ANTIGENICITY OF THE MU (B.1.621) AND A.2.5 SARS-COV-2 SPIKES

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Background:

The rapid emergence of SARS-CoV-2 variants is fueling the recent waves of the COVID-19 pandemic.The Mu (B.1.621) and A.2.5 variants carry some mutations shared by other variants of concerns (VOCs). For example, N501Y and E484K mutations in the receptor-binding domain (RBD) domain detected in B.1.1.7 (Alpha), B.1.351 (Beta) and P.1 (Gamma). Similarly, the L452R mutation of B.1.617.2 (Delta) variant is now present in A.2.5. Here, we evaluated the capacity of Mu and A.2.5 Spikes to interact with angiotensin-converting enzyme 2 (ACE2) and performed binding and neutralization assays with plasma from vaccinated individuals. Finally, we also compared the antigenic properties of both Mu and A.2.5 with Beta and Delta VOCs Spikes.

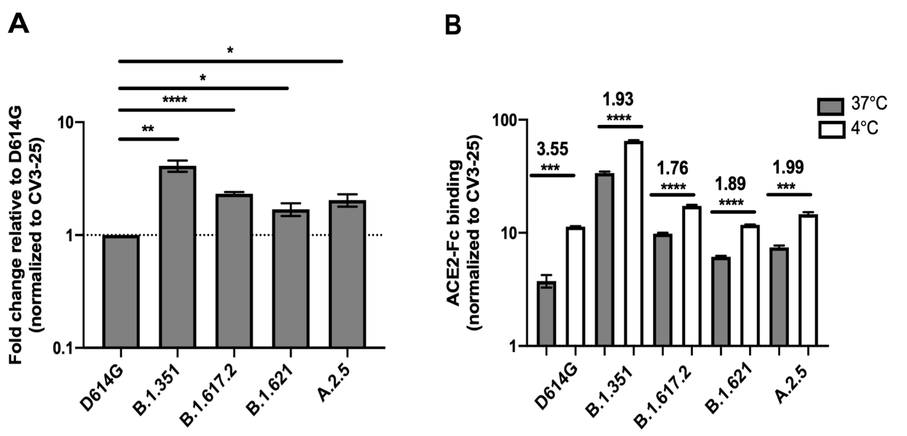


Figure 1. Spike glycoproteins interaction with ACE2.
HEK 293T cells were transfected with the indicated SARS-CoV-2 Spike variants. 48 hrs post transfection, cells were stained with ACE2-Fc or with CV3-25 Ab and analyzed by flow cytometry.

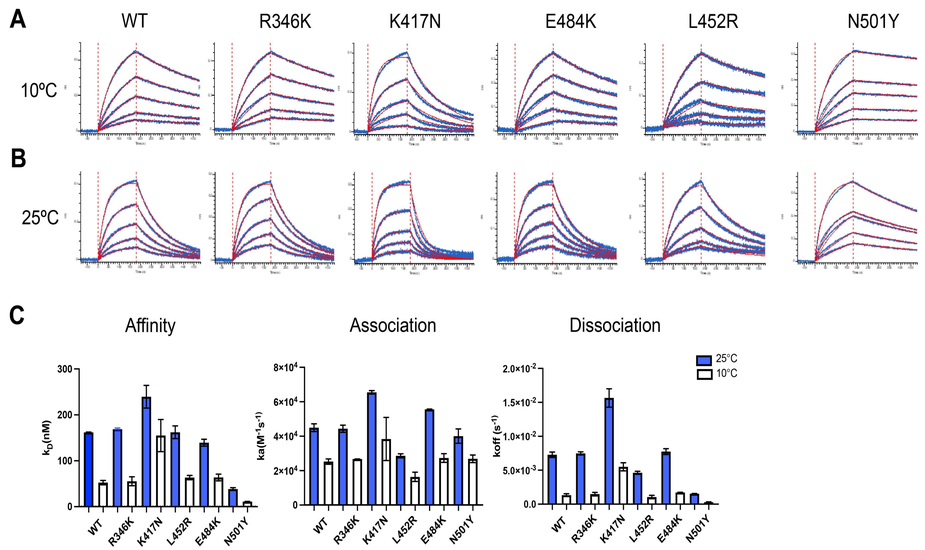


Figure2. Analysis of hACE2-RBD binding affinity by Biolayer Interferometry.

Table: Binding Kinetics of the interaction between SARS-CoV-2 RBD and sACE2 quantified by Biolayer Interferometry.

Ligands	Temperature	ACE2 binding (RBD/biolayer interferometry)		
		KD (nM)	Ka (1/Ms)	Kdis (1/s)
WT	10°C	57.19	$2.68x10^4$	$1.53x10^{-3}$
	25°C	162.6	$4.72x10^4$	$7.68x10^{-3}$
R346K	10°C	45.71	$2.67x10^4$	$1.22x10^{-3}$
	25°C	166.4	$4.64x10^4$	$7.72x10^{-3}$
K417N	10°C	120	$5.09x10^4$	$6.11x10^{-3}$
	25°C	264.2	$6.45x10^4$	$1.70x10^{-2}$
L452R	10°C	68.17	$1.91x10^4$	$1.30x10^{-3}$
	25°C	148.3	$2.98x10^4$	$4.41x10^{-3}$
E484K	10°C	56.39	$2.99x10^4$	$1.69x10^{-3}$
	25°C	146.8	$5.58x10^4$	$8.18x10^{-3}$
N501Y	10°C	11.47	$2.91x10^4$	$3.33x10^4$
	25°C	35.45	$4.42x10^4$	$1.57x10^{-3}$

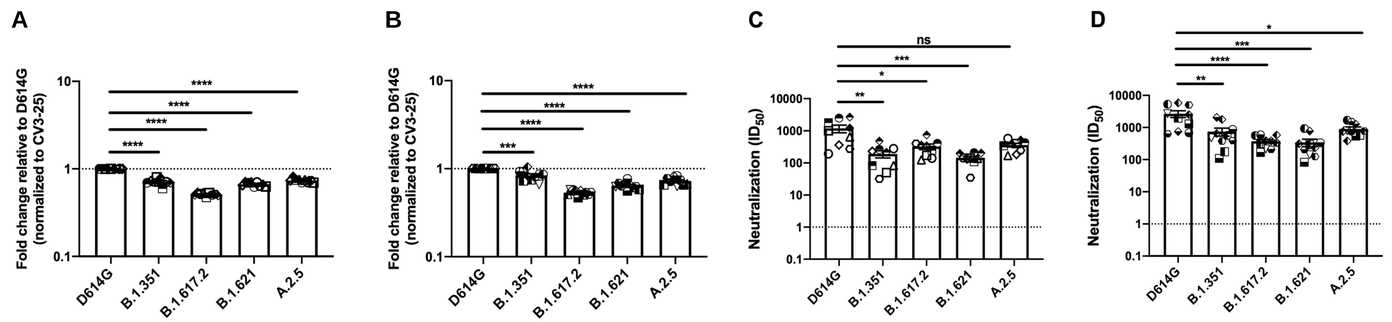


Figure 3. Evaluation of plasma recognition and neutralization ability of SARS-CoV-2 Spike variants of naïve or previously infected vaccinated individuals

Conclusion: Plasma from vaccinated SARS-CoV-2 naïve and previously-infected individuals efficiently recognized all tested Spikes. The decreased neutralization susceptibility of pseudoviral particles expressing the Mu Spike was similar to Beta and Delta. Our results highlight the importance of measuring critical parameters such as ACE2 interaction, plasma recognition and neutralization from each emerging variant.

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