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STRAIN-SPECIFIC SEROLOGICAL RESPONSE FOLLOWING SARS-COV-2 VOC INFECTION

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BACKGROUND

The introduction of new SARS-CoV-2 variants of concern (VOCs) raises the question how these VOCs differ in the serological antibody responses elicited, which is important to assess the risk of re-infections after natural infection and COVID-19 vaccination. Here we studied the virus (cross-) neutralization of sera from convalescent COVID-19 patients infected with a VOC and used this data as input for antigenic cartography to map the antigenic evolution of SARS-CoV-2.

METHODS

- We included PCR proven SARS-CoV-2 infected patients with a primary VOCs infection and without a history of COVID-19 vaccination in two observational cohort studies, the COSCA (NL 73281.018.20) and RECoVERED study (NL73759.018.20)
- Participants were included from June 2020 to July 2021 at the Amsterdam UMC, the Netherlands, and via the Dutch SARS-CoV-2 sequence surveillance program.
- Serum was collected 3-9 weeks after symptom onset and tested in a lentivirus-based SARS-CoV-2 pseudovirus neutralization assay for its neutralization capacity against the ancestral (D416), Alpha, Beta, Gamma, Delta and Omicron variant.
- The Wilcoxon signed rank test with Benjamini Hochberg correction was used to compare median virus cross-neutralization titers with the homologous neutralization.
- The antigenic map was constructed by using multidimensional scaling to position viruses and sera.
- One antigenic unit resembles a 2-fold change in neutralization titers.

Variant of Concern	N= (%)	Age (years) median (range)	Male	Hospital admission
Ancestral	20 (38 %)	53 (22 to 74)	9 (45 %)	9 (45 %)
Alpha	8 (17 %)	34 (25 to 72)	5 (63 %)	6 (75 %)
Alpha + E484K	2 (4 %)	62 (48 to 76)	0 (0 %)	2 (100 %)
Beta	7 (13 %)	43 (18 to 53)	3 (43 %)	0 (0%)
Gamma	4 (8 %)	35 (27 to 40)	2 (50 %)	0 (0%)
Delta	10 (19 %)	34 (19 to 63)	5 (50 %)	1 (10 %)
Total	51 (100%)	45(18 to 76)	25 (49 %)	18 (35 %)

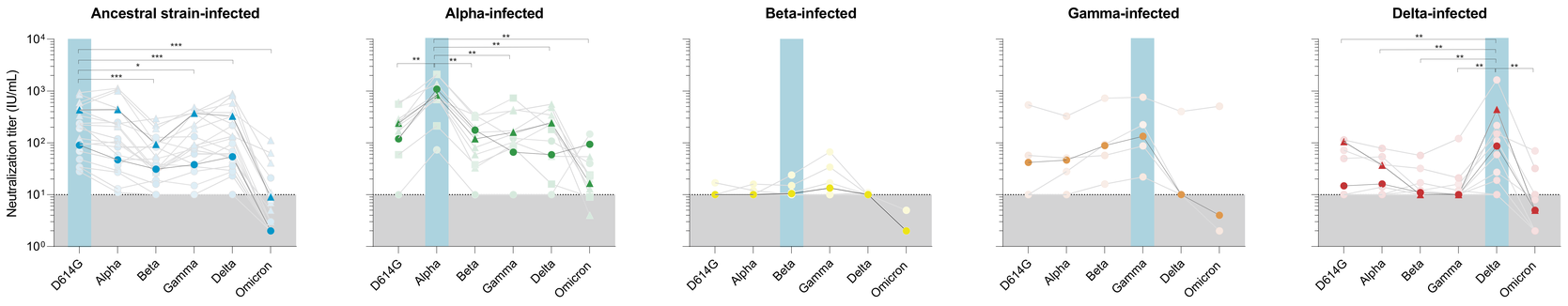
Manuscript available via: Mapping the antigenic diversification of SARS-CoV-2 | medRxiv

Convalescent COVID-19 patients infected with the ancestral, Alpha, Beta, Gamma or Delta variant are at risk of a **re-infection** with the **Omicron** variant.

This data supports the usage of the ancestral strain based COVID-19 vaccinations, but an Omicron specific update is currently indicated.

RESULTS (1) – SUBMITTED

- Generally, the homologous virus induced the highest neutralization titers (light blue bars)
- Hospitalized patients (triangles) showed higher neutralization titers compared to non-hospitalized (dots) patients
- When comparing non-hospitalized patients, patients infected with the Alpha variant (ID_{50} 1088 IU/mL) showed the strongest median homologous virus neutralization, followed by Gamma variant (ID_{50} 156 IU/mL), ancestral strain (ID_{50} 90 IU/mL) and Delta variant (ID_{50} 85 IU/mL) infected patients.
- None of the Beta variant infected patients showed strong virus (cross-)neutralization
- Omicron neutralization dropped below the limit of detection in 21/51 of the studied patients (<2 IU/mL)
- The ancestral, Alpha, Beta, Gamma and Delta variants cluster together in the antigenic map with < 3 antigenic units apart. The Omicron is > 5 antigenic units (>32-fold change in neutralization) apart.



CONCLUSIONS

- Some SARS-CoV-2 VOCs induce a strain specific neutralization pattern, resulting in a strain specific risk of re-infections when exposed to VOCs.
- The substantial reduction of neutralization in all groups against the Omicron variant and the distinct position of the Omicron variant in the antigenic map should warrant for a Omicron specific update of the current COVID-19 vaccinations.
- Limitations: this study has been conducted on a small number of COVID-19 patients and should therefore be confirmed by further research.

ADDITIONAL KEY INFORMATION

We thank all public health services in the Netherlands for their help in contacting participants. We are also thankful to the study personnel and the participants for their contribution to this research.

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