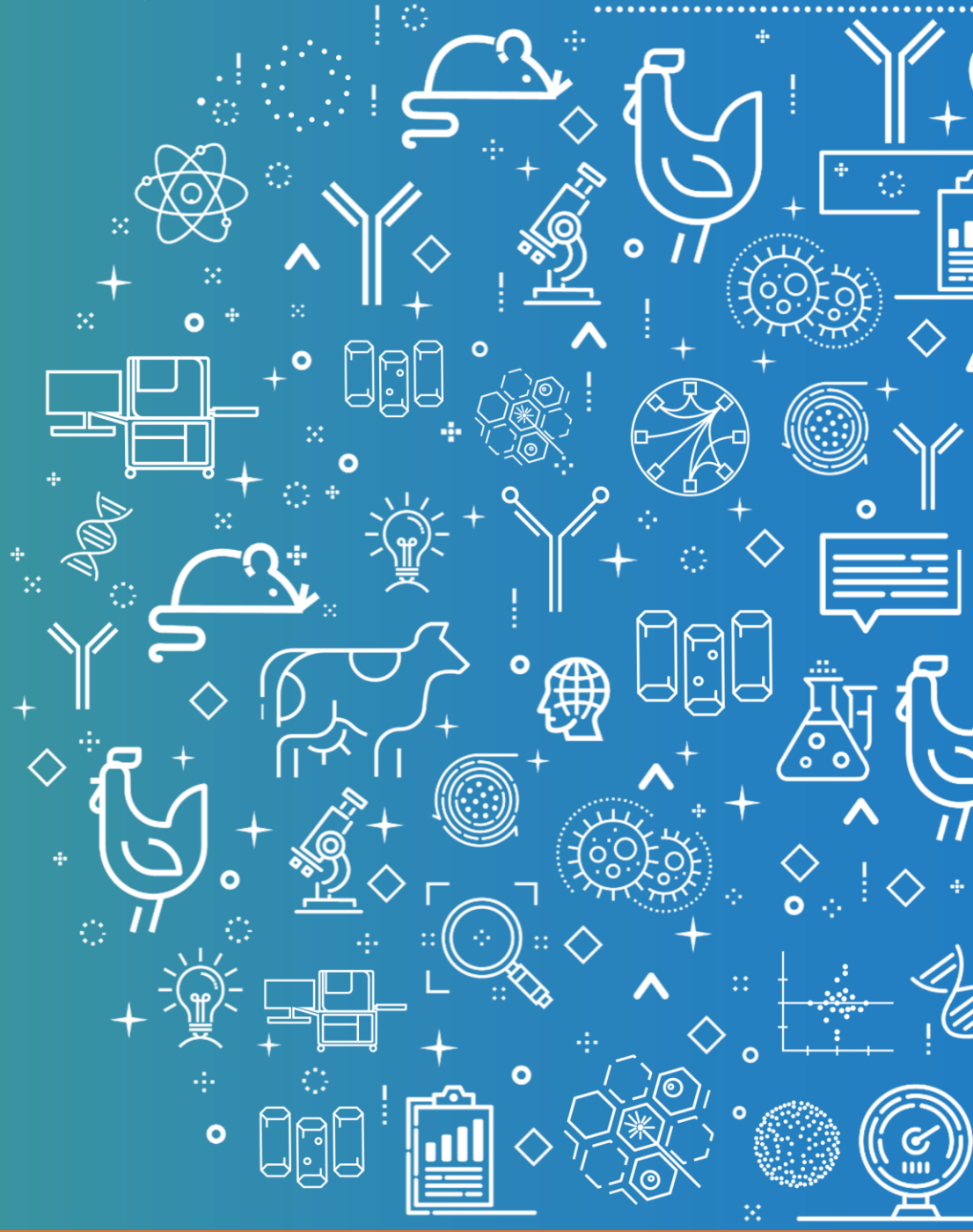
OmniAb®

OmniUltra™

A New *In Vivo* Platform for Discovery of Novel Mini-Proteins and Structured Peptides

AETC: Monday, December 15, 2025

Scientific Briefing #6: 12:15-1:15pm



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

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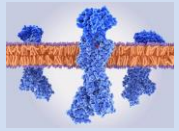
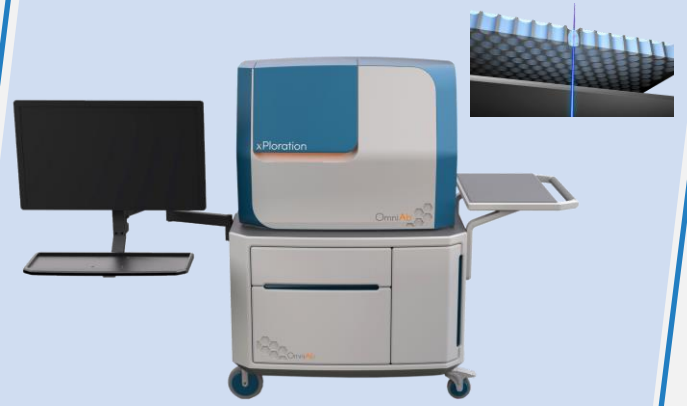
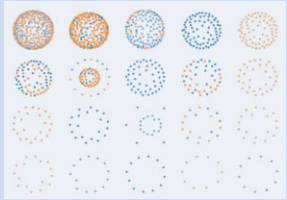
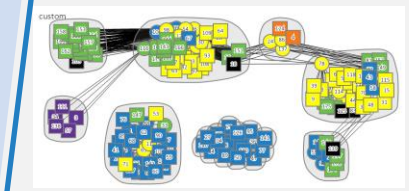
OmniAb Technologies

TECHNOLOGY OFFERINGS ADDRESSES THE MOST CRITICAL CHALLENGES OF ANTIBODY DISCOVERY

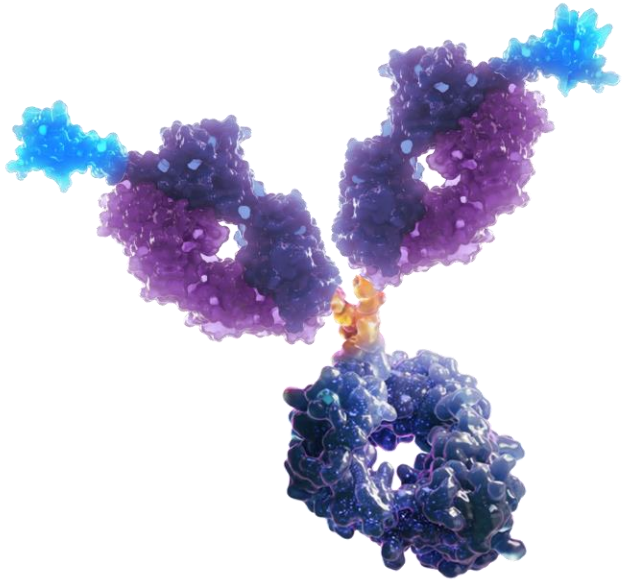
Create	Screen	Deliver
Create Diverse Repertoires of High-Quality Antibodies	***Screen Millions of Cells to Find Potential Therapeutic Candidates***	***Further Characterize, Select and Optimize the Right Therapeutic Candidate***
 *Antigen Design & Proprietary Reagents*	xPloration® 	• *Custom Bioinformatics*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

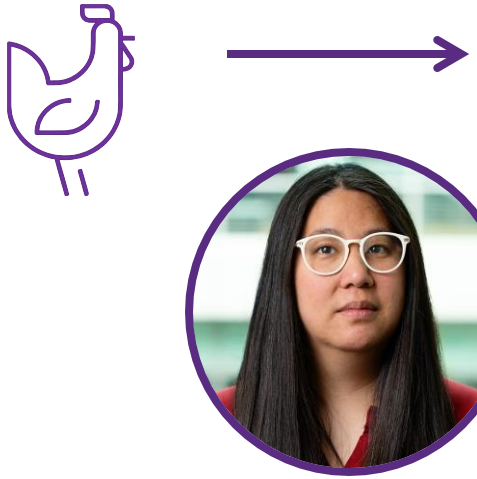
*OmniAb entered into an agreement with mAbsolve Ltd. for STR, mAbsolve's Fc-silencing platform technology, which provides OmniAb with non-exclusive, sublicensable right to incorporate the STR technology with antibodies that have been generated using OmniAb's antibody discovery platform.

Introducing OmniUltra™

Leveraging evolutionary distance for discovery of ultralong CDRH3 antibodies with broad epitope coverage



A new *in vivo* platform for discovery of novel mini-proteins and structured peptides



Christine Vuong, Ph.D.
Tuesday, December 16, 2025
Scientific Briefing #5: 12:35-1:05pm
Pacific Ballroom 15

Yasmina Abdiche, Ph.D.
Monday, December 15, 2025
Scientific Briefing #6: 12:15-1:15pm
San Diego Ballroom AB

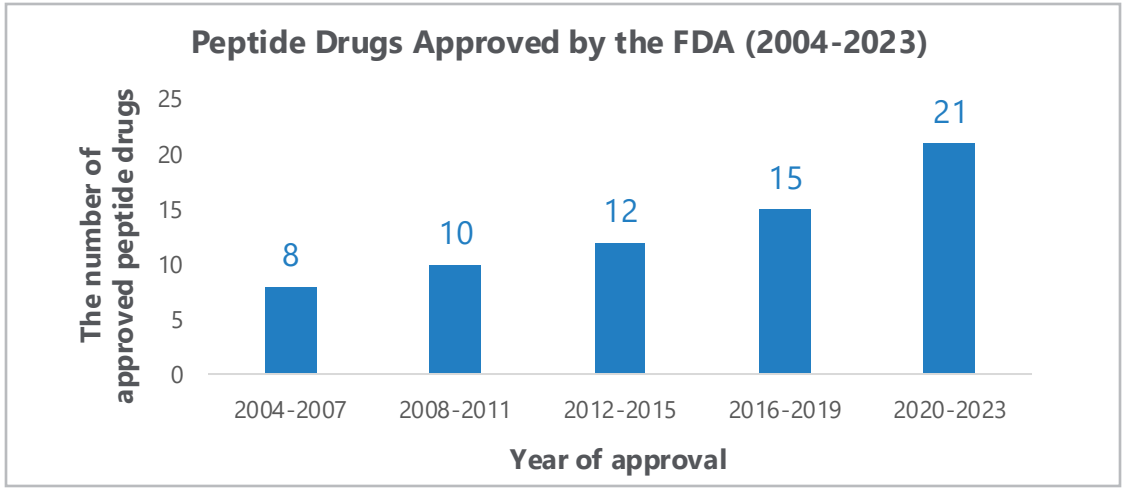
OmniAb

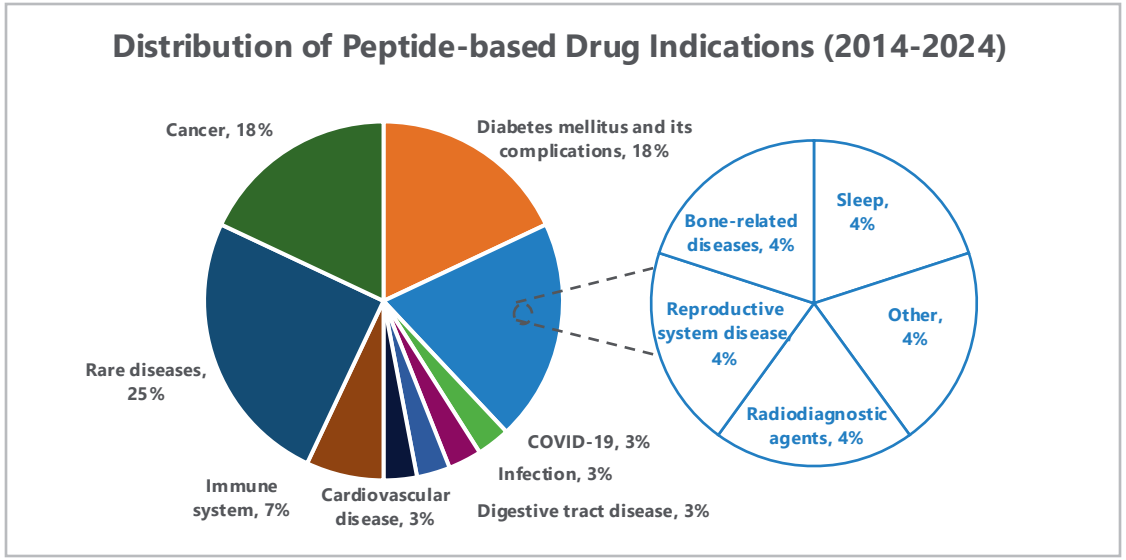
Overview

- Therapeutic Peptides: An Emerging Drug Class
  - High specificity, low toxicity, and structural adaptability to target diverse biological interfaces
  - Enhanced drug-like properties of structured vs linear peptides
- Nature as a Blueprint
  - Across the biosphere, convergent structural motifs provide inspiration for novel drug design
- OmniUltra™ Platform: A New Paradigm
  - *In vivo* affinity maturation of engineered natural scaffolds within a divergent host species
  - Embedding structured peptides (called *picobodies*) within context of antibody genes
- Picobodies™
  - Can be tethered or isolated as autonomous binding units to enable diverse applications
- OmniAb's Expansion
  - Extending discovery capabilities into peptide-based modalities
  - Leveraging decades of expertise in *in vivo* selection and natural diversity to unlock new therapeutic modalities

Importance of Therapeutic Peptides as a Drug Class

PEPTIDE DRUGS FULFILL A UNIQUE ROLE IN THE PHARMACEUTICAL INDUSTRY





- Peptides are a distinct and growing class of drugs blending properties of small molecules and antibodies
- Diverse therapeutic areas including metabolism (diabetes & weight management), heart disease, infectious disease, rare diseases, and cancer, with **GLP-1 receptor agonists** currently dominating sales and growing rapidly
- **Advantages**:
  - High target specificity
  - Structural versatility
  - Low immunogenicity risk
  - Rapid tissue penetration and clearance
- **Historical Limitations**:
  - Intrinsically poor physicochemical properties
  - Synthesis and manufacturing challenges

Adapted from Xiao et al, Sig Transduct Target Ther 2025

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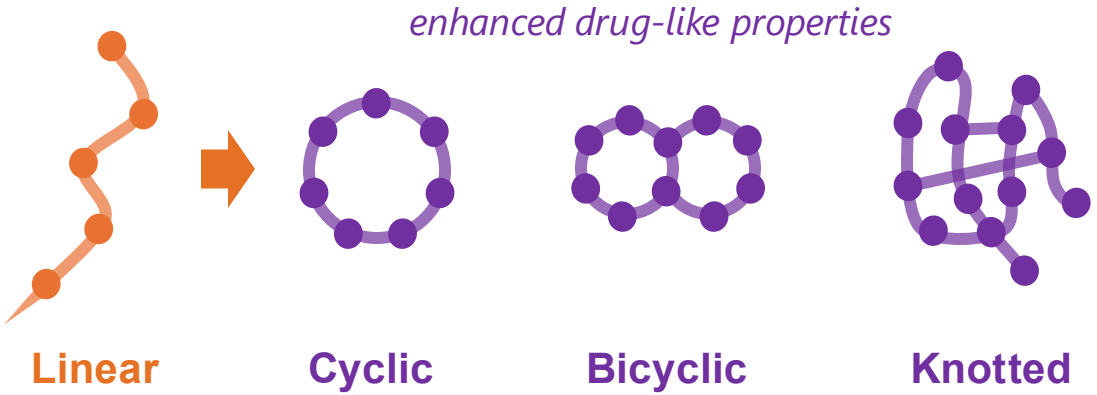
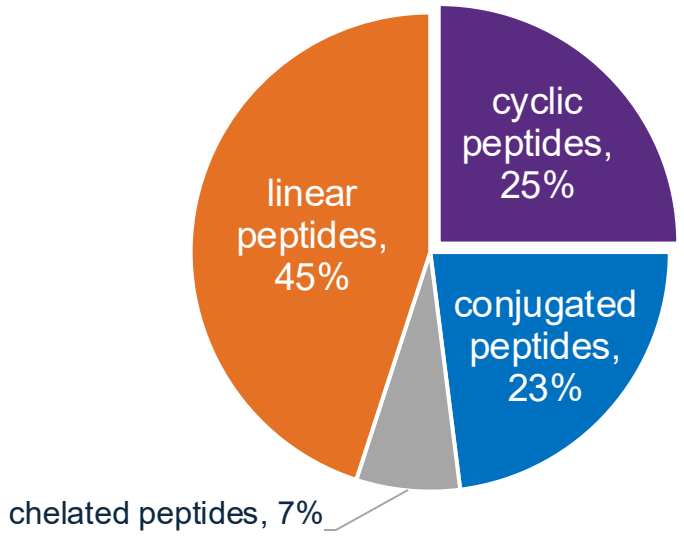
Advantages of Structured Peptides for Drug Discovery





FDA-Approved Peptides
Adapted from Sharma et al, Drug Discovery Today 2023

- **Peptides are structurally adaptable**
- **Structured peptides** can be engineered using **nature-inspired and synthetic** approaches
- Techniques include **constrained peptides** (cyclic, stapled, knotted) and **CDR-grafting** into non-Ig scaffolds
- Structured peptides may overcome some of the limitations of linear peptides:
  - Enhanced proteolytic stability
  - Antibody-like affinity and specificity through structural rigidity
  - Ability to target diverse epitopes
  - Improved cell permeability and bioavailability
  - Reduced immunogenicity
  - Tunable pharmacological properties

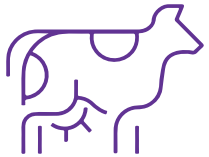
Convergent Structural Motifs in the Biosphere

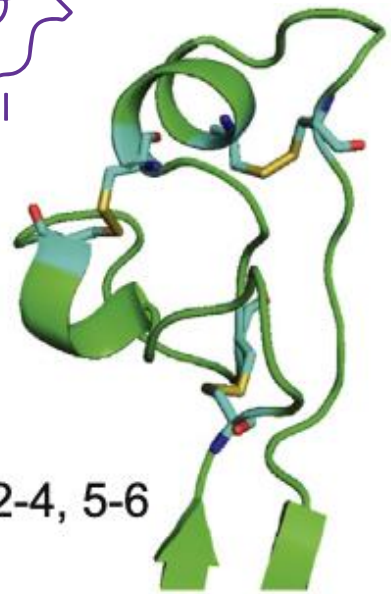
ShK peptide (potent Kv1.3 inhibitor)

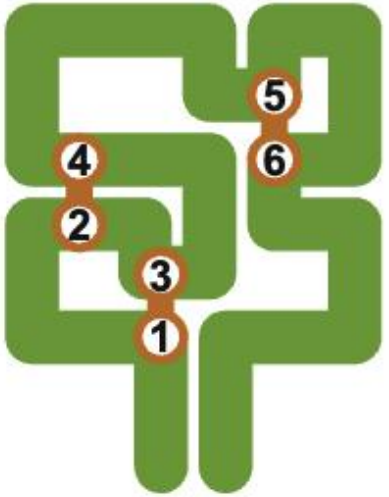
RSCIDTIPKSRCTAFQCKHSMKYRLSFCRKTCGTC

Pohl et al, Lett Pept Sci 1995

Cow antibody 'knob'







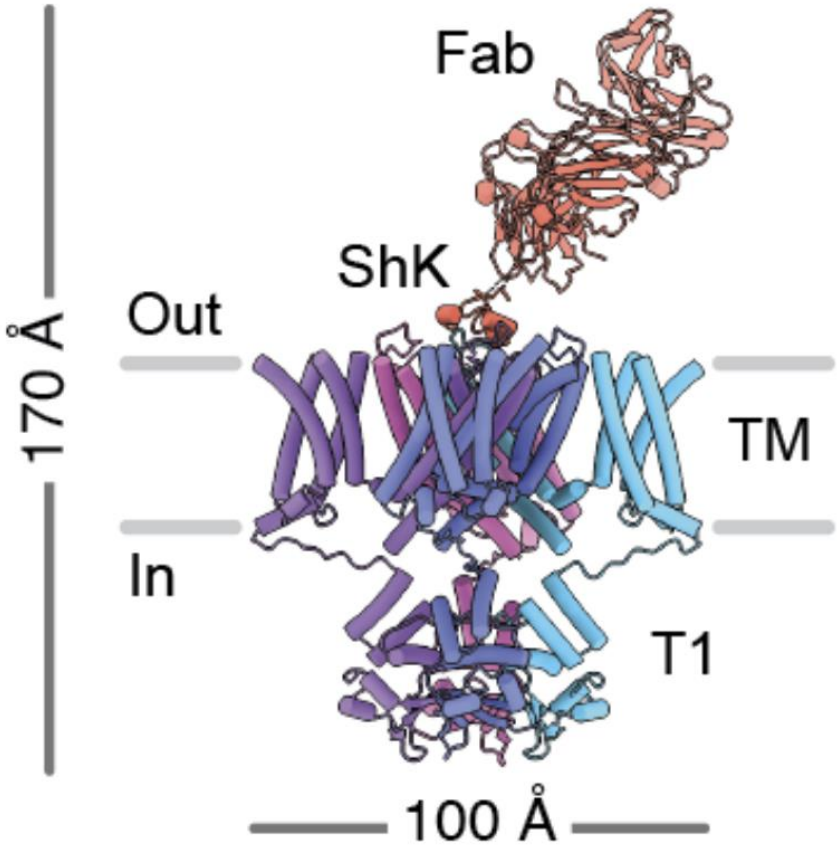
CSDGYIAVDSCGRGQSDGCVNDCNSCYYGWRNCRRQPAIHSYEF

Wang et al, Cell 2013

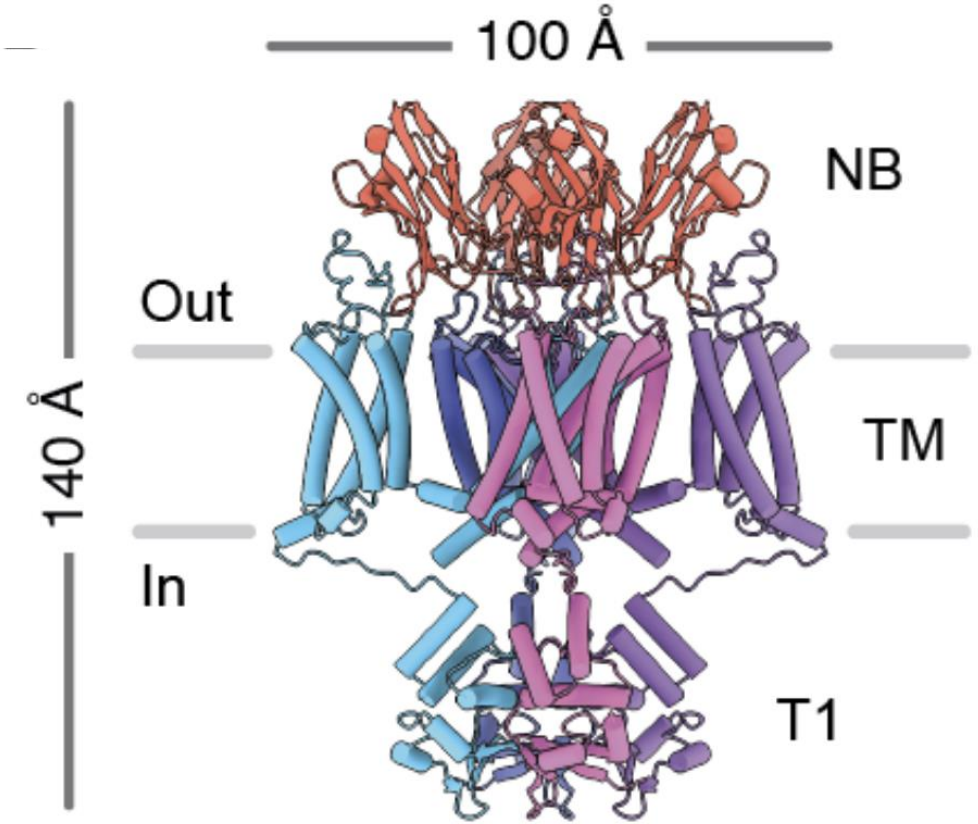
Ultralong CDRH3 antibodies potentially combine **biological potency** with **high target specificity**

Alternative Antibody Binding Modes to Kv1.3 Ion Channel

CRYO-EM STRUCTURES REVEAL HOW CDRH3 LENGTH IMPACTS BINDING MODE



Fusing the ShK peptide (from sea anemone) onto a human Fab ***mimics an UL CDRH3*** antibody and binds ***within*** pore



*Nanobodies (~15kDa) bind turret loops ***atop*** (not within) pore

Selvakumar et al, Nat Commun. 2022

*Nanobody® is a registered trademark of ABLYNX

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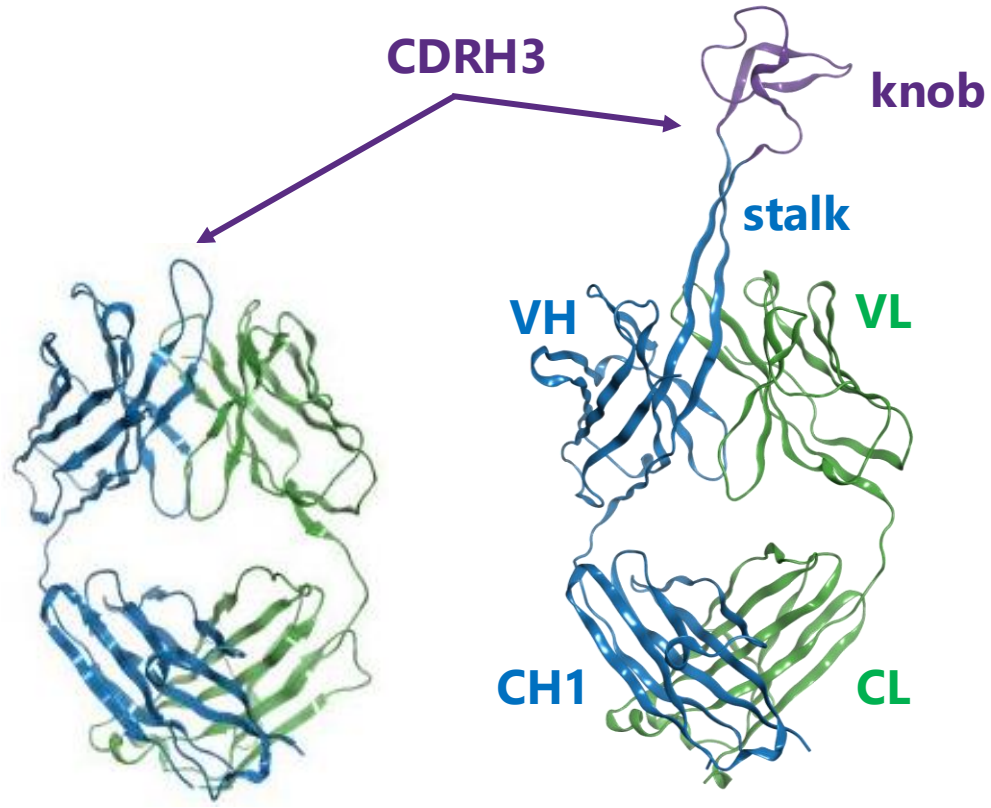
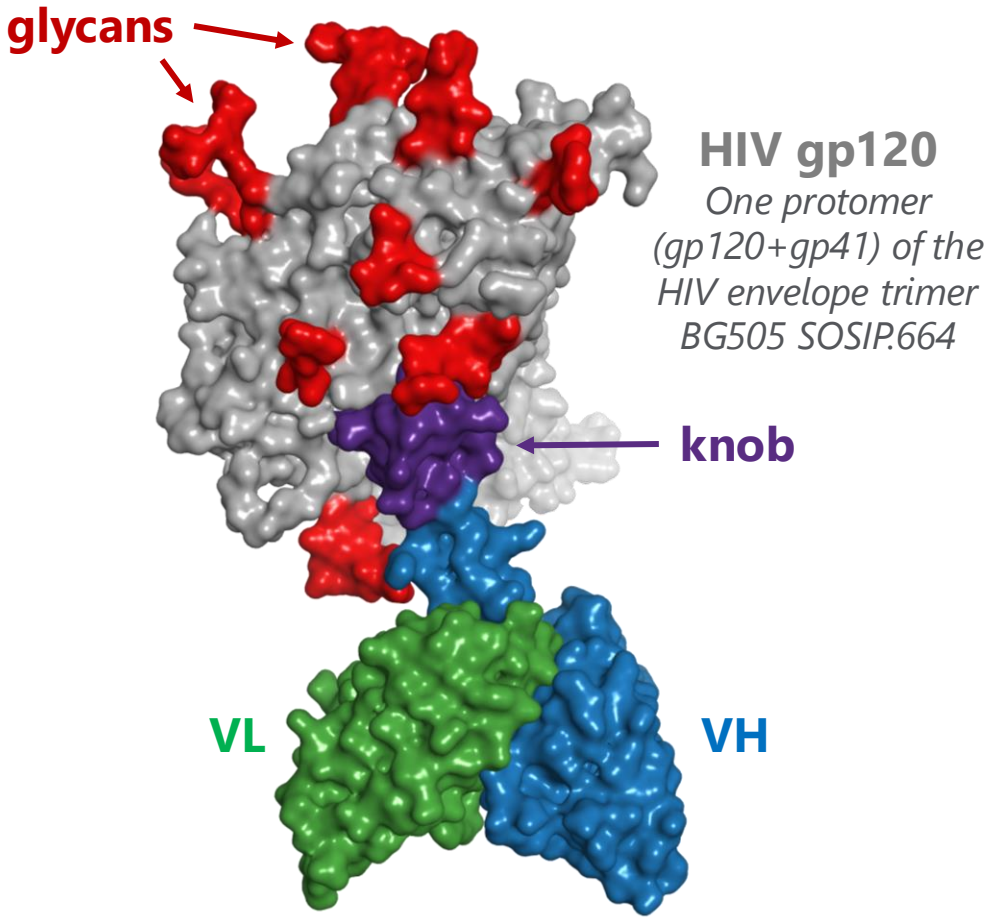
Ultralong CDRH3: Cow *vs.* Human



Human Fab

Cow Fab

Vadnais et al, Curr Opin Struct Biol 2016



Cows can generate antibodies with ***knob-defined paratopes***

Stanfield et al, Sci Adv 2020

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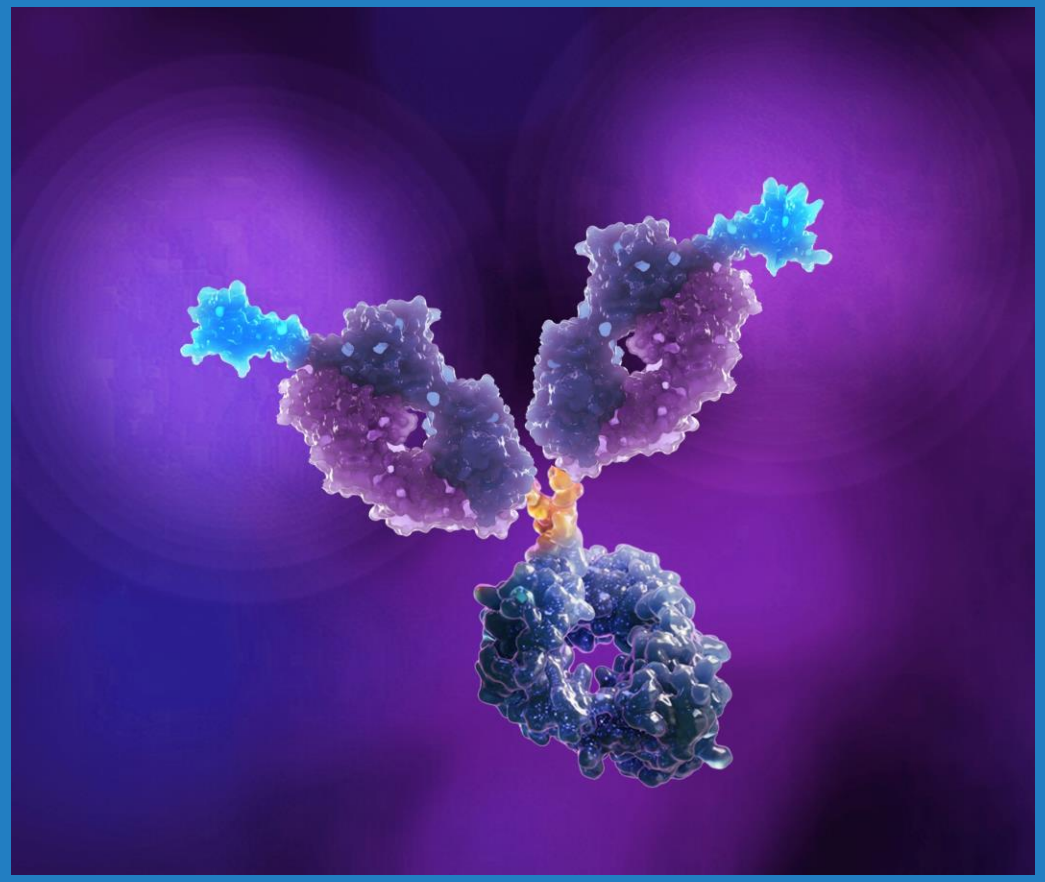
OmniUltra™

NEW *IN VIVO* TECHNOLOGY FOR PEPTIDE DRUG DISCOVERY



Uses ***in vivo* optimization** of ultralong CDRH3 ***'knob'*** sequences expressed in the context of a human variable (V) framework

Generates **structured peptides** that autonomously bind to human drug targets

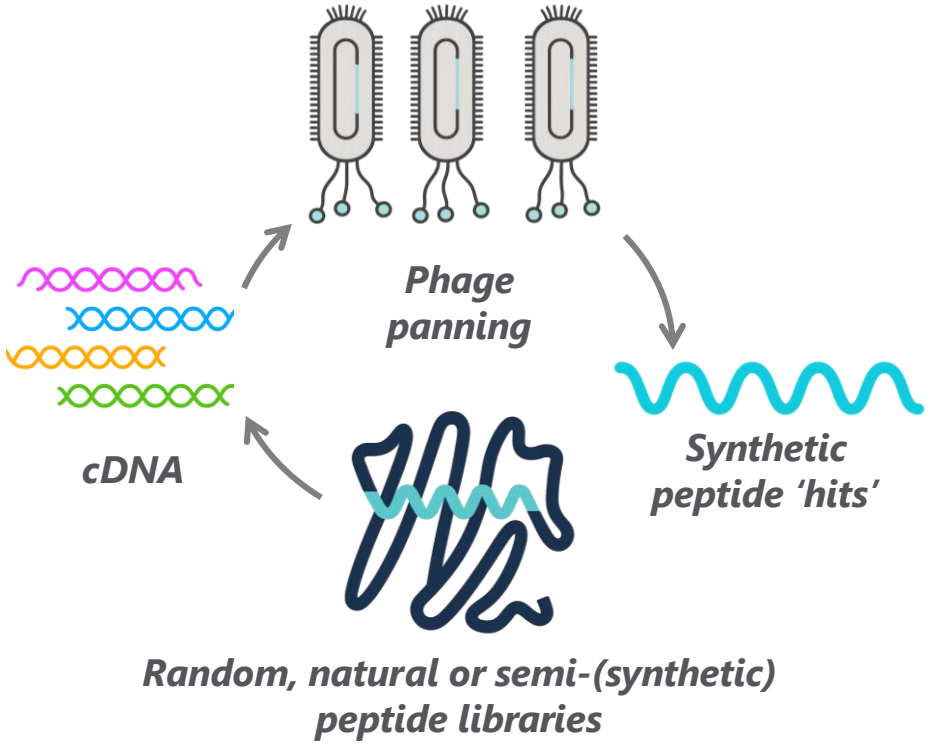
Leverages a **divergent host species** to evolve these peptides, potentially expanding the diversity and functionality of peptide libraries against human targets

Offers a **potentially more dynamic and effective method** for discovering therapeutic peptides beyond traditional rational design or *in vitro* optimization approaches

Traditional Methods for Peptide Drug Discovery

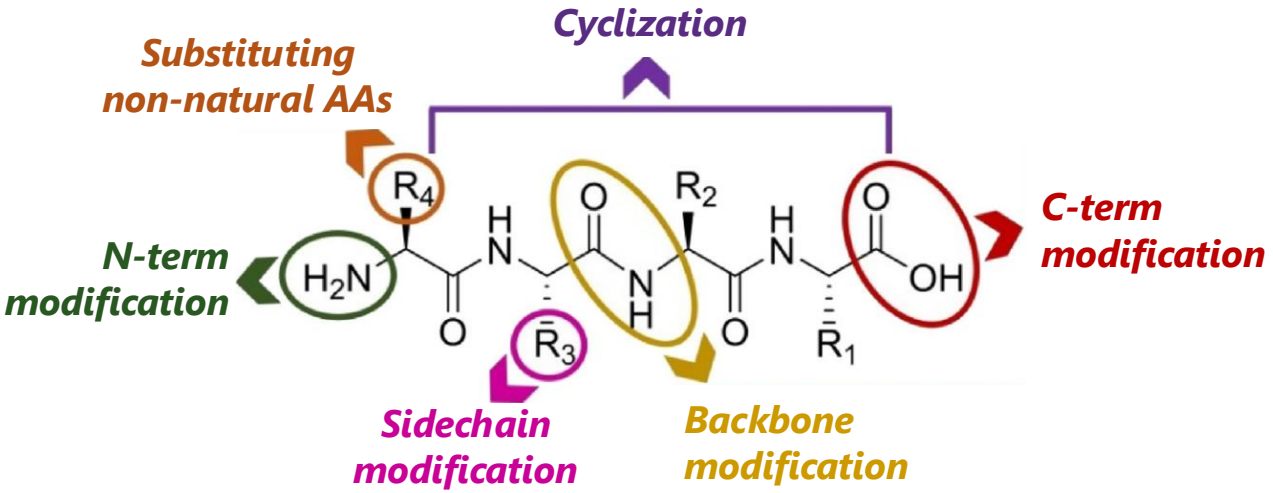
COMBINATORIAL CHEMISTRY & RATIONAL DESIGN: CONCEPTUALLY DISTINCT YET COMPLEMENTARY

Phage Display of Combinatorial Libraries
Discovery-oriented



Adapted from Zhang et al, Int J Mol Sci. 2022

Rationally-Designed Libraries
Optimization-focused



Adapted from Sharma et al, Drug Discovery Today 2023

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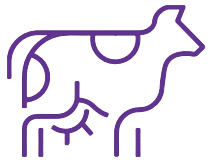
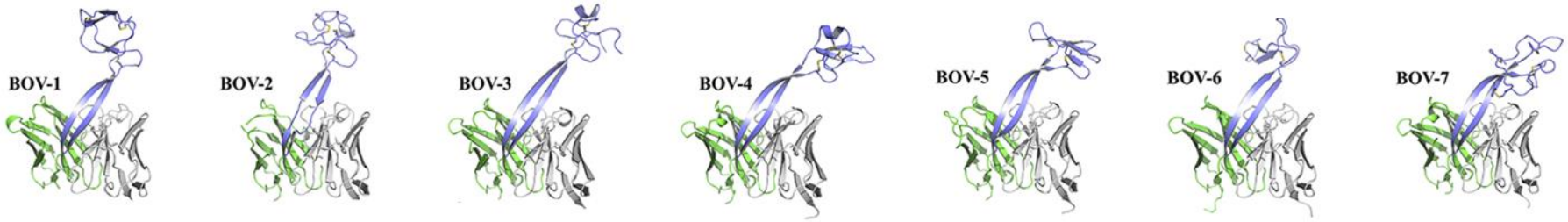
Complementary Peptide Discovery Approaches

Method	Pros	Cons
Combinatorial Chemistry Synthesizes libraries of diverse compounds to 'cast a wide net' and then screens for activity	Chemical diversity	Fixed libraries Limited by synthesis
Display Technologies Empirical selections from (often random) peptide libraries displayed on Phage/Yeast/mRNA	Screens millions of variants Can find novel binders	Fixed libraries Primarily *in vitro*
Rational Design Uses structural, functional, and computational models to design peptides with specific properties	High precision on fewer candidates Faster optimization (if knowledge exists)	Relies on existing knowledge May miss novel structures
***In vivo* Optimization** OmniUltra™ Generates peptides sourced directly from natural immune diversification	**Peptides are inherently biologically active and evolved for stability** **High diversity**	Limited to non-toxic antigens

Advantages of OmniUltra *vs.* Cow



- **Only 10% of cow antibodies contain the UL CDRH3 feature**, and all rely on a bovine framework
- **Knob domain structures vary**, and not all cysteine patterns enable independent binding
- **Discovery campaigns generally use one or two cows** instead of standard laboratory animals
- **The workflow is limited** and relies solely on phage display



Example of bovine Fv crystal structures; Dong et al, Front Immunol. 2019

OmniUltra™

Divergent host species expands epitope coverage of human targets

- **UL CDRH3 integration** designed into most of the antibody repertoire
- **Validated knob scaffold** enables chemical synthesis of knob-derived peptides and **humanized scaffold expression** obviates the need for *ex vivo* humanization
- **Multiple birds per campaign** boosts sequence diversity
- **Display and B cell workflow compatibility** broadens screening options

OmniUltra Workflow: From Knobs to Picobodies

REDEFINING PEPTIDE INNOVATION: PRECISION PEPTIDES OPTIMIZED IN VIVO

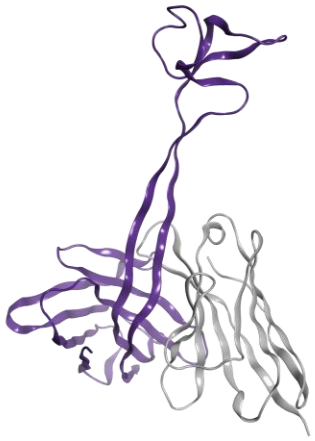
Hit ID

Native VH+VL

All CDRs and FWs ***diversified in vivo*** – amenable to single B cell screening **(xPloration)**

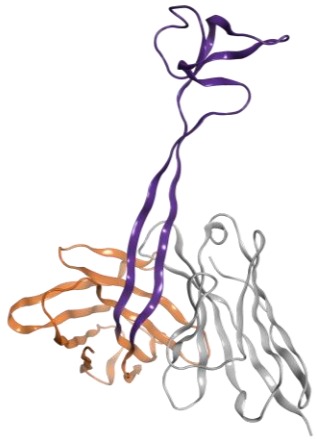
Hit Confirmation

Native VH



Germline VL

Native stalk + knob



Germline VH + Germline VL

Native knob

Germline VH + stalk + Germline VL

Recombinant expression in different IgG-based formats

Peptide production

Picobodies

6 kDa

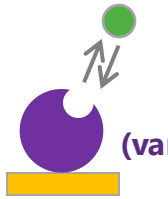
4 kDa

Chemical Synthesis

Cleaved from recombinant Fc fusion protein

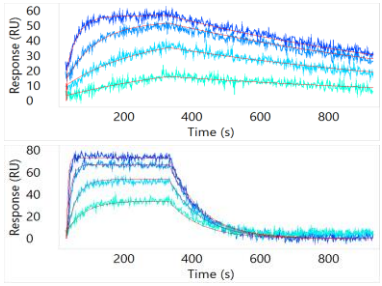
SPR Binding Characterization

Monovalent target

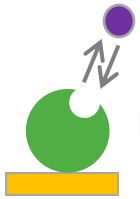


Ultra IgG (various formats)

Anti-human-Fc-coated chip



Picobody (monovalent analyte)



Fc-fused target

Protein A-coated chip

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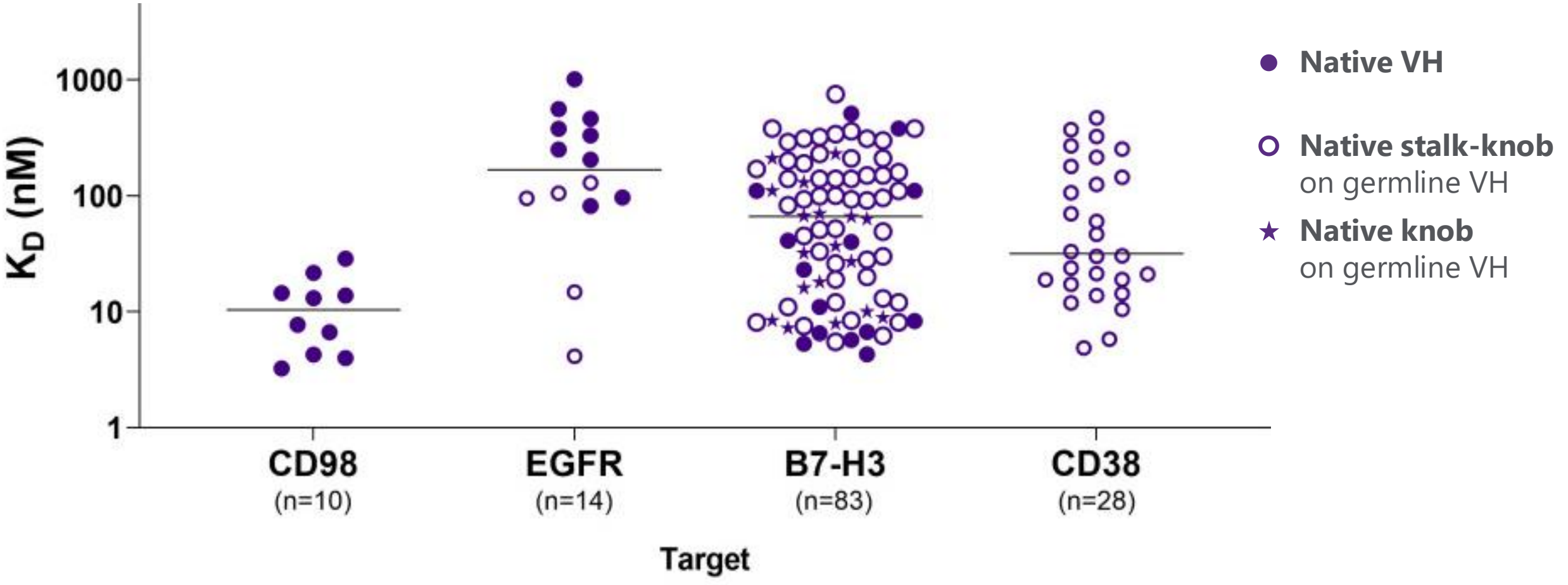
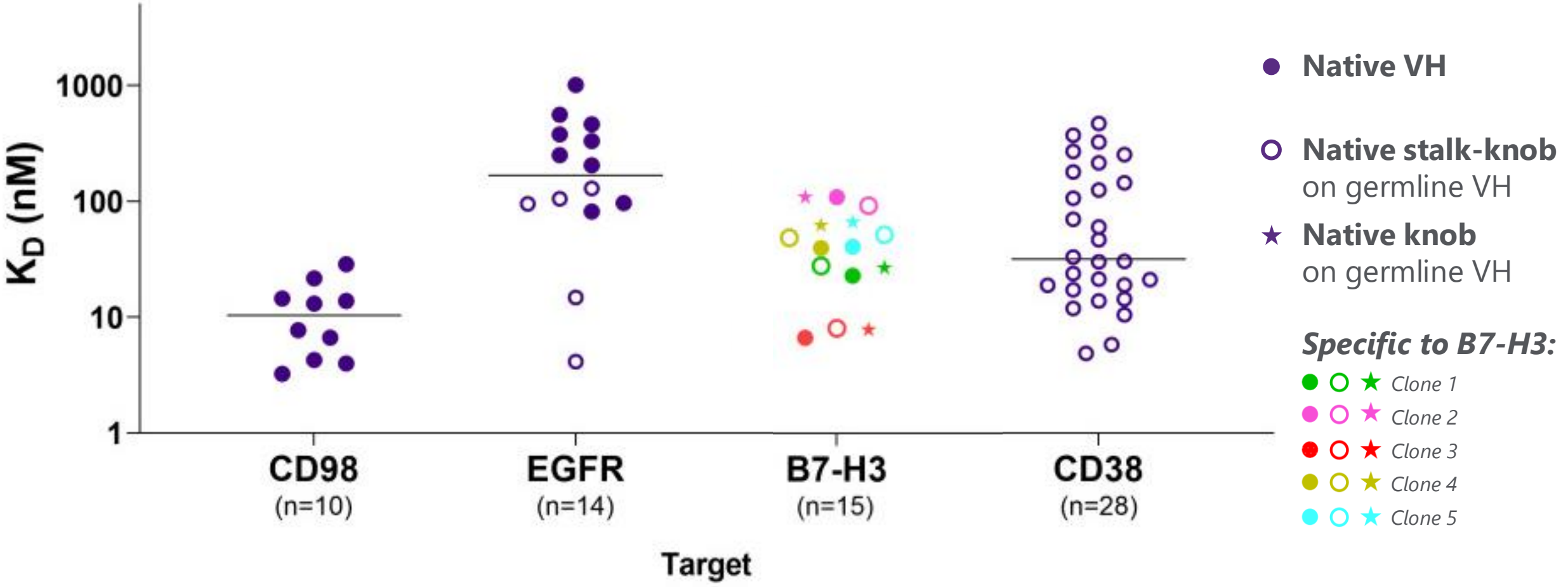
OmniUltra Clones with Knob-Restricted Paratopes

SPR BINDING KINETICS CONFIRM HIGH AFFINITY BINDERS TO MULTIPLE TARGETS



OmniUltra Clones with Knob-Restricted Paratopes

SPR BINDING KINETICS CONFIRM HIGH AFFINITY BINDERS TO MULTIPLE TARGETS



Knobs that retain ***high affinity*** within a fully germline VH scaffold are ideal candidates for tethering or chemical synthesis as stand-alone peptides

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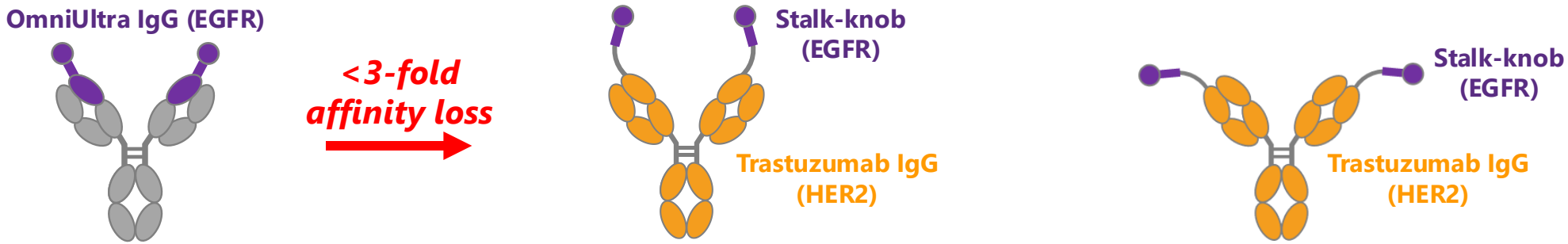
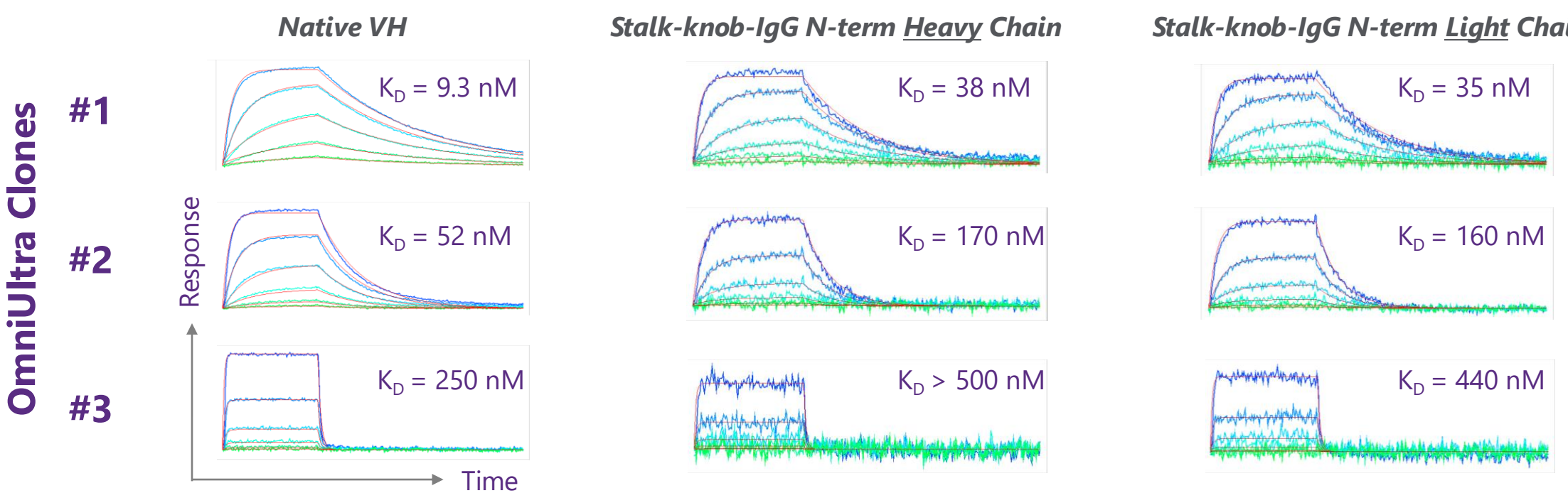
Tethering OmniUltra Stalk-Knobs for Bispecifics: EGFR





OmniUltra clones can be converted to ***stalk-knob***-tethered bispecifics on an unrelated IgG backbone with ***minimal loss of binding affinity***

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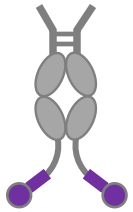
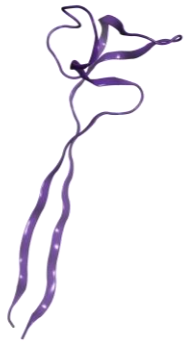
Isolating Knobs as Autonomous Binding Units: EGFR

CONVERTING OMNIULTRA ANTIBODIES INTO SYNTHETIC PEPTIDES WHILE PRESERVING AFFINITY



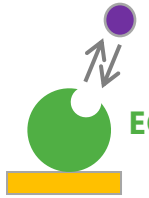
Stalk-knob
C-term Fc fusion

Cleavage and isolation



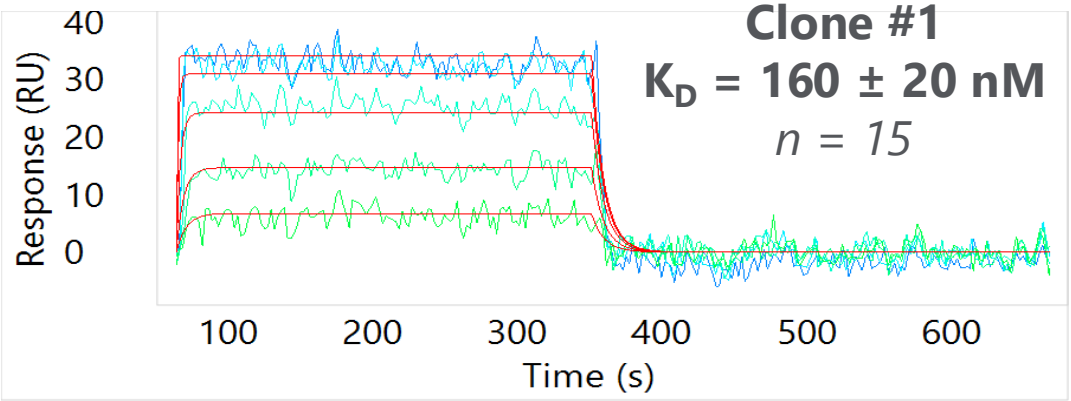
Recombinant
stalk-knob peptide
(6 kDa)

Anti-EGFR picobody (monovalent analyte)

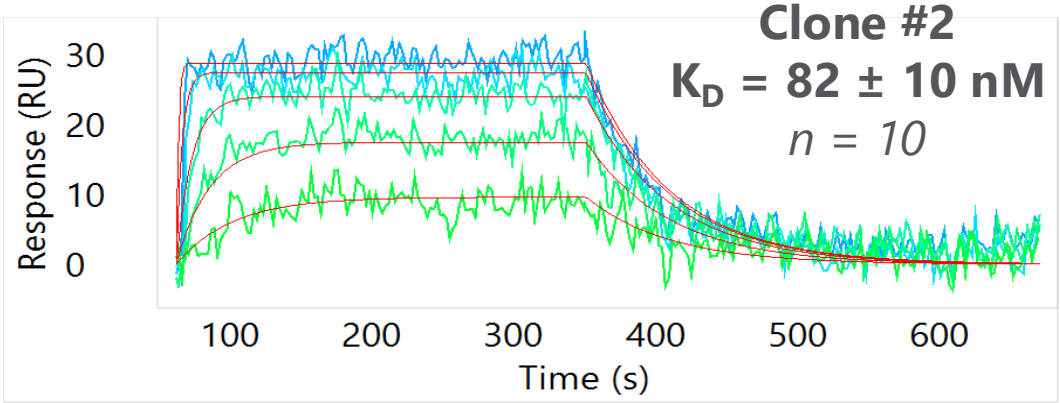


Protein A-coated chip

Chemically synthesized
knob peptide
(4 kDa)



Clone #1
K_D = 160 ± 20 nM
n = 15



Clone #2
K_D = 82 ± 10 nM
n = 10

OmniUltra clones can be produced as ***picobodies*** by cleaving them from recombinant Fc fusions or via chemical synthesis

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OmniUltra™ Nature-Inspired Peptide Innovation

Key Advantages

- **Proprietary *In Vivo* Platform** – A breakthrough approach for peptide discovery that's potentially more dynamic and efficient than traditional methods or cow-based immunization
- **Knob-Derived Peptides** – Deliver antibody-like binding precision with peptide-like tunable clearance, unlocking new pharmacokinetic possibilities
- **Flexible Production** – Compatible with both chemical synthesis and recombinant manufacturing, for scalability

Impact

- **Broadens Therapeutic Discovery** – Opens new frontiers across multiple modalities and indications, including multispecifics, conjugates, CART, radiopharma and more
- **Extends OmniAb's Leadership** – Bringing our proven discovery engine into the ***peptide space*** for novel applications

OmniAb®

Tuesday, December 16th 12:35 p.m. – 1:05 p.m.
Pacific Ballroom 15

OmniUltra™: Leveraging evolutionary distance for the discovery of ultralong CDRH3 antibodies with broad epitope coverage

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