TWIST BIOPHARMA

Synthetic DNA Technologies Enable Antibody Discovery and Optimization

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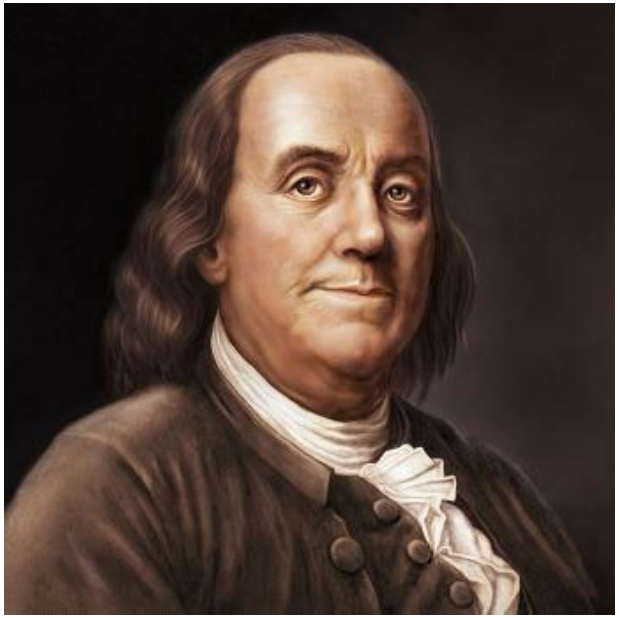
@TwistBioscience #WeMakeDNA

Making the Impossible Possible …

My Idol: Benjamin Franklin

- Technology improvements allow us to do things we've never done before …
- Within the antibody engineering community, there are others like me who to invent new antibody technologies that do just that …
- Assessing new drug targets
  - Therapeutic rationale
  - Unmet medical need
  - Technological feasibility: Does the tech exist?

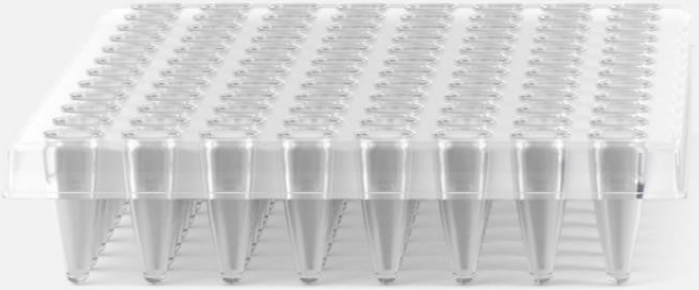


Do whatever it takes to make the impossible possible, including collaborating with others!

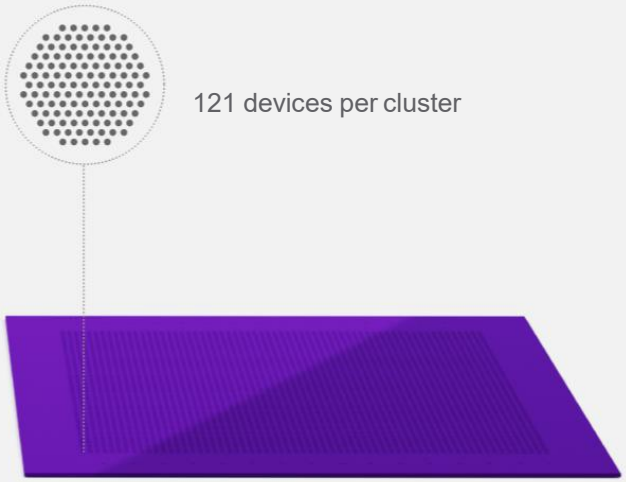
The One Thing

Curly and Mitch

Rewriting DNA with the Power of Silicon – Our One Thing!



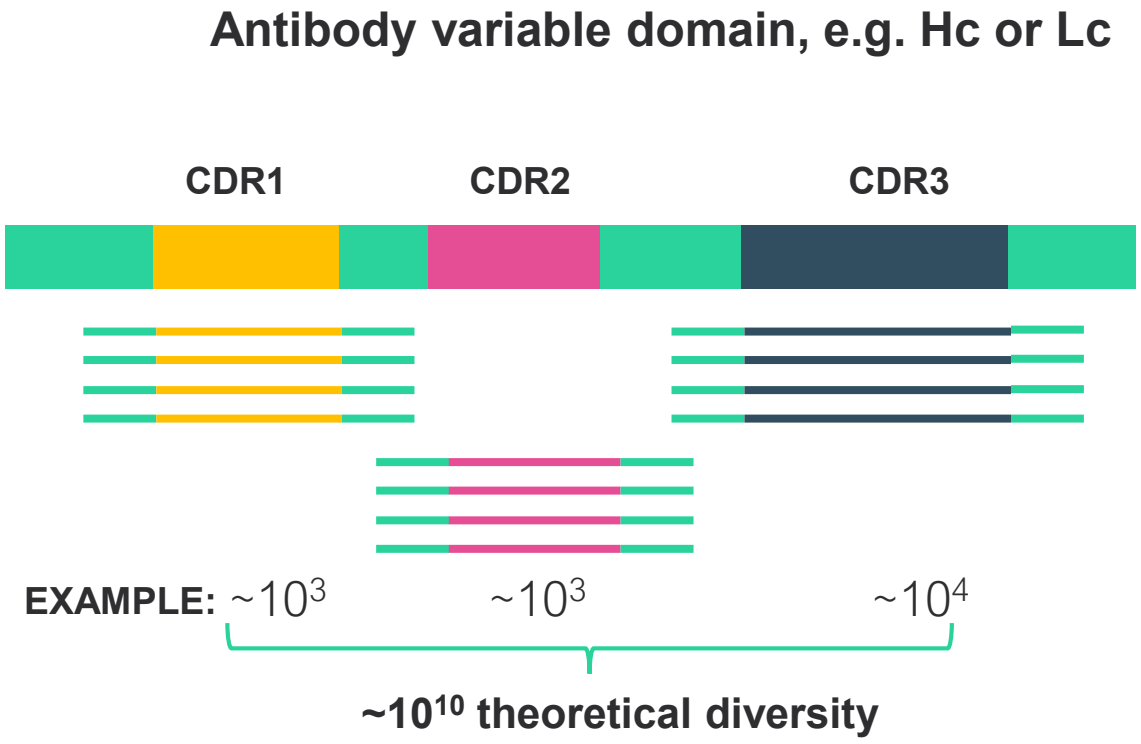
96 WELL PLATE
makes 1 gene

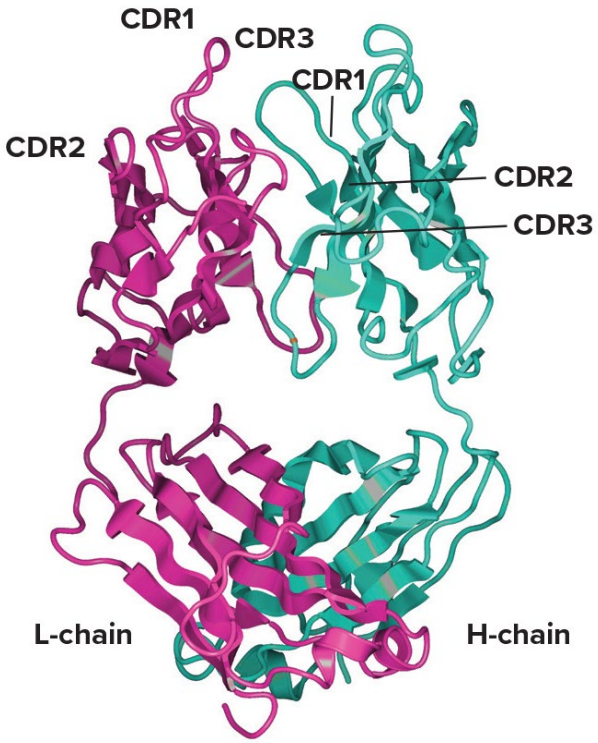


TWIST SILICON PLATFORM
can make 9,600 genes

Developing Game-Changing Throughput and Cost through Quality and Speed at Scale

The Use of Oligo Pools to Build Unprecedented Libraries Our One Thing for Antibody Libraries





- Oligo pools are designed to match the natural CDR repertoire
- Liabilities can be removed, e.g. isomerization, cleavage, deamidation, glycosylation sites
- Rational sampling from desired sequence space
- Accurate representation, e.g. motif sequences can be explicated encoded in oligos

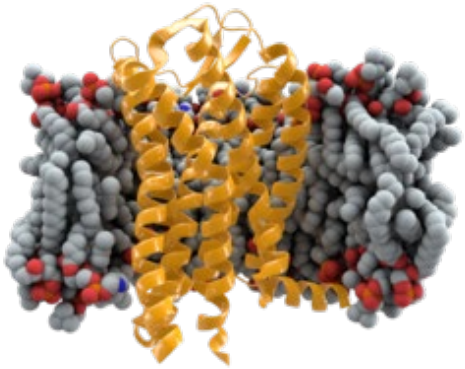
Oligo Technologies to Generate CDR Diversity
The Advantages of Oligo Pools for Library Generation

TECHNOLOGY	FULL CONTROL OVER AMINO ACID DISTRIBUTION	NO STOP CODONS OR CYS	LACK OF OUT-OF-FRAME MUTATIONS	NO LIABILITY DIPEPTIDE MOTIFS	MATCH NATURAL CDR REPERTOIRE OR CONTAIN SEQUENCE MOTIFS
NNS/NNK	✗	✗	✗	✗	✗
TRIM	✓	✓	✓	✗	✗
Twist Oligo Pools	✓	✓	✓	✓	✓

Twist Synthetic libraries have significant technical advantages over NNS/NNK and TRIM

My GPCR Story

- My Dyax Days … so a long time ago
- Client came to us to discover antibodies against CCR5
- Semi-synthetic phage display library and over 10 different selection strategies
- After over a year, we gave up and had to abandon the project as the library did not have any GPCR leads in it!
- *How many of you have similar GPCR stories?*
- What are the technologies required to address GPCRs?
  - A library technology that has anti-GPCR antibodies
  - A GPCR technology to present the target



Twist Pharma Initiative to Discover
Anti-GPCR Antibodies

GPCRS ARE ATTRACTIVE DRUG TARGETS

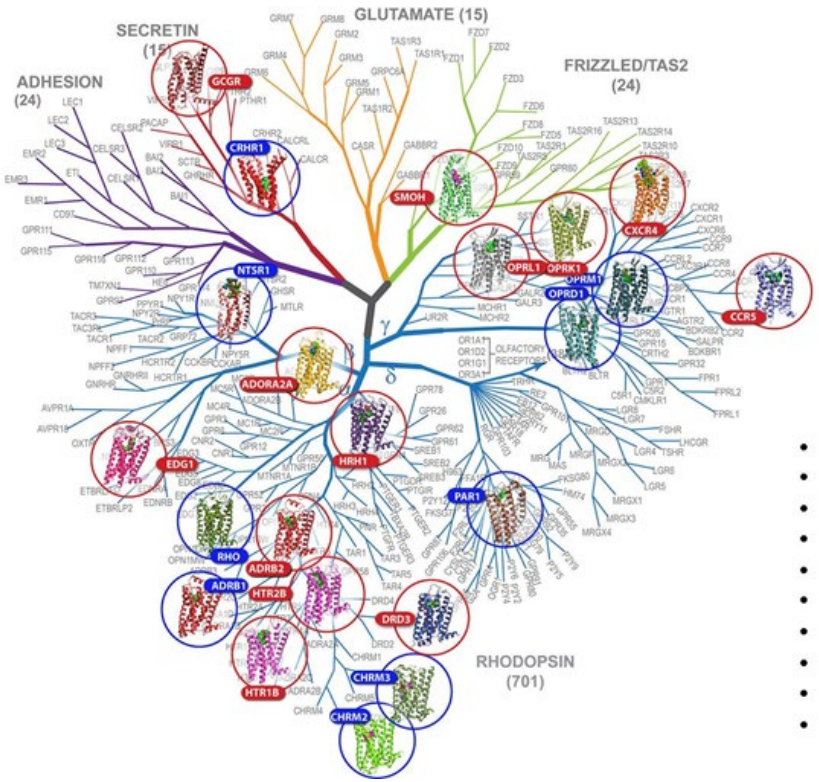
- 30-50% of current drug targets are GPCRs
- Broad indications

GPCRS ARE HARD-TO-DRUG: 2 FDA APPROVED ANTIBODIES

- Current antibody drug development methods do not work
- GPCR antigens immunizations produce binders to epitopes not available biologically
- Panning with random mutagenesis libraries is too inefficient to explore the effective sequence space

SYNTHETIC LIBRARY ADVANTAGE

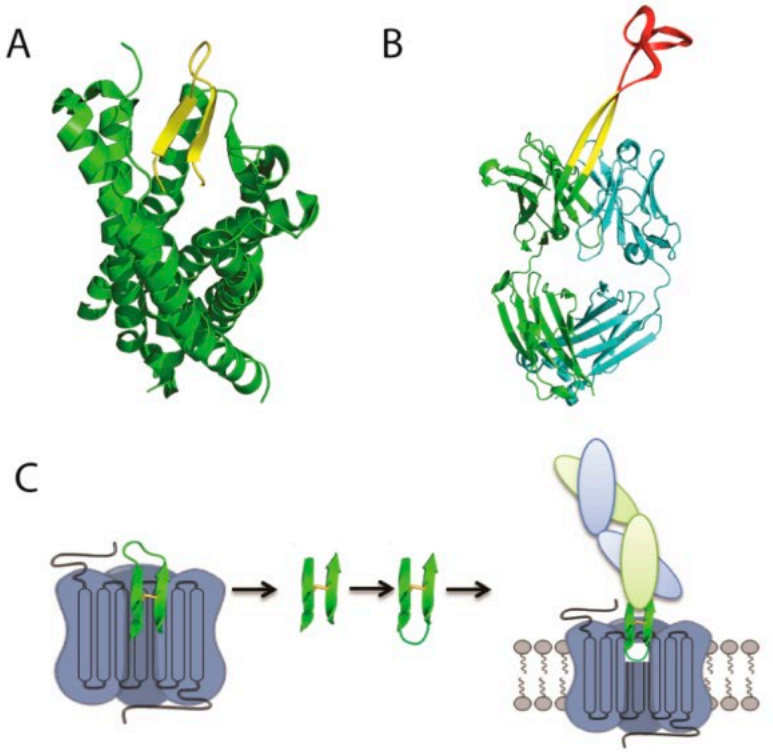
- No immunization required
- Design and synthesis of explicit mAb libraries to focus on effective sequence space
- Simultaneous screening against multiple targets

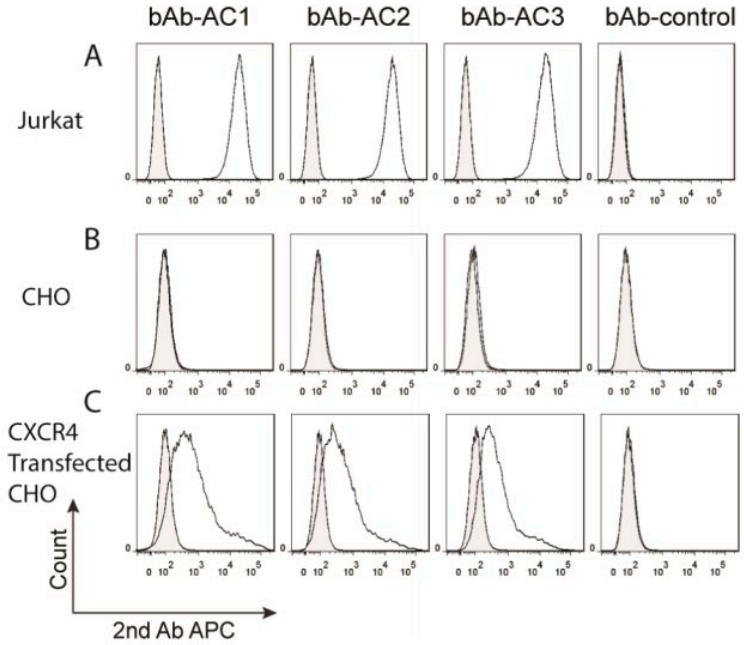


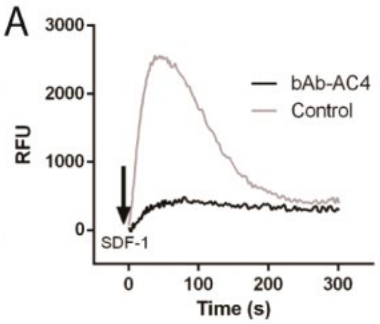
Initial GPCR Library Concept from Literature

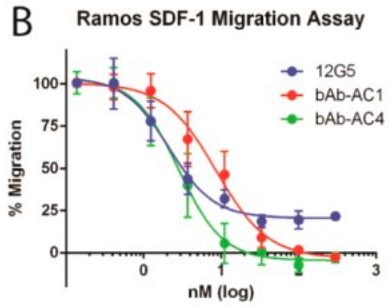
CVX15-CXCR4 complex

Bovine BLV1H12





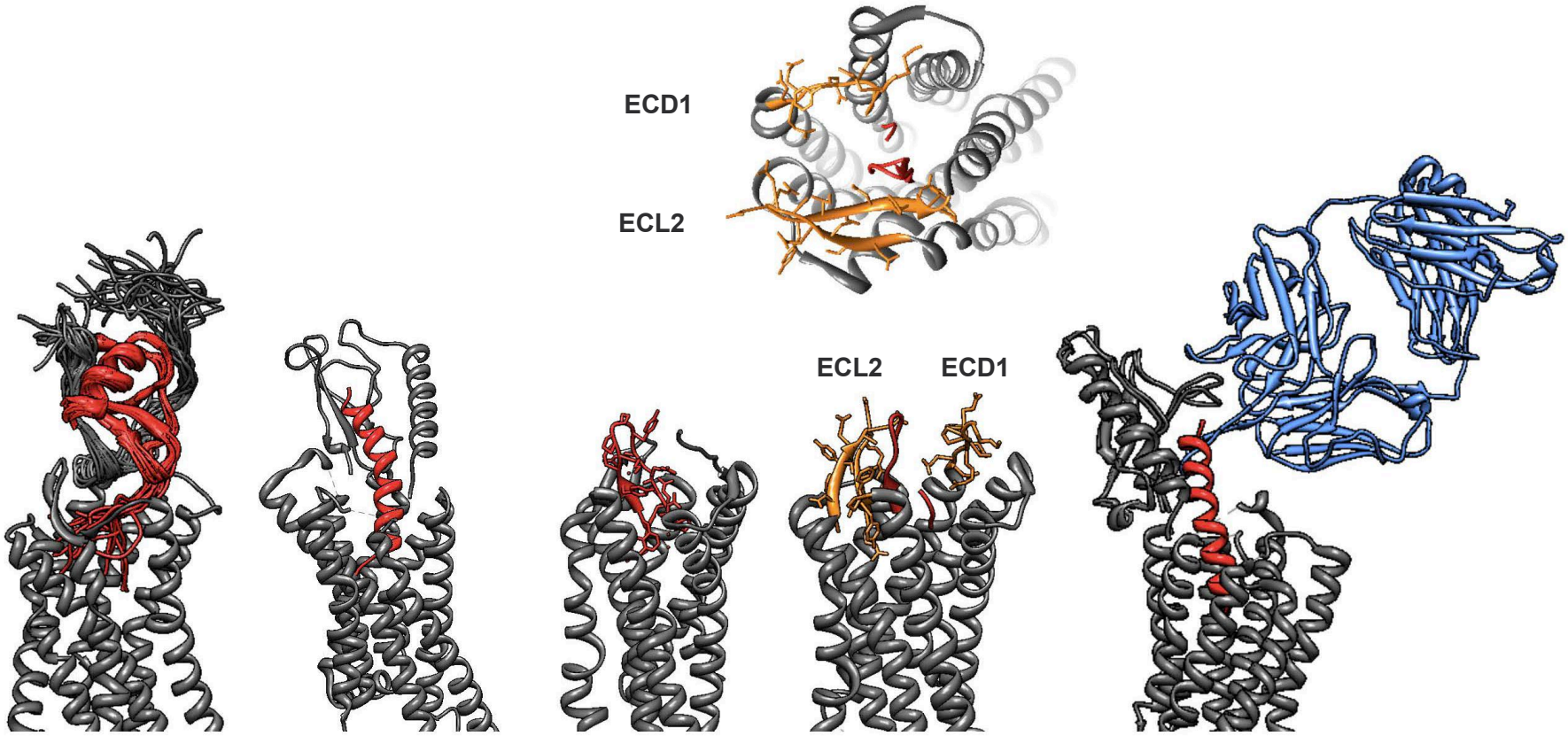




Liu, Tao, et al. "Rational design of CXCR4 specific antibodies with elongated CDR " *Journal of the American Chemical Society* 136.30 (2014): 10557-10560.

Known GPCR Interacting Partners: Source of Motifs

Increasing diversity: These motifs were introduced into our library heavy chain CDR3 (HCDR3)



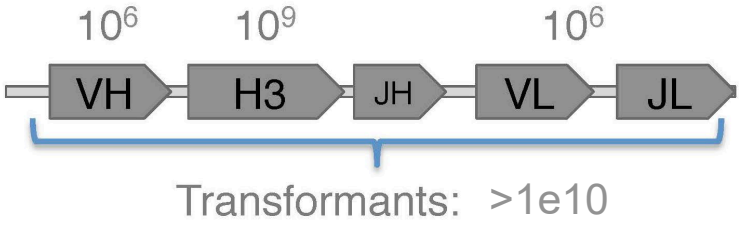
Final GPCR Library > 10 Billion Different Antibodies with Motifs Incorporated into HCDR3 Loop

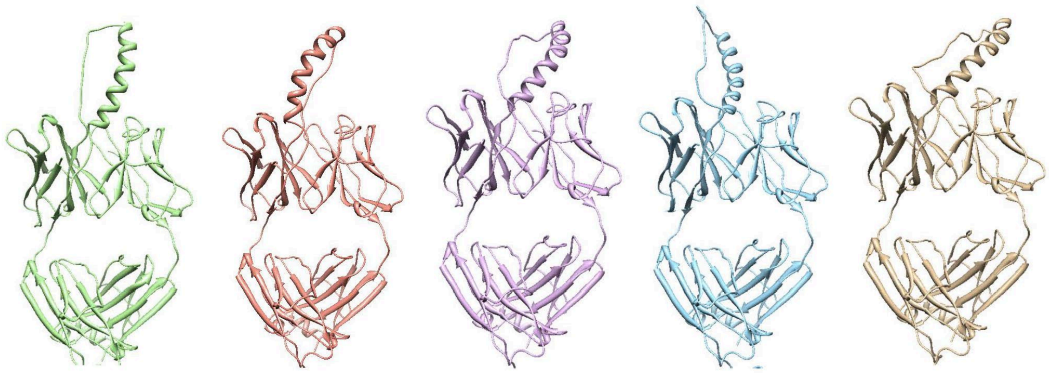
GPCR Crystal Structure to Antibody Scaffold — Done

First Library for Proof of "Displayability" — Done

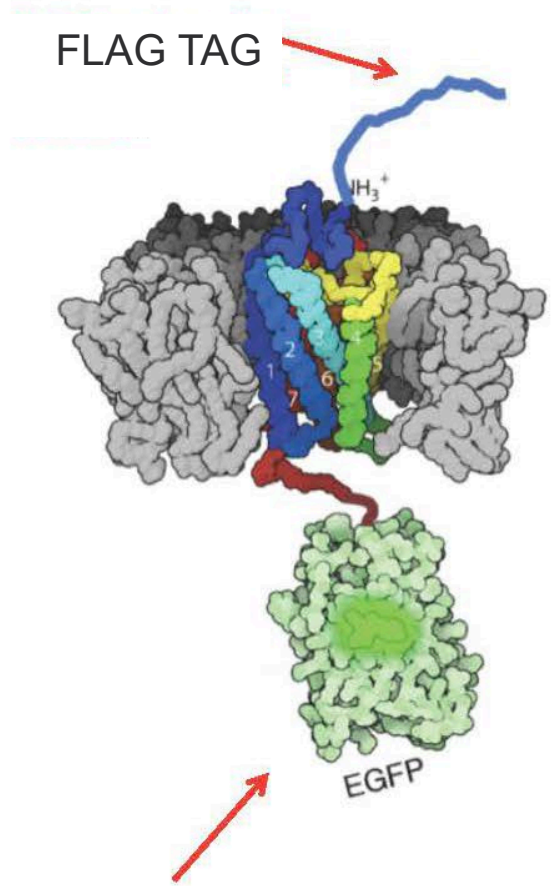
Second Library with Hyper-Variation for Screening — Done

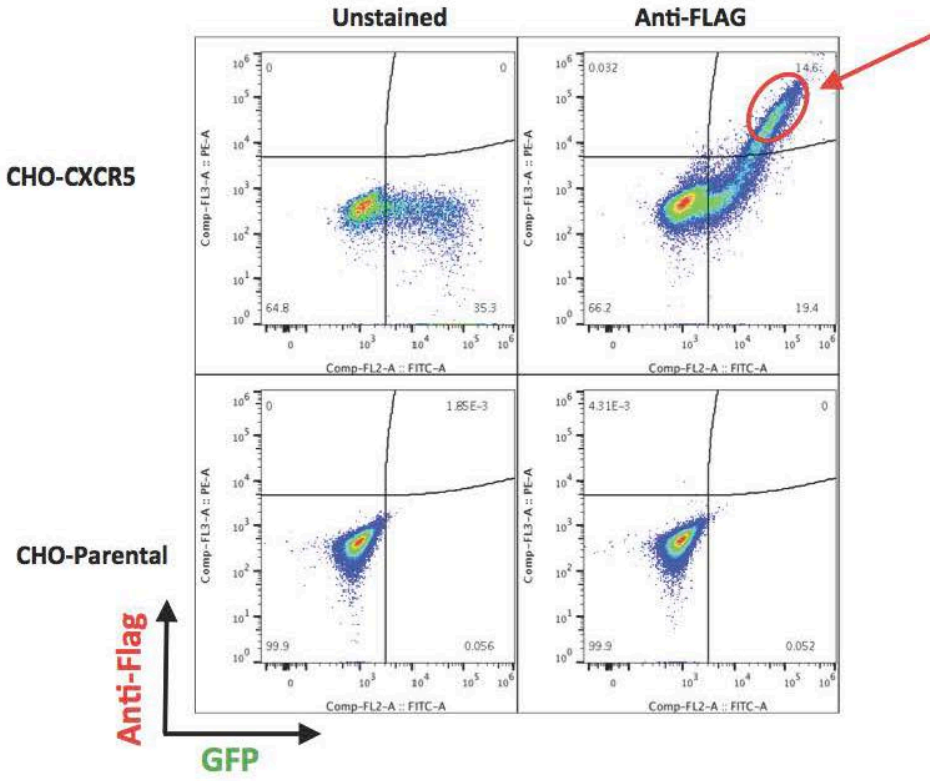
- Completed detailed "displayability" analysis
- Completed computational structural modeling
- Final library design leveraging rules of human repertoire
- Synthesis of 10^{10} high variation library





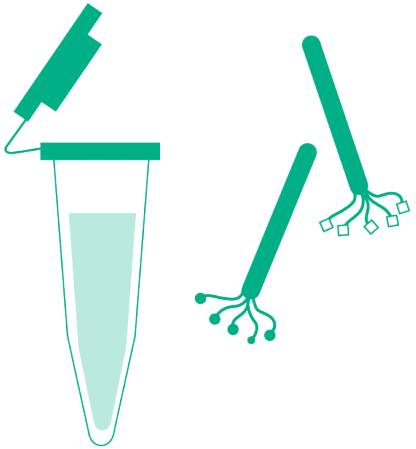
GPCR Design for Creating Over-expressing Lines



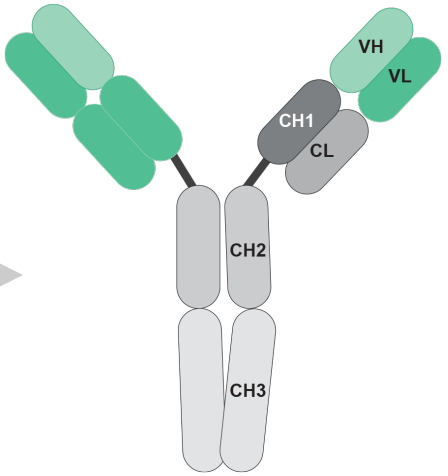


Twist Biopharma is also partnering with other GPCR target companies that can access to provide high quality antigens!

Twist Biopharma's 2 Month Discovery Cycle



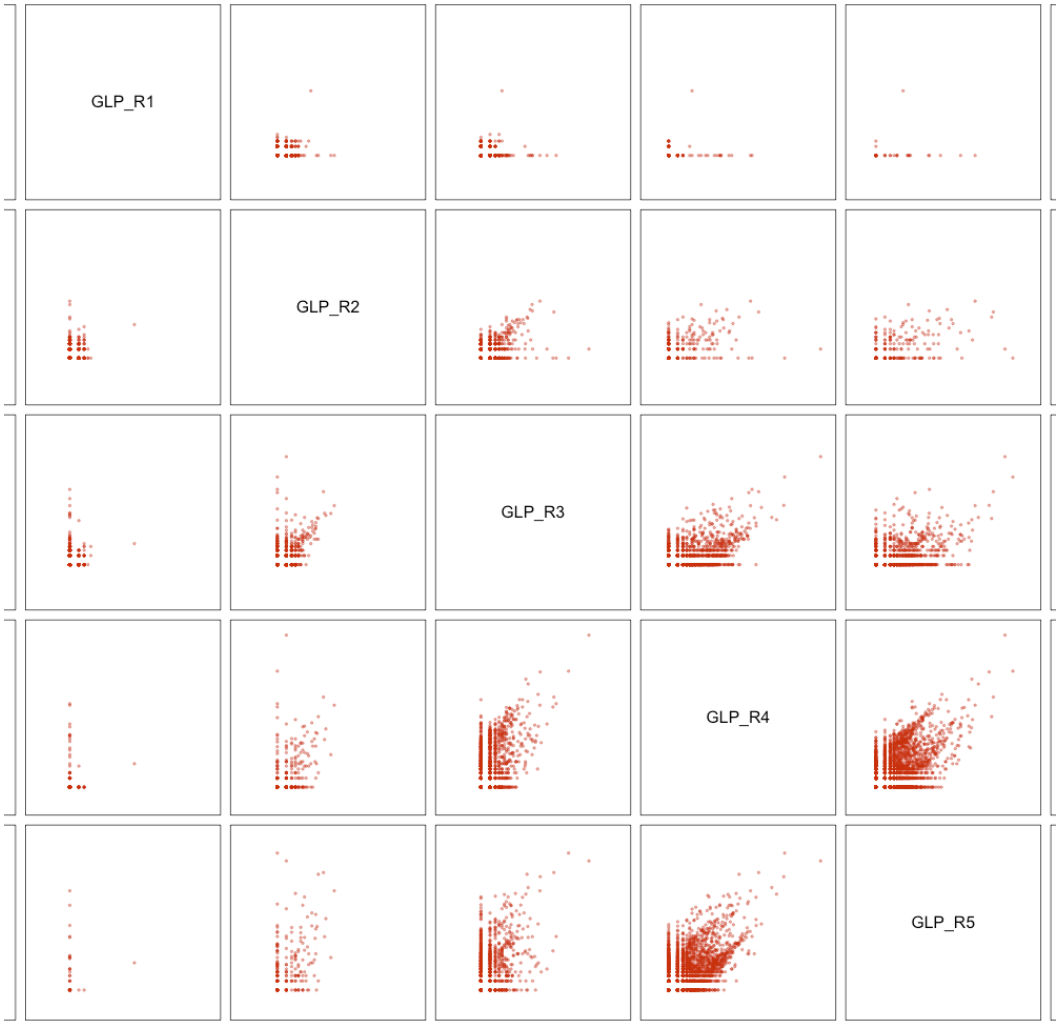
GPCR-focused
scFv phage library
(Library diversity: >1 x 10^{10})



High affinity and potency
target specific IgG

Cell-based Selections	NGS & Sanger Clone Sequencing	Reformatting to IgG and DNA scale-up	High-Throughput IgG Purification	Binding and Functional Assays
2 weeks	1 week	4 weeks	2 week	2-6 weeks

GLP1R POC Panning
Antibody Clones Enrich Significantly in Rounds 4 and 5

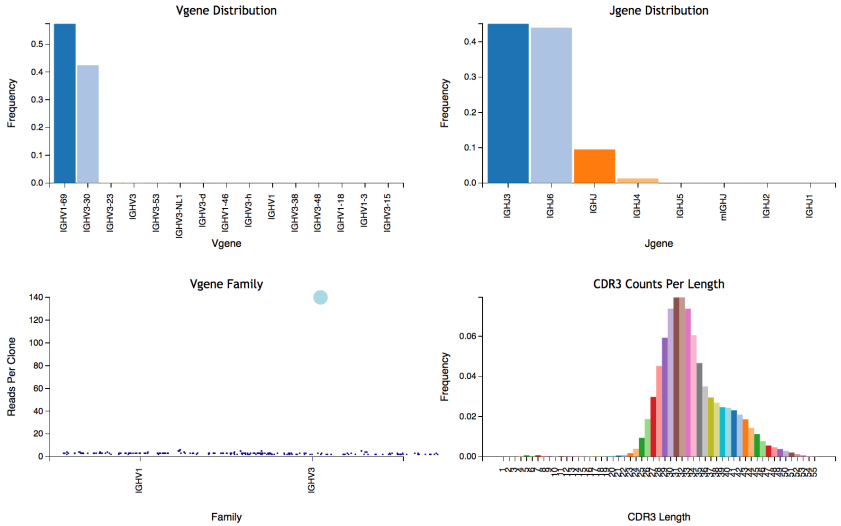


NGS Analysis Reveals Significant Clonal Enrichment

R1

Analytical Distributions: GLP_R1

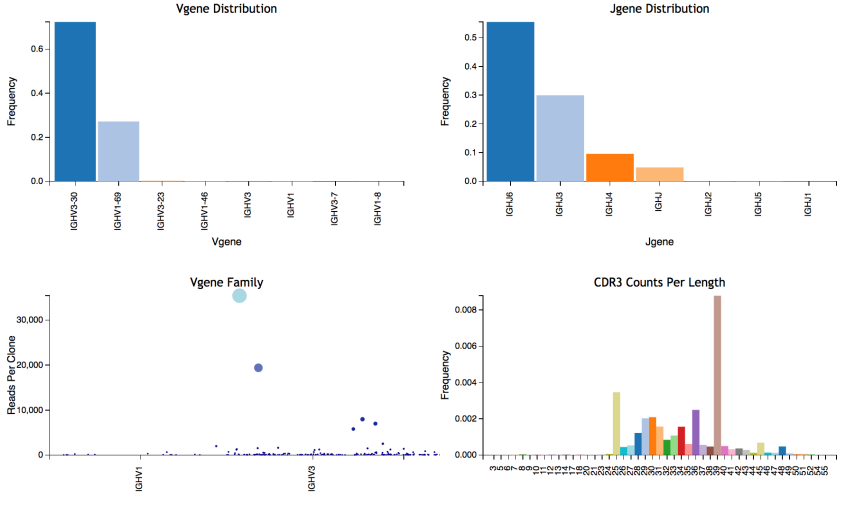
VH distribution



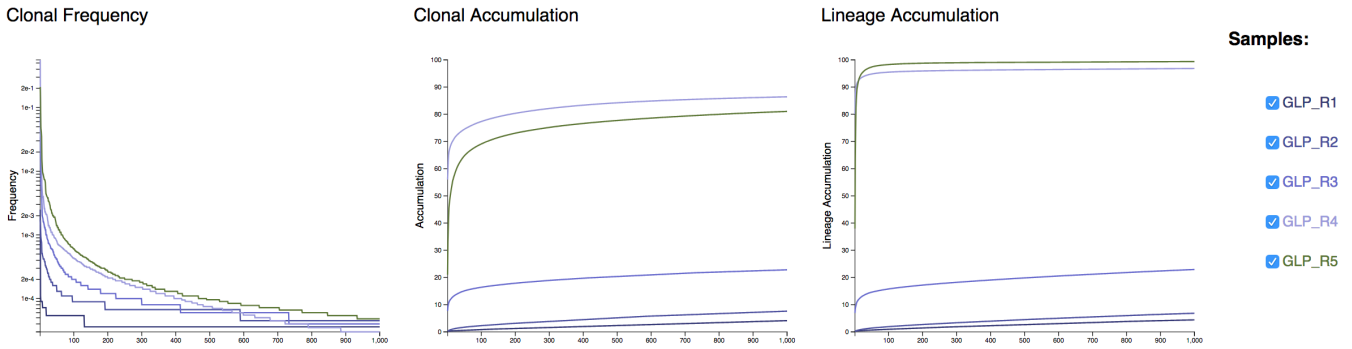
R5

Analytical Distributions: GLP_R5

VH distribution



H Accumulation and Frequency

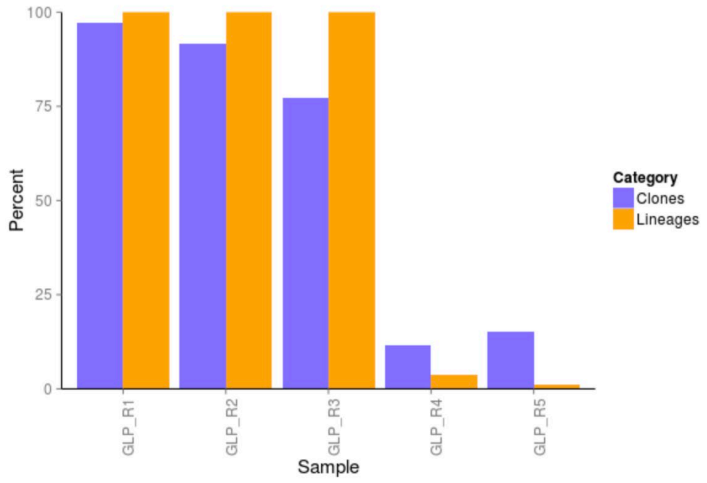


NGS Analysis Reveals Significant Clonal Enrichment

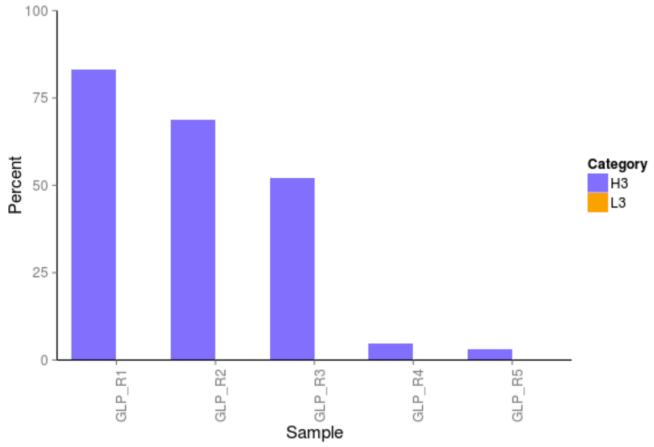
VH

	GLP_R1	GLP_R2	GLP_R3	GLP_R4	GLP_R5
Sequences	106021	126614	129166	212687	174740
Seqs With VH Clones	55409	44864	50223	199502	167449
Clones	53873	41058	38721	23368	25483
Clones (n>1)	1245	2397	2077	3602	4721
Clonotypes	87382	86466	67987	10000	5042
Clonotypes (n>1)	12214	21644	19562	1564	1303
Lineages	85558	82568	63531	7631	2076
Simpsons	9.99975e-01	9.99964e-01	9.93687e-01	6.81153e-01	9.35277e-01

Unique Clones and Lineages



Unique CDR3s

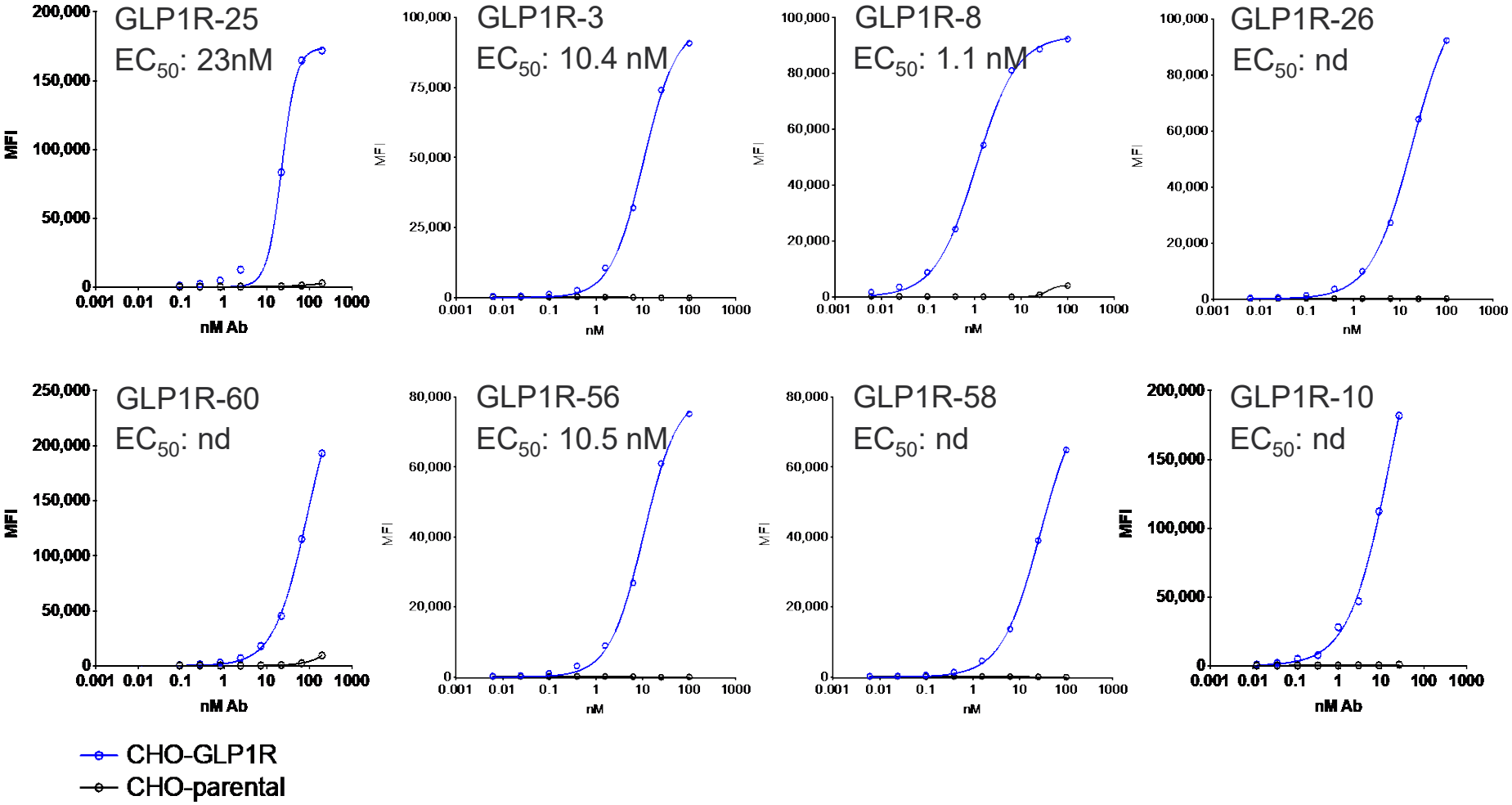


Unique CDR3 % are calculated as the number of unique CDR3s in a sample divided by the total number of sequences that had a CDR3 in that sample, not the total number of sequences.

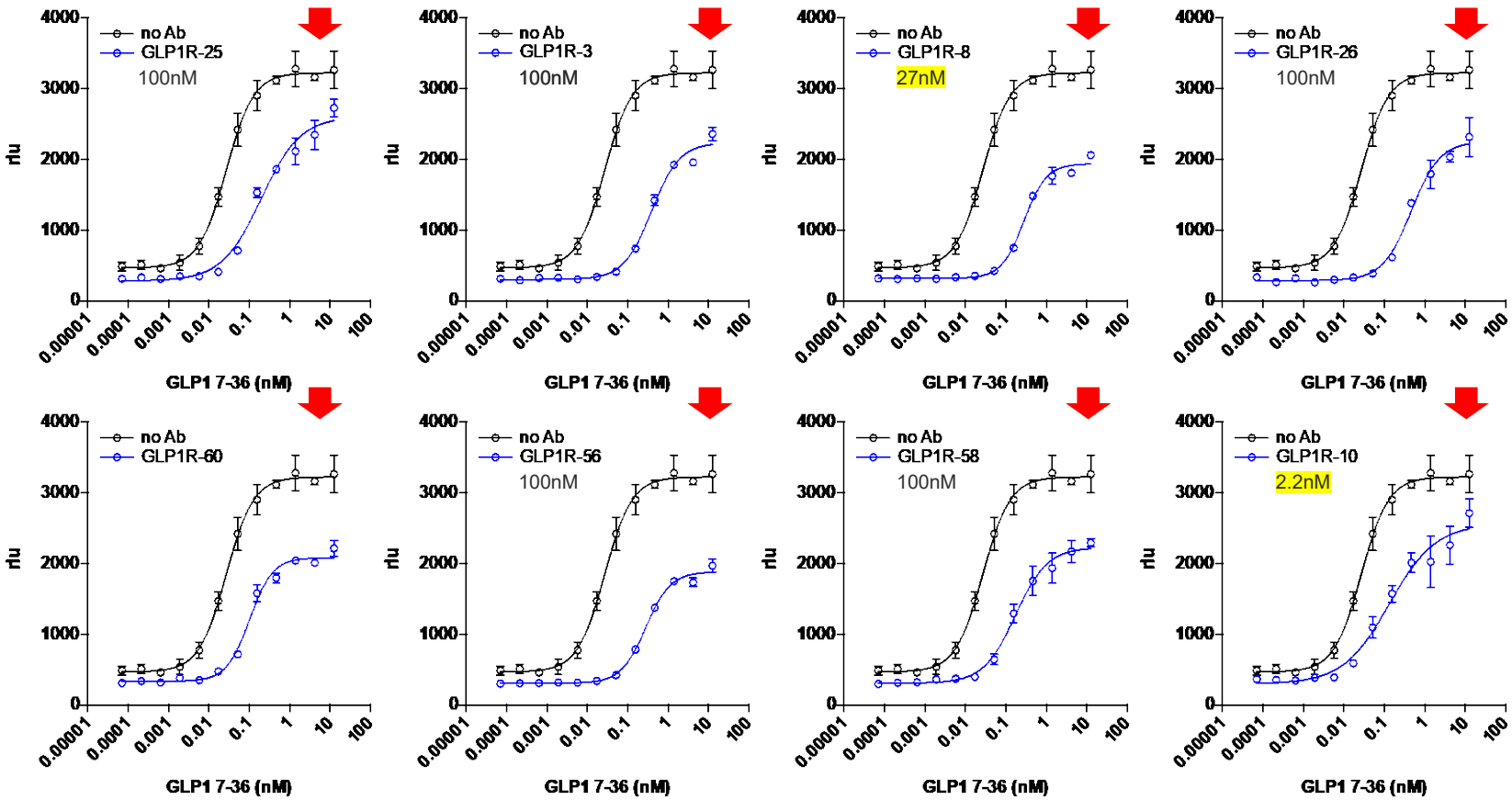
Sample	Reads	Reads with Clones	Unique Clones	% Unique	Unique H	Unique K	Unique L	Lineage Count
GLP_R1	119929	106021	53873	97.23	53873	0	0	85558
GLP_R2	145159	126614	41058	91.52	41058	0	0	82568
GLP_R3	142207	129166	38721	77.10	38721	0	0	63531
GLP_R4	214356	212687	23368	11.71	23368	0	0	7631
GLP_R5	176274	174740	25483	15.22	25483	0	0	2076

Over 15 FACS Positive Antibodies Found

Example: 8 of 15 antibodies



Multiple Antibodies Show Negative Allosteric Inhibition of GLP 7-36 peptide in cAMP Assay!



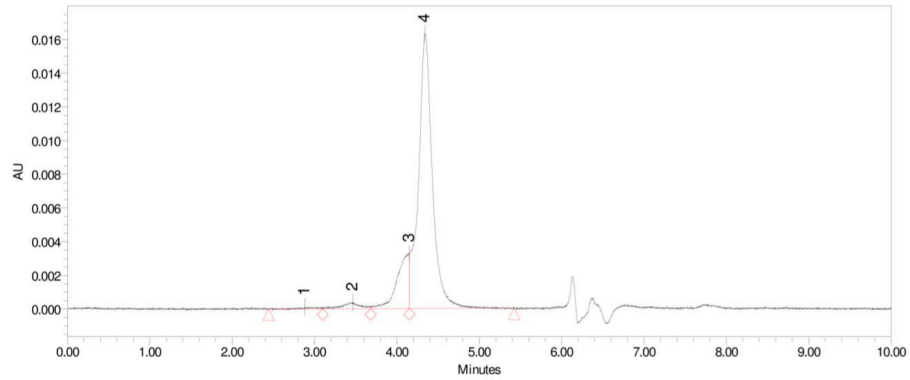
Large Number of GLP & GLP 2 Motifs: FACS Positive GLP1-R Hits

1. 15 positives: GLP1R 2, 3, 8,10, 25, 26, 30, 56, 58, 60, 70, 72, 83, 93, and 98
2. There are three unique sequences, GLP1R 2, 10 and 26 that are also identified positives
3. Positives include the GLP-1 motif (Yellow), and GLP-2 motif (Orange)

FACS +	HCDR3
GLP1R2	CARDMYYDFETVVEGIQWYEALKAGKLGEVVPADDAFDIW
GLP1R3	CAKHMSMQEGAVTG**EGQAAKEFIAWLVKGR**VRADLVGDAFDVW
GLP1R8	CARDGRGSLPRPKGGPQTVG**EGQAAKEFIAWLVKG**GLTYDSSEDSGGAFDIW
GLP1R10	CARANQHFFVPGSLKVWLKGVAPESSSEYDSSEDSGGAFDIW
GLP1R25	CARANQHFLSHAG**AARDFINWLIQTKIT**GLGSGYHYYGMDVW
GLP1R26	CAKHMSMQEGVLQGQIPSTIDWEGLLHLIRADLVGDAFDVW
GLP1R30	CARDMYYDFLKIG**DNLAARDFINWLIQTKITD**GTDTEVVPADDAFDIW
GLP1R56	CARANQHFFSGAEG**EGQAAKEFIAWLVKG**IIPGYHYYGMDVW
GLP1R58	CARANQHFGLHAQG**EGQAAKEFIAWLVKG**SGTYGYHYYGMDVW
GLP1R60	CAKHMSMQDYLVIG**EGQAAKEFIAWLVKG**GPARADLVGDAFDVW
GLP1R70	CARDGRGSLPRPKGGPPSSG**RDFINWLIQTKITD**GFRYDSSEDSGGAFDIW
GLP1R-72	CARDMYYDFHPEGTFTSDVSSYL**EGQAAKEFIAWLVKG**SLIYEVVPADDAFDIW
GLP1R-83	CAKHMSMQEGAVTG**EGQAAKEFIAWLVKG**RVRADLVGDAFDVW
GLP1R-93	CARANQHFLSHAG**AARDFINWLIQTKIT**GLGSGYHYYGMDVW
GLP1R-98	CARDMYYDFGYFTG**MNTILDNLAARDFINWLIQTKITDR**GGGSGGSGGSGGSGGSGEVVPADDAFDIW

IgGs are Monomeric and not Prone to Aggregation

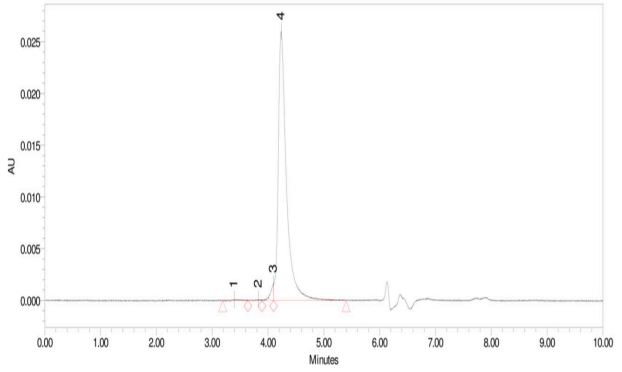
#30



82.64 % monomer (~150Kd)

1	2.882	0.59	---	Peak 1
2	3.466	2.33	---	Peak 2
3	4.151	14.44	---	Peak 3
4	4.339	82.64	---	Peak 4

#56



97.40 % monomer (~150Kd)

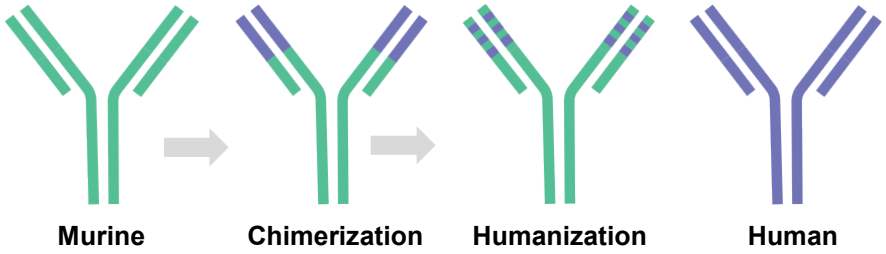
1	3.393	0.34	---	Peak 1
2	3.829	0.15	---	Peak 2
3	4.098	2.11	---	Peak 3
4	4.238	97.40	---	Peak 4

Seeking GPCR Technology Partnerships

1. Over-expressing Cell Lines
2. Nanodiscs and Virus-like-particles
3. Soluble Receptors
4. Viruses, e.g. vaccinia, baculovirus, others
5. Other Innovations in this space …

TAO: Twist Antibody Optimization

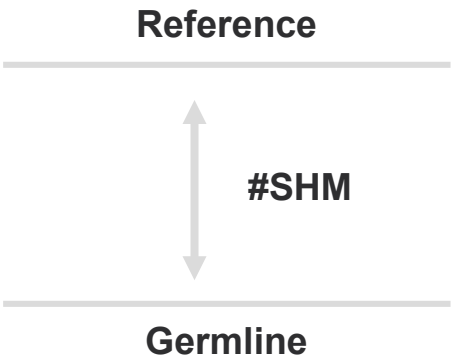
Input: Murine, Chimeric, Humanized or Fully Human Antibody Hits



How many of you have leads that need optimization?

"Human Repertoire Inspired"

Output: Fully Human Optimized Lead



- Explore mutation space from parent reference sequence and germline using natural LCDR1-3 and HCDR1-2 sequences derived from NGS data
- Exclude liabilities and competitive/prior art IP
- Control # the number of subjects that contain these the designed repertoire

POC: PD1 Antibody Optimization

MUTATIONS FROM GERMLINE

Heavy Chain

								FW1		SDR1		FW2		SDR2		FW3		SDR3		FW4
									1		1		0		0		1			0
Germ	d1	d2	V	FW	CDR	H/L	FW1		SDR1		FW2		SDR2		FW3		SDR3		FW4	
donor	0	0	97.1%	97.6%	95.6%	100%	EVQLVQSGAEVKKPGASVKVSCKASG		YRFTSYGIS		WVRQAPGQGLEW		MGWISAYNGNTNYA		QKLQGRVTMTTDTSTNTAYMELRSLRSDDTAVYYC		ARDADYSSGSGY		WGQGTLVTVSS	
IGHV1-18							QVQLVQSGAEVKKPGASVKVSCKASG		YTFTSYGIS		WVRQAPGQGLEW		MGWISAYNGNTNYA		QKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYC		----------		WGQGTLVTVSS	

Light Chain

								FW1		SDR1		FW2		SDR2		FW3		SDR3		FW4
									0		0		1		1		1		6	1
Germ	d1	d2	V	FW	CDR	H/L	FW1		SDR1		FW2		SDR2		FW3		SDR3		FW4	
donor	0	0	96%	96.3%	94.4%	94.7%	---LTQP-PSVSVSPGQTARITC		SGDALPKQYAY		WYQQKPGQAPVMVIY		KDTERPS		GIPERFSGSSSGTKVTLTISGVQAEDEADYYC		QSADNSITYRV		FGGGTKVT--	
IGLV3-25							---LTQP-PSVSVSPGQTARITC		SGDALPKQYAY		WYQQKPGQAPVLVIY		KDSERPS		GIPERFSGSSSGTTVTLTISGVQAEDEADYYC		LSADSSGTWV		FGGGTKLT--	

TAO CRITERIA:

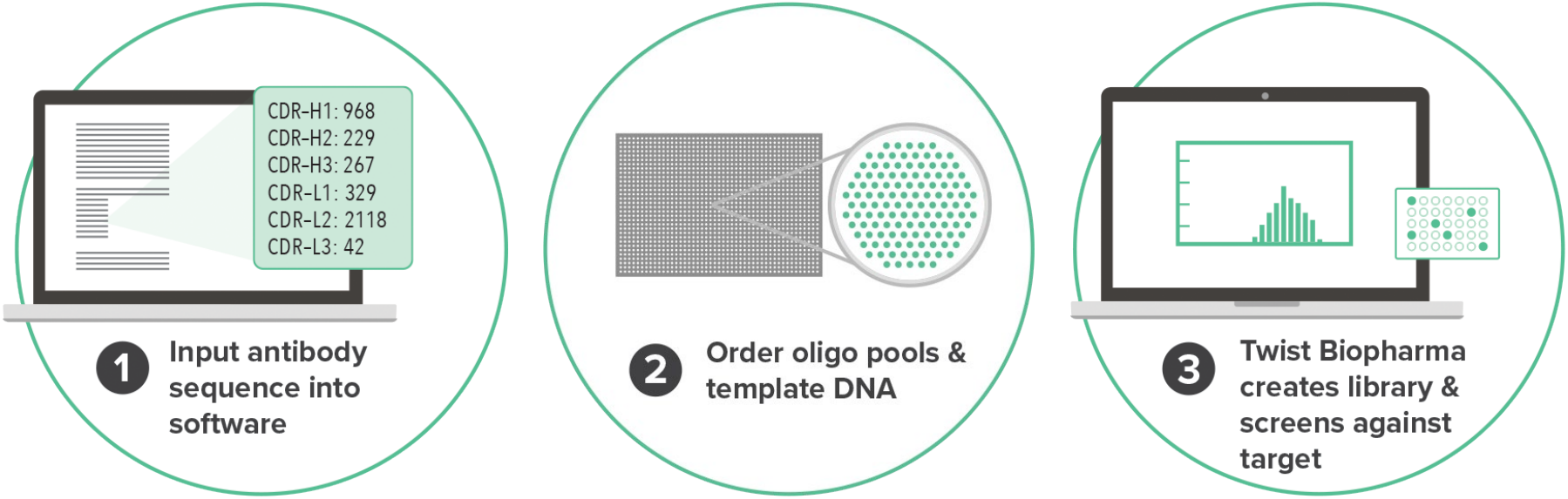
natural-fitness-scan	distance 1, 2, or 3 (default 1)
min_subjects	min number of people with CDR (default 2)
suppress-liabilities	default yes
explore-germline	distance 1, 2, or 3 (default 1)
amino-scan=H,D,E	charge and feature scan
custom_cdrs=mycdrs.txt	custom CDRs that the user can force include
perform_h3_scan=0	single amino acid scan of H3 (default yes)

Uses NGS database from 12 people

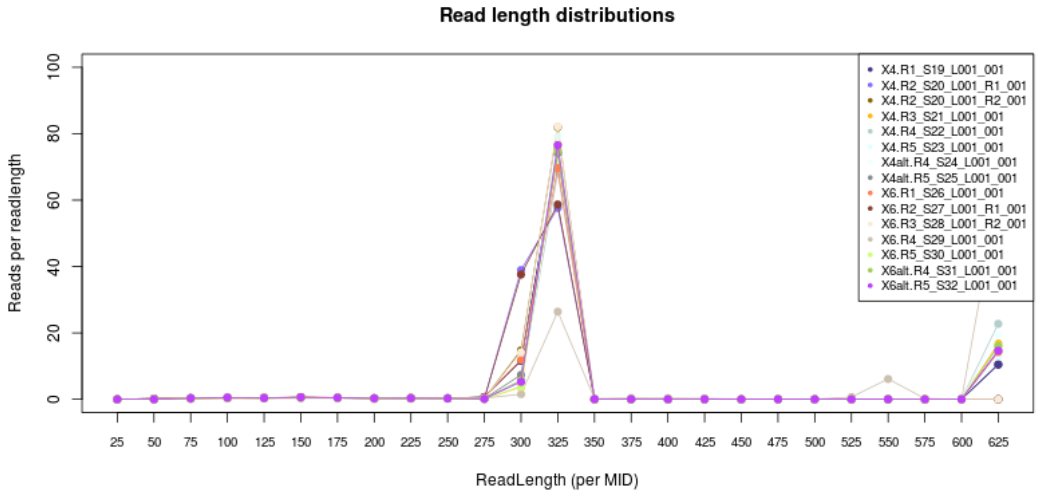
POC: PD-1 Antibody TAO Output (SHM = 3, min_subjects = 2)

Twist Antibody Optimization: Generate high-diversity, high quality molecules inspired by the human repertoire in months

4 months

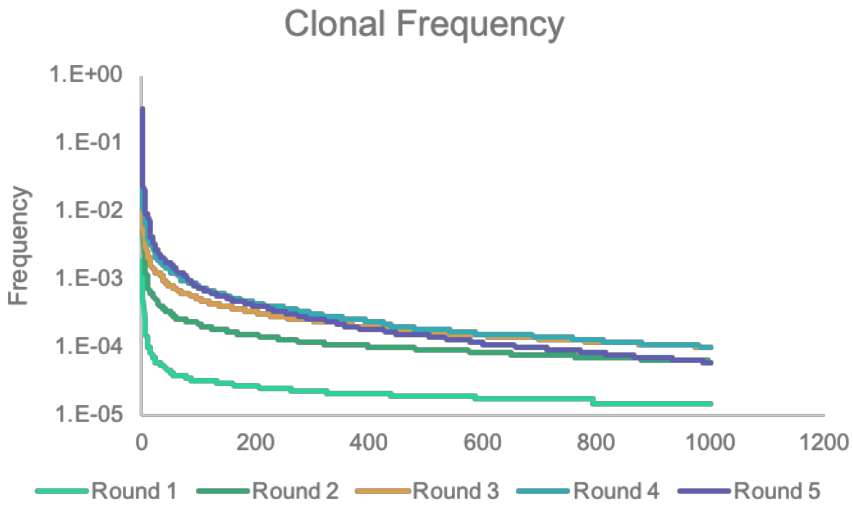


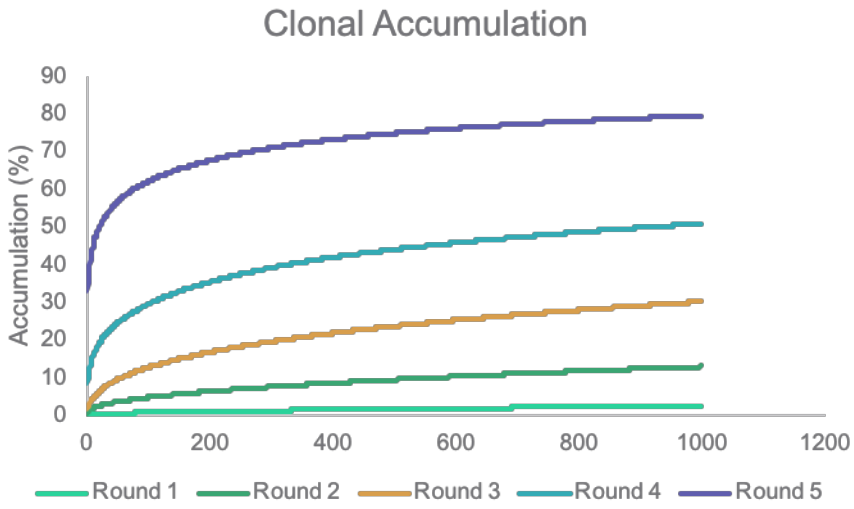
Panning NGS Analysis Reveals Significant Clonal Enrichment in Round 5



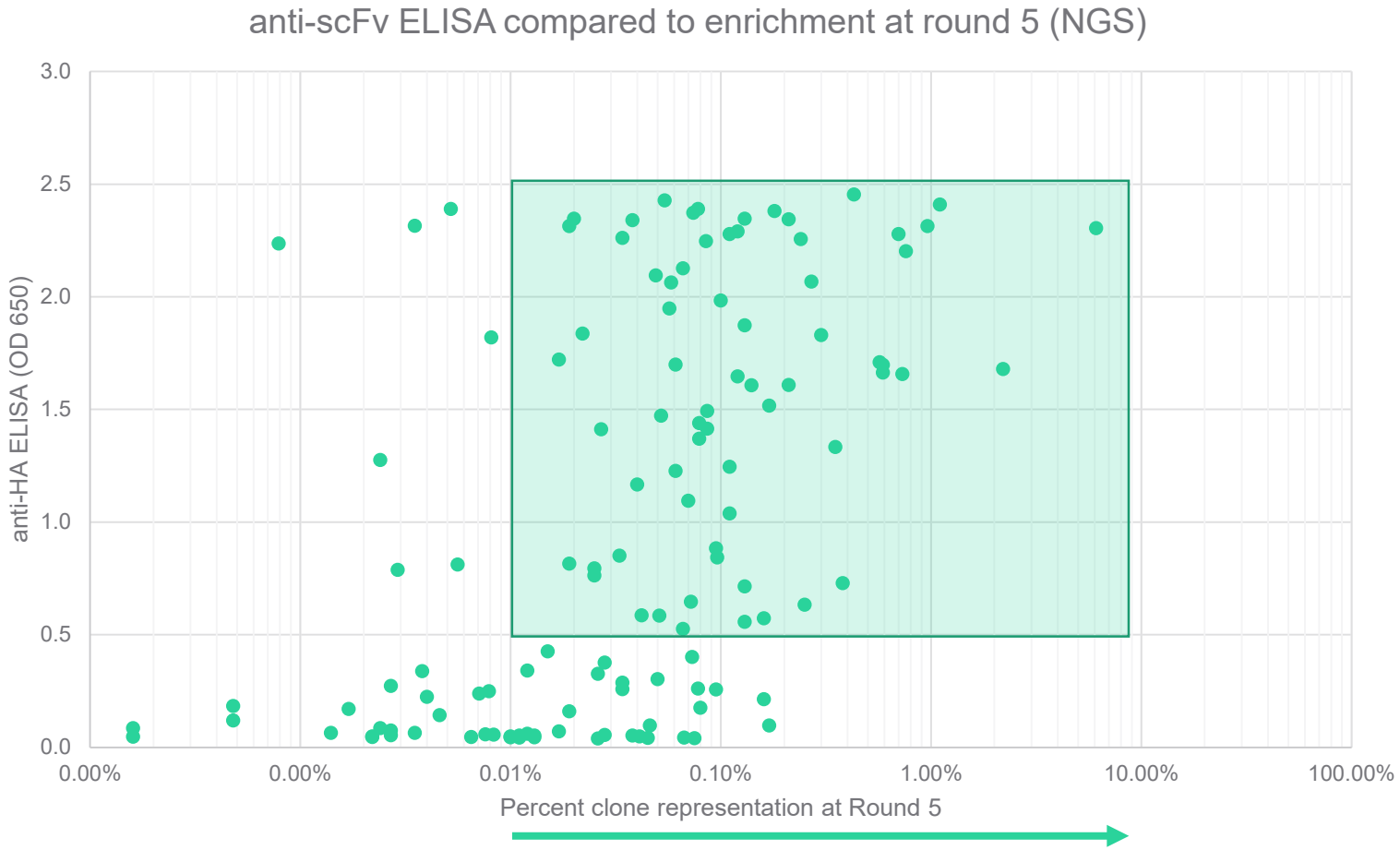
Variable heavy chain PCR amplified from Round 1 – 5 (including alternate Round 4 and Round 5 panning conditions using off-rate based screening)

10 million reads
400k unique clones identified





Majority of High-affinity scFv Binders Enriched at Round 5

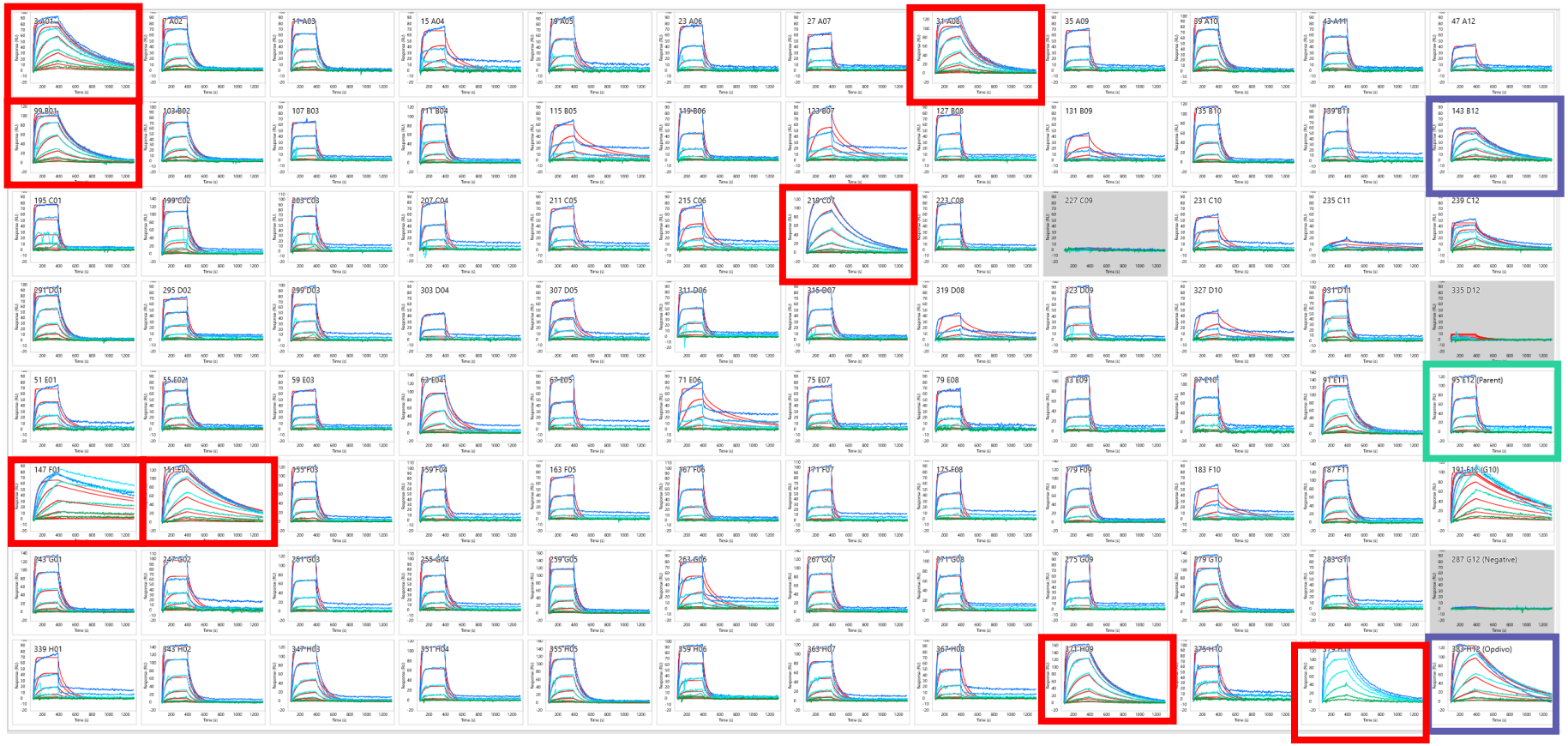


- >90% (68/75) of clones 5x over background in ELISA measuring scFv binding to PD-1 were enriched to > 0.01%
- ~1000 clones represented in Round 5 enrich > 0.01% of population
  → amenable to high-throughput IgG screening

TAO Optimized IgGs Bind with Similar or Improved Affinity to Commercial PD-1 Antibodies Pembro, Nivo

Affinity increased 80x

Bind leads with higher affinity than control antibodies



Top binding Ab | Commercial Ab | Parental Ab

Multiple TAO Optimized IgGs Bind Better than Commercial Antibodies

Common substitutions

- Polar (+) charged → Hydrophobic or uncharged
- Polar uncharged → Polar charged
- Asparagine → Serine
- Uncharged → Polar charged
- Small hydrophobic → Bulky hydrophobic

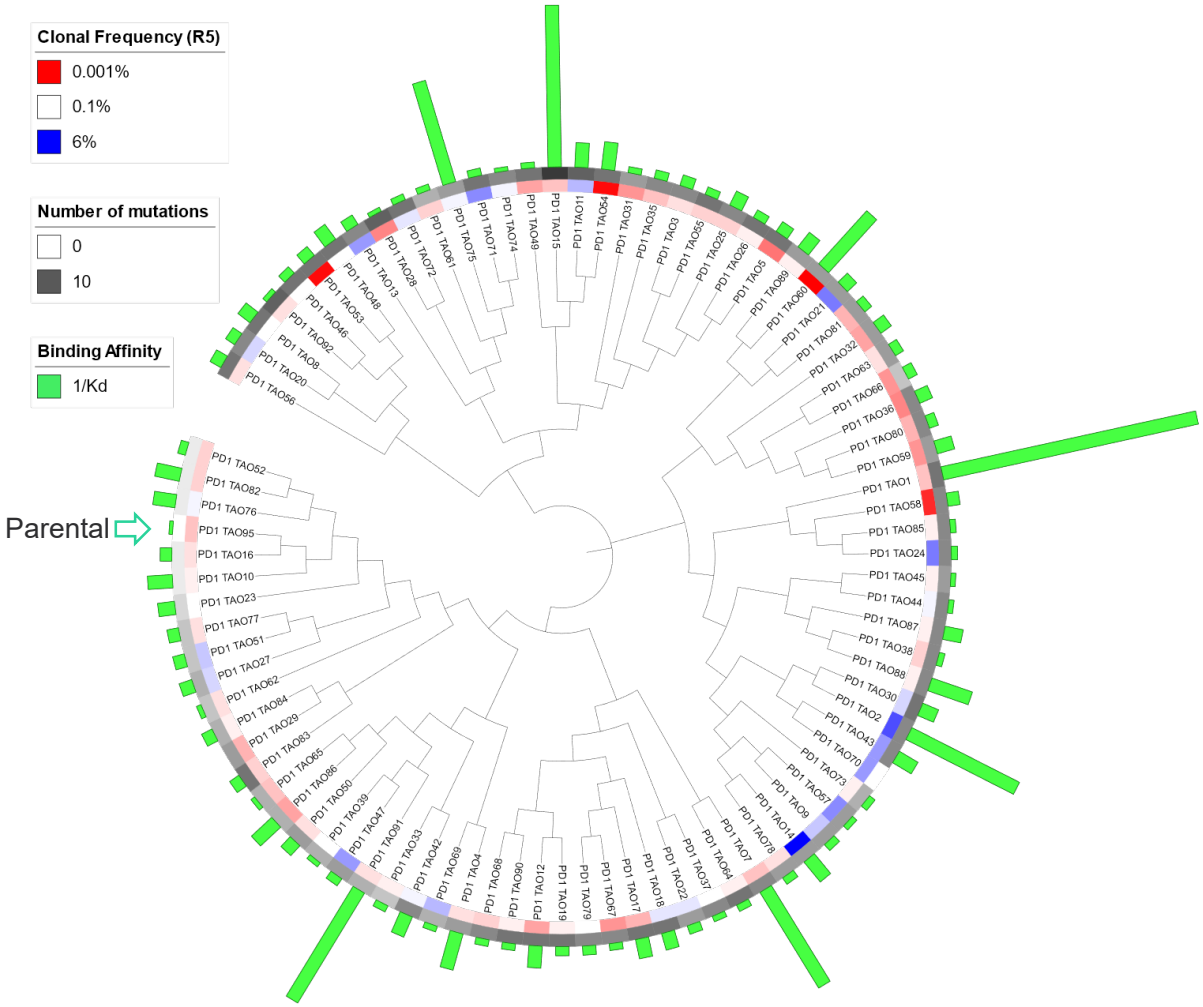
Commercial Ab

Parental Ab

Binding affinity (IgG)

	SPR (Carterra)			FACS				
Clone	KD (nM)	ka (M-1 s-1)	kd (s-1)	KD (nM)	Yield (ug/ml)	CDRH1	CDRH2	CDRH3
						Y R F T S Y G I S	G W I S A Y N G N T N Y A	C A R D A D Y S S G S G Y W
PD1_TAO1	4.52	6.E+05	2.94E-03	3.37	19.7	Y T F S H Y G I S	G W V S A Y S G N T R Y A	C A R D A T Y S S G S G Y W
PD1_TAO15	7.29	2.E+05	1.76E-03	11.52	8.8	Y T F T D Y G V S	Y T I S P Y S G K T D Y A	C A R D A D Y S I G S G Y W
PD1_TAO91	9.17	6.E+05	5.12E-03	4.18	9.7	Y T F A D Y G I S	G W I S A Y N G N T N Y A	C A R D W D Y S S G S G Y W
PD1_TAO2	9.76	7.E+05	7.29E-03	4.81	30.7	Y S F S N Y G I S	G W V S A Y S G N T N Y A	C A R D A D Y A S G S G Y W
PD1_TAO7	10.4	7.E+04	7.37E-04	1.23	14.8	Y T F T H Y G I T	G W I S A Y S G S T N Y A	C A R D A D Y S I G S G Y W
PD1_TAO75	11.1	5.E+05	5.60E-03	ND	8.5	Y P F T N Y G I S	G W I S P Y S G N T N Y A	C A R D F D Y S S G S G Y W
nivolumab	14.5	2.E+06	2.80E-02	1.30	13.4	Y T F T N Y Y M Y	G G I N P S N G G T N F N	C A R R D Y R F D M G F D Y
pembrolizumab	16.3	2.E+05	2.96E-03	18.60	21.3	I T F S N S G M H	V I W W Y D G S K R Y Y A	C A T N D D Y
PD1_TAO60	16.4	3.E+05	5.23E-03	3.46	53.5	Y D F S S Y G I S	G W I S A Y S G N T R Y A	C A R D A D Y S V G S G Y W
PD1_TAO88	27.5	5.E+05	1.36E-02	4.08	8.1	Y T F N R Y G I S	G W I S A Y S G N T R Y A	C A R D A D Y A S G S G Y W
PD1_TAO4	31.3	9.E+05	2.67E-02	6.90	15.1	Y T F S T S G I S	G W I S A Y N G N T N Y A	C A R D F D Y S S G S G Y W
PD1_TAO86	42.6	3.E+04	1.39E-03	ND	10.5	Y T F D D Y G I S	G W I S A Y N G N T N Y A	C A R D A T Y S S G S G Y W
PD1_TAO54	42.9	8.E+04	3.23E-03	9.18	7.3	Y A F S N Y G I S	G W I S P Y S G N T K Y A	C A R D A D Y S I G S G Y W
PD1_TAO14	45.8	1.E+07	6.42E-01	ND	10.8	Y P F T N Y G I S	G W T S A Y S G N T N Y A	C A R D F D Y S S G S G Y W
PD1_TAO82	46.9	6.E+05	2.76E-02	7.46	12.5	Y R F T S Y G I S	G W I S A Y N G N T N Y A	C A R D W D Y S S G S G Y W
PD1_TAO10	47.3	4.E+06	1.66E-01	1.99	15.4	Y R F T S Y G I S	G W I S A Y N G N T N Y A	C A R D A D Y A S G S G Y W
PD1_TAO11	48.1	8.E+05	3.97E-02	4.26	10.5	Y T F S N Y G F S	G W I S P Y S G N T K Y A	C A R D A D Y S I G S G Y W
PD1_TAO76	52.6	7.E+05	3.85E-02	5.27	13.4	Y R F T S Y G I S	G W I S A Y N G N T N Y A	C A R D F D Y S S G S G Y W
PD1_TAO12	53.5	8.E+08	4.05E+01	3.01	119.7	Y T F N T Y G V S	G W I S A Y S G N T R Y A	C A R D F D Y S S G S G Y W
PD1_TAO42	53.6	1.E+07	7.55E-01	2.09	9.1	Y T F N N F G I S	G W I S A Y N G N T D Y A	C A R D M D Y S S G S G Y W
PD1_TAO43	54.4	5.E+05	2.86E-02	4.12	8.4	Y T F S N Y G I S	G W I S A Y S G N T K Y A	C A R D A D Y A S G S G Y W
PD1_TAO17	60.0	8.E+05	5.07E-02	2.65	9.2	Y T F S K Y G I S	G W I S A Y S G H T D Y A	C A R D F D Y S S G S G Y W
PD1_TAO89	63.8	9.E+05	5.66E-02	3.37	11.5	Y S F T K Y G I S	G W I S A Y S G N T R Y A	C A R D A D Y S I G S G Y W
PD1_TAO87	63.9	3.E+06	1.65E-01	2.72	7.7	Y T F D R Y G I S	G W I S A Y S G N T R Y A	C A R D V D Y S S G S G Y W
PD1_TAO48	64.3	1.E+09	6.43E+01	ND	59.4	Y T F S H Y G I S	G W I S P Y S G N T K Y A	C A R D A D Y W S G S G Y W
PD1_TAO59	65.9	7.E+05	4.87E-02	8.37	8.3	Y D F S S Y G I S	G W I S A Y S G Y T N Y A	C A R D A V Y S S G S G Y W
PD1_TAO18	68.4	8.E+05	5.15E-02	2.55	12.6	Y T F N N Y G I S	G W I S A Y S G H T D Y A	C A R D W D Y S S G S G Y W
PD1_TAO30	68.7	4.E+05	2.61E-02	3.62	8.0	Y T F N N Y G V S	G W V S A Y S G N T N Y A	C A R D A D Y A S G S G Y W
PD1_TAO23	69.2	2.E+06	1.41E-01	10.76	8.0	Y P F T S Y G I S	G W I S A Y N G N T N Y A	C A R D V D Y S S G S G Y W
PD1_TAO25	76.0	3.E+05	2.18E-02	5.28	7.3	Y S F T R Y G I S	G W I S P Y S G N T K Y A	C A R D A D Y G S G S G Y W
PD1_TAO8	78.0	8.E+05	6.39E-02	1.44	9.4	Y T F S H Y G I S	G W I S P Y S G N T K Y A	C A R D N D Y S S G S G Y W
PD1_TAO36	84.8	1.E+09	8.49E+01	ND	7.1	Y T F S S Y G V S	G W I S A Y S G S T N Y A	C A R D A V Y S S G S G Y W
PD1_TAO50	87.4	7.E+08	6.21E+01	12.67	15.8	Y T F R N Y G I S	G W T S A Y N G N T N Y A	C A R D A T Y S S G S G Y W
PD1_TAO27	88.6	1.E+06	1.07E-01	4.33	11.8	Y P F T N Y G I T	G W I S A Y N G N T N Y A	C A R D W D Y S S G S G Y W
Parental	325.5	9.E+04	2.85E-02	ND	10.4	Y R F T S Y G I S	G W I S A Y N G N T N Y A	C A R D A D Y S S G S G Y W

TAO-Optimized IgG binders are Derived from a Wide Sequence Space



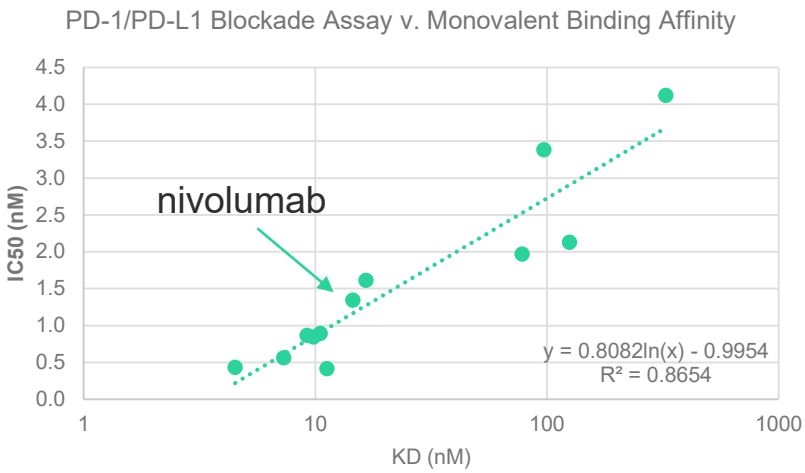
Clone	Frequency	Mutations	KD
PD1_TAO1	0.05%	7	4.5
PD1_TAO15	0.05%	10	7.3
PD1_TAO91	0.09%	4	9.2
PD1_TAO2	2.20%	6	9.8
PD1_TAO7	0.05%	6	10.5
PD1_TAO75	0.16%	5	11.1
PD1_TAO60	0.00%	5	16.5
PD1_TAO88	0.11%	6	27.5
PD1_TAO4	0.09%	5	31.4
PD1_TAO86	0.03%	4	42.6
PD1_TAO54	0.00%	7	42.9
PD1_TAO14	6.10%	5	45.9
PD1_TAO82	0.07%	1	47.0
PD1_TAO10	0.11%	1	47.4
PD1_TAO11	0.38%	8	48.1
PD1_TAO76	0.15%	1	52.6
PD1_TAO12	0.03%	7	53.5
PD1_TAO42	0.16%	6	53.6
PD1_TAO43	0.59%	6	54.4
PD1_TAO17	0.04%	7	60.1
PD1_TAO89	0.10%	5	63.9
PD1_TAO87	0.11%	6	63.9
PD1_TAO48	0.12%	7	64.3
PD1_TAO59	0.03%	5	65.9
PD1_TAO18	0.21%	7	68.4
PD1_TAO30	0.27%	7	68.8
PD1_TAO23	0.14%	2	69.2
PD1_TAO25	0.06%	6	76.0
PD1_TAO8	0.13%	7	78.1
PD1_TAO36	0.02%	6	84.9
PD1_TAO50	0.09%	5	87.5
PD1_TAO27	0.25%	4	88.6
PD1_TAO21	0.96%	5	92.0
PD1_TAO32	0.03%	5	92.2
PD1_TAO56	0.08%	7	94.8
PD1_TAO58	0.01%	6	96.7
PD1_TAO51	0.35%	3	98.8
PD1_TAO16	0.08%	1	100.8
PD1_TAO77	0.08%	3	100.9
PD1_TAO5	0.02%	7	101.0
PD1_TAO84	0.09%	4	101.2
PD1_TAO53	0.00%	7	102.8
PD1_TAO83	0.06%	7	105.7
PD1_TAO13	0.57%	6	106.4
PD1_TAO3	0.07%	6	107.3
PD1_TAO20	0.24%	6	109.4
PD1_TAO66	0.03%	3	118.9
PD1_TAO80	0.04%	6	125.2
PD1_TAO63	0.08%	5	125.8
PD1_TAO79	0.12%	6	129.2
PD1_TAO19	0.10%	7	129.5
PD1_TAO22	0.21%	5	132.5
PD1_TAO81	0.04%	5	134.0
PD1_TAO46	0.12%	7	136.4
PD1_TAO26	0.10%	7	137.5
PD1_TAO35	0.05%	6	139.1
PD1_TAO47	0.70%	5	139.1
PD1_TAO9	0.30%	5	148.4
PD1_TAO55	0.07%	7	149.3
PD1_TAO52	0.06%	1	149.4
PD1_TAO78	0.07%	5	152.0
PD1_TAO71	0.73%	7	160.9
PD1_TAO64	0.10%	7	166.9
PD1_TAO73	0.11%	4	170.5
PD1_TAO67	0.03%	6	171.5
PD1_TAO68	0.07%	6	173.2
PD1_TAO33	0.10%	3	173.6
PD1_TAO90	0.09%	7	174.3
PD1_TAO72	0.18%	7	188.1
PD1_TAO24	1.10%	6	189.8
PD1_TAO31	0.03%	5	194.5
PD1_TAO61	0.06%	4	194.5
PD1_TAO37	0.13%	6	198.6
PD1_TAO49	0.03%	7	201.4
PD1_TAO69	0.43%	4	201.5
PD1_TAO38	0.06%	6	203.6
PD1_TAO57	0.76%	5	204.3
PD1_TAO85	0.11%	6	209.6
PD1_TAO44	0.17%	6	226.5
PD1_TAO92	0.09%	8	235.8
PD1_TAO62	0.09%	3	240.2
PD1_TAO39	0.13%	4	240.5
PD1_TAO45	0.11%	5	242.9
PD1_TAO65	0.05%	4	260.6
PD1_TAO28	0.02%	8	267.0
PD1_TAO74	0.16%	6	285.7
PD1_TAO95	0.05%	0	325.5

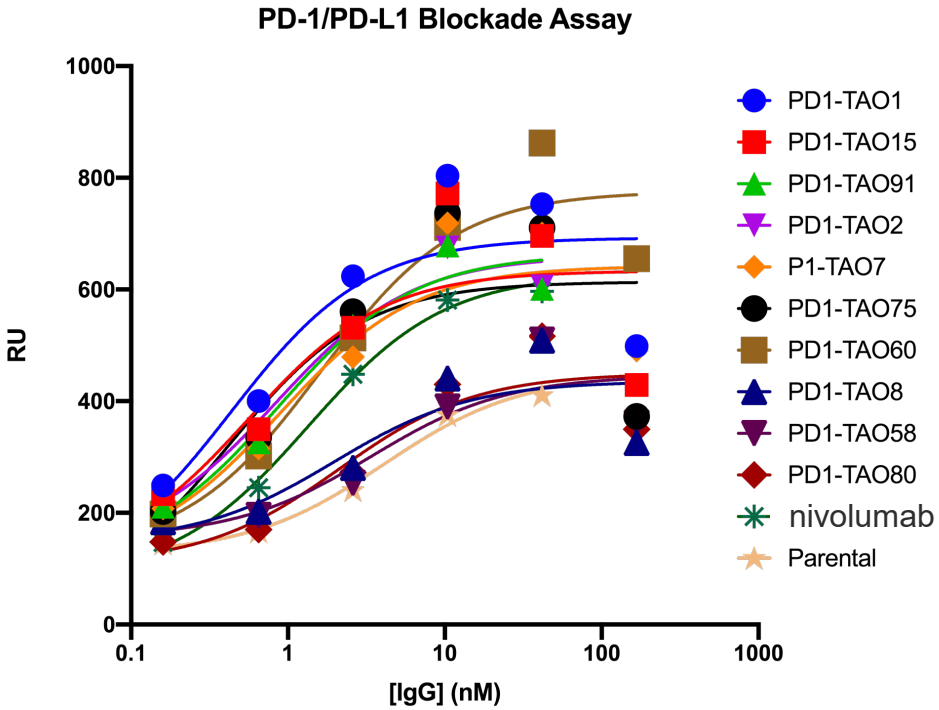
>90% of clones contain unique light chains that are never repeated

TAO Optimized IgGs Block PD-1/PD-L1 Interaction

Binding affinity (IgG)

Clone	SPR K_D (nM)	IC50 (nM)	Bmax (RU)
PD1_TAO1	4.5	0.434	693
PD1_TAO15	7.3	0.562	634
PD1_TAO91	9.2	0.868	664
PD1_TAO2	9.8	0.848	661
PD1_TAO7	10.5	0.896	642
PD1_TAO75	11.2	0.418	614
nivolumab	14.5	1.345	628
PD1_TAO60	16.5	1.614	776
PD1_TAO8	78.1	1.968	436
PD1_TAO58	96.7	3.384	446
PD1_TAO80	125	2.129	450
Parental	325	4.122	449





Addition of anti-PD1 antibody blocks the PD-1/PD-L1 interaction, releases inhibitory signal and results in TCR activation and NFAT-RE-mediated luminescence (RU)

Ways to Work with Us

1. License libraries
2. Partnership around generating new leads against any GPCR of interest
3. Partnership around optimizing existing leads with Twist Antibody Optimization
4. Partner/Collaborate around select leads generated from initial POC

Twist Biopharma Strategic Areas

Multiple Antibody Discovery Tools to Ensure a Successful Campaign

TWIST ANTIBODY DISPLAY LIBRARIES

- Wide range antibody library scaffold libraries (Fab, scFv, VHH)
- Virtual target specific synthetic libraries enabled by modeling or immunization

GPCR ANTIBODY LIBRARY

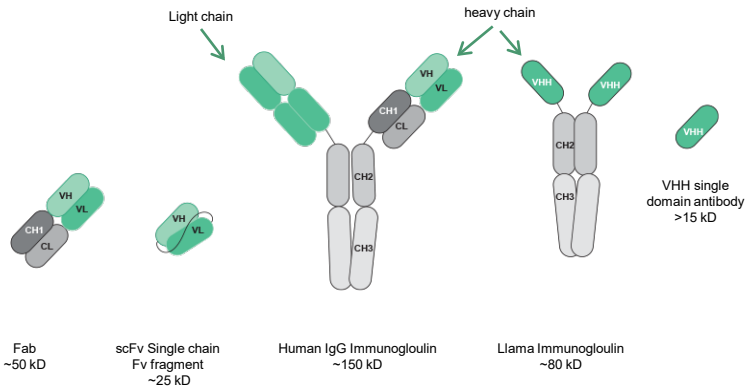
- Unlock and enable the discover of antibodies to this difficult target class

TWIST ANTIBODY OPTIMIZATION (TAO)

HIGH THROUGHPUT ANTIBODY PRODUCTION

- Enabled by HT Gene Synthesis and Automation

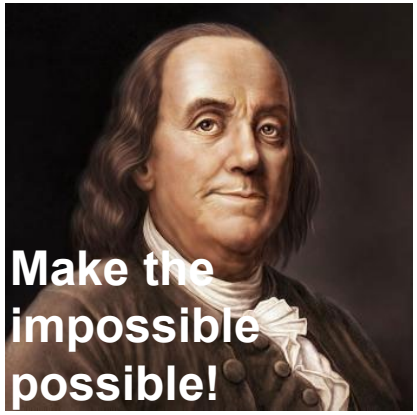
IgG, scFv, VHH



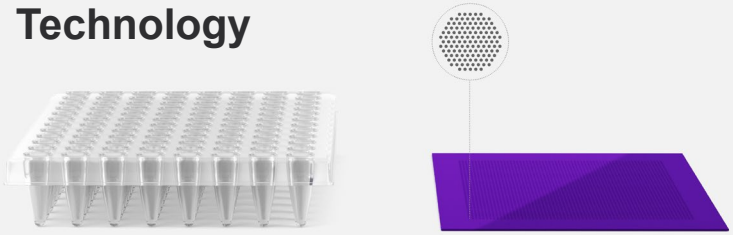
Our Competitive Advantage

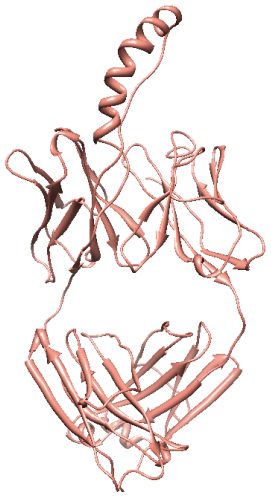
Utilize “writing” of precisely defined libraries to create unprecedented synthetic antibody libraries that are devoid of liability issues and can match the natural CDR repertoire or contain specific sequence motifs

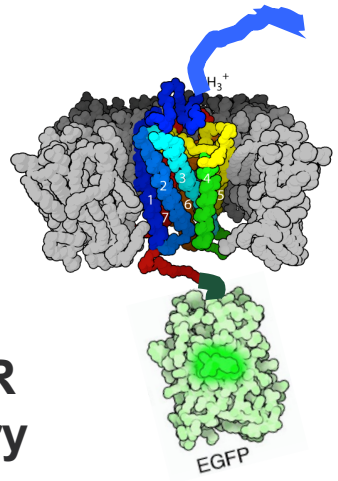
Wrap up



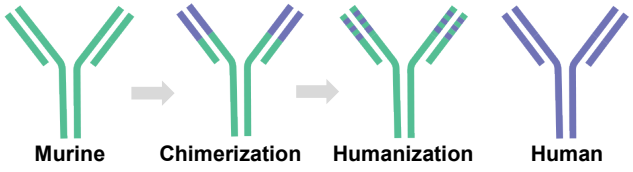
Enabling Twist Technology





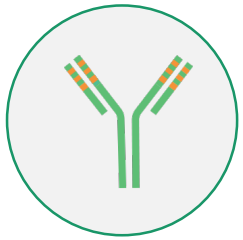


GPCR Library



TAO

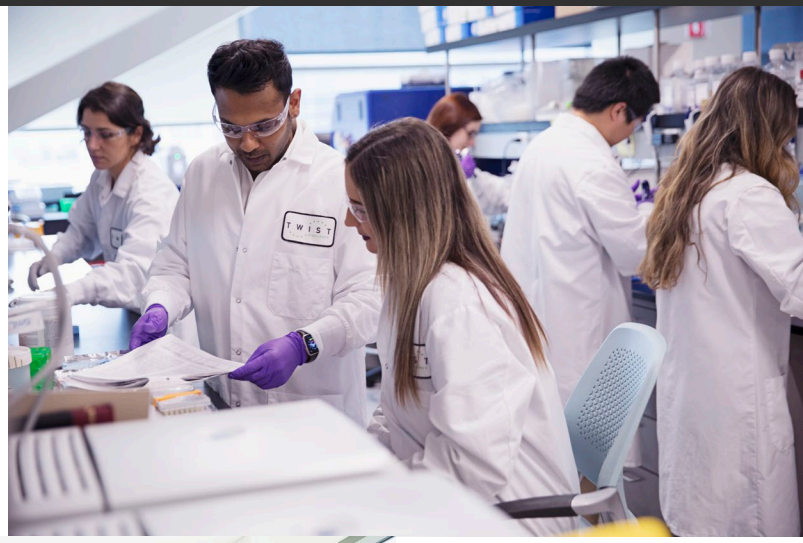
CUSTOM SOFTWARE



"Human Repertoire Inspired"

Building a Library of Libraries

Big Thanks to the Team!



Check out the Twist Bioscience posters …

Date: Monday, April 8, 2019
Time: 5:40 pm – 7:15 pm
Location: Commonwealth Hall
Poster Session: A

Poster Number: A103
Precision Synthesis of Variant Libraries Enables Comprehensive Interrogation of Single Site Variant Space

Poster Number: A104
A High-Throughput Platform to Develop Highly Potent and Functional Antibodies Against G-Protein Coupled Receptors

Poster Number: A105
Twist Bioscience's Silicon-Based DNA Synthesis Platform Enables the Construction of Focused Variant Libraries with Unprecedented Precision

Poster Number: A106
Rapid Optimization and Humanization of an Anti-PD1 Antibody