



SARS-CoV-2 Neutralising Antibodies in US and EU Plasma, and Cross Reactivity with Variants and Seasonal Coronaviruses



Thomas R. Kreil

Global Pathogen Safety

IPFA/PEI 28th International Workshop on Surveillance and Screening of Blood-borne Pathogens

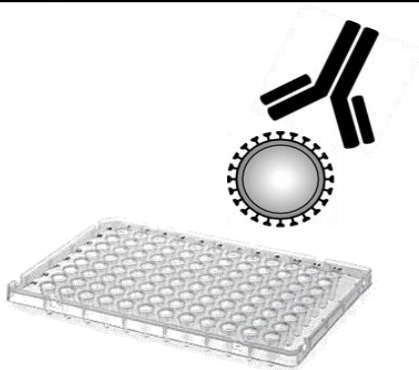
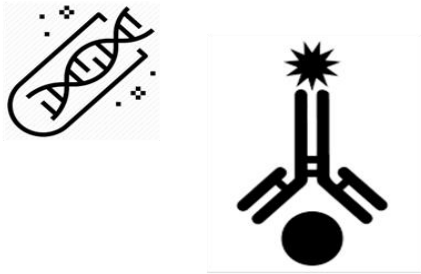
September 21, 2022 – Porto

Viruses and Virus Neutralizing Antibodies



Function Matters

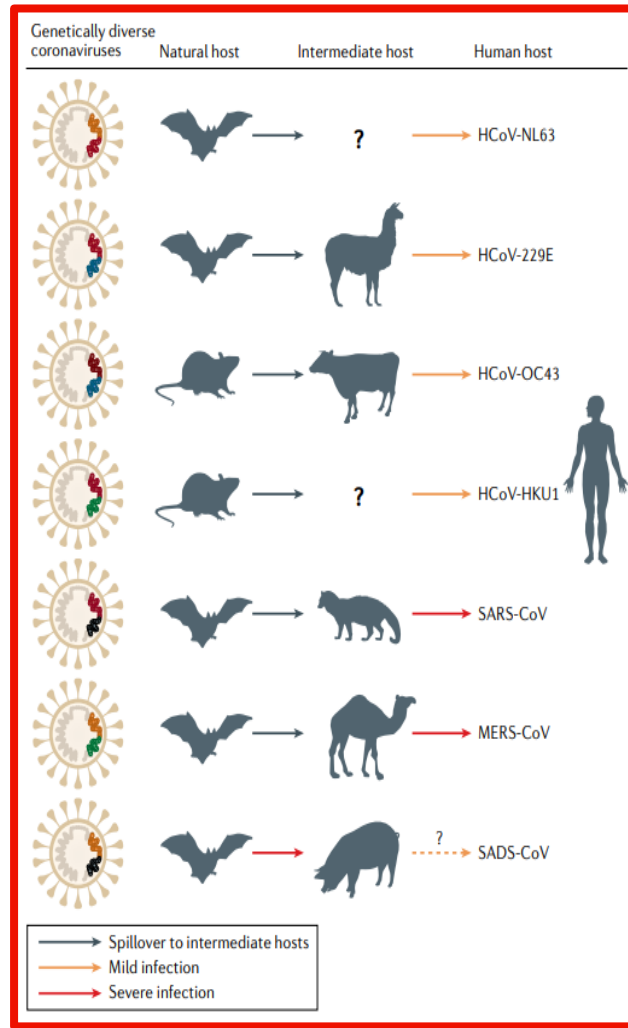
- Virus **infectivity**, rather than presence of nucleic acids
- Virus **neutralization**, rather binding of virus
- Basis: cell culture work, under biocontainment

Virus	Infectivity test	Nucleic acid test (e.g. PCR)
Antibody	Neutralization test, gold standard reference	Binding-assay (e.g. ELISA), unclear cross-reactivity
	 • Biocontainment laboratory, BSL 3 • Cell culture • Sterile work bench	 • More simple diagnostic lab • PoC (?)

Zoonotic Coronavirus Infections of Humans



- Alpha
 - NL63
 - 229E
 - **Canine (?)**
- Beta
 - OC43
 - HKU1
 - SARS-CoV
 - MERS-CoV
 - **SARS-CoV-2**
- Delta
 - **Porcine (?)**



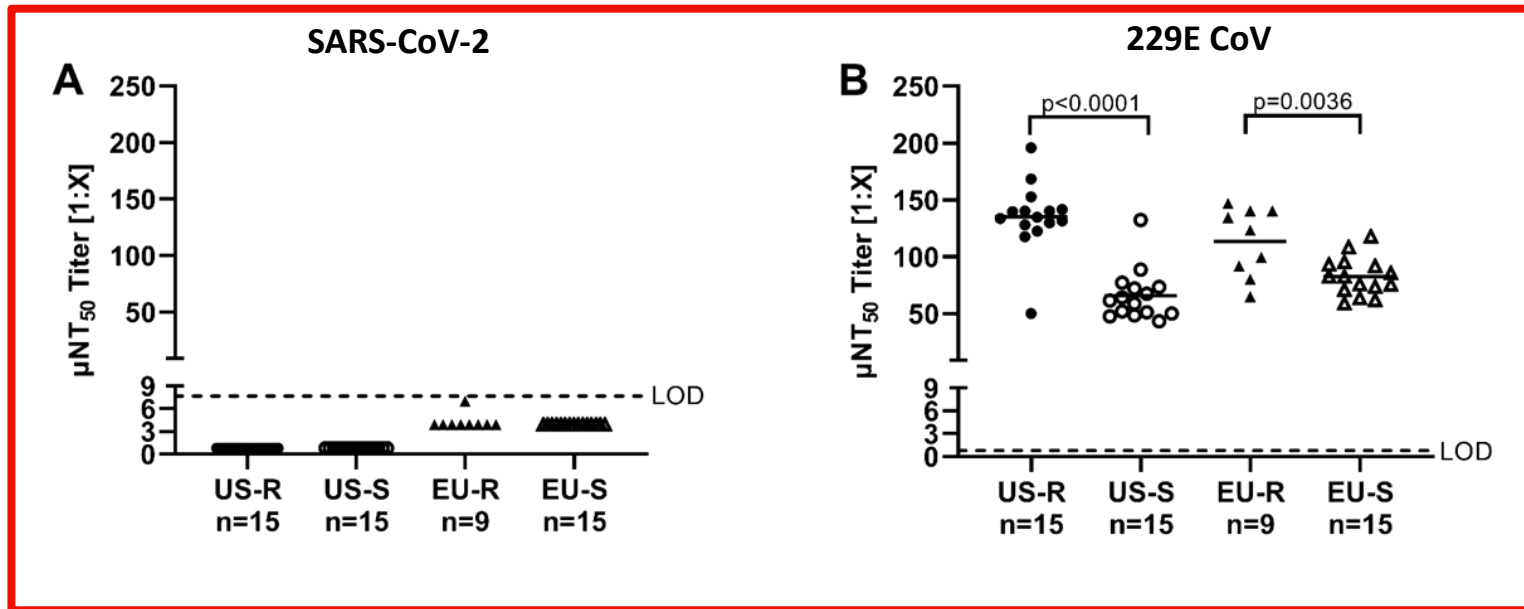
- **COVID-19 Pandemic**
 - 556 million cases
 - 6.4 million deaths (*at least*)
 - 12 billion vaccine doses

Johns Hopkins COVID-19 dashboard, updated July 07, 2022
- „Luck is not a strategy“
 - Andy Plump, statnews.com

Emergence of SARS-CoV-2 in the US, and **Antibodies in IG: NO**



- **Cross-reaction** between seasonal and pandemic coronavirus ?
 - SARS-CoV-2 antibody neutralization: no
 - 229E CoV antibody neutralization: US ~ EU; R > S



The Journal of Infectious Diseases

BRIEF REPORT

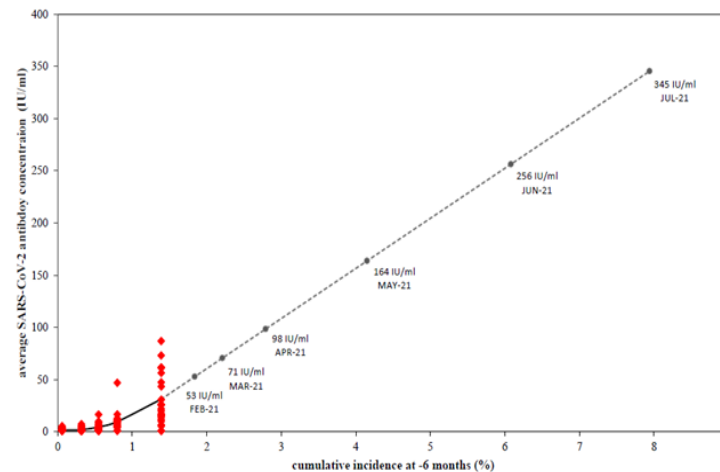
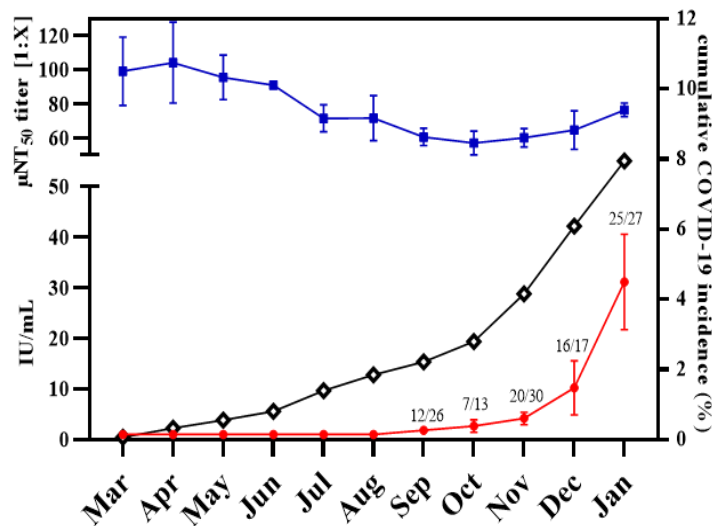
No SARS-CoV-2 Neutralization
by Intravenous Immunoglobulins
Produced From Plasma Collected
Before the 2020 Pandemic

Julia Schwaiger,¹ Michael Karbiener,¹ Claudia Aberham,² Maria R. Farcet,¹ and Thomas R. Kreil¹

SARS-CoV-2 in the US, and Antibodies in IG: Rapidly Increasing



- 229E Coronavirus neutralization: stable
- Cumulative post COVID-19 incidence
- SARS-CoV-2 neutralization: increasing → prediction (?)



The Journal of Infectious Diseases BRIEF REPORT

Rapidly Increasing Severe Acute Respiratory Syndrome Coronavirus 2 Neutralization by Intravenous Immunoglobulins Produced From Plasma Collected During the 2020 Pandemic

Maria R. Farcet,¹ Michael Karbiener,¹ Julia Schwaiger,¹ Reinhard Ilk,² and Thomas R. Kreil¹

May 4, 2021 – virtual IPFA-PEI

- Prediction, based on correlation of
 - SARS-CoV-2 incidence, and
 - IG-mediated neutralization of SARS-CoV-2 ~6 months later

→ Given a ***cumulative incidence*** of 7.94% in January 2021, IG lots to be released in **July 2021** can be expected to contain a mean SARS-CoV-2 nAb concentration of around **345 IU/mL** (Figure 1B).
- *Prediction is very difficult, especially if it's about the future !*
 - Niels Bohr, Nobel laureate in Physics and father of the atomic model

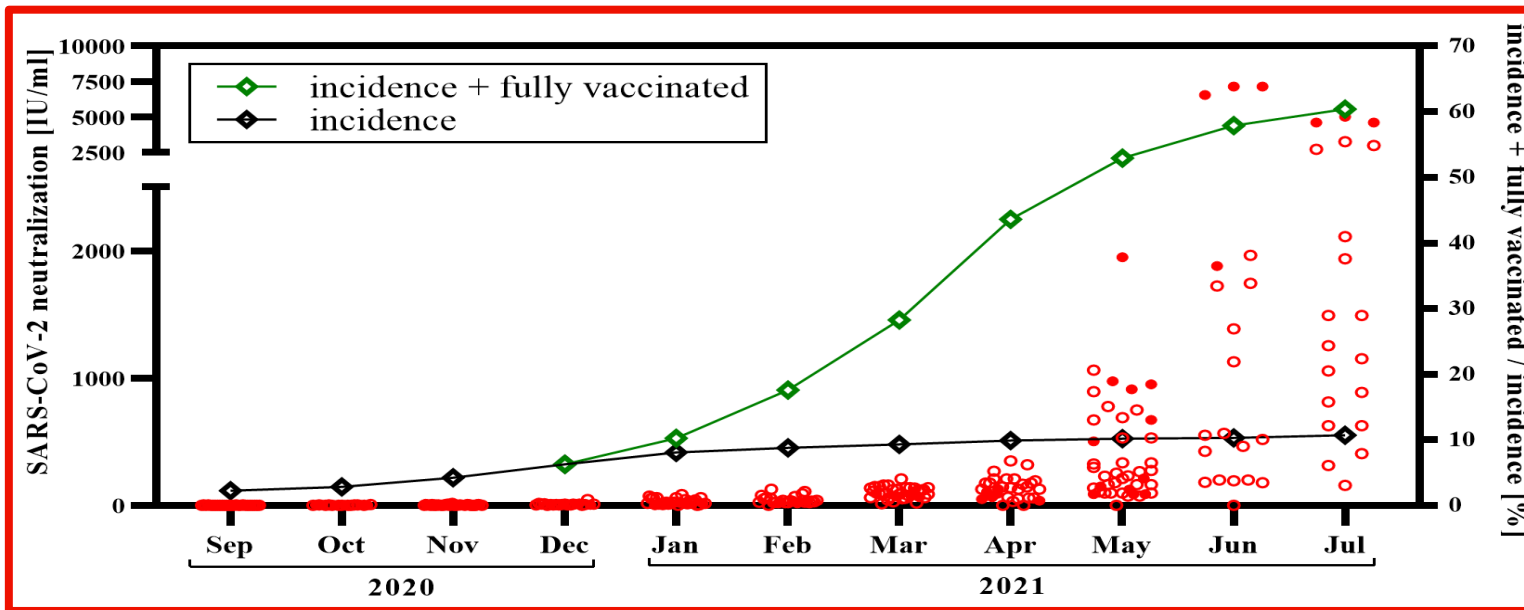
July 2021

- Prediction
 - Given a cumulative incidence of 7.94% in January 2021, IG lots to be released in July 2021 can be expected to contain a mean SARS-CoV-2 nAb concentration of around 345 IU/mL (Figure 1B).
- Reality
 - 848 IU/ml
 - vaccination had started, on top of cumulative incidence (only)

SARS-CoV-2 in the US, and Antibodies in IG: Highly Potent



- **SARS-CoV-2 neutralization: increasing**
- **Cumulative post COVID-19 incidence**
- **Cumulative post COVID-19 + COVID-19 vaccinated**



The Journal of Infectious Diseases

BRIEF REPORT

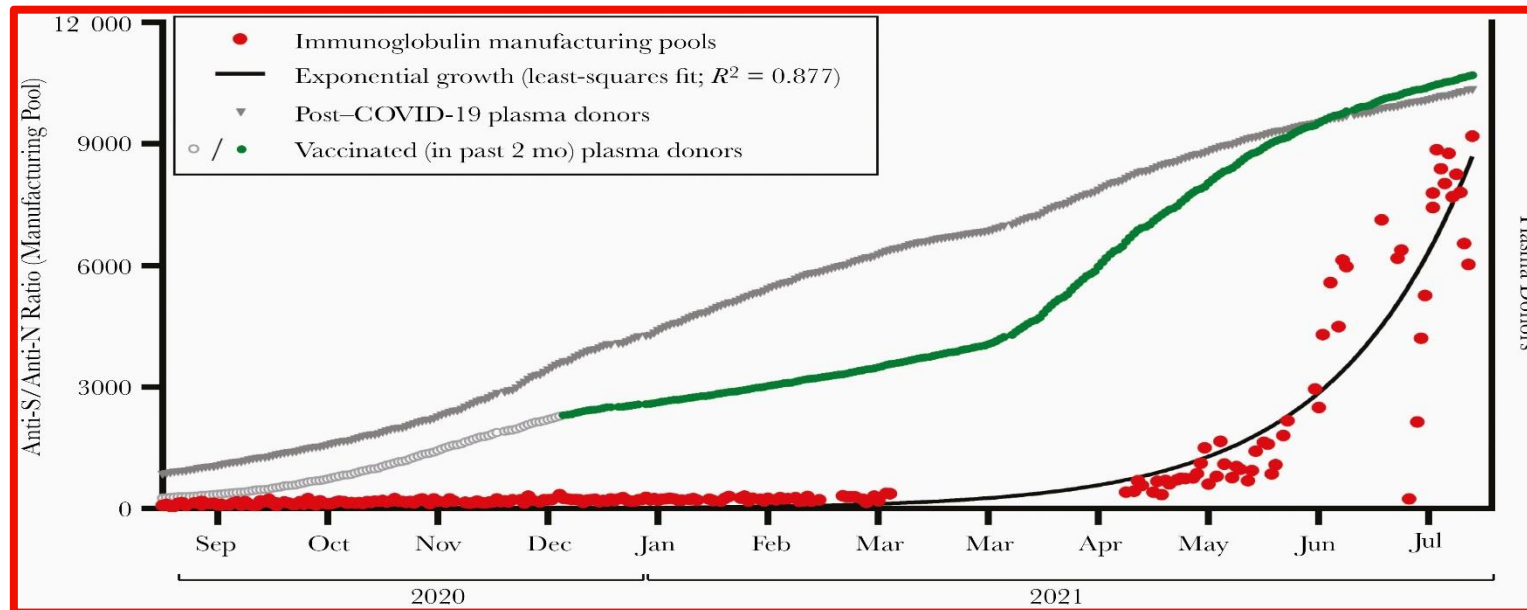
Highly Potent SARS-CoV-2
Neutralization by Intravenous
Immunoglobulins manufactured from
Post-COVID-19 and COVID-19-
Vaccinated Plasma Donations

Michael Karbiener,^{1,*} Maria R. Farcet,^{1,*} Julia Schwaiger,¹ Nicholas Powers,²
James Lenart,² Joseph M. Stewart,² Hema Tallman,² and Thomas R. Kreil¹

SARS-CoV-2 in the US, and Antibodies in IG: Highly Potent



- **Ratio anti-S : anti-N antibodies**
- „Vaccinated“,
before and **after COVID-19 vaccine availability**



The Journal of Infectious Diseases

BRIEF REPORT

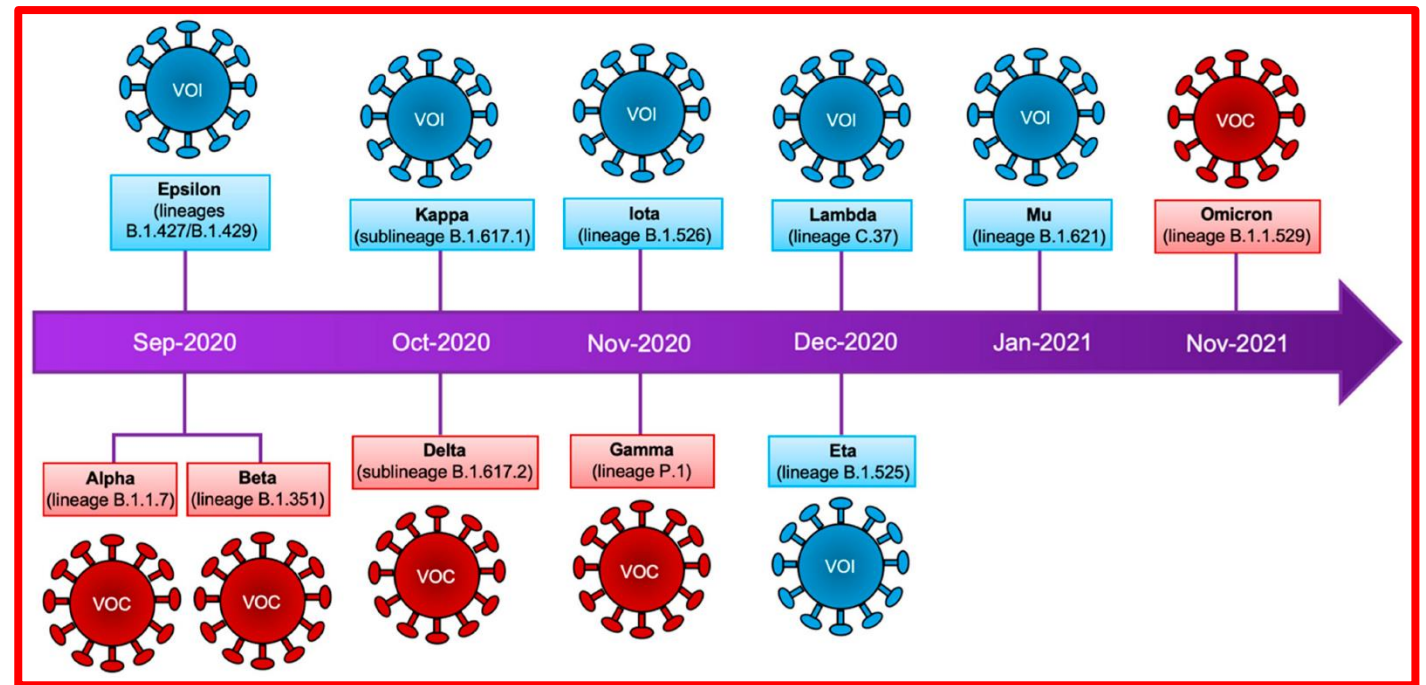
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SARS-CoV-2 in the US, and **Antibodies in IG: Highly Potent**



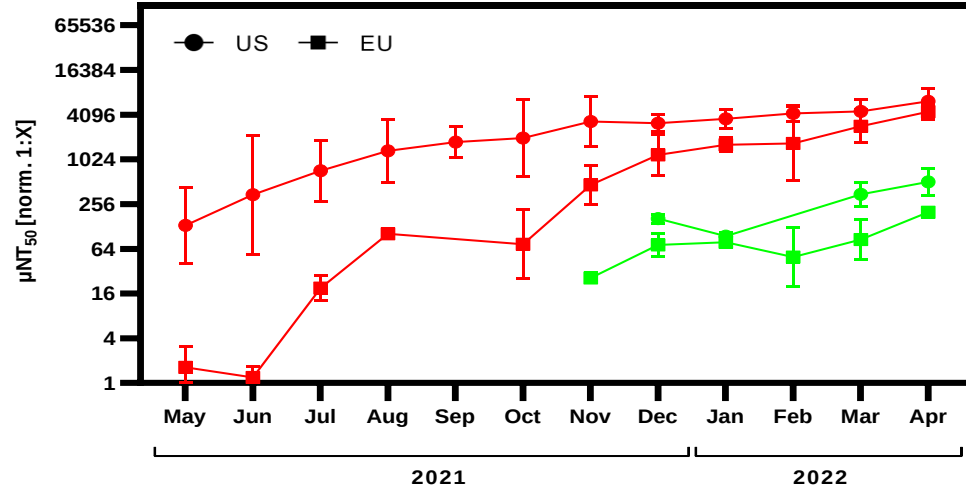
- „Highly potent “ → against the Wuhan SARS-CoV-2 prototype
- Virus variants ? Immune escape ?



SARS-CoV-2 Omicron, and Antibodies in IG



- **SARS-CoV-2 neutralization: high and consistent**
- **SARS-CoV-2 Omicron: ≤ 20 -fold lower, increasing**



JOURNAL ARTICLE ACCEPTED MANUSCRIPT

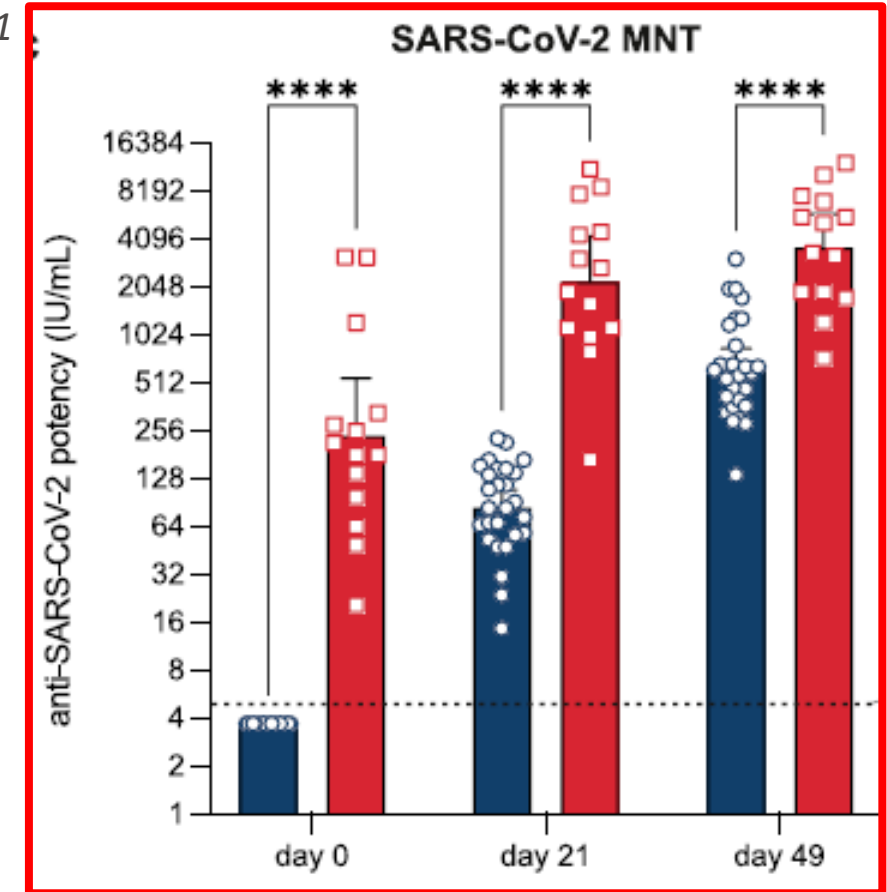
Omicron SARS-CoV-2 Neutralization by Immunoglobulin Preparations Manufactured from Plasma Collected in the US and Europe

Maria R Farcet, Michael Karbiener, Simone Knotzer, Julia Schwaiger, Thomas R Kreil

SARS-CoV-2 Neutralization by Plasma and IG: Medical Significance ?



- **Convalescent plasma**
 - 801 IU/mL GMT for top 20% of CP samples (n = 88).¹
- **Naive and convalescent + 2x vaccinated plasma**
 - 633 and 3,600 IU/ml GMT ²
- **IGs, April 2022**
 - Wuhan: US 11.226 and EU 8.146 IU/ml mean
 - Omicron: approx. 10 to 20-fold lower ³



1) Farcet MR, Karbiener M, Schwaiger J, Ilk R, and Kreil TR. Rapidly increasing ... *The Journal of Infectious Diseases* [2021] March 16

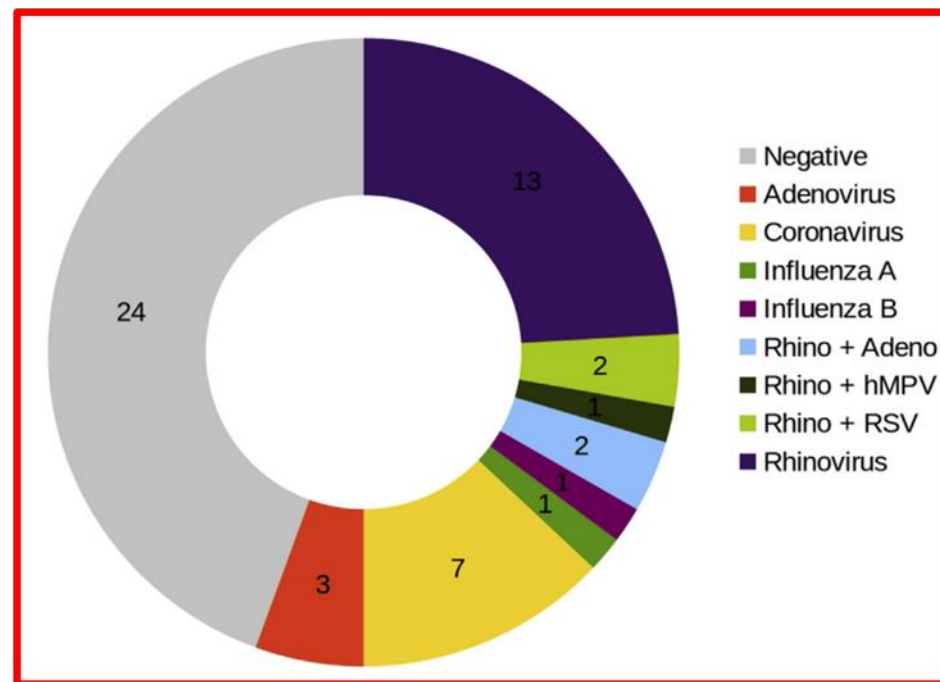
2) Zollner A, Watschinger C, Rössler A, Farcet MR, Penner A, Böhm V, Kiechl SJ, Stampfl G, Hintenberger R, Tilg H, Koch R, Antlanger M, Kreil TR, Kimpel J, Moschen AR. *EBioMed* 2021 70: 103539

3) Farcet MR, Karbiener M, Knotzer S, Schwaiger J, and Kreil TR. Omicron ... *The Journal of Infectious Diseases*, published 02 September 2022: jiac358, accessed at <https://doi.org/10.1093/infdis/jiac358>

- **CVID**

- *Even with immunoglobulin replacement, respiratory tract infections remain the commonest clinical feature in common variable immunodeficiency (CVID) and impair quality of life.*
- 69 patients, 6210 days of symptoms:
56% of respiratory exacerbations
→ pathogenic virus isolated
- 7 / 54 events, i.e. 13%, caused by Coronavirus

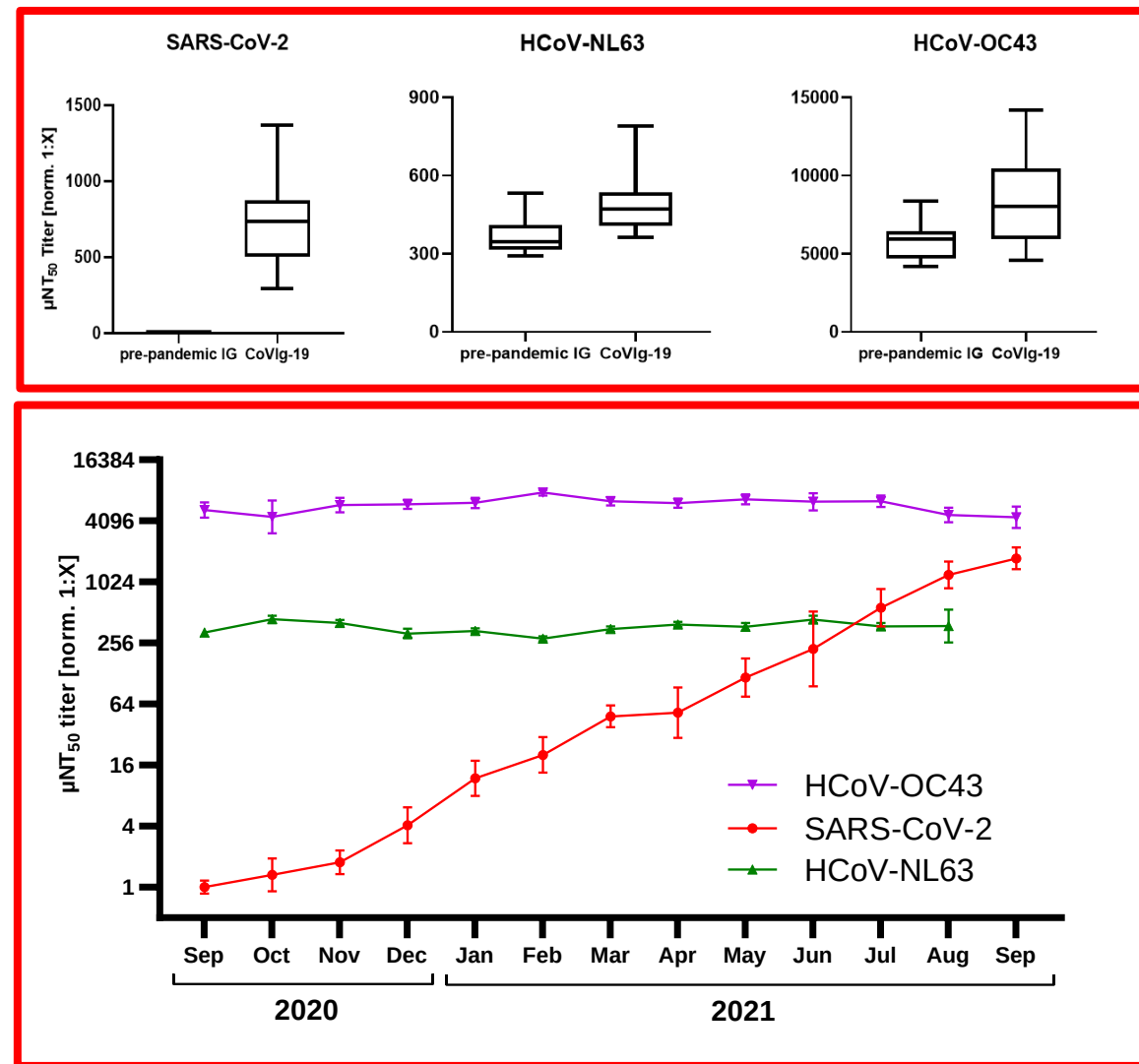
- Rising SARS-CoV-2 antibodies
→ protection against seasonal coronavirus ?



Cross-Coronavirus antibodies



- **Binding – YES** ¹
- **Neutralizing – NO** ²
 - CoVlg-19 versus pre-pandemic IG: minimally different neutralization
 - SARS-CoV-2 neutralization increase over time, but did **not** change for
 - OC43, another beta coronavirus
 - NL63, an alpha coronavirus that uses the same receptor as SARS-CoV-2



SARS-CoV-2 Antibodies in IG: **Summary**



- No SARS-CoV-2 Neutralization by IGs Produced From Plasma Collected Before the 2020 Pandemic ¹
- Rapidly Increasing SARS-CoV-2 Neutralization by IGs Produced From Plasma Collected During the 2020 Pandemic ²
- Highly Potent SARS-CoV-2 Neutralization by Intravenous Immunoglobulins manufactured from Post-COVID-19 and COVID-19-Vaccinated Plasma Donations ³
- Omicron SARS-CoV-2 Neutralization by Immunoglobulin Preparations Manufactured from Plasma Collected in the US and Europe ⁴
- Function matters: Coronavirus cross-binding antibodies do not cross-neutralize ⁵

THANK YOU !



Global Pathogen Safety

- Our Values „Up-Front“
 - Patient
 - Trust
 - Reputation
 - Business
- Living Our Values Every Day

