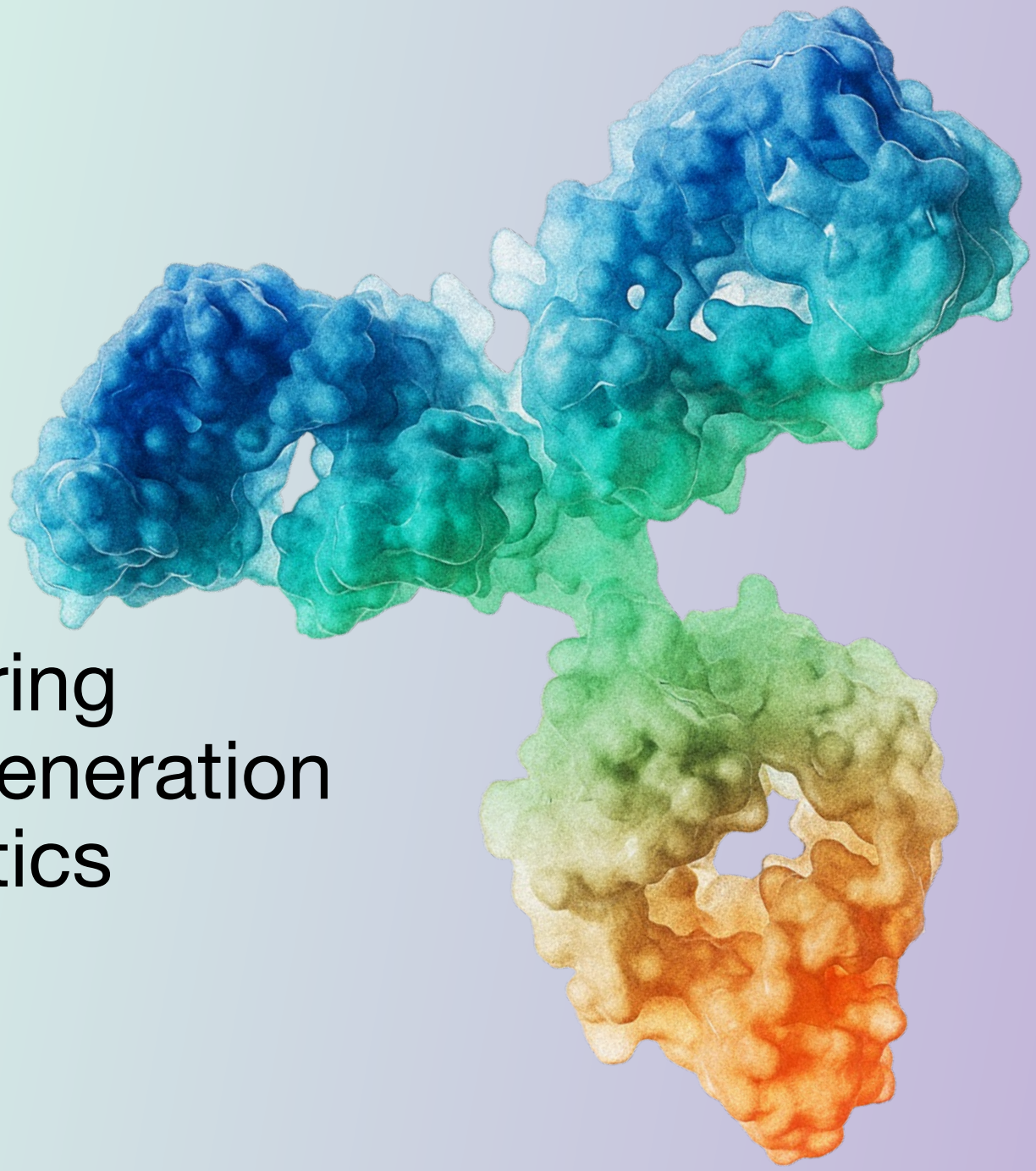
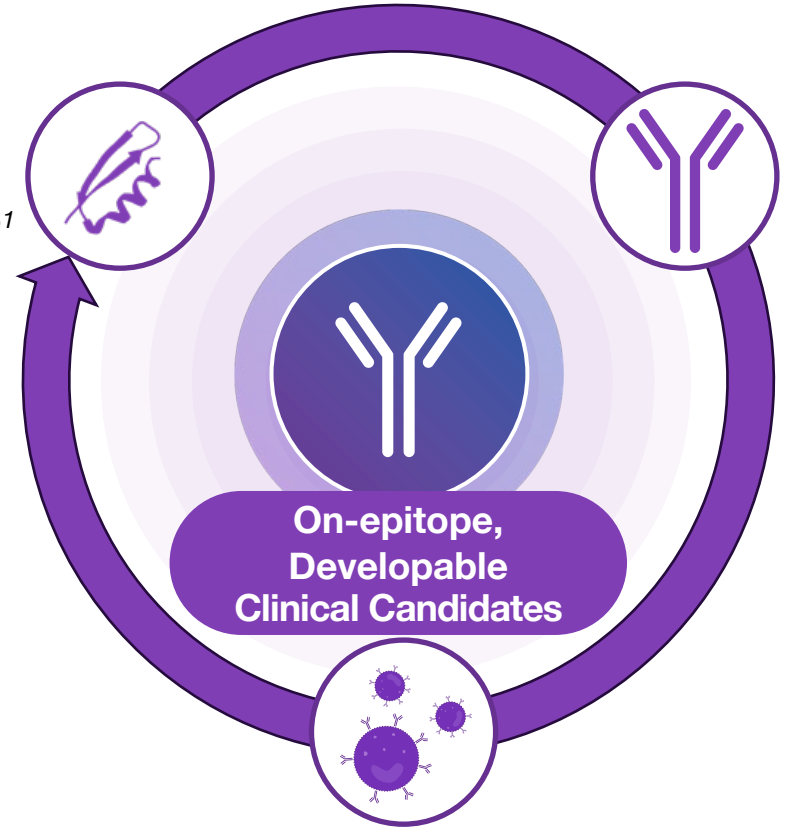


Beyond Peptides: Engineering GPCR Agonists for Next-Generation Cardiometabolic Therapeutics

Cody Moore

November 2026

End-to-End Antibody Discovery Platform Accelerates Path to IND



Target Engineering

Epitope-selective antibody discovery with AI protein design[1]

Human Antibody Diversity

Naïve human CDR libraries in clinically validated frameworks

Mammalian Display

Multi-Dimensional optimization in production cell-lines

[1]*U.S. Patent No. 11,545,238 (issued January 3, 2023)*

Amylin Peptide Analogues: Understanding the Optimal Profile

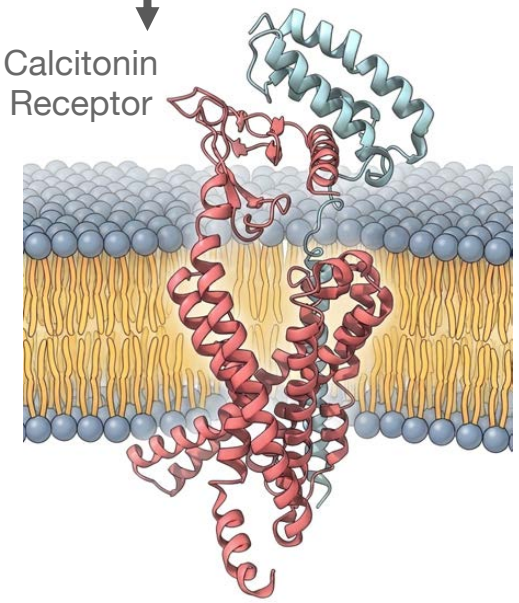
37 aa pancreatic hormone, reduces food intake, distinct mechanism from GLP-1s

***SARA**: Selective Amylin Receptor (AMYR) Agonist*

RAMP-1/3

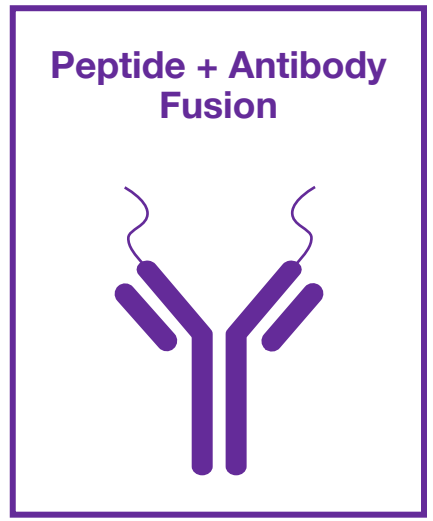
***DACRA**: Dual Amylin and Calcitonin Receptor (CTR) Agonist*

Calcitonin Receptor



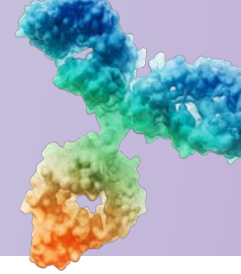
Existing peptide agonists retain CTR activity, leaving the optimal therapeutic profile undefined

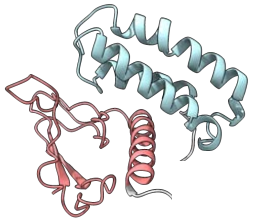
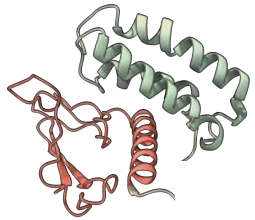
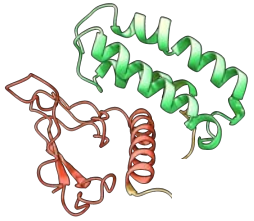
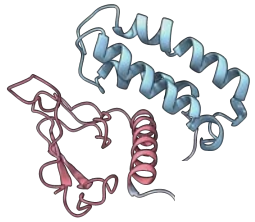
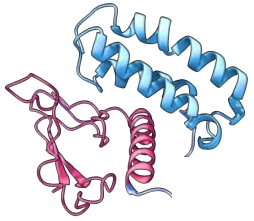
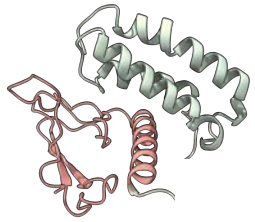
Goal: Improve therapeutic specificity and longevity with antibody fusion



Antibody-delivered agonists could provide the selectivity and half-life to define the optimal profile

Amylin Peptide Analogues: Understanding the Optimal Profile



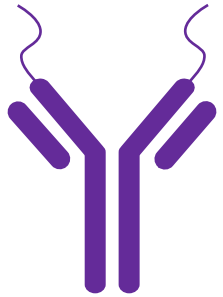
	AMY1R	AMY3R
Human		
Cyno		
Rat		

76% CTR cross-species sequence conservation

28% RAMP-1/3 cross-species sequence conservation

Goal: Improve therapeutic specificity and longevity with antibody fusion

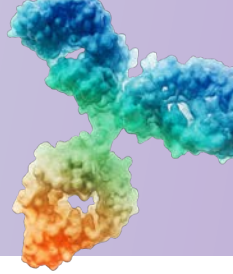
Peptide + Antibody Fusion

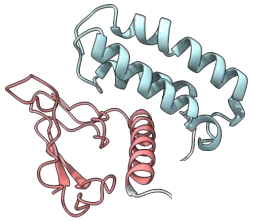
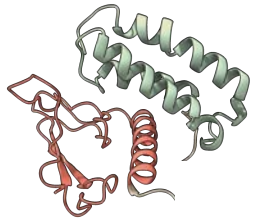
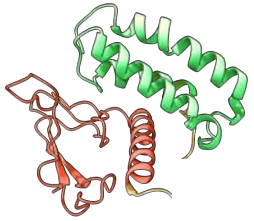
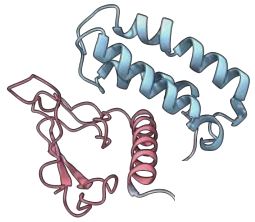
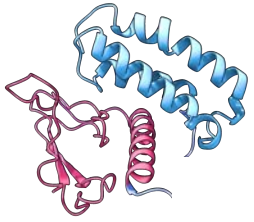
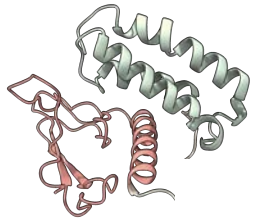


Antibody-delivered agonists could provide the selectivity and half-life to define the optimal profile

AMY1R: Amylin Receptor 1
AMY3R: Amylin Receptor 3

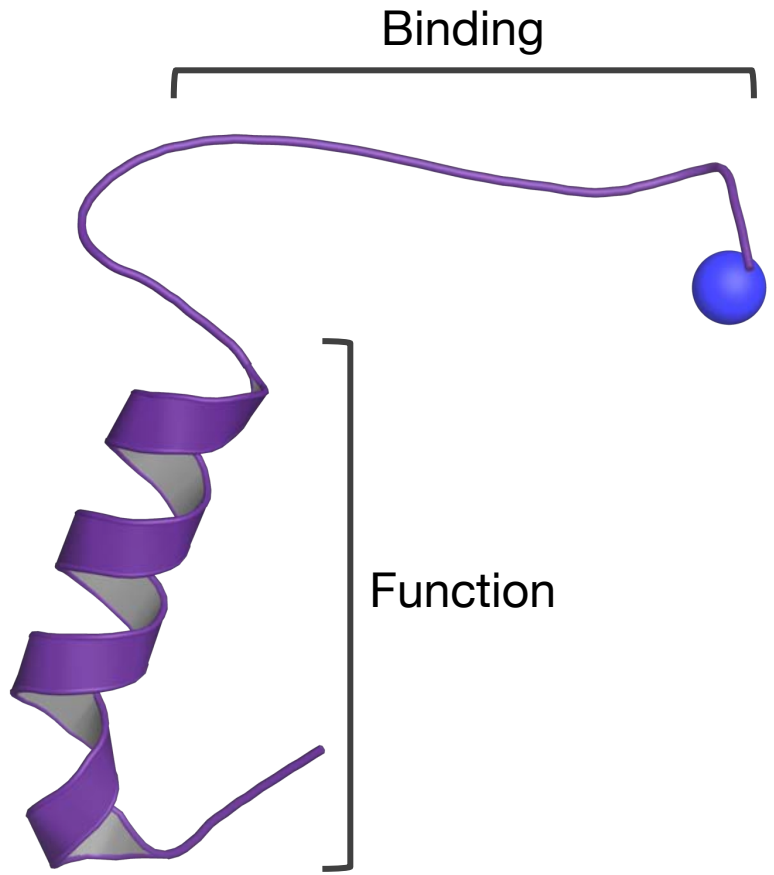
Amylin Peptide Analogues: Understanding the Optimal Profile



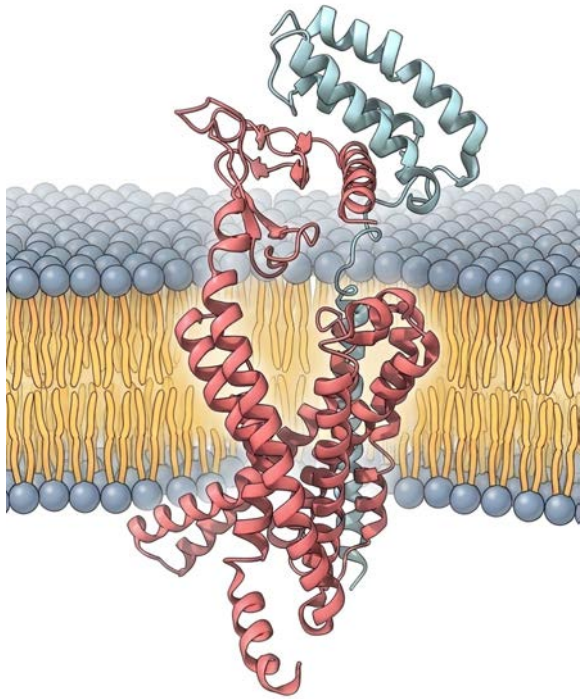
	AMY1R	AMY3R
Human		
Cyno		
Rat		

76% CTR cross-species sequence conservation

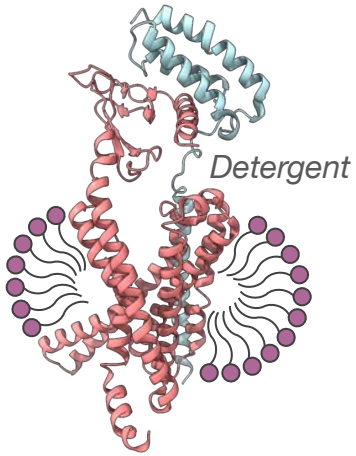
28% RAMP-1/3 cross-species sequence conservation

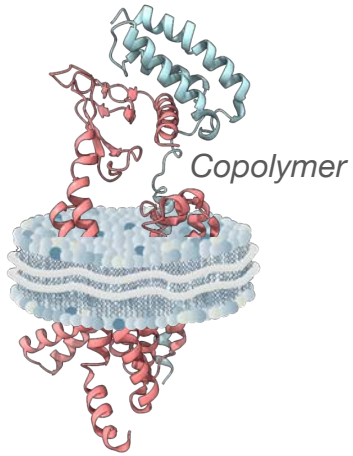


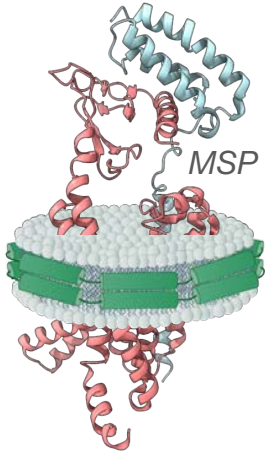
GPCR Paradox: Prime Targets, Tough Antigens to Produce

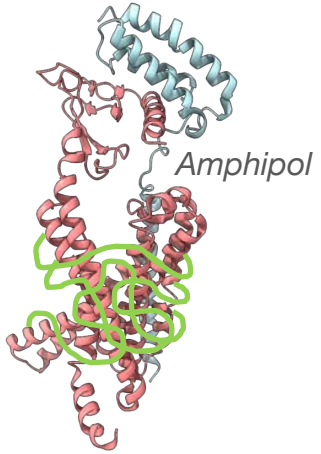


Solubilization









Benefits

- *Native sequence*
- *Native-like structure*

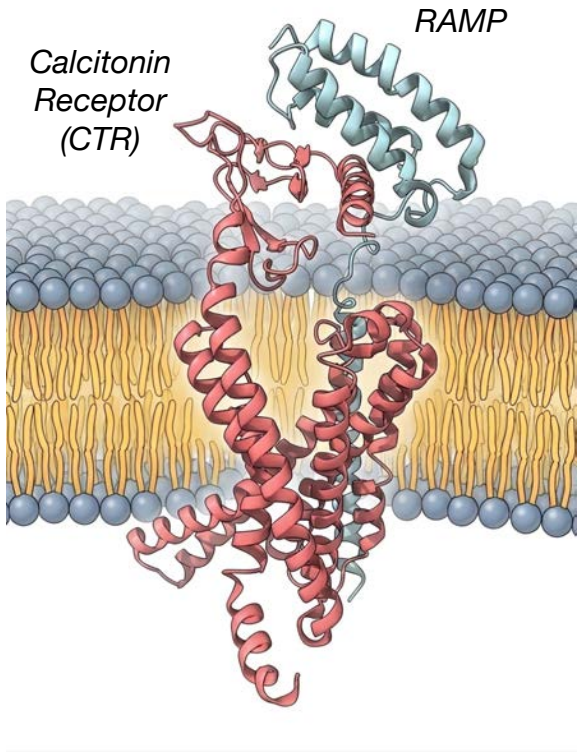
Complications

- *Time consuming*
- *Stability issues*
- *Heterogeneity*

Engineered Epitopes: Defined, Stable, and Easy to Express

Input Target

Amylin Receptor

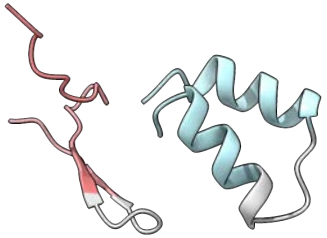


Generative AI

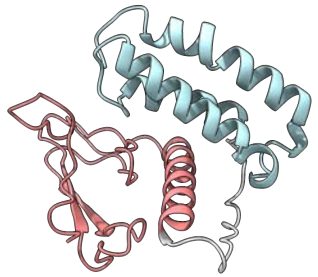


Epitope Designs

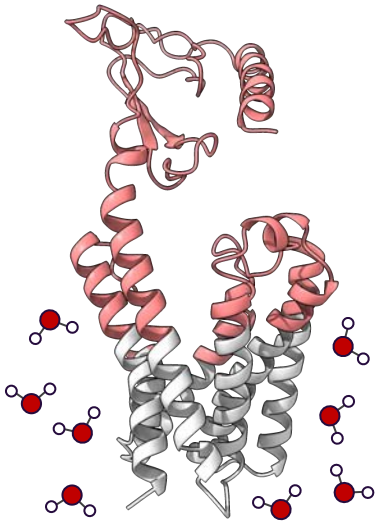
Individual Epitopes



CTR-RAMP Junction

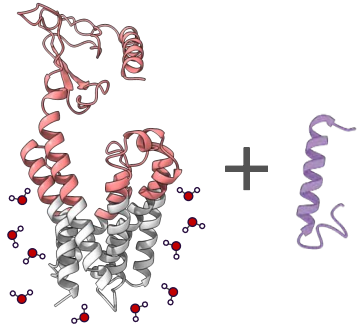


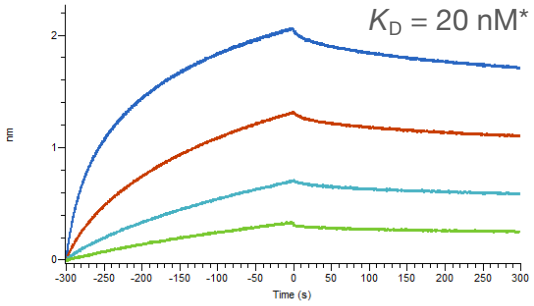
Soluble CTR



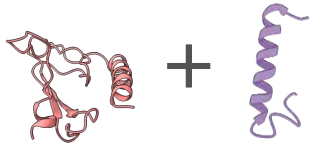
CTR Solubilization Validated by Salmon Calcitonin Binding

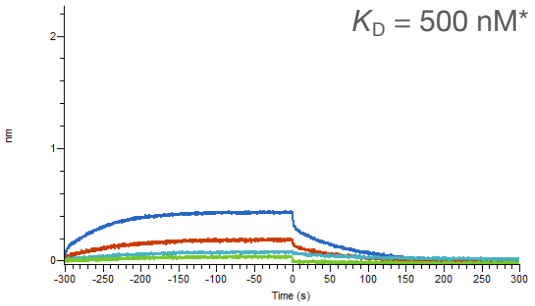
Soluble Receptor



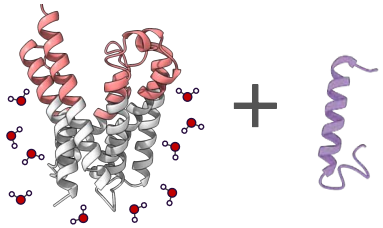


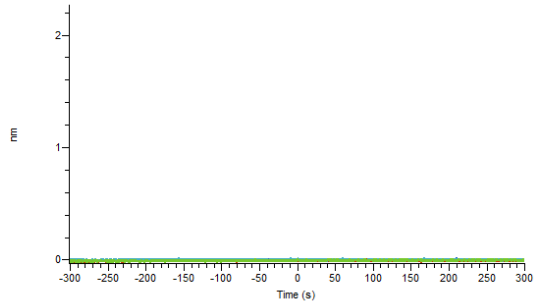
Extracellular Domain





Transmembrane Domain



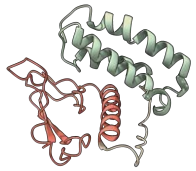


Multi-Round Selections Drive Exquisite Selectivity

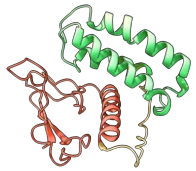
Naïve Library Phage Panning



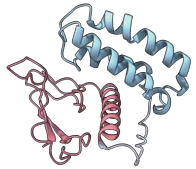
Human Amylin Receptor 1 (AMYR1)



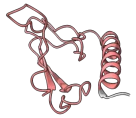
Human Amylin Receptor 3 (AMYR3)



Rat Amylin Receptor 1 (AMYR1)



Rat Amylin Receptor 3 (AMYR3)

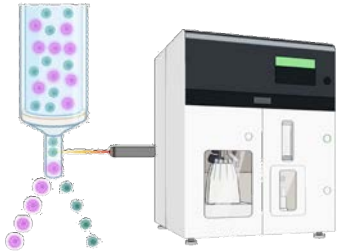


Human Calcitonin Receptor (CTR)

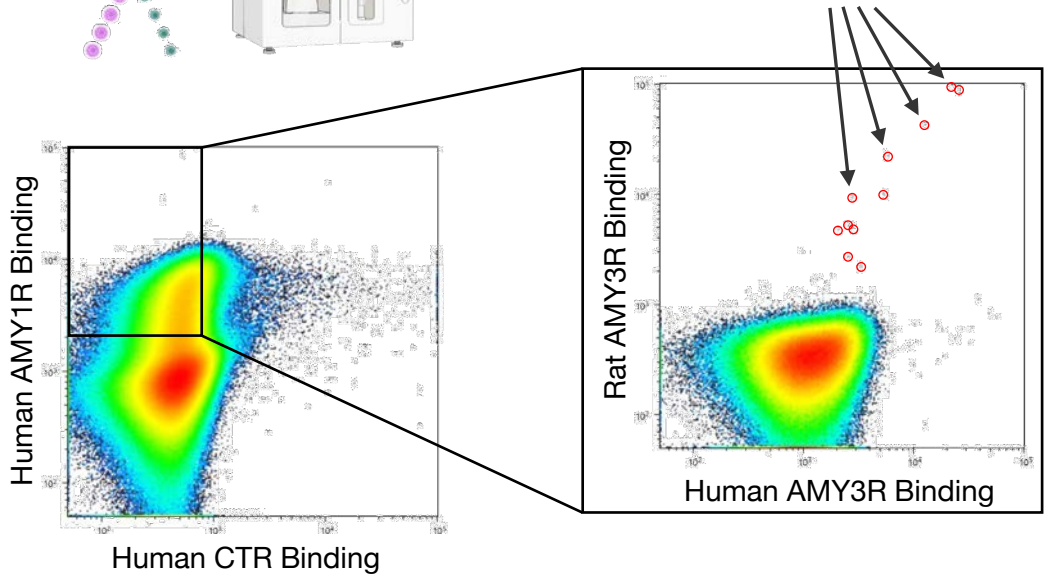


CTR, AMY1R, or AMY3R Cells

Multi-Dimensional Mammalian Display Sorting

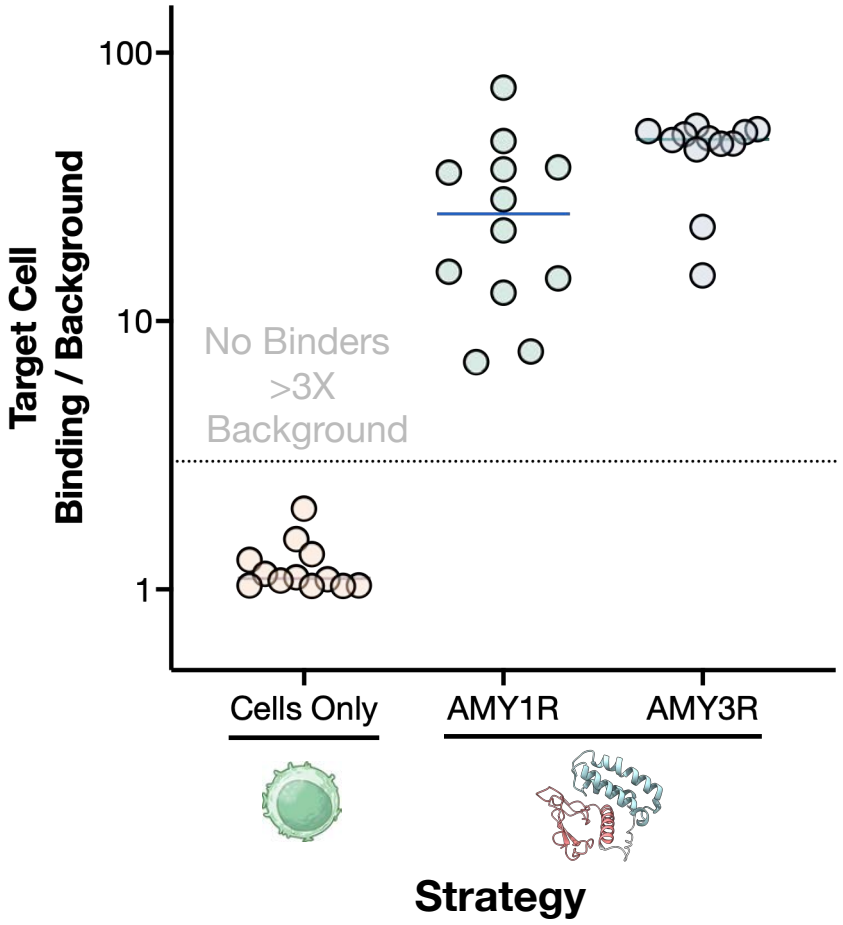


Simultaneous Amylin Receptor Specificity and Species Cross-Reactivity

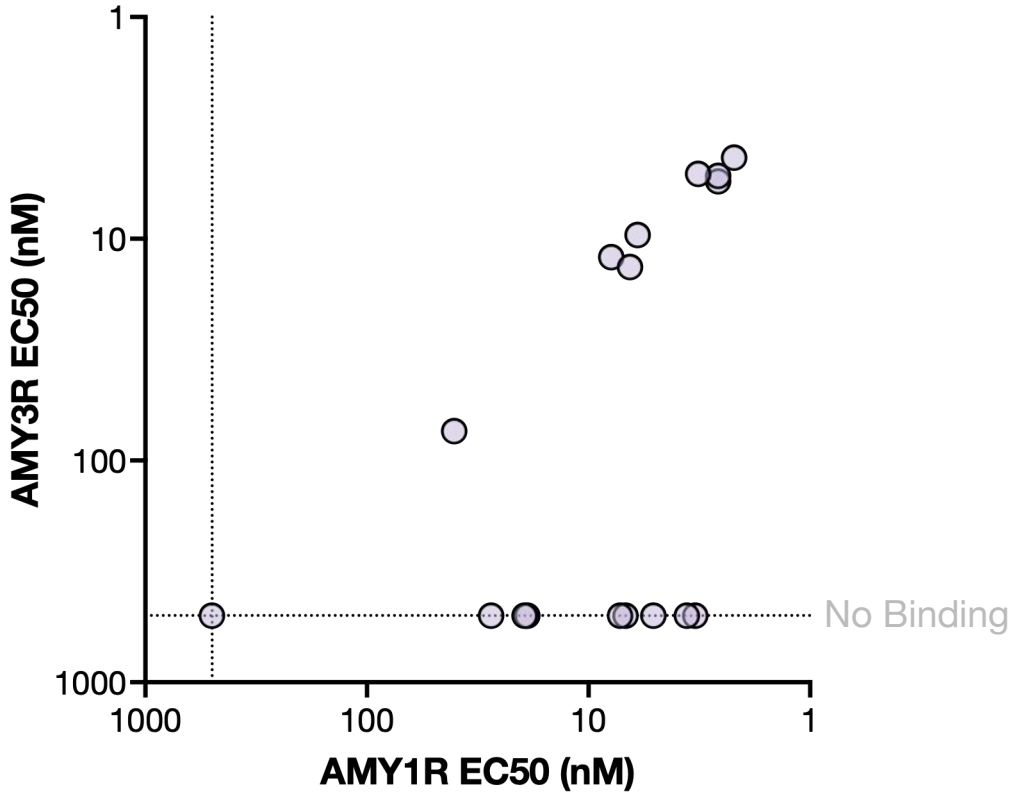


Engineered Epitopes are Required to Generate Cell Binders

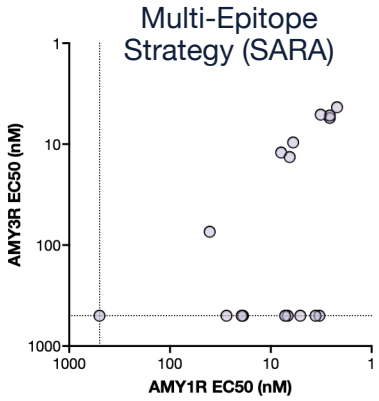
Single Epitope Strategies



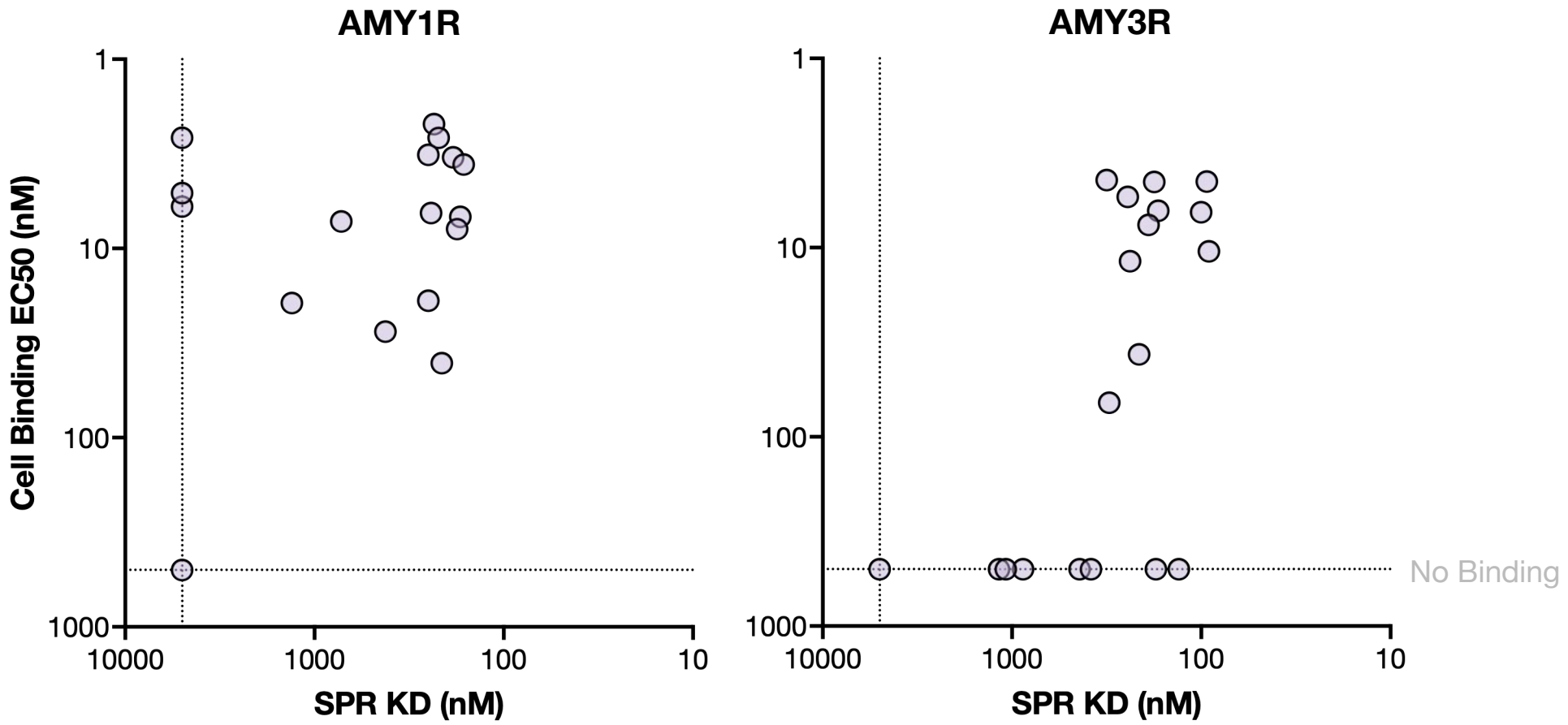
Multi-Epitope Strategy (SARA)



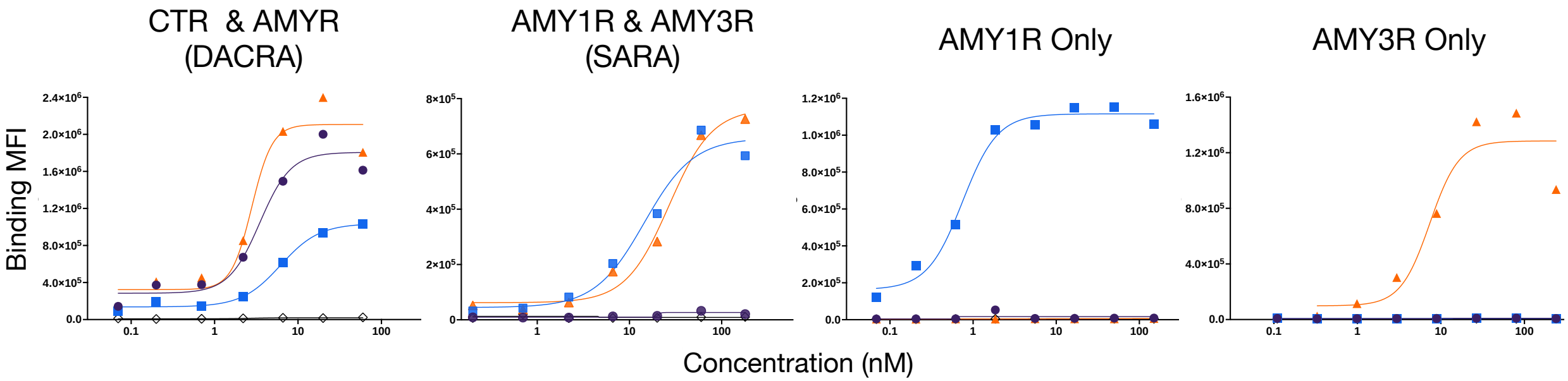
Engineered Epitope Binding Translates to Cell Binding



AMYR Cell Binding vs SPR Epitope KD



Selections Yield 4 Distinct Specificity Profiles



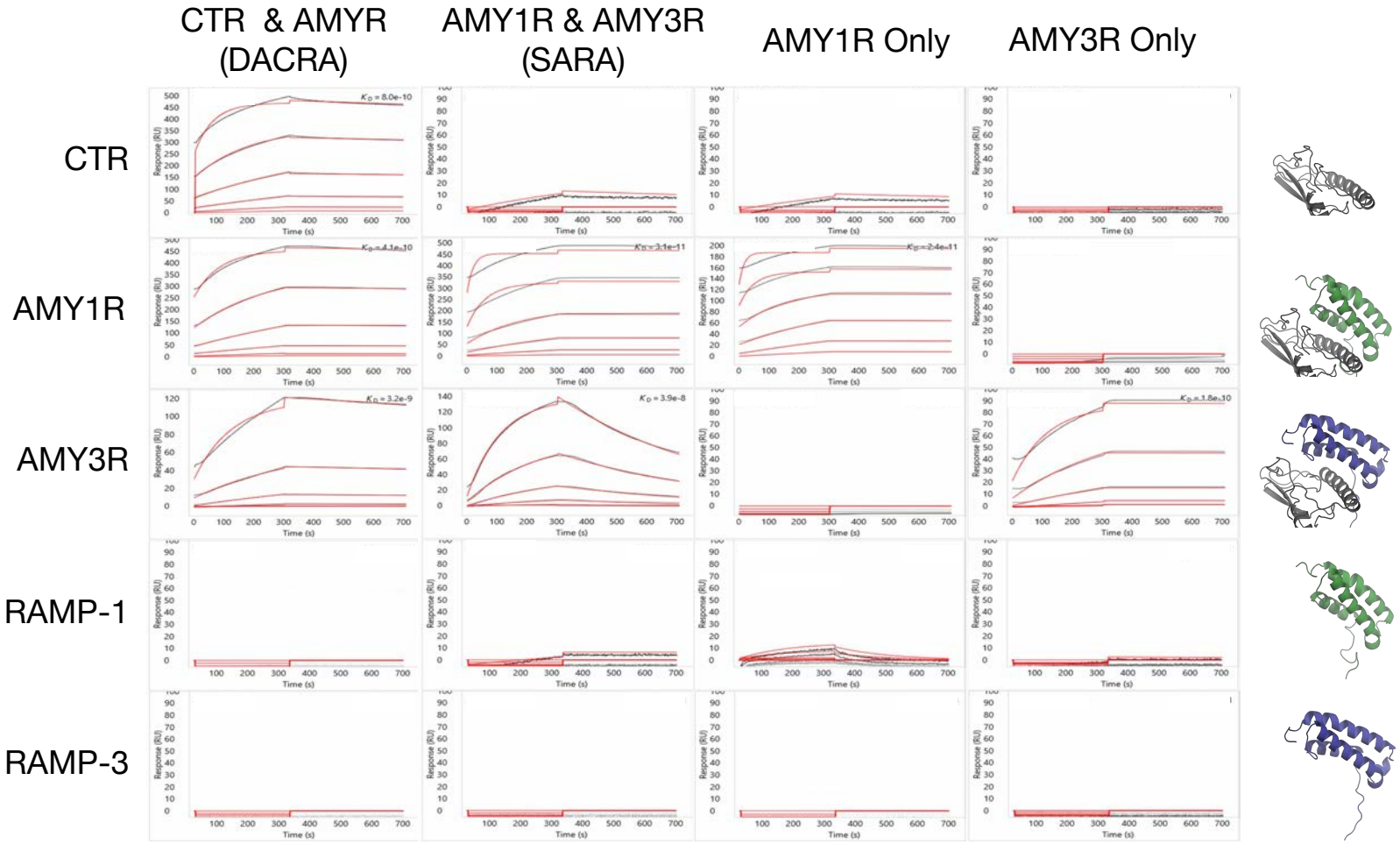
IgG
Species Cross-Reactive

VHH
Species Cross-Reactive

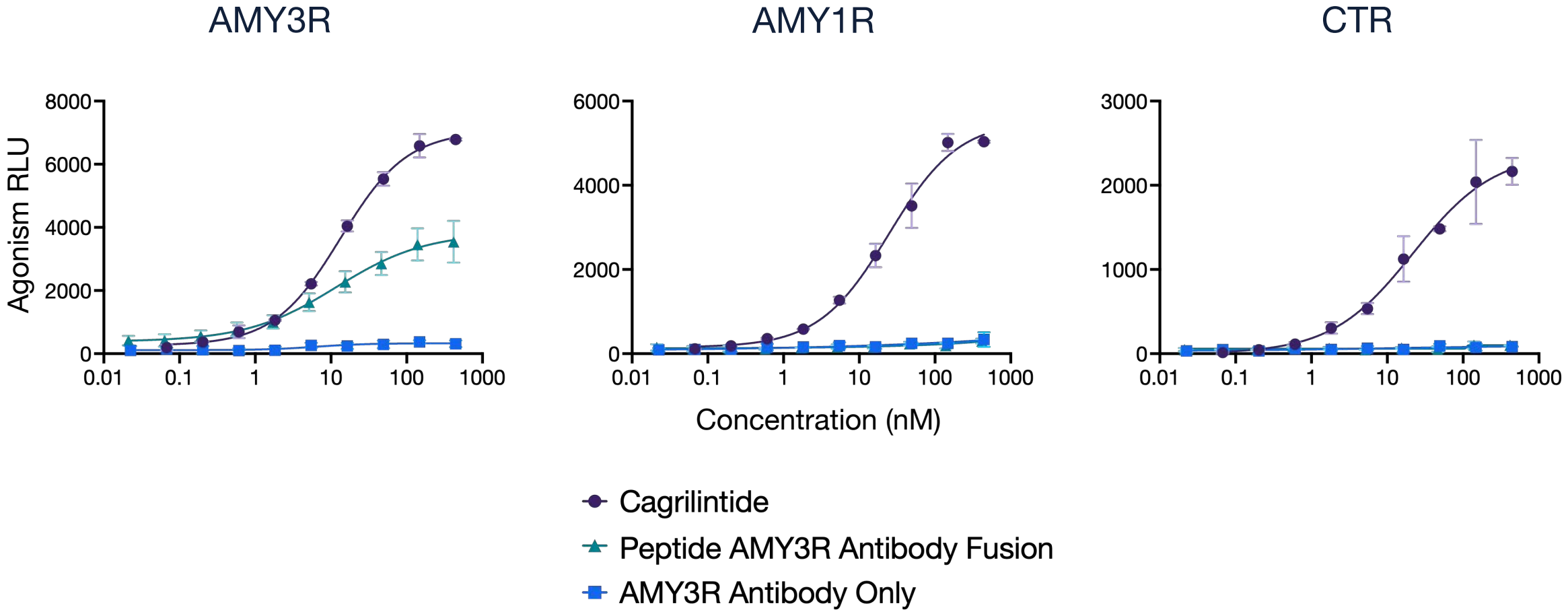
IgG and VHH
Species Cross-Reactive

IgG

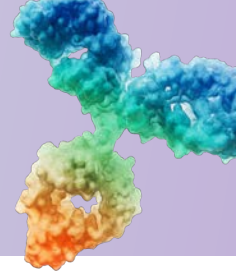
Engineered Epitopes Confirm Junctional Epitope Recognition



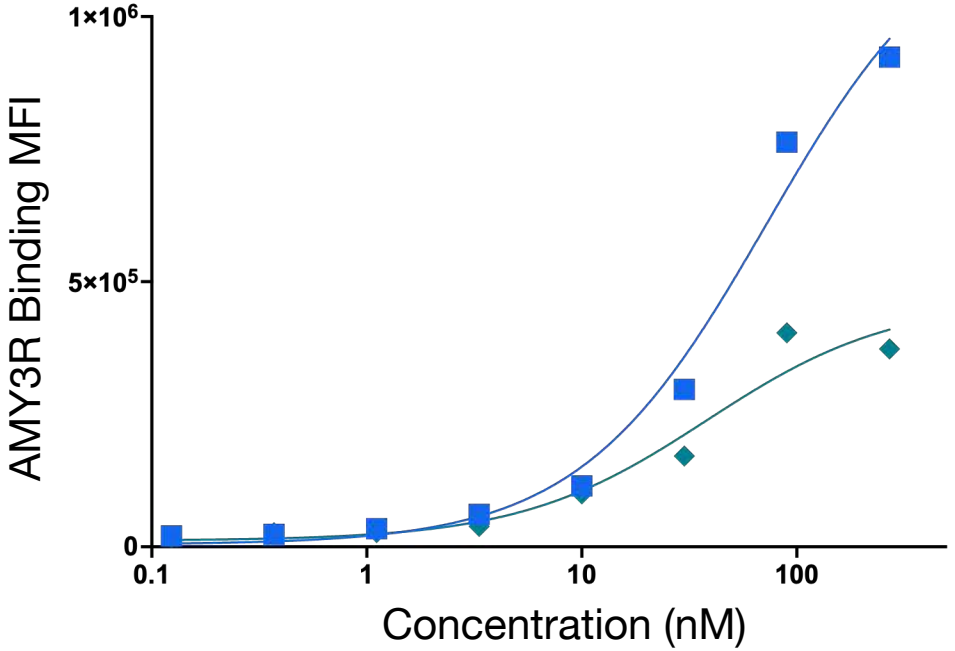
Peptides Confer Function and Maintain Specificity



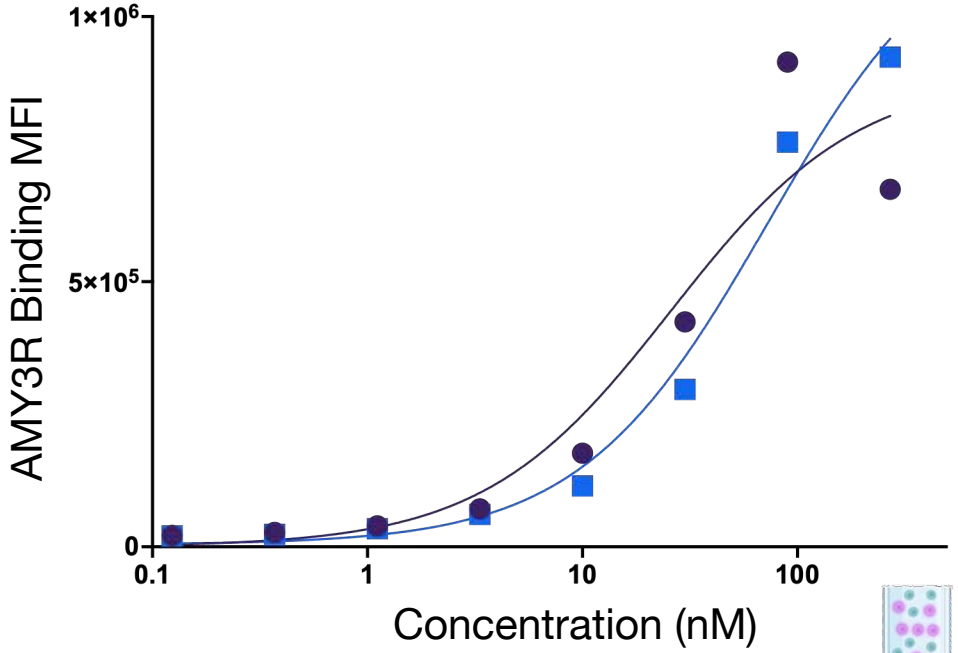
Whole Molecule Co-Optimization Recovers Binding Activity

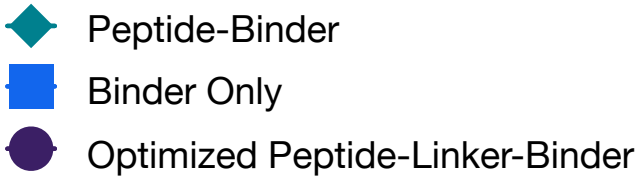


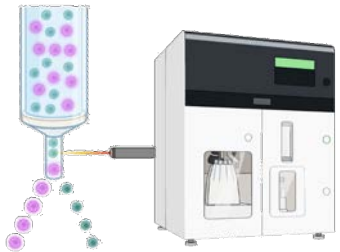
Problem: Original peptide fusion measurably reduced cell binding potency



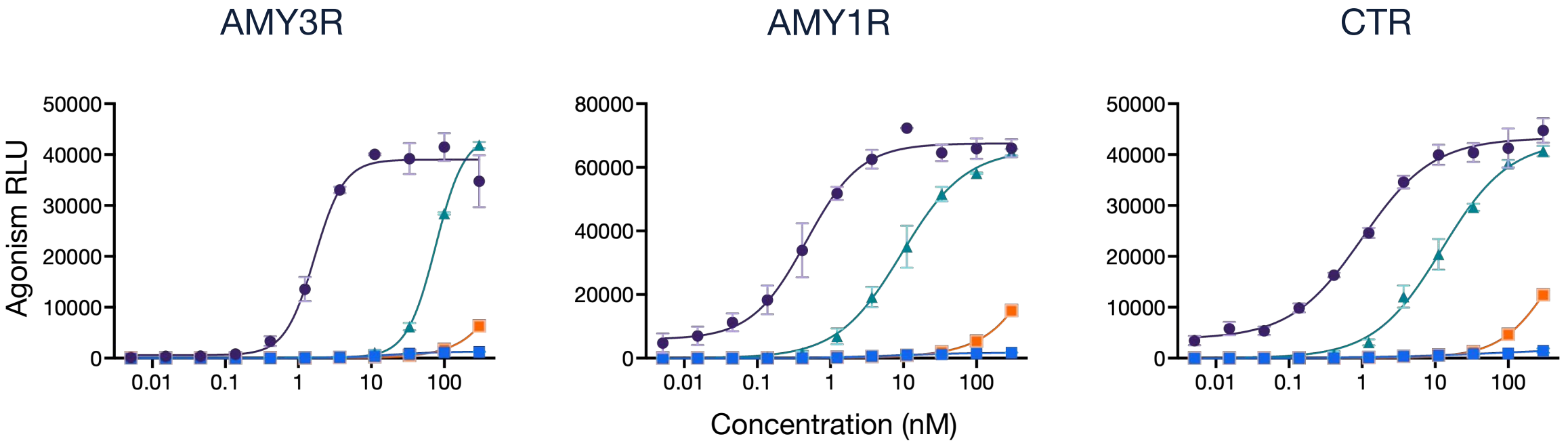
Solution: Co-optimize peptide-linker-binder in mammalian display







Optimized Peptides Retain Functional Activity



IBIO-DACRA Demonstrates Viability *In Vivo*

In Vivo Study



DIO Sprague Dawley rats

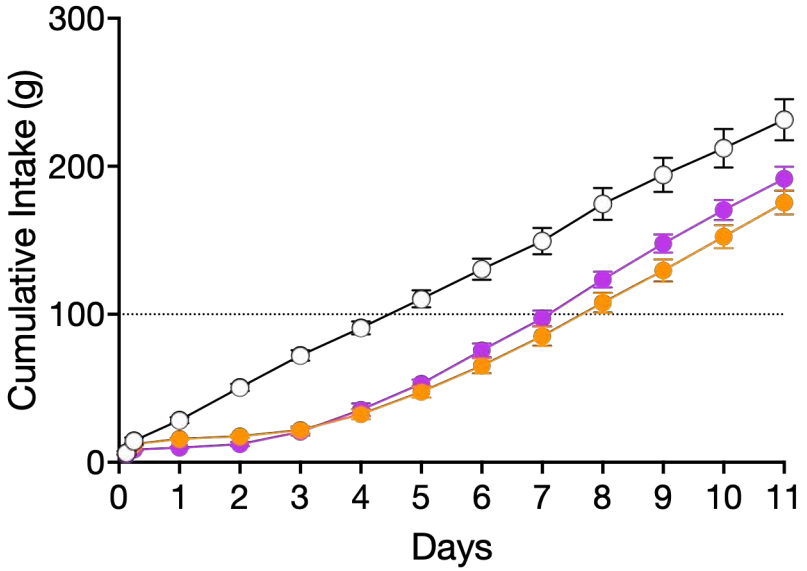


Single dose (S.C)

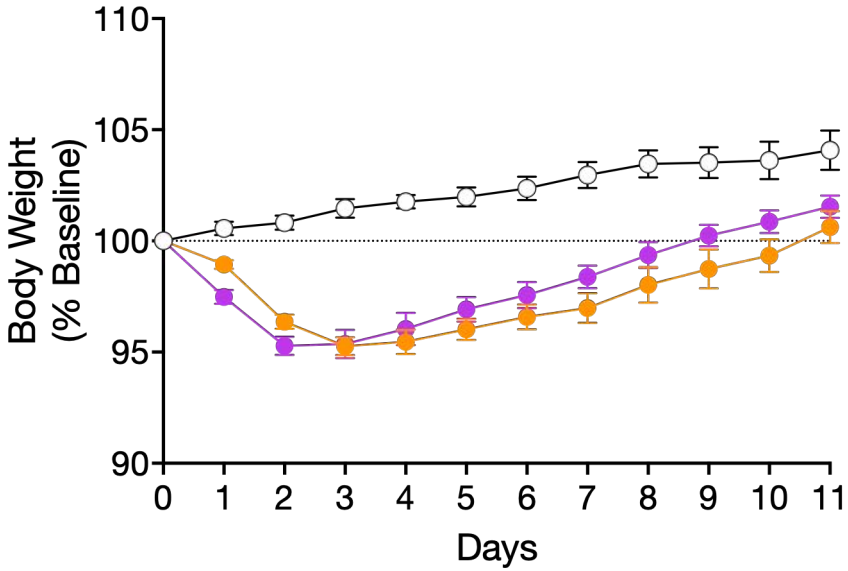


Monitor food intake & BW daily

Reduced Food Intake up to 11 Days



5% Bodyweight Loss After 1 Dose



Vehicle

IBIO-DACRA (15 mg/kg)

Cagrilintide (10 nmol/kg)

IBIO-SARA Reduces Food Intake Exclusively Through Amylin Receptors 1 and 3

In Vivo Study



Lean Sprague Dawley rats

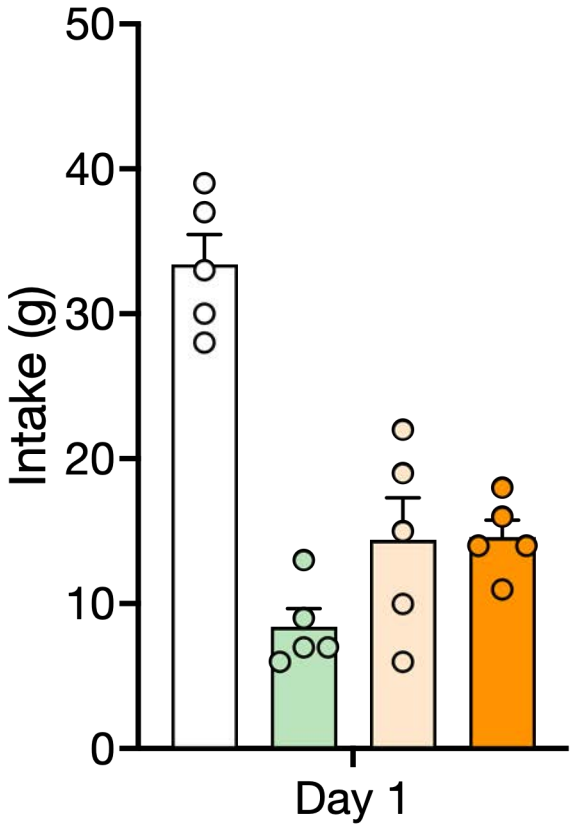


Single dose (S.C)



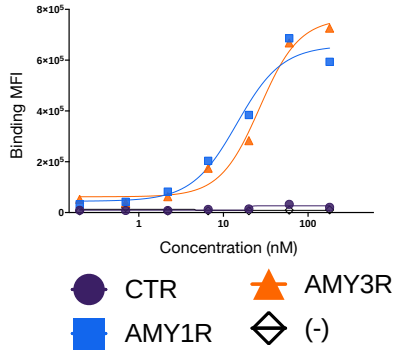
Monitor food intake & BW daily

24-Hour Food Intake

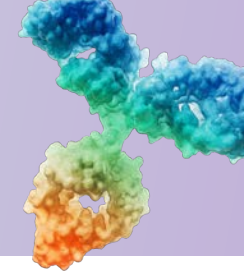


- Vehicle
- Cagrilintide (10 nmol/kg)
- iBIO-DACRA (30 mg/kg)
- iBIO-SARA (30 mg/kg)

iBIO-SARA Cell Binding



Summary



1. Soluble engineered epitopes embody amylin receptor heterodimers with high fidelity

2. Engineered epitopes are required to generate specific cell binders

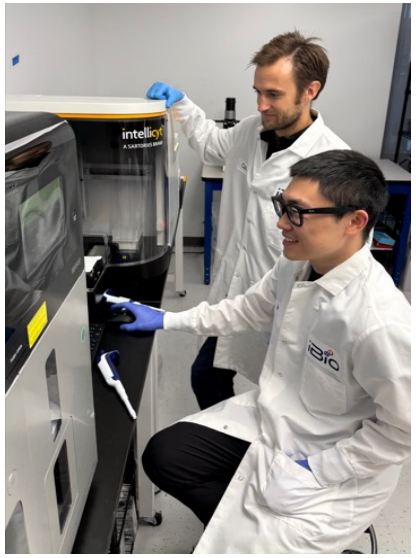
3. Mammalian display enables optimization across specificity and function

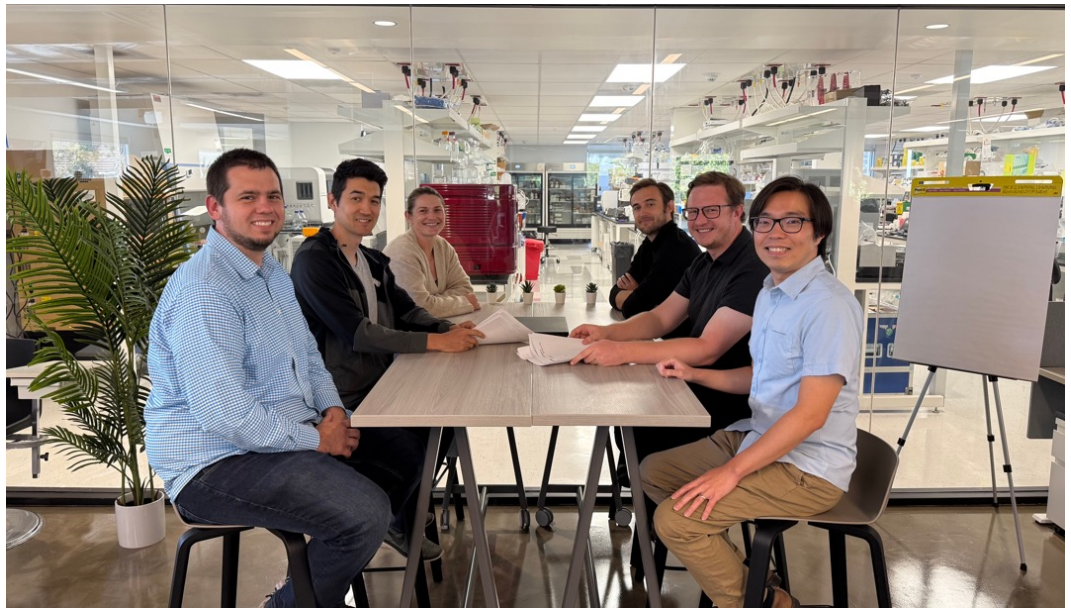
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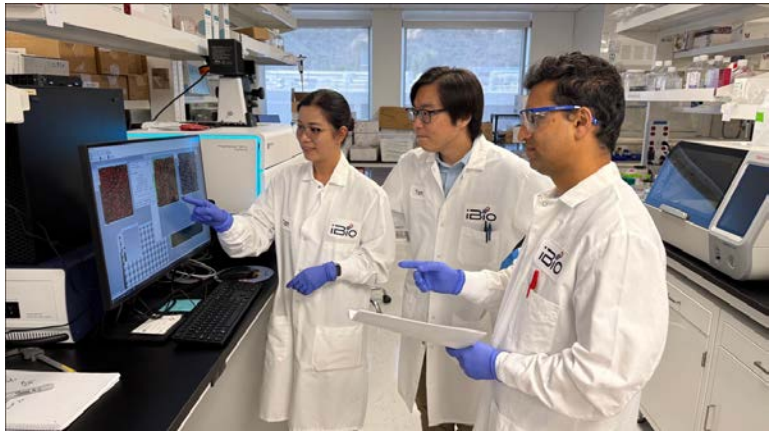
Moving selective molecules into rat and/or cyno DIO models

Acknowledgements









Thank You

