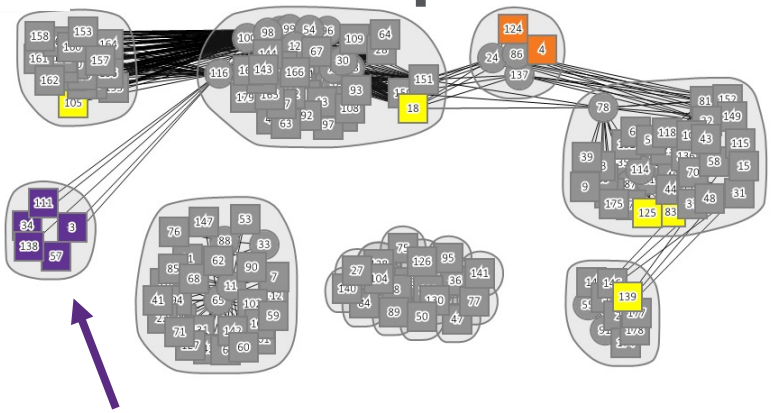
NATIVE KNOB ON GERMLINED VH MAINTAINS BINDING AFFINITY



Ultralong CDRH3 IgG clones cover a broad range of binding affinity, depending on the target

Epitope Coverage of Ultralong Antibodies

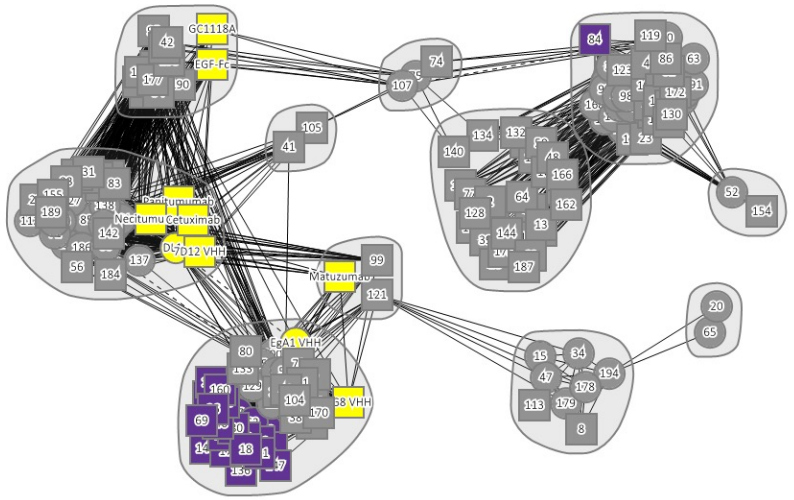
NKp46



OmniUltra - 1 unique epitope bin not represented by any other repertoire tested

	OmniUltra, n=5
	OmniTaur (cow), n=2
	Benchmarks, n=5
	OmniFlic + OmniClic + OmnidAb, n=167

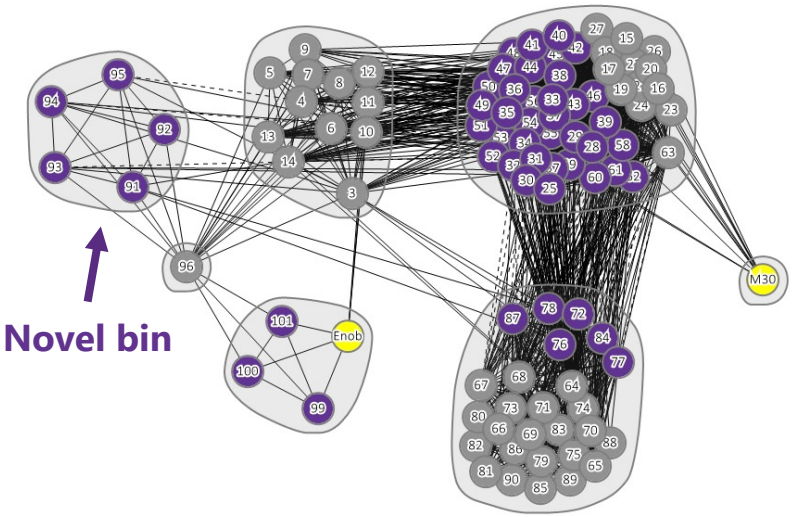
EGFR



OmniUltra - 2 epitope bins

	OmniUltra, n=22
	Benchmarks & EGF ligand, n=10
	OmniChicken + OmniClic + OmnidAb, n=153

B7-H3



OmniUltra - 4 epitope bins (including a novel bin)

	OmniUltra, n=50
	Benchmarks, n=2
	OmniChicken, n=47

Ultralong CDRH3 IgG clones bind to overlapping and novel epitopes

*NKp46 and B7-H3 Benchmarks represent clinical or literature Abs sourced from mouse immunization
**EGFR structural benchmarks (Abs with PDB IDs) sourced from immunization of llama or mouse, or phage display of non-immune human repertoires

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OmniUltra™

- OmniUltra chickens are engineered to express ultralong CDRH3 in the context of human V frameworks
- Like wild-type chickens, OmniUltra chickens produce robust immune titers to a variety of human targets
- Pseudogenes participate in gene conversion of ultralong CDRH3
- Ultralong CDRH3 cover the same epitopes as previous platforms, with the potential to also bind to novel epitopes
- Ultralong CDRH3 can be tethered for bispecifics or produced as autonomous binding units (picobodies™)

Acknowledgements

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Poster 126: Development of OmniUltra™: A transgenic chicken system for the generation of ultralong CDRH3 antibodies, mini-proteins, and structured proteins

Poster 139: Empowering the efficient discovery of ultra-long CDRH3 antibodies with high-throughput xPloration® workflows

Booth 300