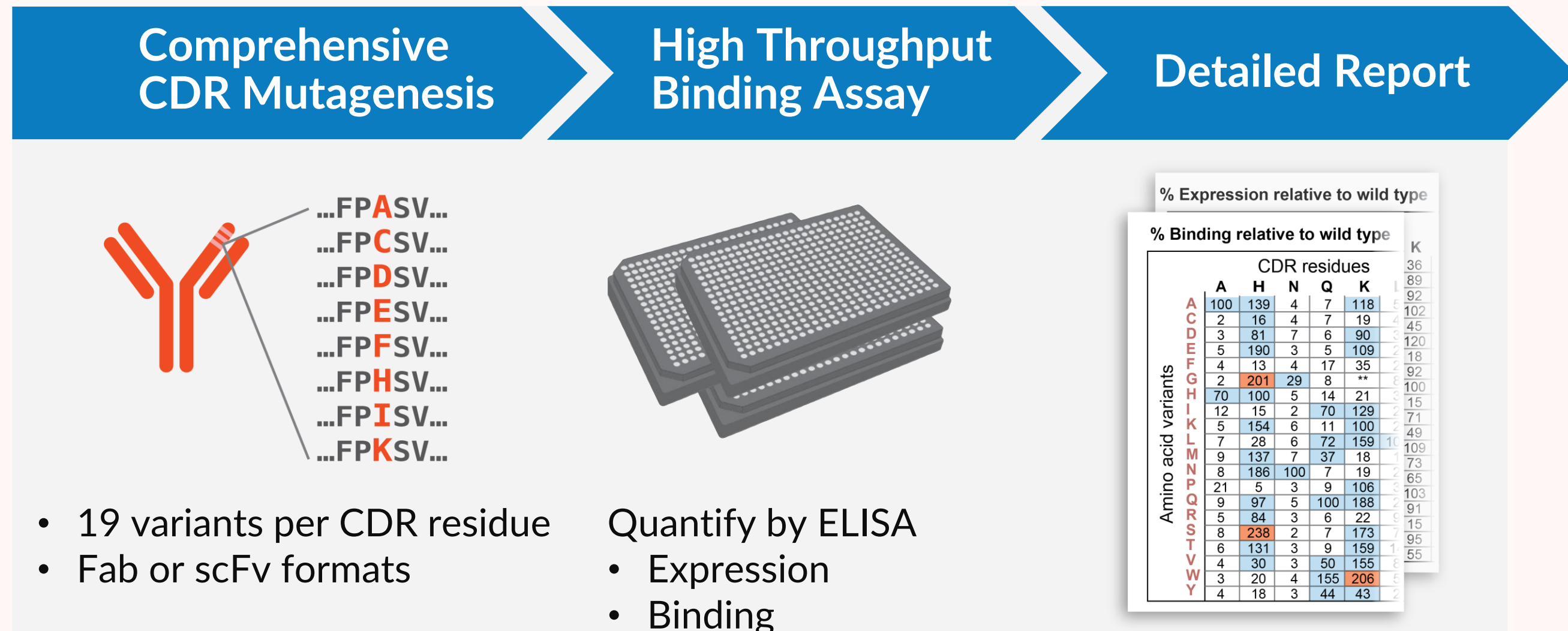


Paratope-PLUS™ CDR-Scanning



Report Containing All Data

- Critical residues encompassing paratope
- Data describing CDR variations that can yield improved binding and developability
- Draft patent claims
- AI/ML suggested combination mutations

As described in Banik et al., 2025

Patents
nature biotechnology
Redefining antibody patent protection using paratope mapping and CDR-scanning

Enabling Multiparametric Engineering

- Improve binding
- Remove off-target binding
- Introduce pH sensitivity (His substitutions)
- Improve developability motifs: reduced polyreactivity, oxidation, deamidation, isomerization, hydrolysis, glycosylation, etc.
- Introduce reactivity against non-human primate (NHP) orthologs

Case Study GPRC5D: CDR-Scanning for MAb Optimization

Scanning revealed key functions at each CDR residue

		HC WGH Binding Sequences																			
HC	Parental Residue	A	C	D	E	F	G	H	I	K	L	M	N	P	Q	R	S	T	V	W	Y
HCDR1	152	101	14	72	77	90	91	103	111	105	90	97	85	102	94	103	122	70	93	88	
HCDR1	153	102	10	126	127	109	90	127	126	110	100	103	111	111	110	111	121	104	103	104	
HCDR1	154	112	13	8	7	107	20	14	110	110	113	110	110	110	110	110	110	110	110	110	
HCDR1	155	9	10	6	8	106	7	9	9	11	8	9	9	9	9	9	9	9	9	9	
HCDR1	157	219	32	140	143	113	114	113	113	113	113	113	113	113	113	113	113	113	113	113	
HCDR2	171	181	17	7	11	114	9	104	11	100	110	110	110	110	110	110	110	110	110	110	
HCDR2	172	8	8	3	5	11	104	6	11	8	ND	7	5	6	6	6	6	6	6	6	
HCDR2	173	181	17	7	11	114	9	104	11	100	110	110	110	110	110	110	110	110	110	110	
HCDR2	174	29	34	137	9	7	15	8	6	7	12	103	6	7	7	14	13	7	7	6	
HCDR2	175	5	8	5	4	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
HCDR2	176	6	127	5	5	8	9	10	101	10	10	10	10	10	10	10	10	10	10	10	
HCDR2	177	160	9	11	6	100	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
HCDR2	178	22	7	4	4	12	101	11	11	11	11	11	11	11	11	11	11	11	11	11	
HCDR2	179	ND	6	5	10	101	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
HCDR2	180	70	42	46	46	127	25	113	113	113	113	113	113	113	113	113	113	113	113	113	
HCDR2	181	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
HCDR3	221	5	13	7	8	6	6	7	7	4	6	10	14	100	6	8	ND	7	6	5	
HCDR3	222	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	223	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	224	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	225	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	226	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	227	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	228	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	229	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	230	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	

Improvements >200% WT
detected at 6 positions, 14 variants

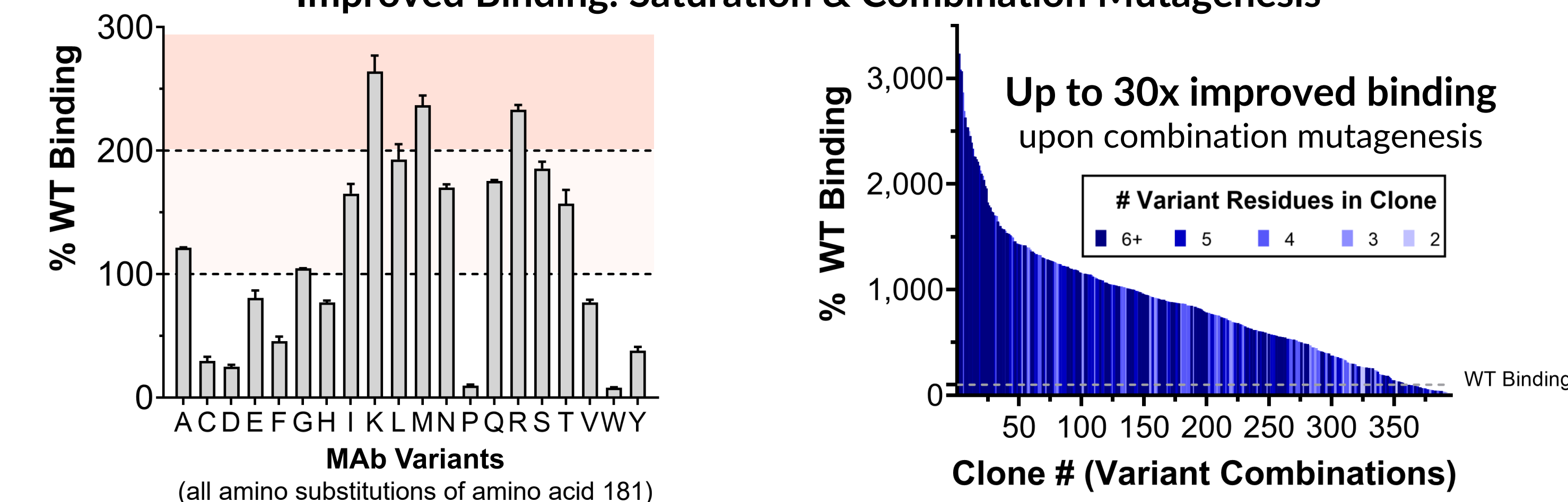
HCDR1	152	101	14	72	77	90	91	103	111	105	90	97	85	102	94	103	122	70	93	88	
HCDR1	153	102	10	126	127	109	90	127	126	110	100	103	111	111	110	111	121	104	103	104	
HCDR1	154	112	13	8	7	107	20	14	110	110	113	110	110	110	110	110	110	110	110	110	
HCDR1	155	9	10	6	8	106	7	9	9	11	8	9	9	9	9	9	9	9	9	9	
HCDR1	157	219	32	140	143	113	114	113	113	113	113	113	113	113	113	113	113	113	113	113	
HCDR2	171	181	17	7	11	114	9	104	11	100	110	110	110	110	110	110	110	110	110	110	
HCDR2	172	8	8	3	5	11	104	6	11	8	ND	7	5	6	6	6	6	6	6	6	
HCDR2	173	181	17	7	11	114	9	104	11	100	110	110	110	110	110	110	110	110	110	110	
HCDR2	174	29	34	137	9	7	15	8	6	7	12	103	6	7	7	14	13	7	7	6	
HCDR2	175	5	8	5	4	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6	
HCDR2	176	6	127	5	5	8	9	10	101	10	10	10	10	10	10	10	10	10	10	10	
HCDR2	177	160	9	11	6	100	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
HCDR2	178	22	7	4	4	12	101	11	11	11	11	11	11	11	11	11	11	11	11	11	
HCDR2	179	ND	6	5	10	101	11	11	11	11	11	11	11	11	11	11	11	11	11	11	
HCDR2	180	70	42	46	46	127	25	113	113	113	113	113	113	113	113	113	113	113	113	113	
HCDR2	181	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	
HCDR3	221	5	13	7	8	6	6	7	7	4	6	10	14	100	6	8	ND	7	6	5	
HCDR3	222	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	223	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	224	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	225	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	226	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	227	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	228	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	229	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	
HCDR3	230	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	

no data (ND) no expression (NE)

- 986 variants, heavy + light chain variants, human antigen

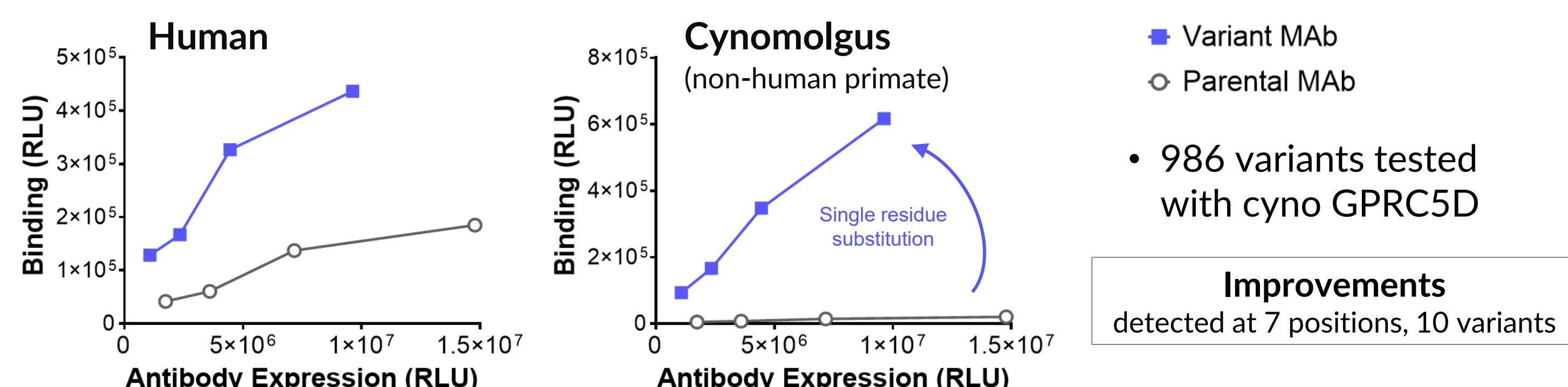
- Permissive binding
- Improved binding

Improved Binding: Saturation & Combination Mutagenesis



Improved variants may yield better efficacy, developability, and novel IP

Engineering Species Cross-Reactivity



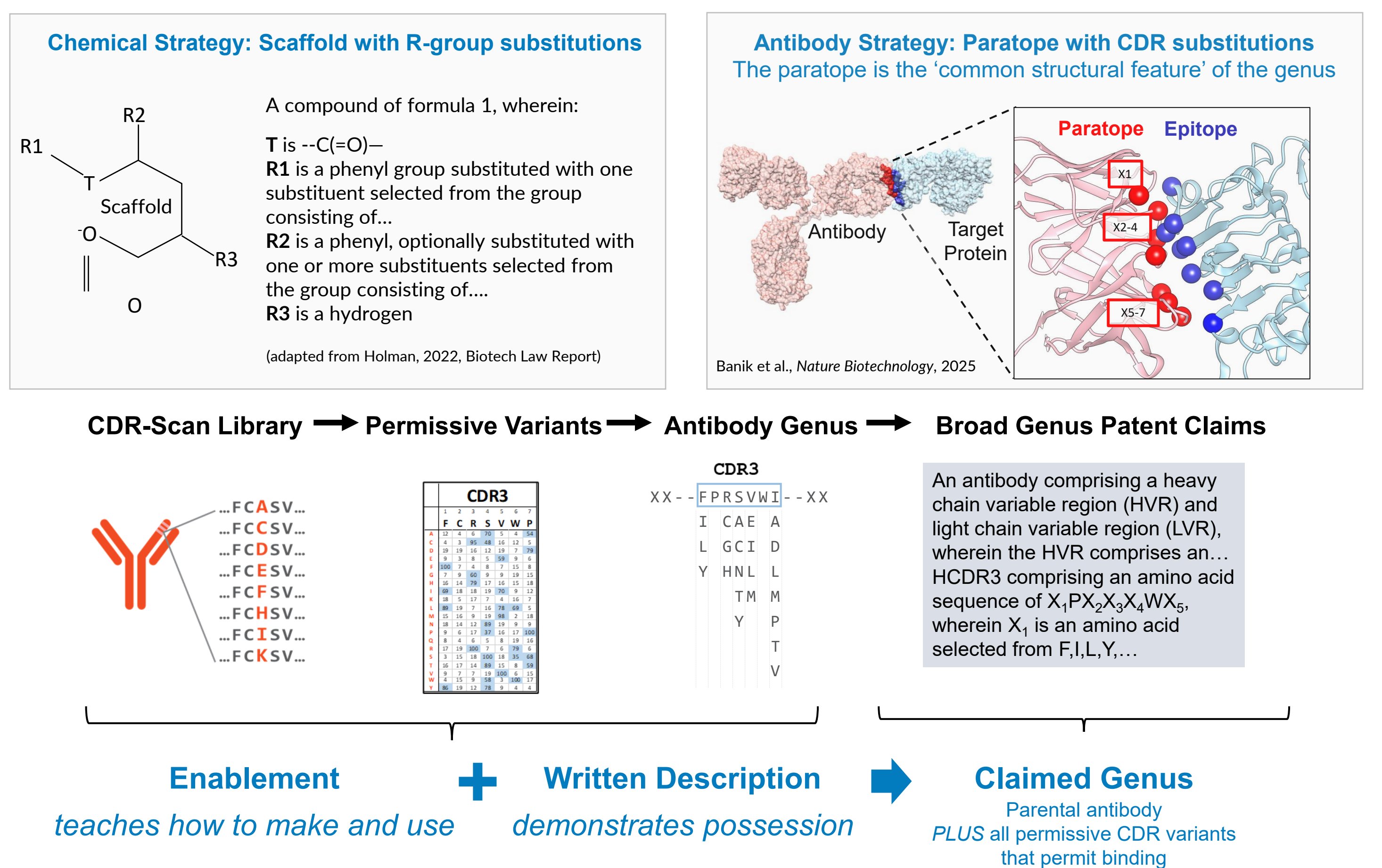
Reactivity to specific orthologs can enable testing in corresponding animal models

USPTO Allowed Antibody Genus Claims

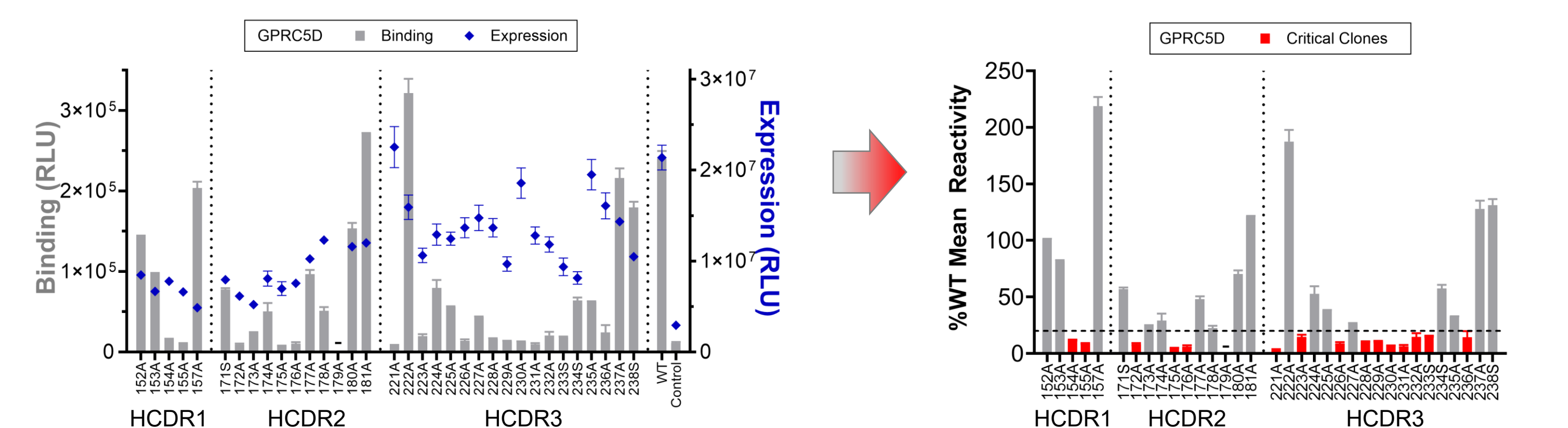
- Patents claiming only 1 antibody 'species' can be easily circumvented, so it is preferable to claim a 'genus' covering a group of related antibodies
- Antibodies patent strategy using extremely broad functional genus claims is no longer viable in the US after the landmark case *Amgen v. Sanofi*

Because of new USPTO guidance and case law, developers must use a new strategy to fulfill antibody patent Enablement and Written Description requirements

CDR-Scanning for better antibody IP is based on established small molecule strategy



CDR-Scanning Reveals Critical Residues Encompassing Paratope



GPRC5D Genus claims are based on the shared 'common structural feature', the paratope; single and combination variants allowed by USPTO in patent claims

US Patent 12,545,726 B1

Why Choose Paratope-PLUS™ to Optimize and Protect Your Antibody

- Robust patent protection of your antibody to meet new USPTO requirements of **Enablement** and **Written Description**
- Quantitative, **unbiased scanning** of all CDR residues and **compatible with all protein targets**, including membrane proteins
- All IP owned by you, including knowledge of permissive and improved variants
- 20+ years expertise in antibody discovery and >1,000 antibody mapping projects

