Technische Universität Braunschweig

Human serum from SARS-CoV-2 vaccinated and COVID-19 patients shows reduced binding to the RBD of SARS-CoV-2 Omicron variant

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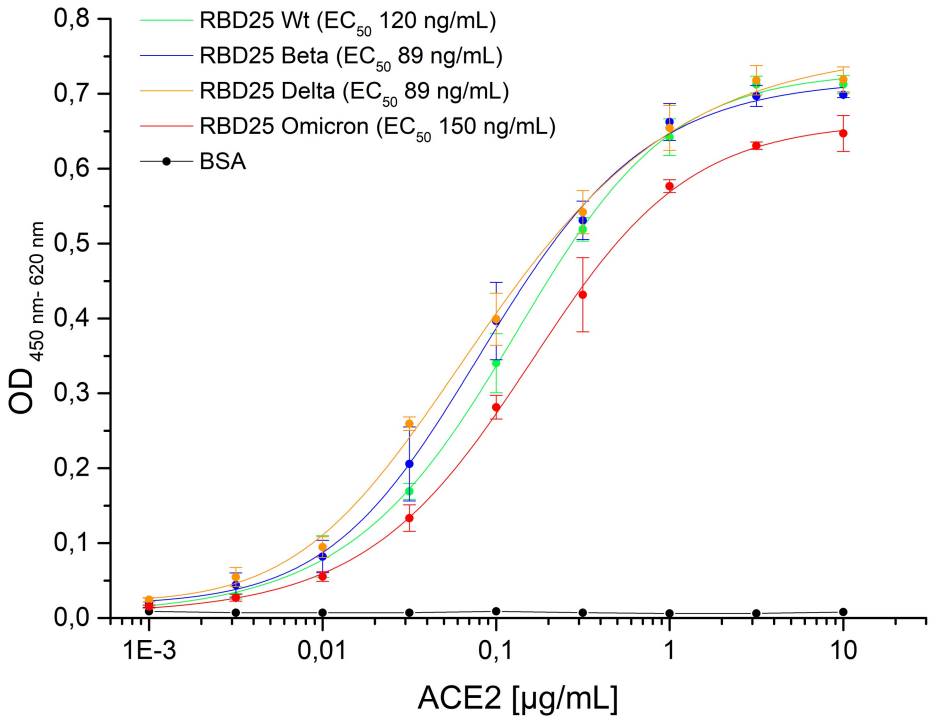
We analyzed the Omicron RBD

- Receptor binding domain (RBD) of SARS-CoV-2 spike produced in insect cells
- „Classic“ Omicron RBD with 15 mutations
- RBD is main target of neutralizing antibodies and therapeutic antibodies, e.g. Casirivimab/Imdevimab (Ronapreve)

RBD wt	Original Wuhan	-
RBD beta	B.1.351	K417N, E484K, N501Y
RBD delta	B.1.617.2	L452R, T478K
RBD omicron	B.1.1.529	G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493K, G496S, Q498R, N501Y, Y505H

Table: RBD variants used in this study (319-541 of GenBank: MN908947)

Omicron RBD – ACE2 binding is reduced



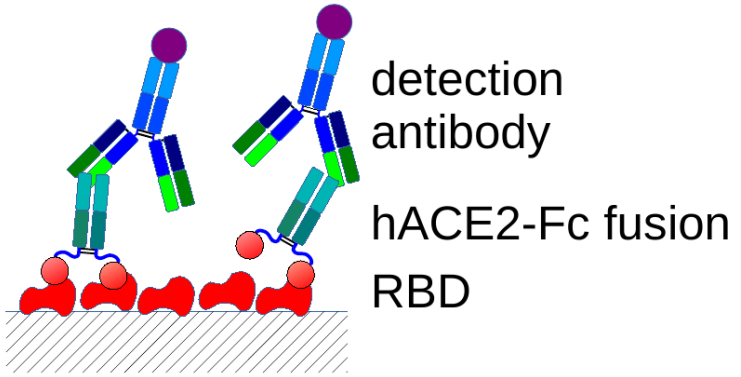


Figure: RBD – ACE2 interaction and ELISA setup

- Binding of RBD-ACE2 is reduced compared to Wuhan wt, Beta and Delta (data confirmed by MST analysis)!
- RBD-ACE2 not reason for increased Omicron infectivity > immune evasion?

We analyzed human sera binding to RBD

- Serum samples from COVID-19 patients, immunized and boost immunized individiuals were analyzed.

		n (female/ male)	*Mean age (range)*	*Time point of sampling*
Patients	severe symptoms, hospitalized	27 (7/20)	65 (39-86)	7-25 days after symptom onset (mean 12 days)
Vaccinated persons	2xBNT162b2	15 (4/11)	36 (25-61)	7-43 days after 2nd dose (mean 16 days)
	1xAd26.COV2.S	6 (2/4)	35 (24-40)	14-33 days after 1st dose (mean 25 days)
	BNT162b2 or mRNA-1273	16 (7/9)	39 (24-64)	5-49 days after 3rd dose (mean 17 days)

Table: Used human serum samples in this study.

Serum binding to Omicron RBD is reduced

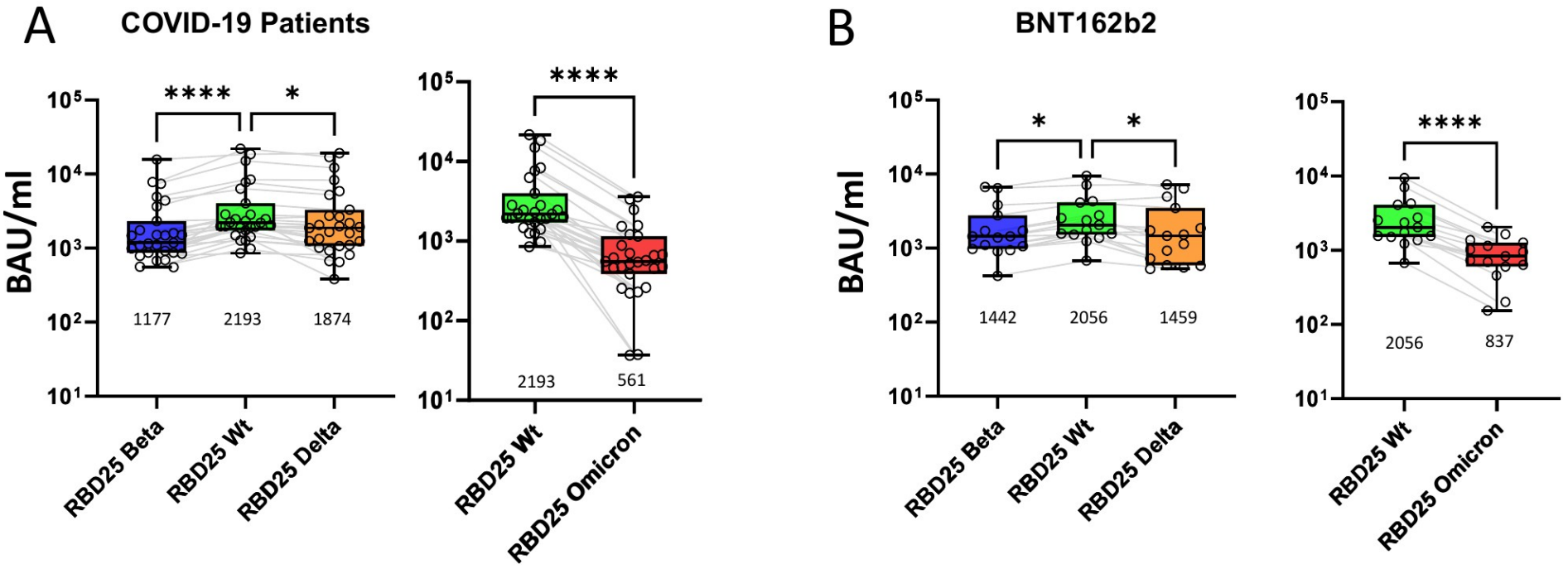
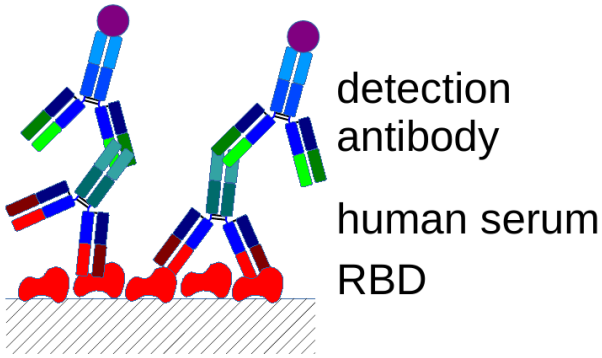
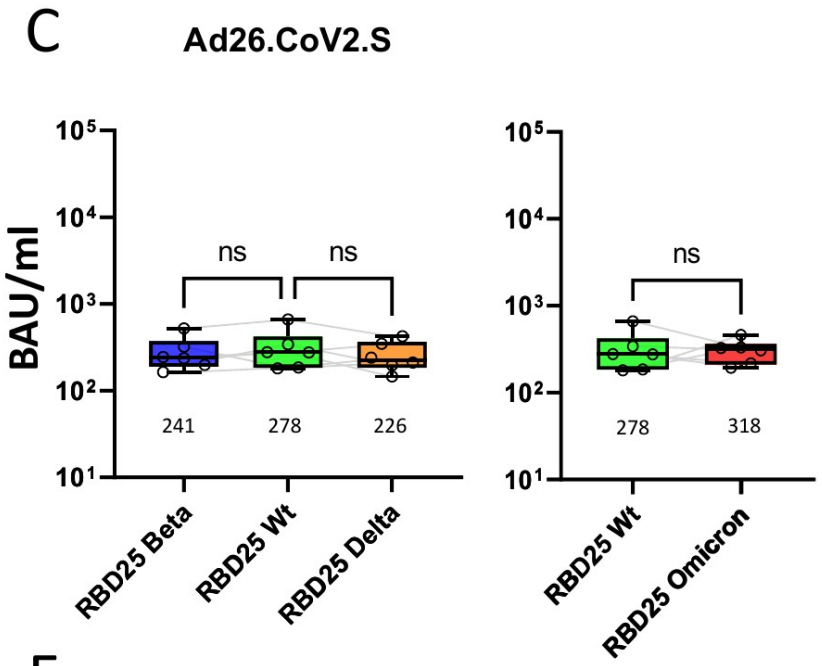


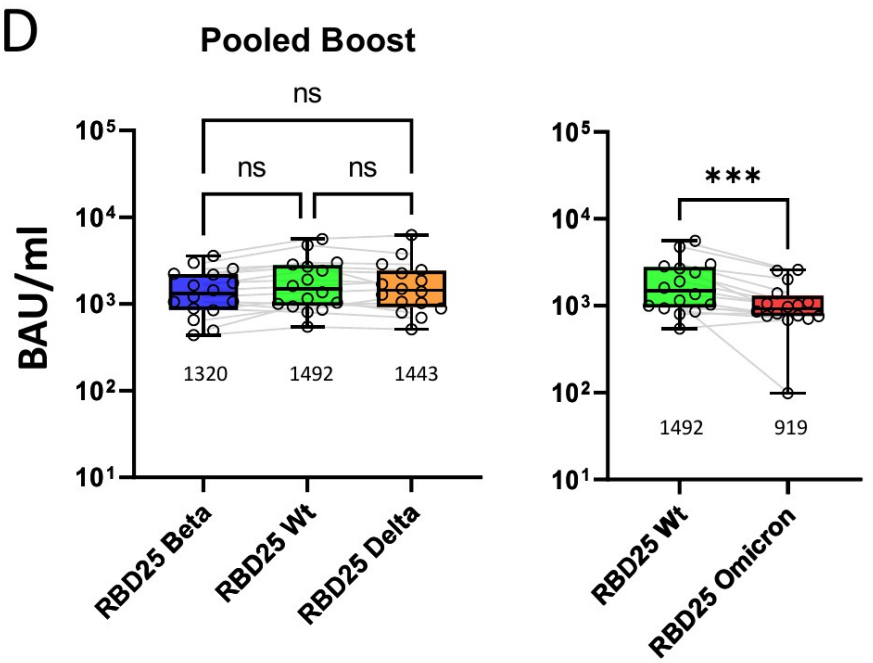
Figure: Human serum binding to RBD and ELISA setup

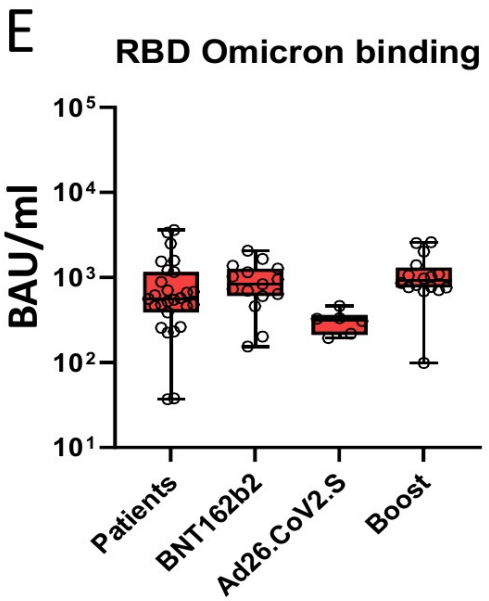
- IgGs are still binding to Omicron RBD!
- Binding to Omicron RBD is reduced!



Serum binding to Omicron RBD is reduced







- Ad26.CoV2.S serum binding is very low compared to BNT162b2
- Boost immunization of Ad26.Cov-2 with mRNA vaccine increases serum answer to all SARS-CoV-2 RBDs.

Conclusion

- Omicron RBD-ACE2 interaction is reduced
  > reason for increased infectivity: immune evasion?
- Hint for immune evasion: reduced binding of Omicron RBD by human COVID-19 patients and vaccinated individuals
- Current results are a snapshot!
- Omicron spike/RBD mutations are highly dynamic!

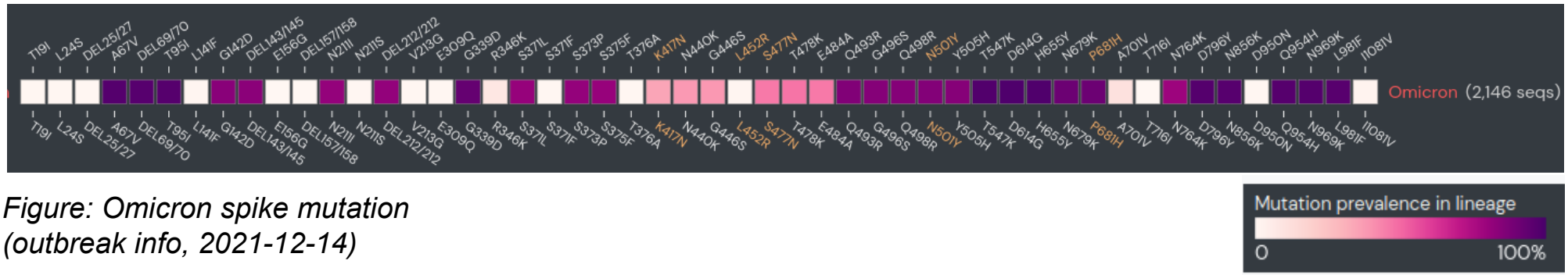


Figure: Omicron spike mutation (outbreak info, 2021-12-14)

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