The ADG20 human monoclonal antibody binds with high affinity and neutralises a wide range of SARS-CoV-2 variants and zoonotic sarbecoviruses

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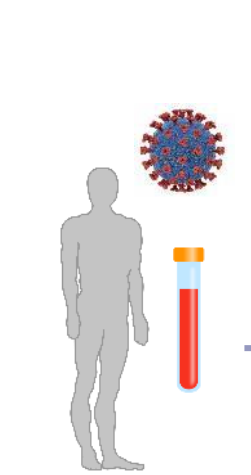
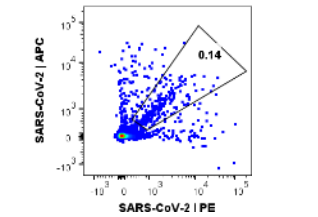
Disclosures

- LMW is an inventor on a patent application submitted by Adagio Therapeutics, Inc., describing the engineered SARS-CoV-2 antibodies
- CIK is an employee of Adagio Therapeutics, Inc.
- ZM has received consulting fees from Adagio Therapeutics, Inc.
- Editorial assistance was provided by Georgiana Manica, BSc, of Parexel, and was funded by Adagio Therapeutics, Inc.

ADG20 is a fully human IgG1 monoclonal antibody isolated from a survivor of the 2003 SARS epidemic



Blood sample
Convalescent SARS donor

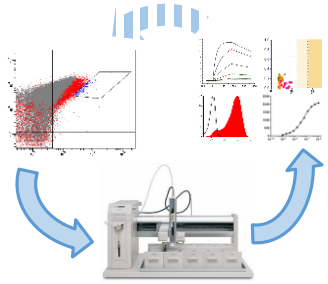


Single B-cell sort against SARS-CoV-2 spike protein

Cross-neutralisers

3 leads optimisation

Yeast surface-display technology

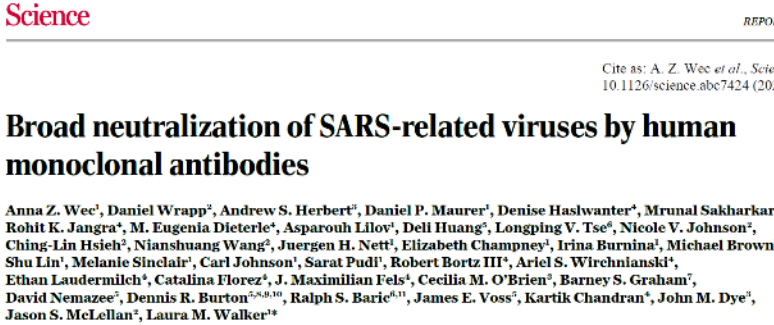


~500-fold increase in binding affinity
~70-fold increase in neutralisation potency

Adagio 2 (ADG2)

Fc modification to extend half-life

Adagio 20 (ADG20)



Science REPORTS

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Broad neutralization of SARS-related viruses by human monoclonal antibodies

Anna Z. Wec[1], Daniel Wrapp[2], Andrew S. Herbert[1], Daniel P. Maurer[1], Denise Haslwanter[1], Mrunal Sakharkar[1], Rohit K. Jangra[1], M. Eugenia Dieterle[1], Asparouh Lilov[1], Deli Huang[1], Longping V. Tse[6], Nicole V. Johnson[2], Ching-Lin Hsieh[2], Nianshuang Wang[2], Juergen H. Nett[1], Elizabeth Champney[1], Irina Burnina[1], Michael Brown[1], Shu Lin[1], Melanie Sinclair[1], Carl Johnson[1], Sarat Pudi[1], Robert Bortz III[1], Ariel S. Wirchnianski[1], Ethan Laudermilch[1], Catalina Florez[1], J. Maximilian Fels[1], Cecilia M. O'Brien[1], Barney S. Graham[7], David Nemazee[5], Dennis R. Burton[2,8,9,10], Ralph S. Baric[6,11], James E. Voss[2], Kartik Chandran[1], John M. Dye[1], Jason S. McLellan[2], Laura M. Walker[1]*

Science RESEARCH ARTICLE

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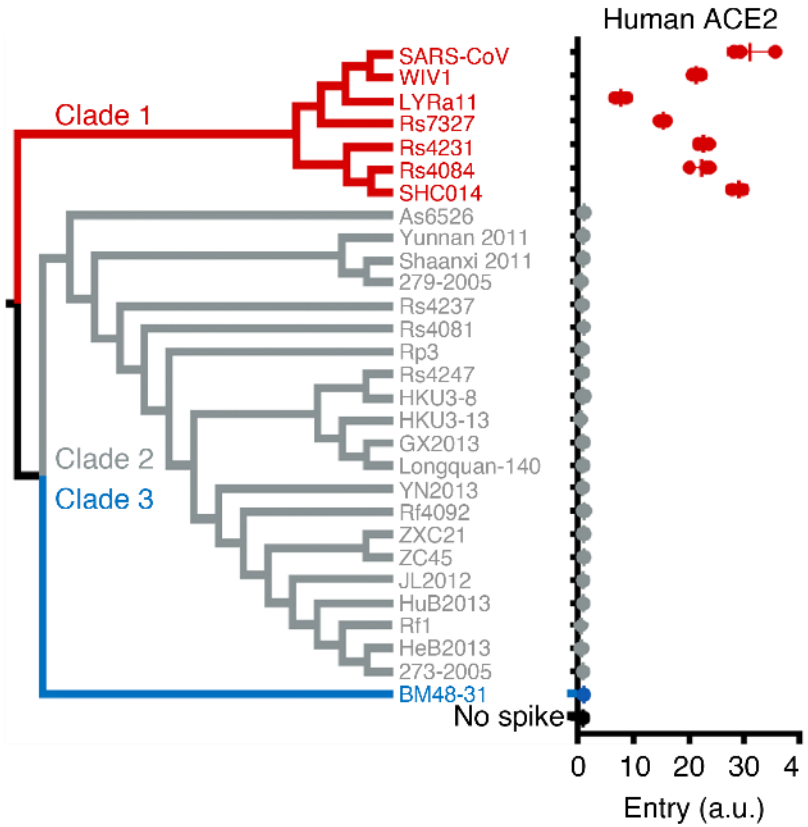
Broad and potent activity against SARS-like viruses by an engineered human monoclonal antibody

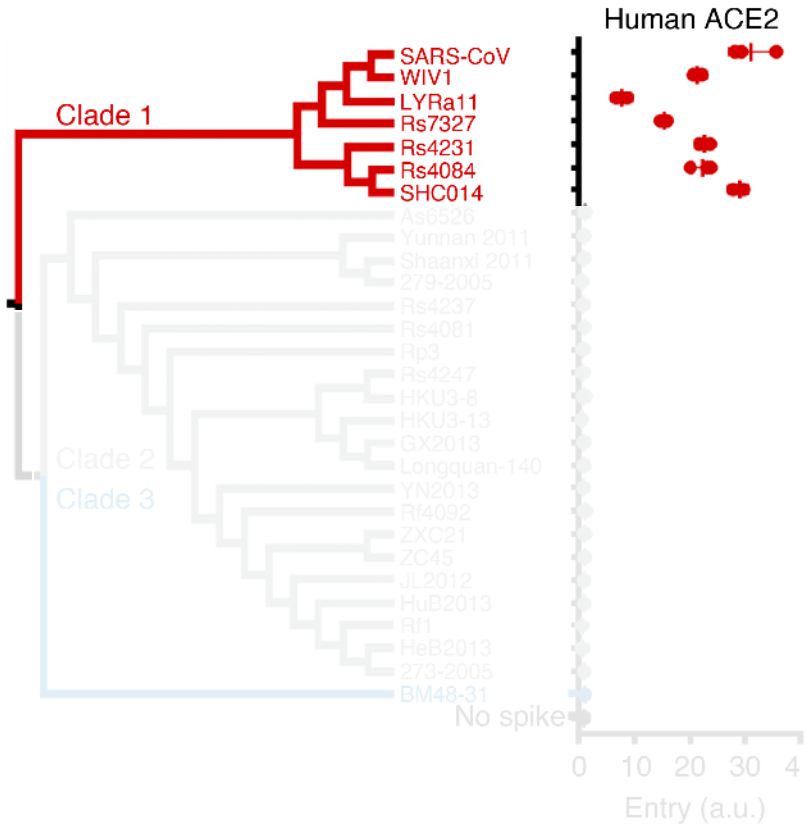
C. Garrett Rappazzo[1*], Longping V. Tse[2*], Chengzi I. Kaku[1], Daniel Wrapp[2], Mrunal Sakharkar[1], Deli Huang[1], Laura M. Deveau[1], Thomas J. Yockachonis[1], Andrew S. Herbert[6,7], Michael B. Battles[1], Cecilia M. O'Brien[6,7], Michael E. Brown[1], James C. Geoghegan[1], Jonathan Belk[1], Linghang Peng[1], Linlin Yang[1], Yixuan Hou[2], Trevor D. Scobey[2], Dennis R. Burton[4,8,9,10], David Nemazee[4], John M. Dye[6], James E. Voss[1], Bronwyn M. Gunn[5], Jason S. McLellan[3], Ralph S. Baric[2,11]†, Lisa E. Gralinski[2]†, Laura M. Walker[1,12]†

In vitro ADG2 shows broad and potent neutralising activity across diverse SARS-related coronaviruses



ACE2, angiotensin-converting enzyme 2.
Letko M, et al. *Nat Microbiol*. 2020;5:562–569 .

In vitro ADG2 shows broad and potent neutralising activity across diverse SARS-related coronaviruses



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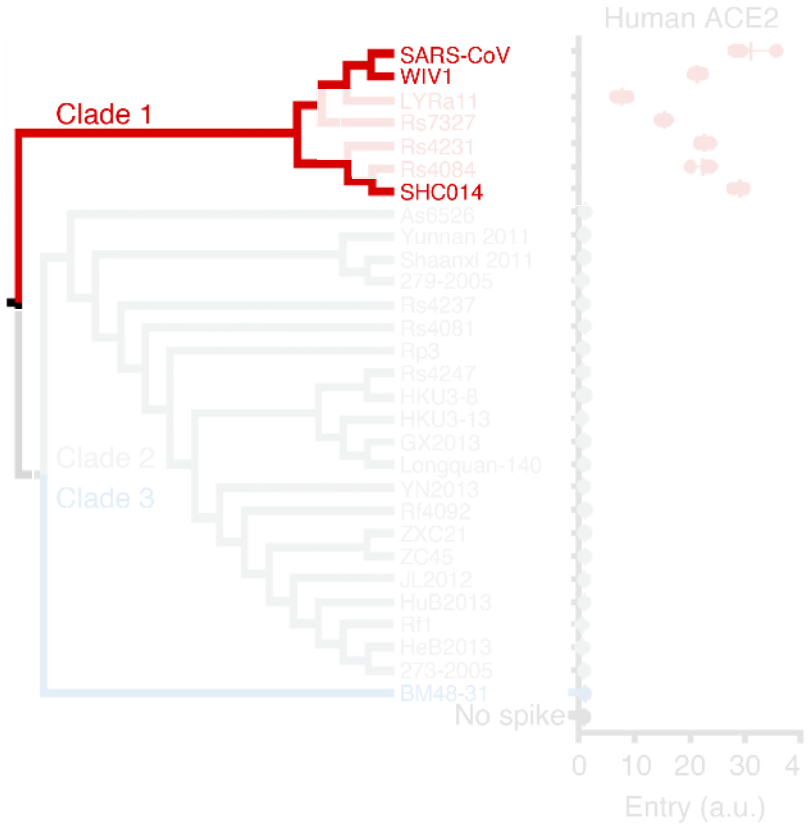
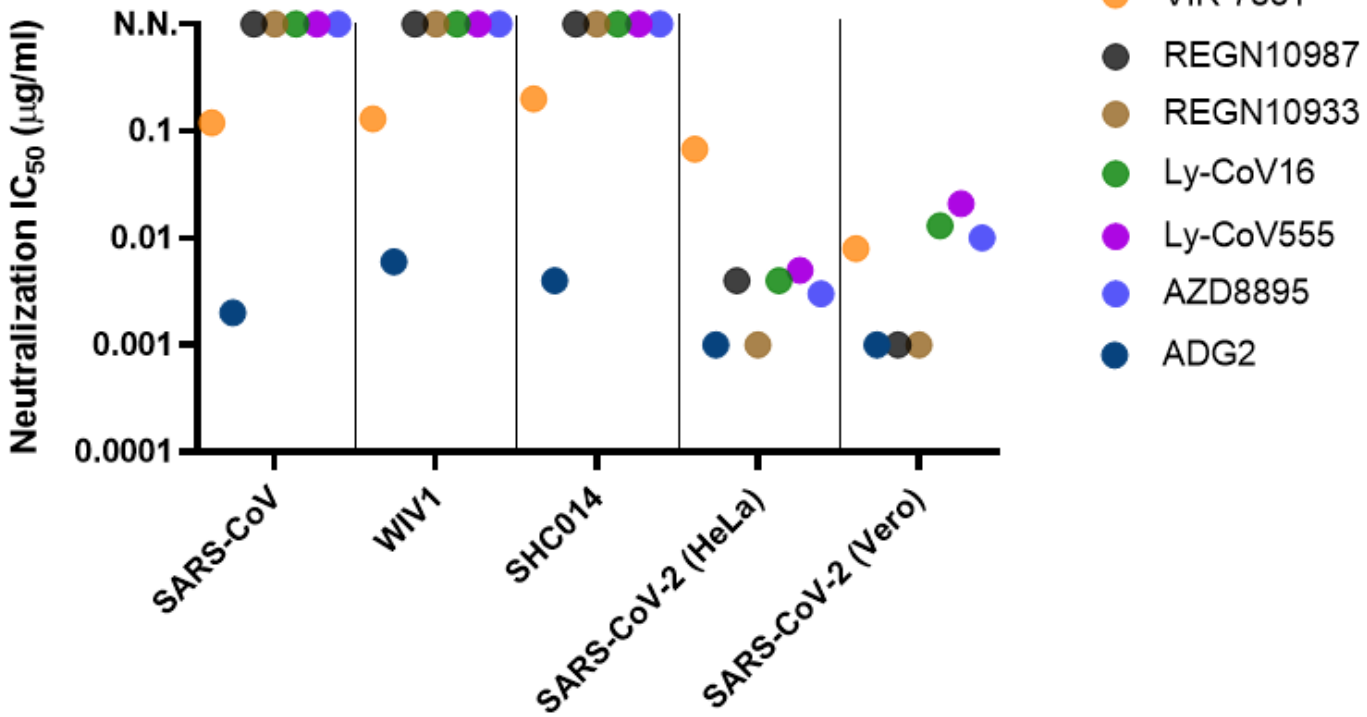
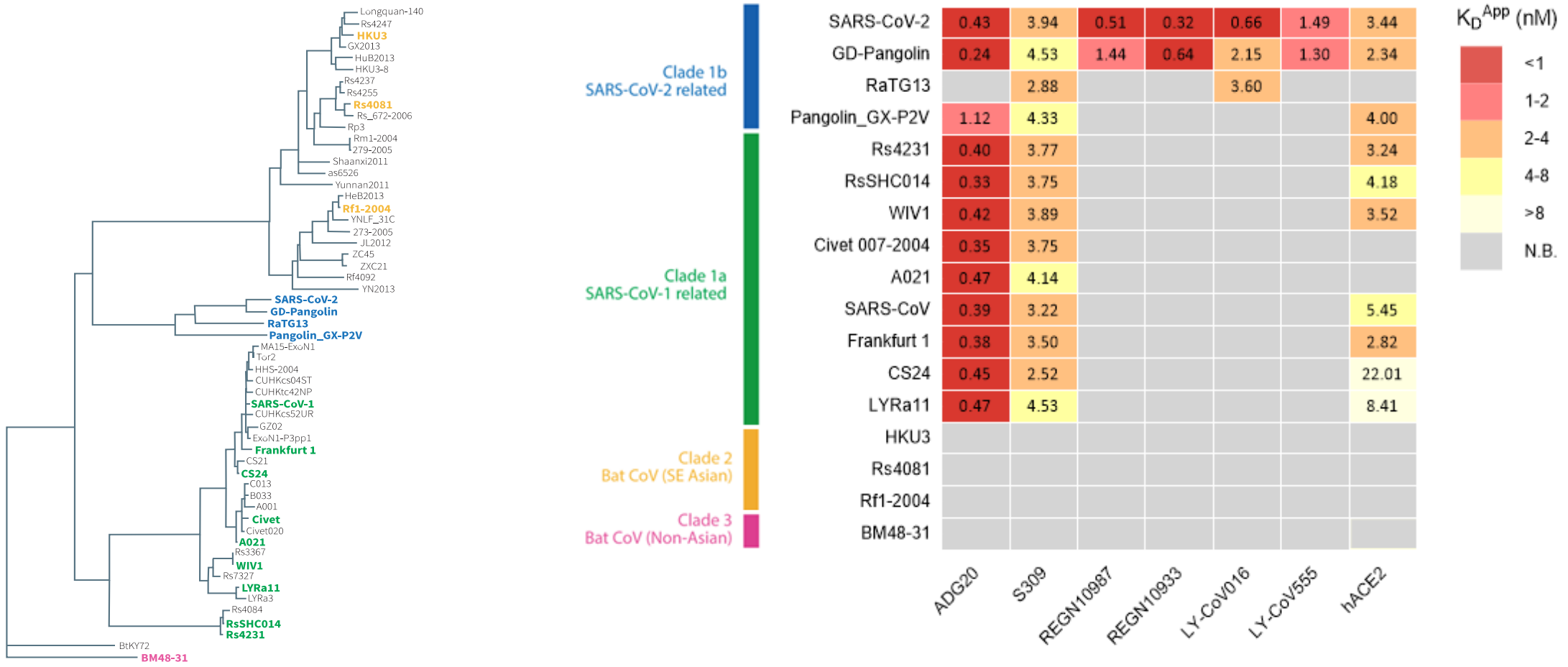
In vitro ADG2 shows broad and potent neutralising activity across diverse SARS-related coronaviruses





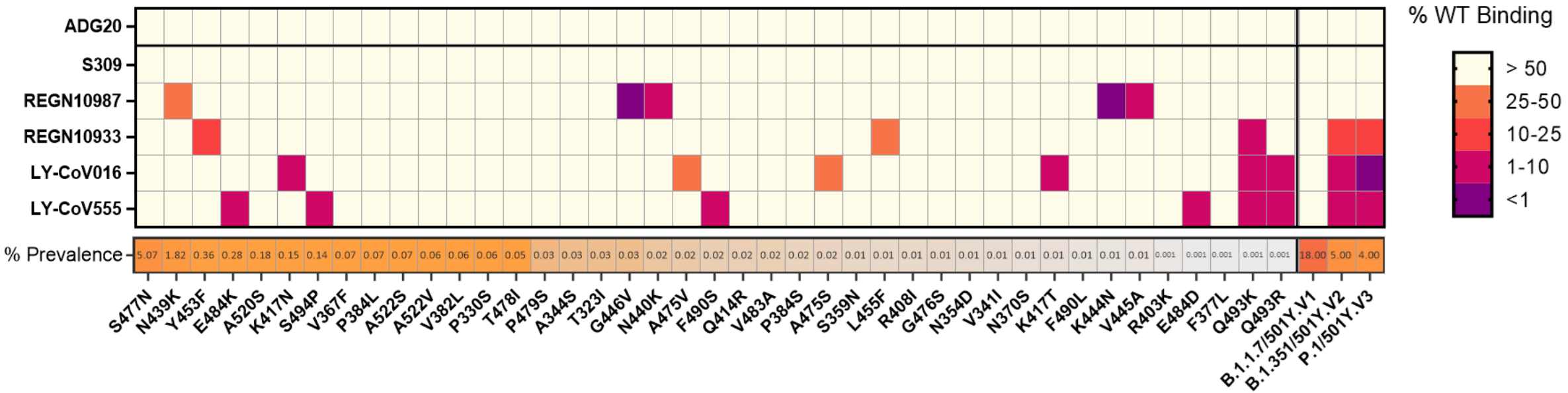
VIR-7831 (sotrovimab); REGN10987 (imdevimab); REGN10933 (casirivimab); Ly-CoV16 (etesevimab); Ly-CoV555 (bamlanivimab); AZD8895 (tixagevimab).
IC_{50}, 50% maximal inhibitory concentration; N.N., non-neutralising.
Letko M, et al. *Nat Microbiol*. 2020;5:562–569.

ADG20 binds with high affinity to clade 1, ACE2-binding sarbecovirus RBDs



S309, the parent antibody of VIR-7831 (sotrovimab); REGN10987 (imdevimab); REGN10933 (casirivimab); Ly-CoV16 (etesevimab); Ly-CoV555 (bamlanivimab).
RBDs, receptor-binding domains; K_D^{App}, apparent dissociation constant; N.B., non-binding.

ADG20 maintains binding activity against commonly circulating SARS-CoV-2 isolates



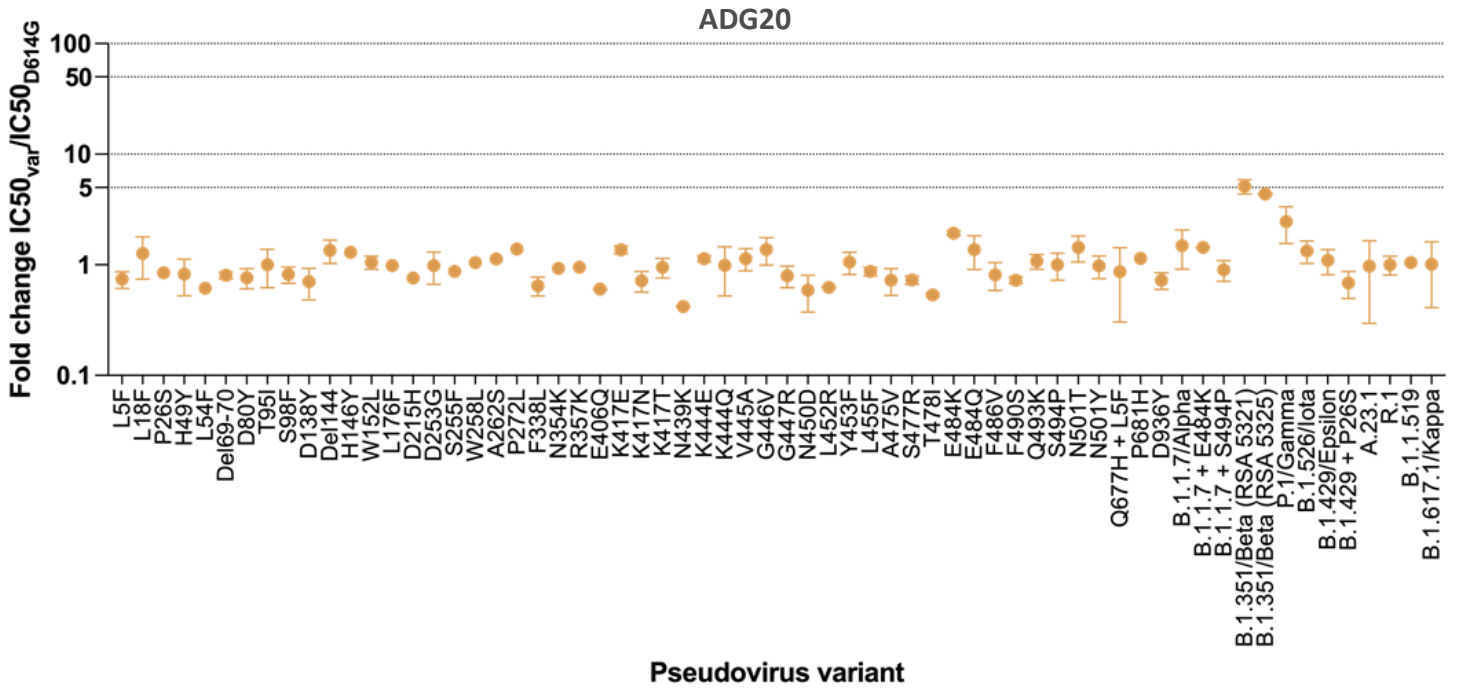
Commonly observed spike mutations in the RBD

S309, the parent antibody of VIR-7831 (sotrovimab); REGN10987 (imdevimab); REGN10933 (casirivimab); Ly-CoV16 (etesevimab); Ly-CoV555 (bamlanivimab).
GISAID, Global Initiative on Sharing All Influenza Data; WT, wild-type.
% Prevalence: SARS-CoV-2 variant frequencies as of 02/06/2021 (GISAID database).

ADG20 maintains neutralising activity against emerging SARS-CoV-2 variants of concern

WHO nomenclature	Victoria	Alpha B.1.1.7	Beta B.1.351	Gamma P.1	Delta B.1.617.2	Kappa B.1.617.1 (PV)
ADG20	0.004	0.006	0.010	0.009	0.006	0.005
VIR-7831	0.040	0.078	0.082	0.076	0.113	0.238
REGN10933	0.004	0.014	3.284	6.177	0.003	0.010
REGN10987	0.032	0.028	0.007	0.013	0.017	0.021
LY-CoV555	0.006	0.009	>10	>10	8.311	>10
LY-CoV16	0.034	3.225	>10	>10	0.012	0.010
AZD1061	0.013	0.012	0.014	0.007	0.038	0.033
AZD8895	0.005	0.011	0.046	0.046	0.003	0.002

IC50 (µg/ml)
<0.02
0.02-0.2
0.2-1
1-10
>10



Broad neutralisers

SARS-CoV-2–only neutralisers

Adagio utilized the non-clinical and pre-clinical services program offered by the US National Institute of Allergy and Infectious Diseases to generate these data.

VIR-7831 (sotrovimab); REGN10933 (casirivimab); REGN10987 (imdevimab); Ly-CoV555 (bamlanivimab); Ly-CoV16 (etesevimab); AZD1061 (cilgavimab); AZD8895 (tixagevimab).
PV, pseudovirus; WHO, World Health Organization.
Rappazzo CG, et al. *Science*. 2021;371:823–829. Liu C, et al. *Cell*. 2021;S0092-8674(21)00755-8.

Conclusions

- In vitro, ADG20 displayed breadth of binding to RBDs of clade 1 sarbecoviruses and SARS-CoV-2 variants resistant to many other antibody therapies
- ADG20 showed potent neutralising activity against emerging SARS-CoV-2 variants of concern and pre-emergent SARS-like CoVs
- ADG20 demonstrated potential to be an effective prophylactic and therapeutic agent against emergent variants of SARS-CoV-2, as well as pre-emergent SARS-like viruses with pandemic potential

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Long Ping Victor Tse
Lisa Gralinski

John Dye
Andrew Herbert
Cecilia O'Brien

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