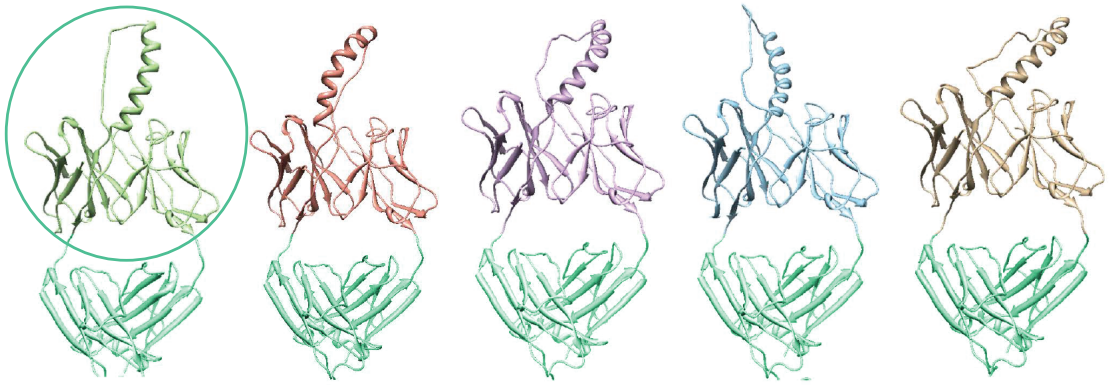
TWIST BIOPHARMA

GPCR Library

Unlock the discovery of antibodies to this difficult target class



>100,000
DIFFERENT GPCR BINDING MOTIFS

Chemokines • Helical peptides • Looped peptide • GPCR • ECD1 • ECL2

Motifs derived from GPCR binding antibodies

- 10^{10} high variation GPCR library
- Final library design leverages rules of human repertoire
- Completed computational structural modeling and detailed displayability analysis
- 100,000 motifs were empirically screened for foldability, expressability and displayability

GPCRs are Hard-to-Drug

- 30-50% of current drug targets are GPCRs but there are only 2 FDA approved antibodies
- Current antibody drug development methods do not work
- Random mutagenesis libraries are too inefficient to explore the effective sequence space

Synthetic Library Advantage

- No immunization required
- Synthetic mAb libraries focus on effective sequence space
- Simultaneous screening against multiple targets

License Twist Biopharma GPCR Libraries

Partner with Twist Biopharma to Generate New Leads Against Any GPCR of Interest

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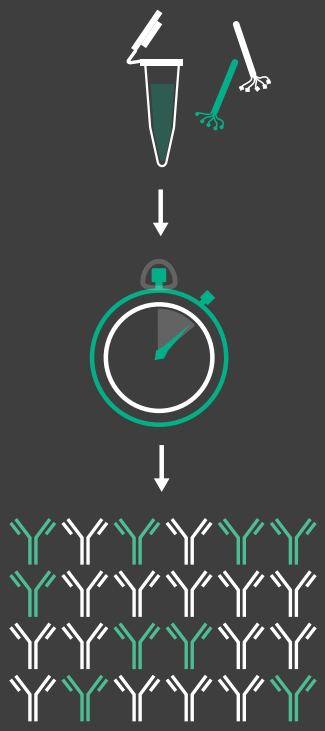
Proof of Concept: GLP1R Target, Class B GPCR

Quickly Find Dozens of Antibodies



Panning
- 5 successive rounds against GLP1R stable CHO line
- Depletion on CHO parental line

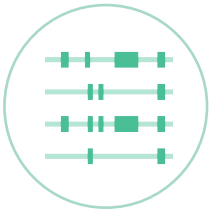
Sequencing
- NGS clonal enrichment monitored at each round
- 1000 picked clones were sequenced and >100 unique paired VH/VL sequences determined

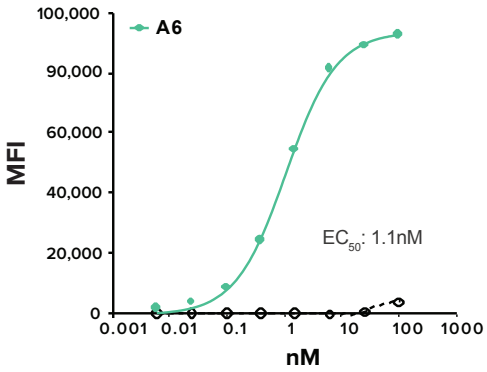
Reformatting to IgG and DNA scale-up
- All unique clones were synthesized as full IgG and expressed/purified in HEK293

Binding and Functional Assays
- GLP1R Cell Binding
- Panel of GPCR functional assays (cAMP, b arrestin, internalization)

Multiple Antibodies Bind GLP1R Over-Expressing CHO Cells and Are Functional in a cAMP Assay

- IgGs are monomeric and not prone to aggregation
- Multiple FACS positive hits in GLP-1 and GLP-2 motifs as well as additional unique sequences.





A Panel of Cell Target (+) IgGs Identified

Cell Binding IgGs with Several Antagonists

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