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 variant       | Original Wuhan | Mutations                                      |
|-------------------|----------------|-----------------------------------------------|
| 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

➢ 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 individuals were analyzed.

|                                | n (female/male) | Mean age (range) | Time point of sampling                           |
|--------------------------------|-----------------|-----------------|--------------------------------------------------|
| Patients with 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!

- 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)