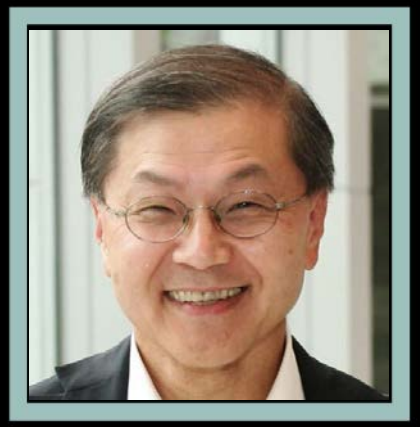
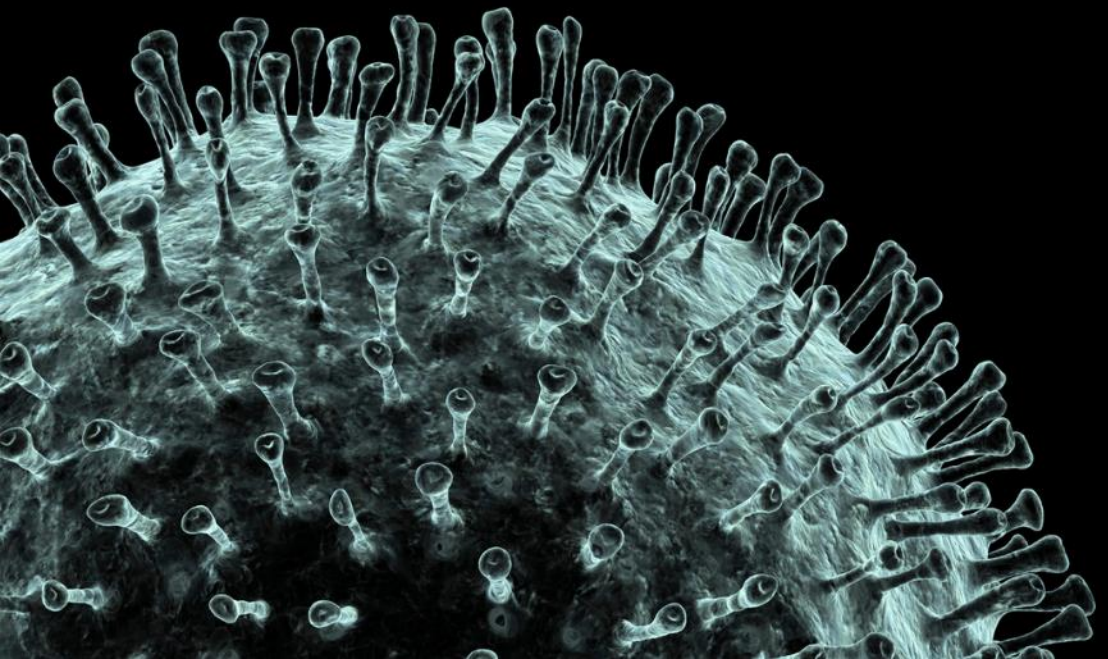
COVID-19 Conversations



David D. Ho

Aaron Diamond AIDS Research Center
Columbia University



COVID19Conversations.org
#COVID19Conversations

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AMERICAN PUBLIC HEALTH ASSOCIATION
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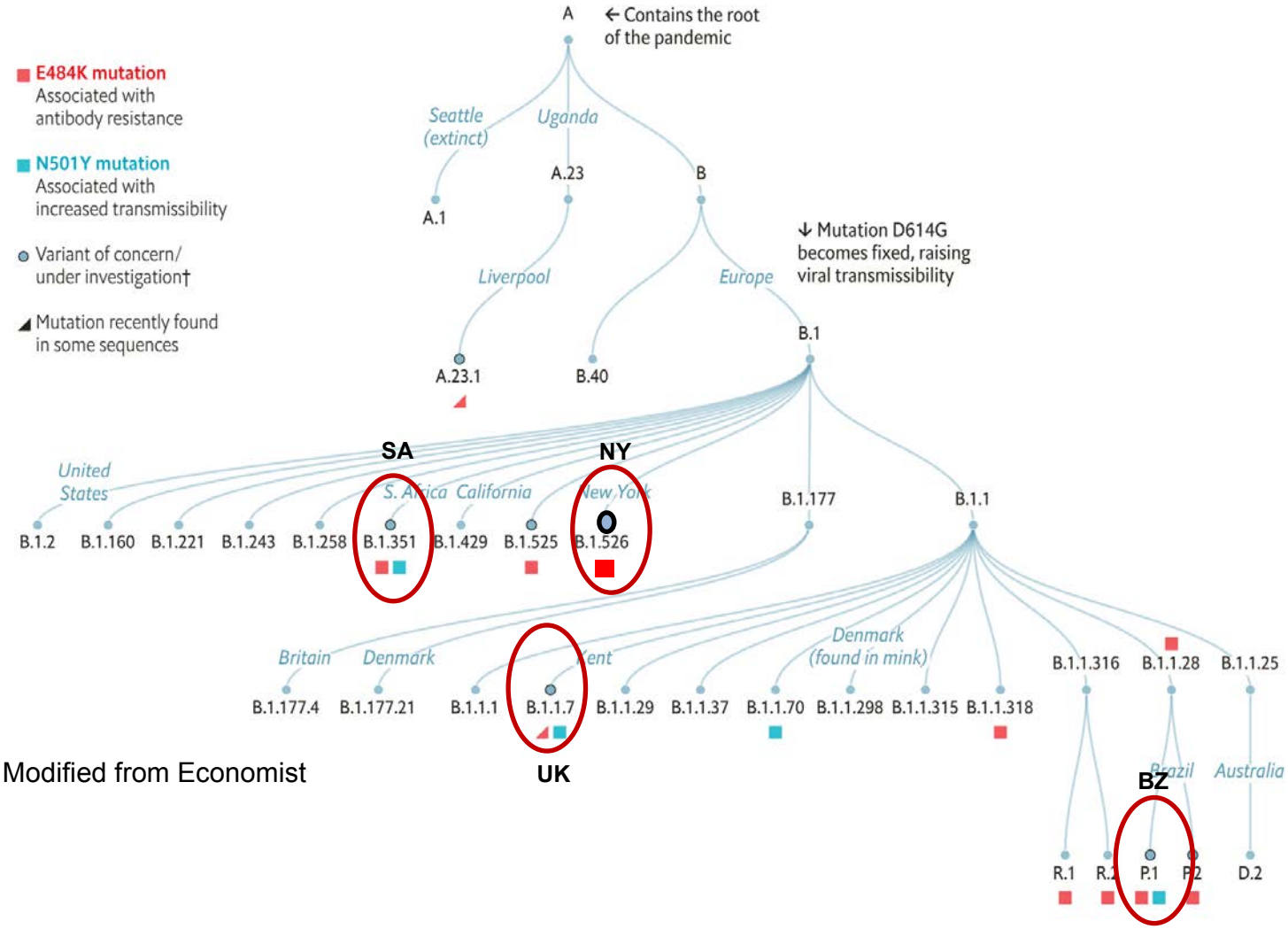
50 years NATIONAL ACADEMY of MEDICINE

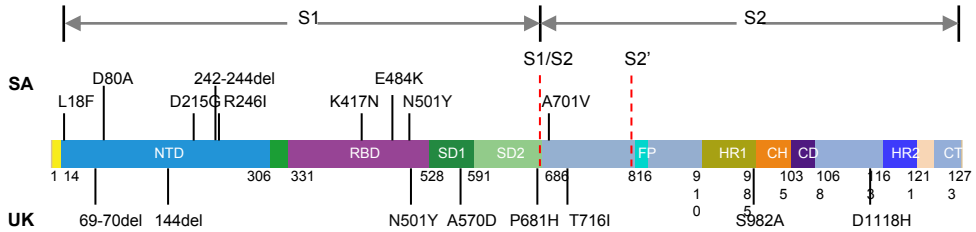
SARS-CoV-2 Variants of Concern

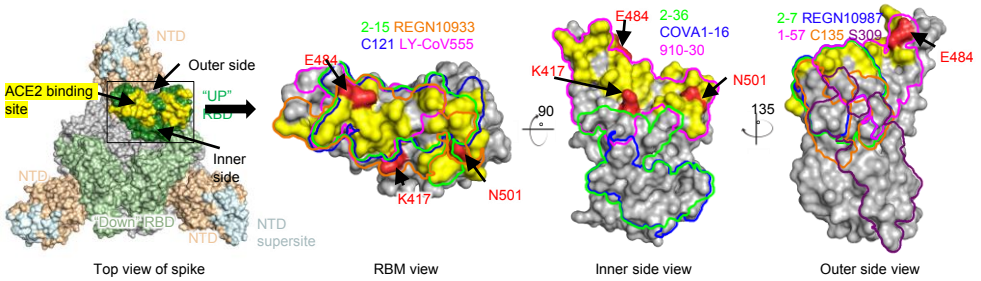
David D. Ho
Aaron Diamond AIDS Research Center
Columbia University Vagelos College of Physicians and Surgeons

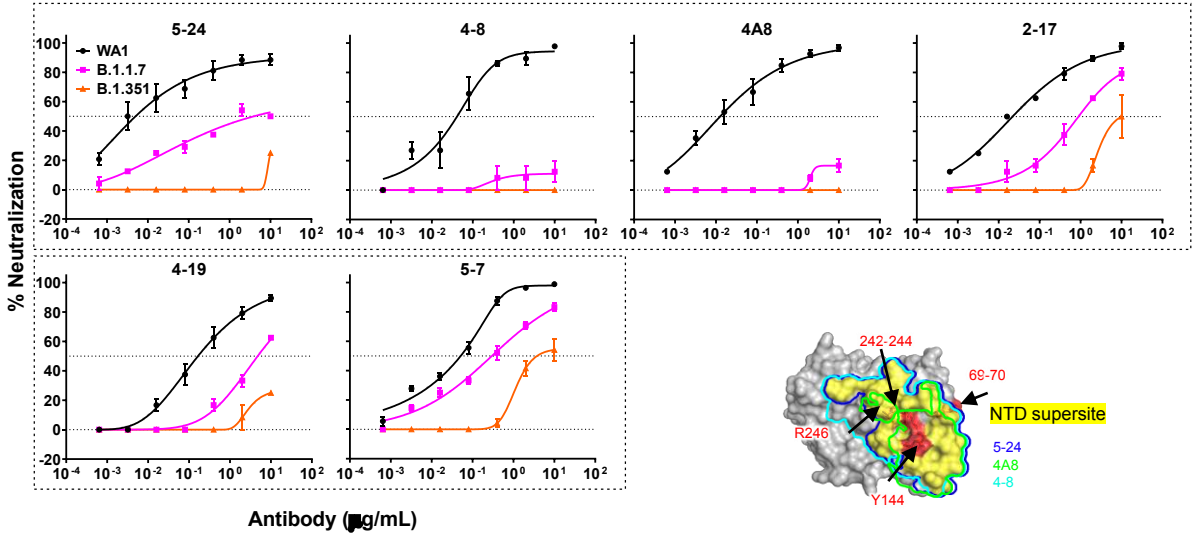


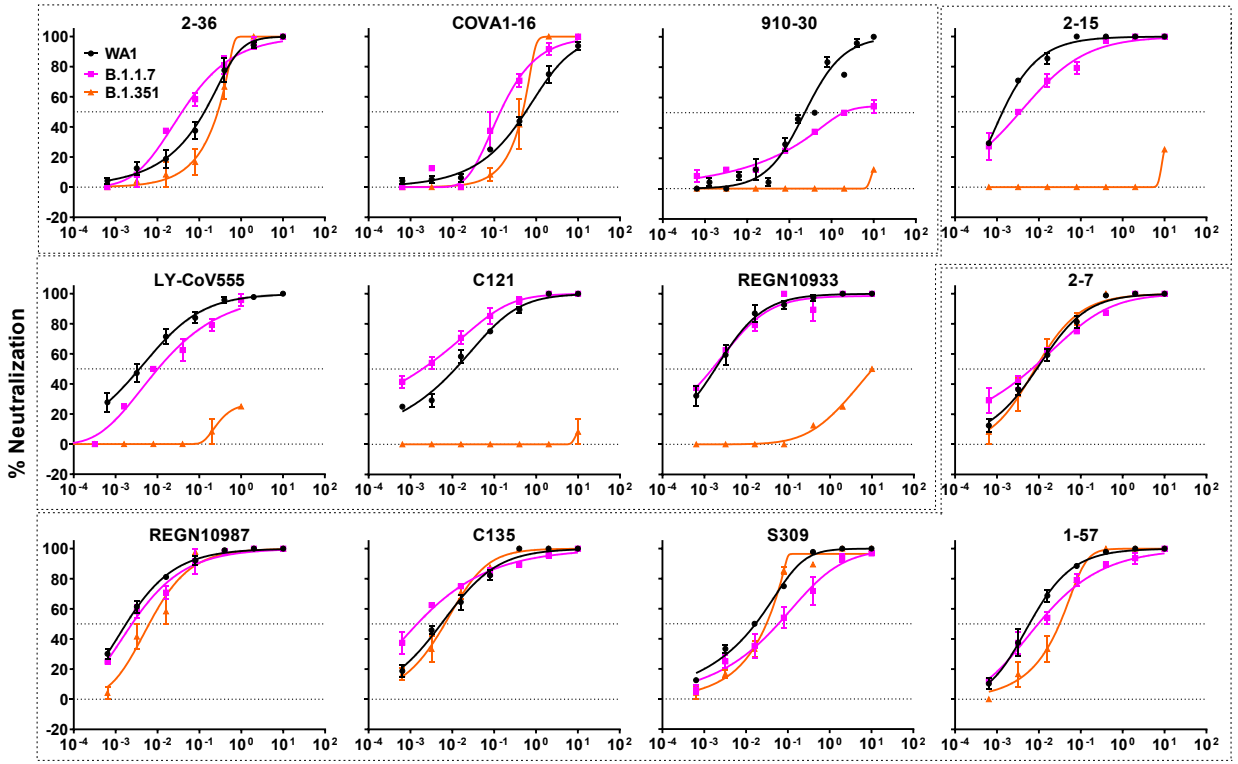
Modified from Economist

Resistance of B.1.1.7 (UK) and B.1.351 (SA) to select monoclonal antibodies







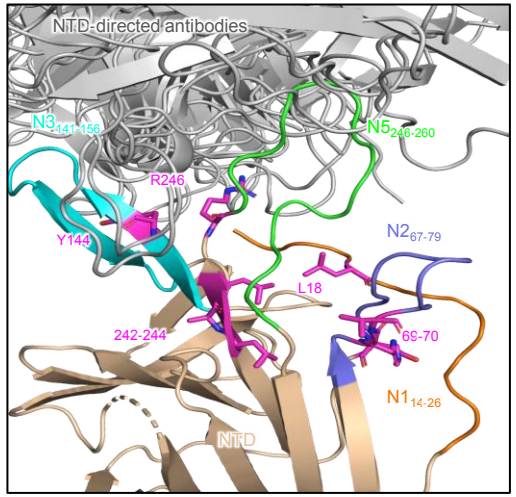


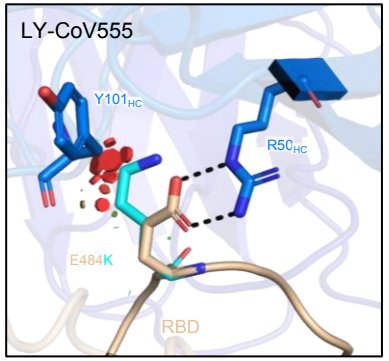
Wang et al, Nature 2021

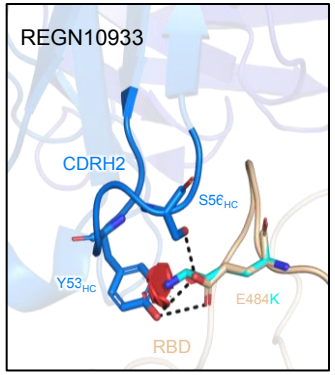
Susceptibility of B.1.1.7 and B.1.351 & mutant pseudoviruses to neutralization by RBD and NTD mAbs (fold change in IC50)

Fold Change of IC50 from WT		RBD-directed mAbs												NTD-directed mAbs					
		Inner side			RBM				Outer side					Supersite				Others	
		2-36	COVA1-16	910-30	2-15	LY-CoV555	C121	REGN10933	2-7	REGN10987	C135	S309	1-57	5-24	4-8	4A8	2-17	4-19	5-7
UK	**B.1.1.7**	3.4	3.4	-10.3	-3.0	-2.8	4.0	1.0	1.5	1.0	3.0	-4.0	-1.5	-330.2	<-1000	<-1000	-42.6	-29.2	-7.5
	UKΔ8	1.2	1.3	-14.0	2.2	1.7	2.3	2.5	1.4	2.1	-1.4	-3.1	2.1	<-1000	<-1000	<-1000	-121.2	-20.5	-11.9
	69-70del	-1.0	1.1	2.7	1.2	1.1	1.7	1.3	-1.2	1.2	1.8	-1.6	1.1	1.1	1.1	1.5	-1.1	-3.6	-4.0
	144del	1.5	-1.3	2.3	1.3	1.1	1.7	1.3	1.2	-1.4	1.4	1.4	1.1	<-1000	<-1000	<-1000	-80.7	1.6	-3.7
	N501Y	-1.2	-1.4	-12.7	1.5	-1.0	1.5	-1.4	-1.0	1.3	1.2	1.2	3.6	-2.9	-6.7	MPI↓	-12.0	-1.4	-3.2
	A570D	4.1	1.9	6.7	1.4	1.7	1.7	4.7	-2.3	-1.6	1.1	-1.2	2.2	1.1	-15.1	-2.9	-4.8	-1.9	-2.2
	P681H	2.0	1.5	2.5	3.1	2.3	-1.0	1.6	-1.4	-1.9	1.3	-1.2	2.9	-1.5	-2.8	1.1	-4.7	-1.2	1.8
	T716I	4.3	3.9	3.9	3.1	3.5	2.0	3.6	-1.1	-1.6	1.2	-1.6	2.9	-3.5	-5.5	MPI↓	-2.6	1.2	-1.0
	S982A	-3.9	-3.0	-2.4	1.1	-2.0	1.4	-2.3	-2.2	-1.2	1.6	-1.0	-1.5	-1.1	-1.1	-2.9	-4.3	1.2	-1.3
	D1118H	-1.1	-3.1	1.0	1.2	1.0	1.7	-1.3	-1.4	-1.7	1.2	1.5	1.1	-1.3	-3.1	1.4	-1.1	-1.1	-1.8
SA	**B.1.351**	-2.1	1.0	-456.6	<-1000	<-1000	<-1000	<-1000	1.1	-3.5	1.0	-2.2	-5.2	<-1000	<-1000	<-1000	-456.4	-595.2	-84.8
	SAΔ9	-2.0	1.3	<-1000	<-1000	<-1000	<-1000	-58.8	1.3	1.8	1.2	1.3	3.3	<-1000	<-1000	<-1000	-406.6	<-1000	-18.1
	L18F	1.5	1.9	2.8	3.0	1.0	1.8	1.4	-1.4	-1.8	1.1	1.2	-1.6	-2.2	1.3	MPI↓	-107.2	<-1000	-8.9
	D80A	-1.4	1.2	2.1	2.0	1.5	2.0	1.4	-2.2	-2.2	1.0	2.2	-2.7	2.3	2.0	-1.0	-2.0	<-1000	-9.8
	D215G	1.9	1.6	1.5	1.8	1.5	2.1	1.5	-1.8	-2.1	-1.2	1.0	2.2	-1.1	-1.8	-2.3	-6.0	1.1	1.1
	242-244del	-1.4	1.2	-1.2	1.4	-1.1	1.1	1.0	-1.2	-3.2	1.8	1.2	-1.3	<-1000	<-1000	<-1000	<-1000	<-1000	-20.7
	R246I	1.3	1.7	2.2	2.4	1.4	2.1	2.2	1.4	-2.1	1.1	2.3	1.7	<-1000	<-1000	<-1000	-2.8	<-1000	-9.2
	K417N	3.2	3.3	<-1000	3.3	8.4	1.2	-13.1	2.1	-1.2	2.9	1.6	7.8	2.9	-1.6	1.7	-1.5	1.2	-1.2
	E484K	-1.2	-1.0	4.3	<-1000	<-1000	<-1000	-10.5	-3.4	-1.1	2.3	2.5	-1.1	-1.6	-3.2	MPI↓	-2.8	-1.1	-1.4
	N501Y	-1.2	-1.4	-12.7	1.5	-1.0	1.5	-1.4	-1.0	1.3	1.2	1.2	3.6	-2.9	-6.7	MPI↓	-12.0	-1.4	-3.2
	A701V	1.9	1.4	2.1	2.8	2.0	1.6	2.3	-1.8	-2.6	1.5	1.1	2.5	-3.3	-2.0	MPI↓	-3.3	-1.2	-1.3

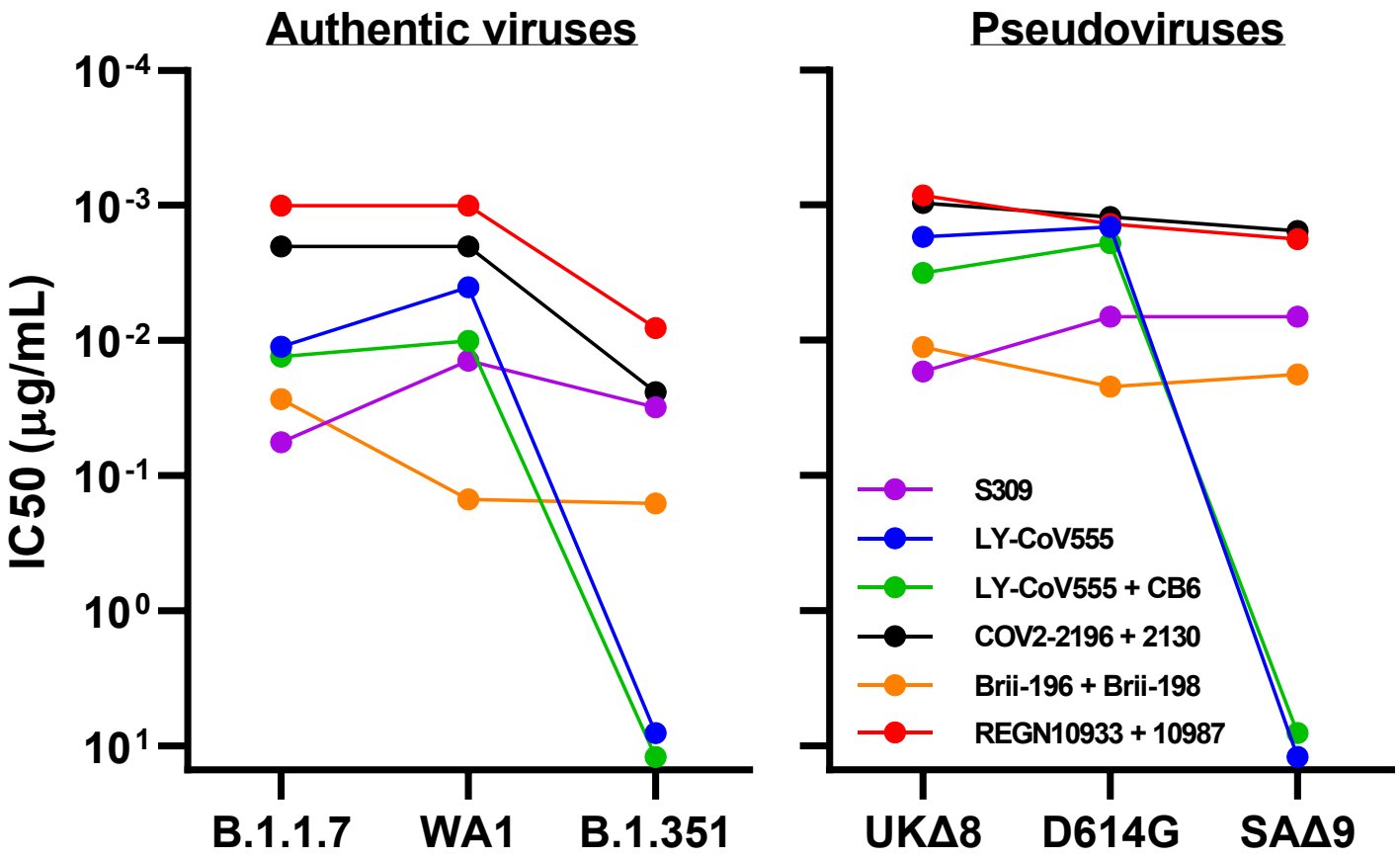
Red: resistance >3 fold; Green: sensitization >3 fold



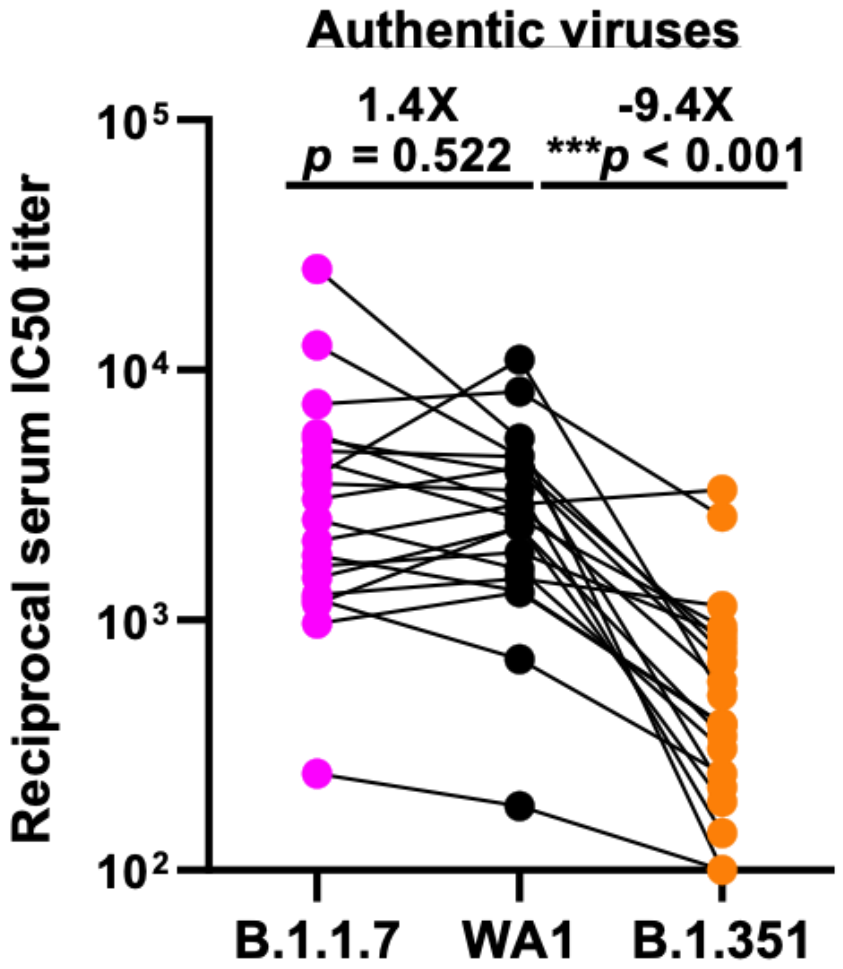




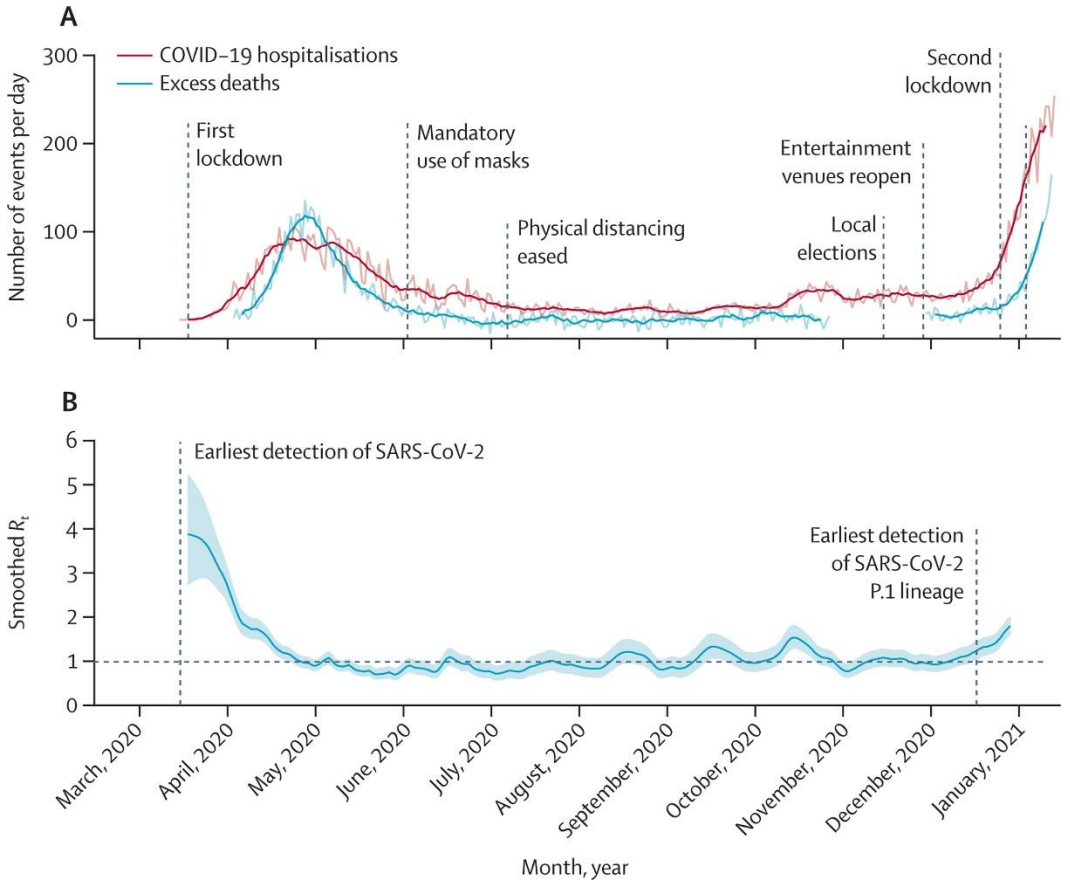
Changes in IC50 of authorized or investigational therapeutic mAbs against B.1.1.7 and B.1.351 as well as UKΔ8 and SAΔ9 relative to the WT



Changes in neutralization IC50 of convalescent plasma against B.1.1.7 and B.1.351 relative to the WT

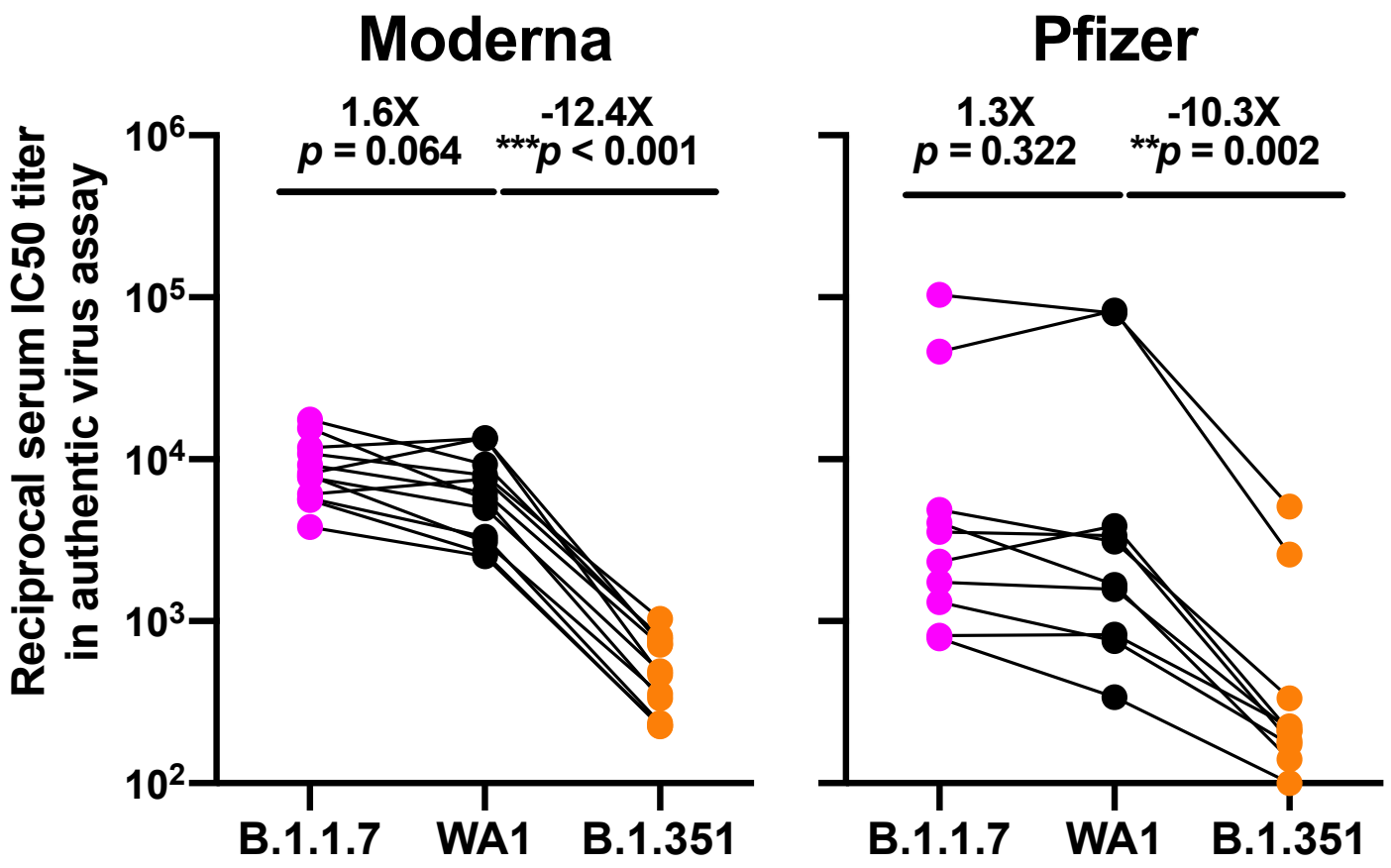


No protection against re-infection in SA in Novavax placebos



From Lancet 2021

Changes in neutralization activity of vaccinee sera against B.1.1.7 and B.1.351



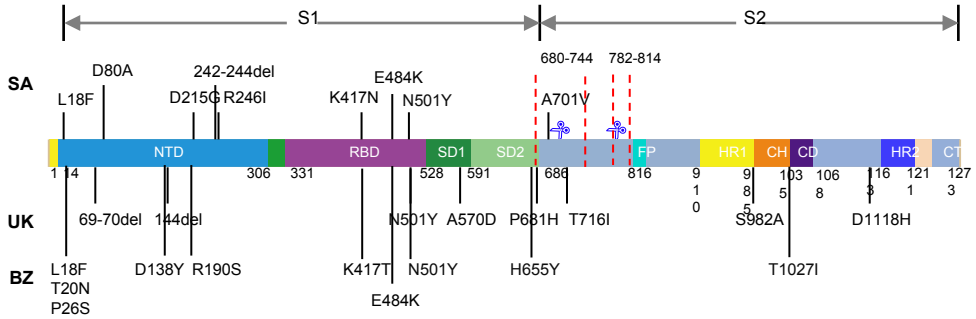
Novavax protective efficacy

WT	96%
B.1.1.7	86%
B.1.351	49%

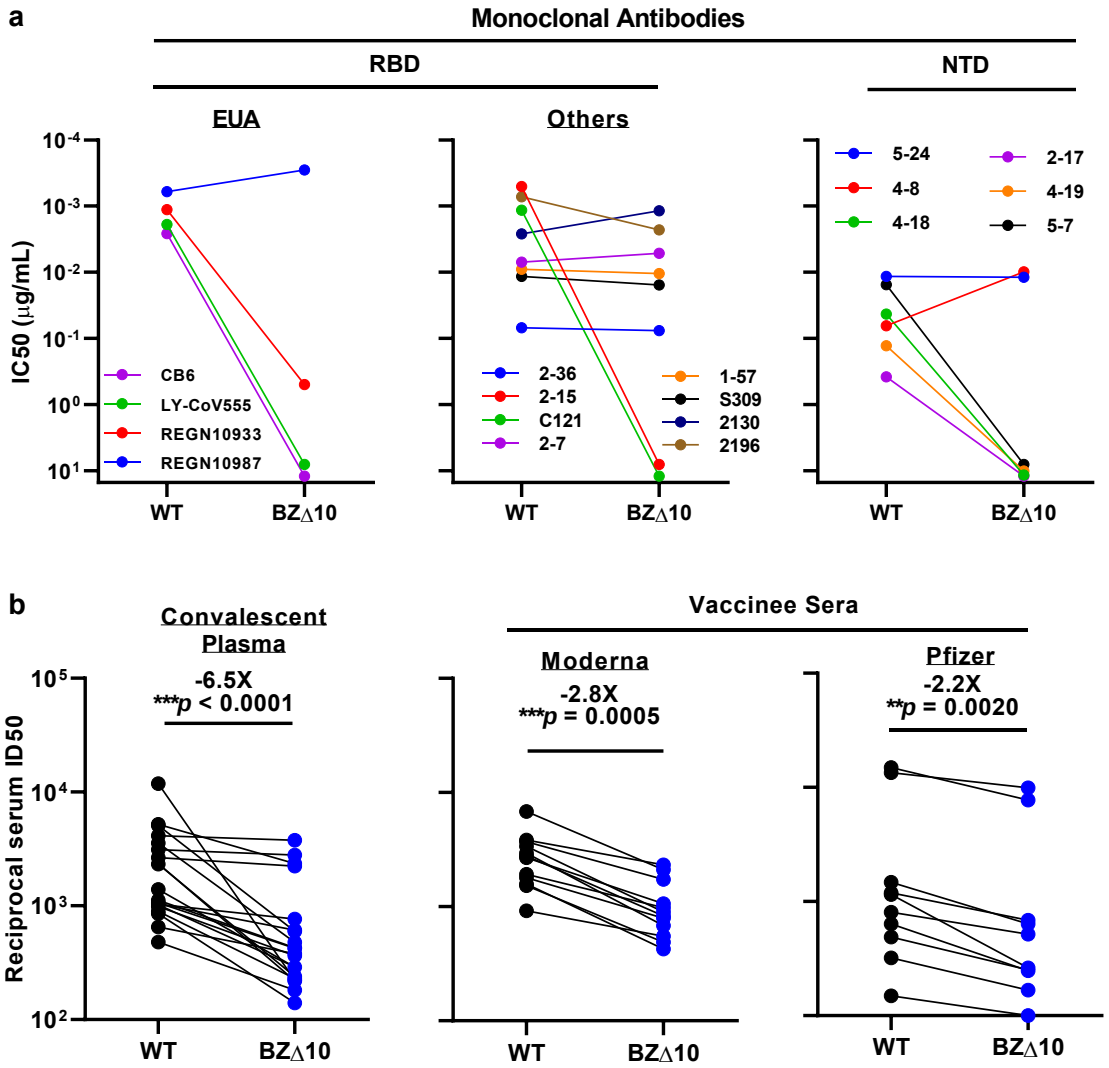
J & J protective efficacy

U.S.	72%
Latin Am	66%
SA	57%

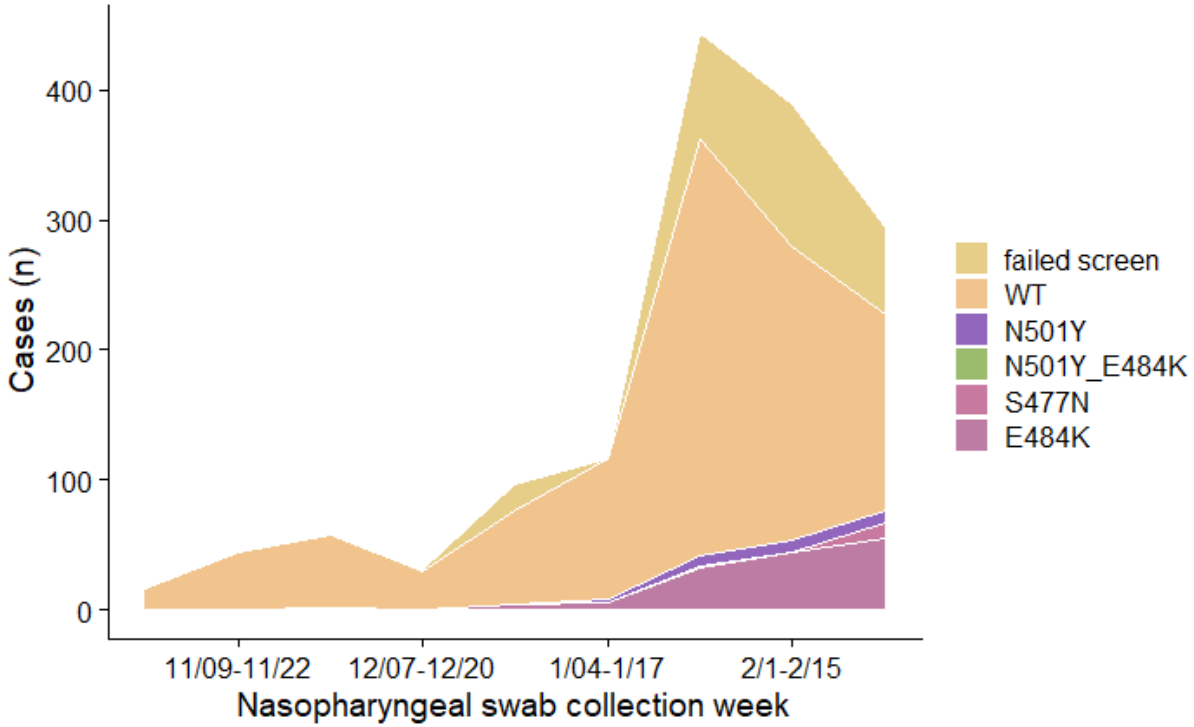
Antibody resistance of P.1 (BZ) variant



Wang et al
https://www.biorxiv.org/content/10.1101/2021.03.01.433466v1



A new SARS-CoV-2 variant in the NY metropolitan area

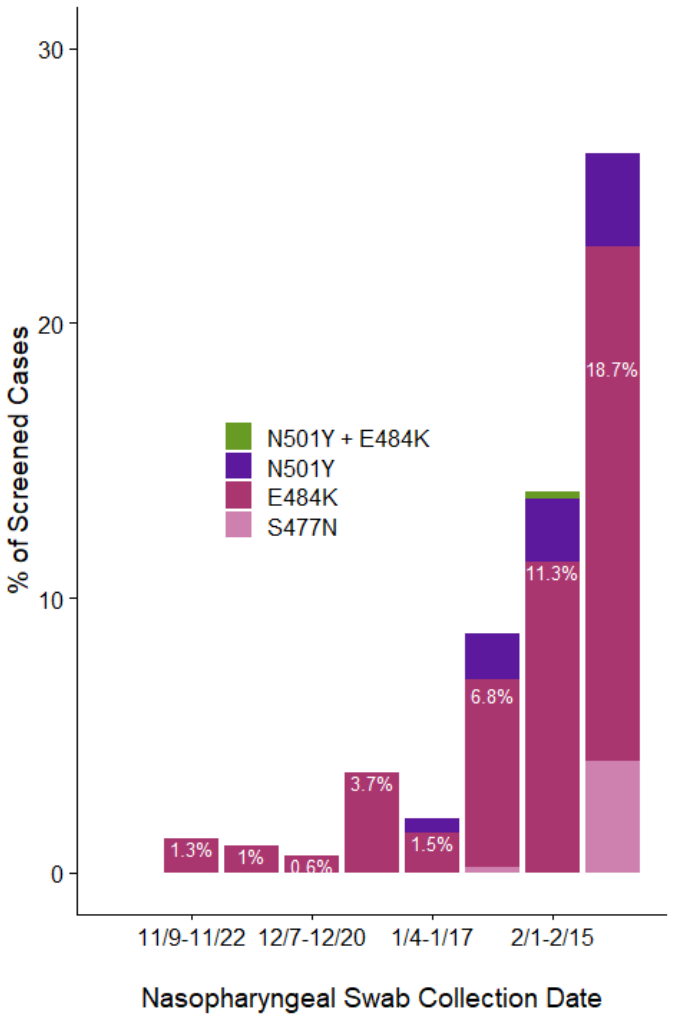


Hiroshi Mohri

Anne-Catrin Uhlemann

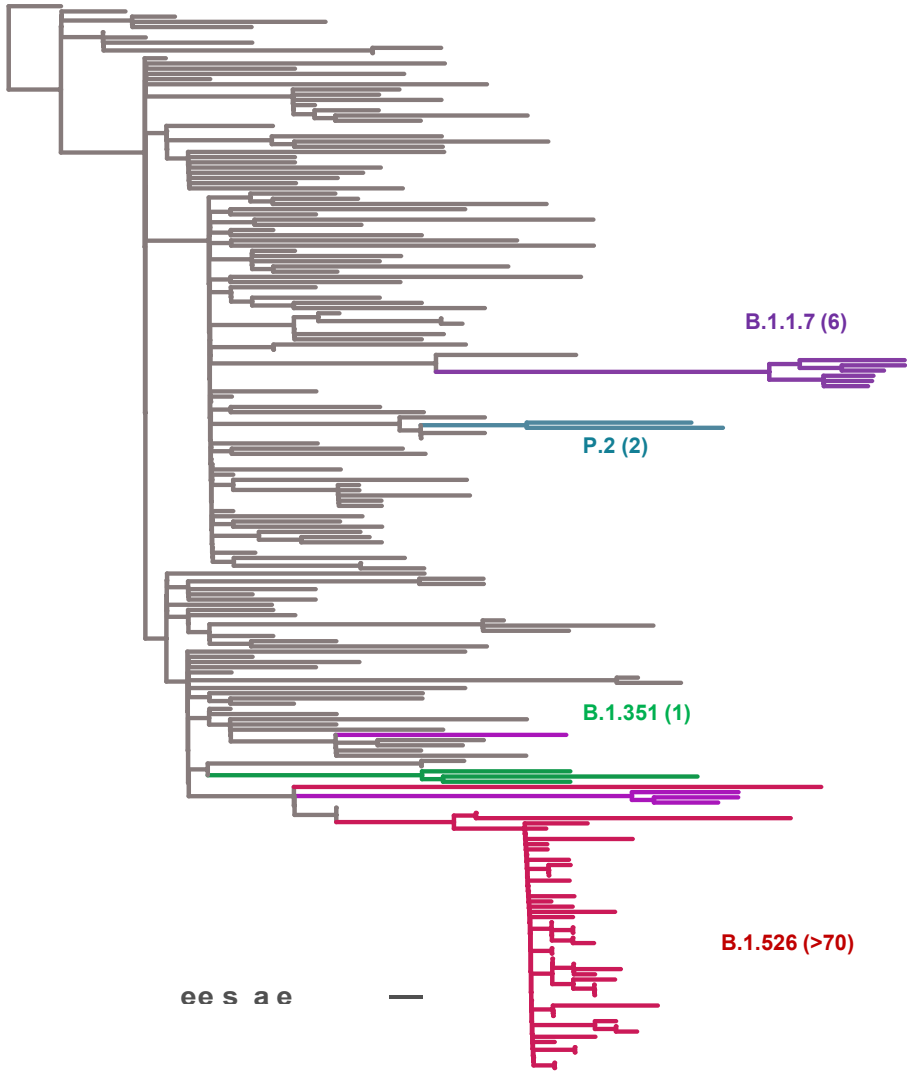
Medini Annavajhala

https://www.medrxiv.org/content/10.1101/2021.02.23.21252259v1

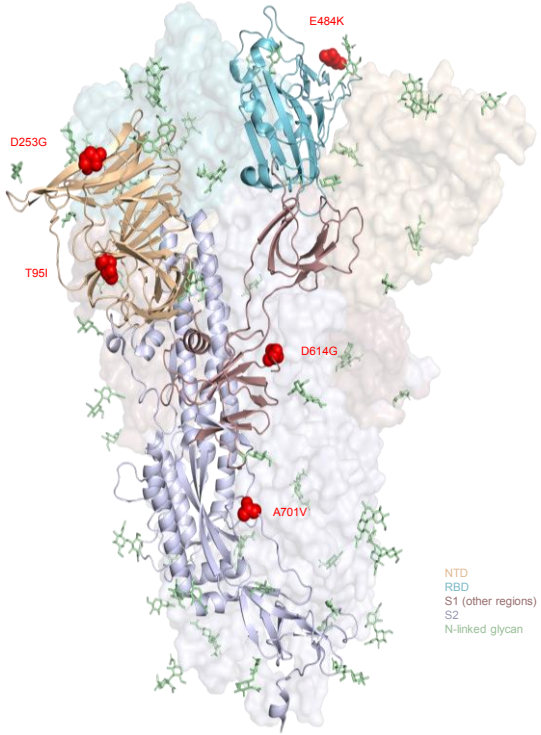


Past week 36%

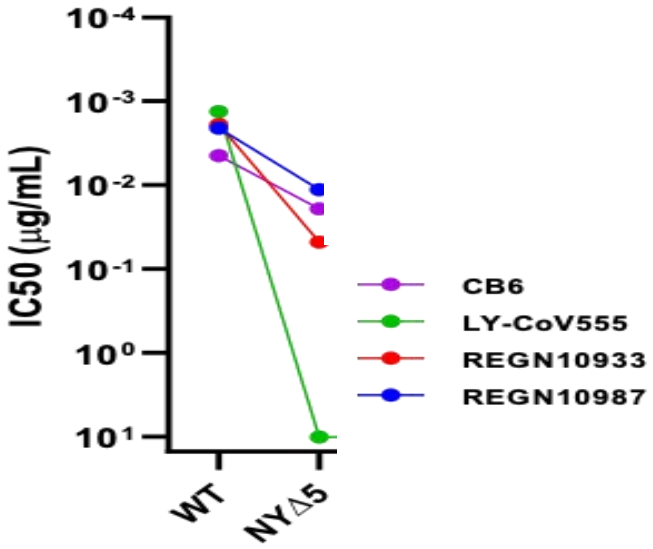
SARS-COV-2 variant of concern identified in New York: B.1.526 with E484K mutation



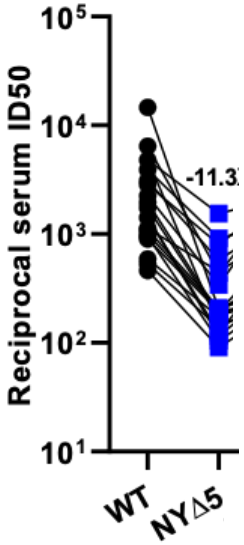
Spike mutations found in B.1.526/E484K and resistance to antibody neutralization



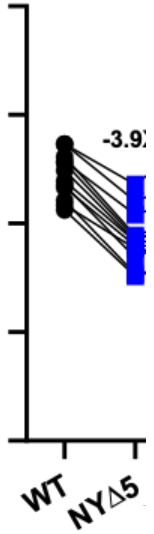
mAbs with EUA



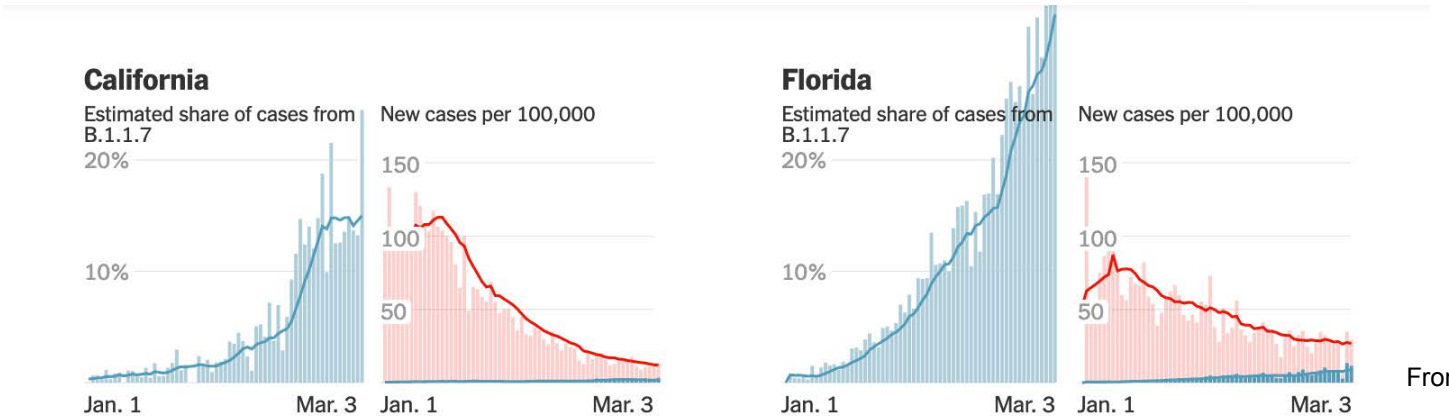
Convalescent plasma



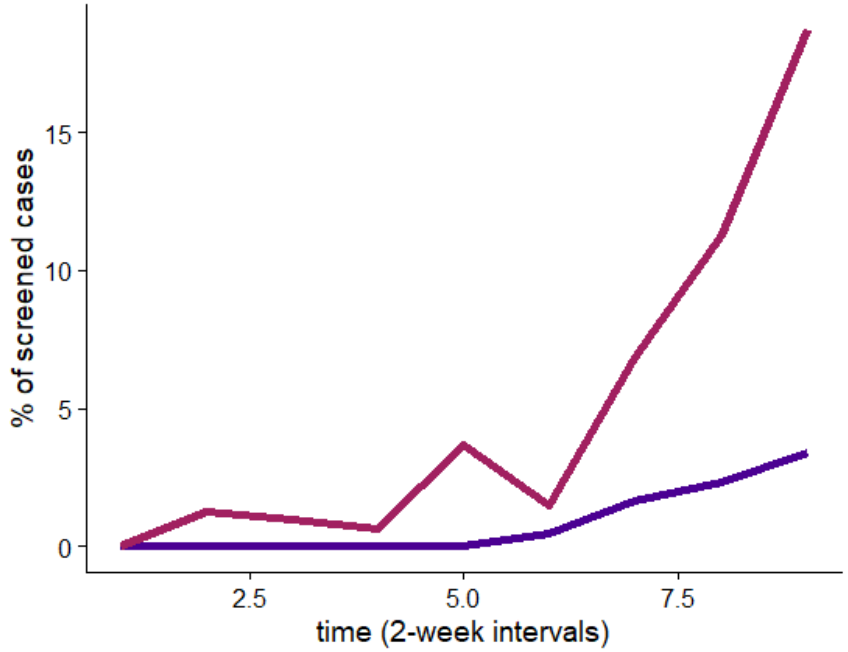
Vaccinee sera



B.1.1.7 is becoming dominant in most parts of US but it is out-competed by B.1.526 in NYC



From NY Times



E484K doubling time:
~ 12 days

NYC DOH:
39% B.1.526
12% B.1.1.7