B.1.1.529 escapes the majority of SARS-CoV-2 neutralizing antibodies of diverse epitopes

Yunlong Richard Cao, Jing Wang, Fanchong Jian, Tianhe Xiao, Weiliang Song, Ayijiang Yisimayi, Weijin Huang, Qianqian Li, Peng Wang, Ran An, Jing Wang, Yao Wang, Xiao Niu, Sijie Yang, Hui Liang, Haiyan Sun, Tao Li, Yuanling Yu, Qianqian Cui, Shuo Liu, Xiaodong Yang, Shuo Du, Zhiying Zhang, Xiaohua Hao, Fei Shao, Ronghua Jin, Xiangxi Wang, Junyu Xiao, Youchun Wang, Xiaoliang Sunney Xie

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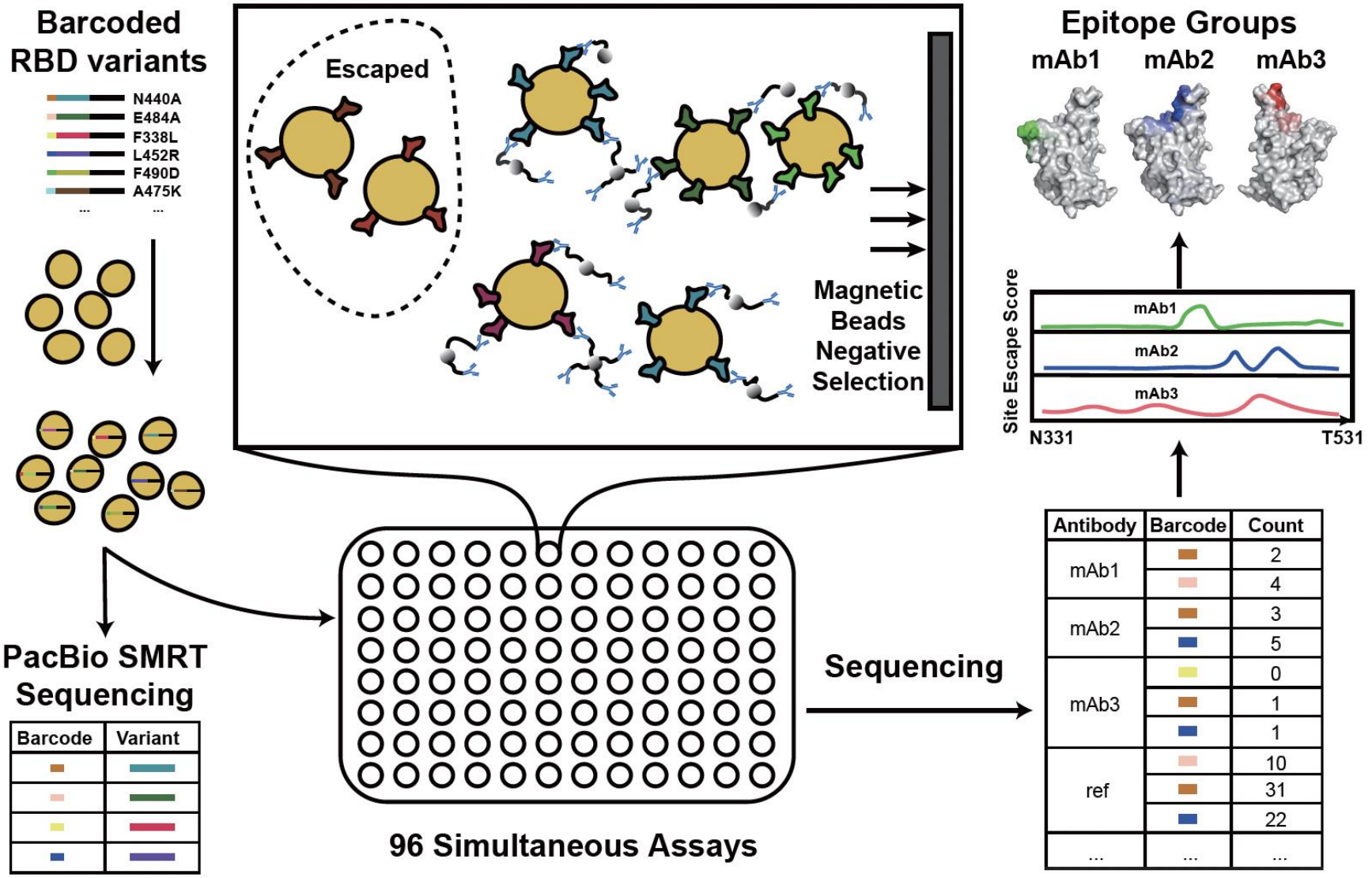
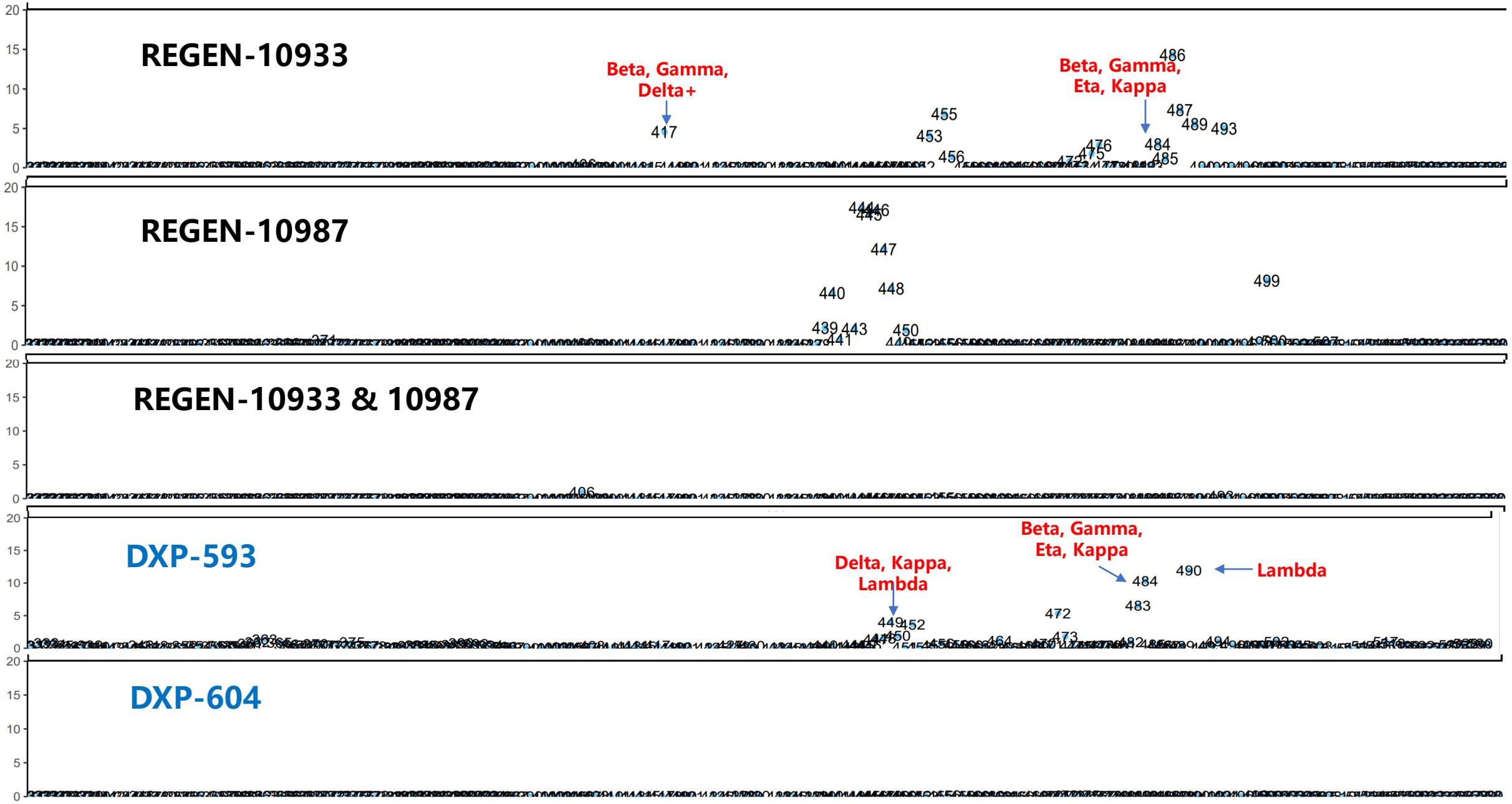
Disclosure

Yunlong Richard Cao and Xiaoliang Sunney Xie are Co-founders of Singlomics Biopharmaceutical

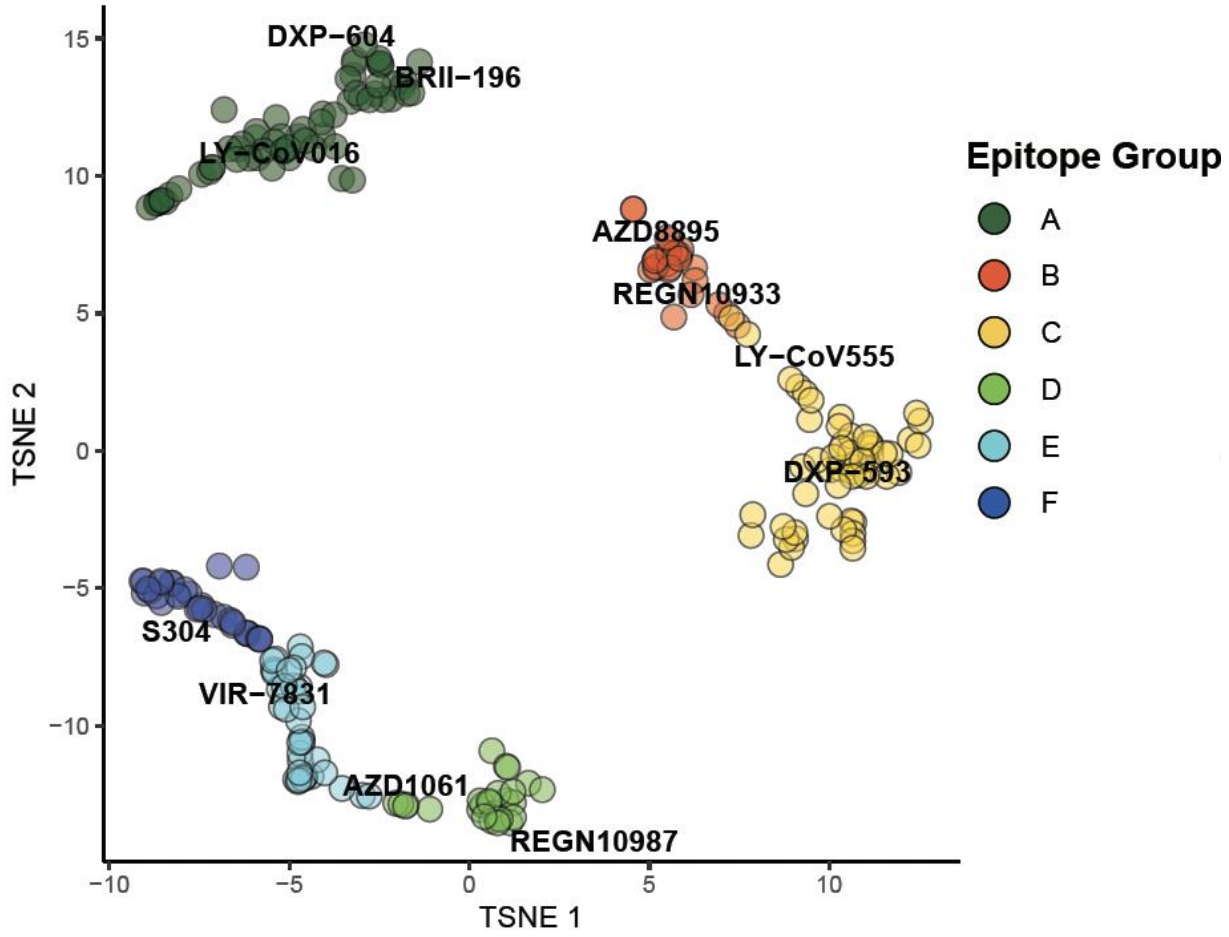
High Throughput Yeast Display Screening of RBD Single-point Mutations Escaping SARS-CoV-2 Neutralizing Antibodies



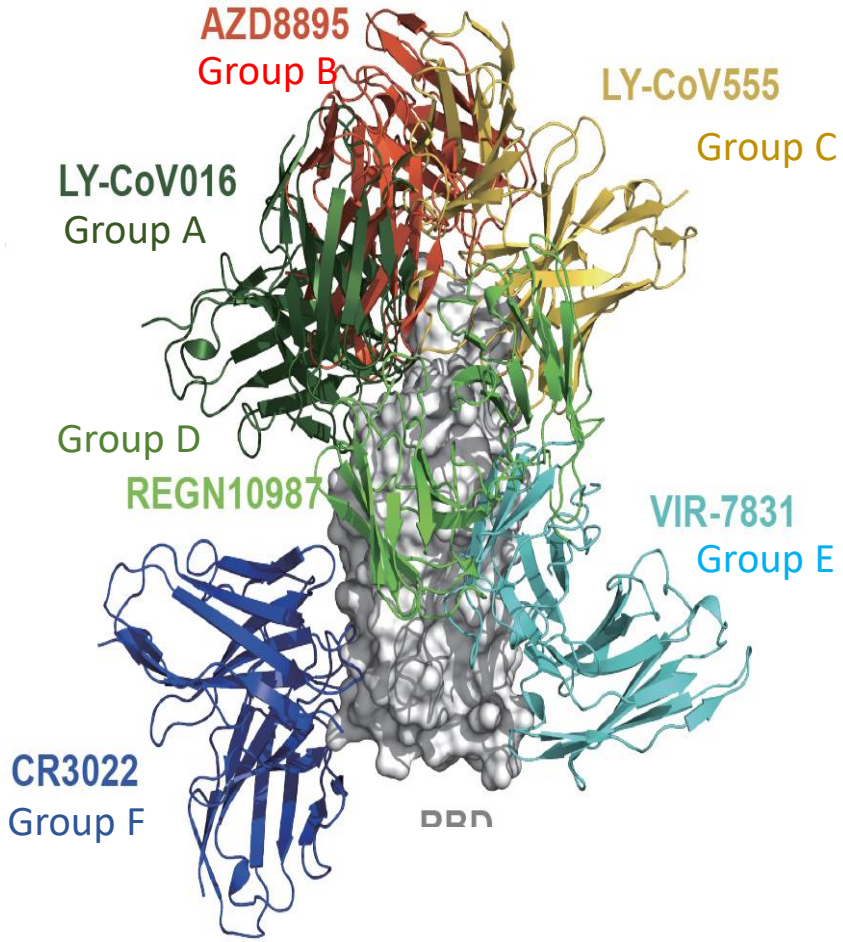
Jessi Bloom, *Cell*, 2020

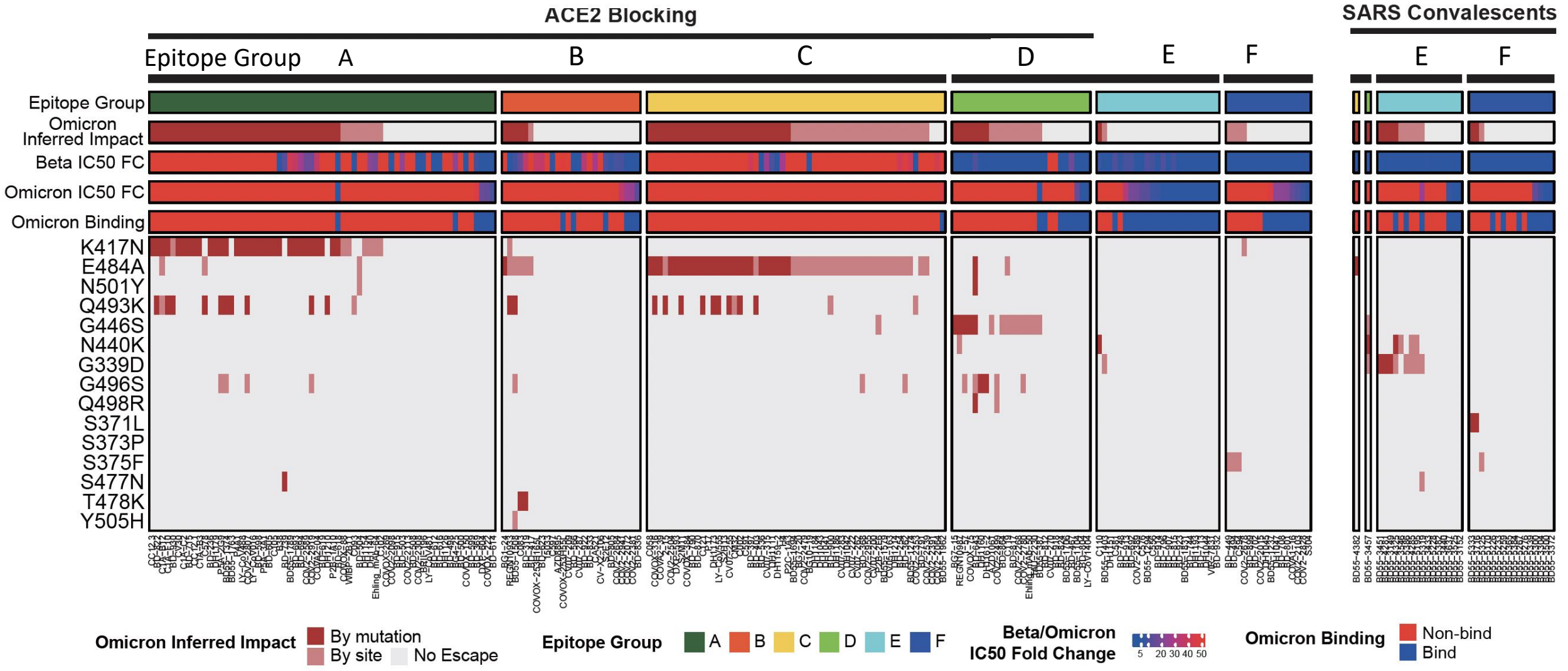

REGEN-10933
Beta, Gamma, Delta+
417
455
453
456
Beta, Gamma, Eta, Kappa
486
487
489
493
484
476
475
485
REGEN-10987
444
446
445
447
440
448
499
439
443
450
441
REGEN-10933 & 10987
406
DXP-593
Delta, Kappa, Lambda
449
452
450
Beta, Gamma, Eta, Kappa
484
490
Lambda
483
472
473
DXP-604

Unsupervised Clustering of 247 SARS-CoV-2 Neutralizing Antibodies into Six Epitope Groups



Corresponding Knowledge-based Structural Classifications





>85% of the 247 neutralizing antibodies are escaped by single-point mutations in Omicron RBD.

北京大学生物医学前沿创新中心
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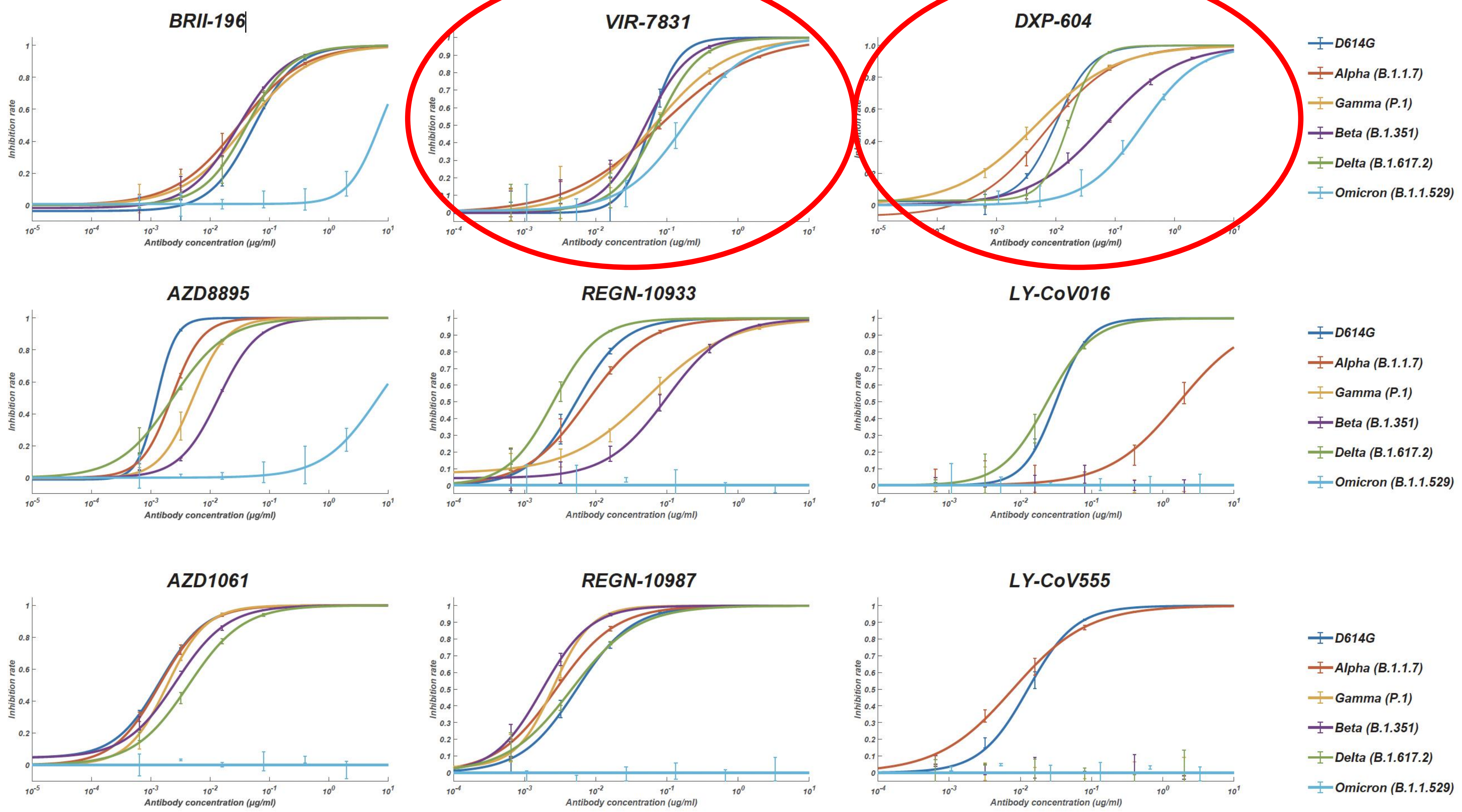
The only two survivors!

北京未来基因诊断高精尖创新中心
Beijing Advanced Innovation Center for Genomics



Vir7831 and DXP-604 are the only two Nab drugs in EUA of compassionate use that survived

	D614G	Alpha	Gamma	Beta	Delta	Omicron
LY−CoV555	0.013	0.008	>10	>10	>10	>10
LY−CoV016	0.032	1.707	>10	>10	0.024	>10
REGN10933	0.005	0.007	0.055	0.098	0.003	>10
REGN10987	0.005	0.003	0.003	0.002	0.005	>10
AZD8895	0.001	0.002	0.012	0.014	0.002	6.860
AZD1061	0.001	0.001	0.002	0.003	0.004	>10
VIR−7831	0.058	0.080	0.066	0.050	0.073	0.181
BRII−196	0.053	0.031	0.041	0.030	0.042	7.258
DXP−604	0.010	0.007	0.005	0.065	0.016	0.287

IC50 (μg/mL)

0 5 10

Potent neutralizing antibodies against Omicron are found from SARS convalescents who received inactive SARS-CoV-2 vaccines

Antibody		BD55-3152	BD55-5319	BD55-5386	BD55-5300	BD55-3372	BD55-3500
Epitope Group		E	E	E	F	F	F
Variants Pseudovirus IC50 (μg/mL)	D614G	0.0105	0.0150	0.0005	0.0051	0.0068	0.1053
	Beta	0.0076	0.0040	0.0011	0.0031	0.0073	0.2326
	Omicron	0.0142	0.3685	0.0584	0.0663	0.0097	0.2610

Summary

- We improved the throughput of yeast display by two order of magnitudes to screen RBD single-point escaping mutations of a large collection of SARS-CoV-2 neutralizing antibodies.
- Omicron escaped >85% of 247 known SARS-CoV-2 neutralizing antibodies, especially those targeting ACE2 binding site.
- Vir7831 and DXP-604 are the only two neutralizing antibody drugs in EUA of compassionate use that survived Omicron.
- Potent neutralizing antibodies against Omicron are found SARS convalescents who received inactive SARS-CoV-2 vaccines.

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- Biomedical Pioneering Innovation Center (BIOPIC) at Peking University
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- National Institutes for Food and Drug Control
- Royal Prince Alfred Hospital
- BeiGene
- Beijing Ditan Hospital
- Beijing Youan Hospital
- Institute of Zoology, Chinese Academy of Sciences
- Institute of Biophysics, Chinese Academy of Sciences