



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

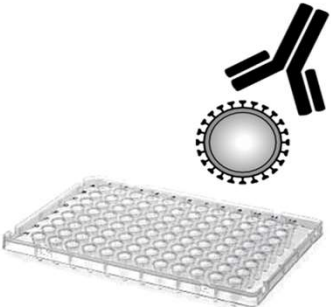
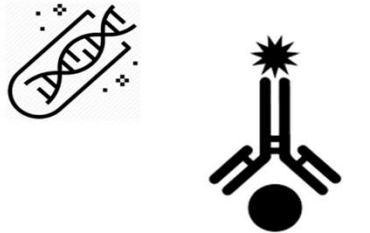
Thomas R. Kreil  
Global Pathogen Safety  
VirusSure Symposium  
September 23, 2022

# Viruses and Virus Neutralizing Antibodies



## Function Matters

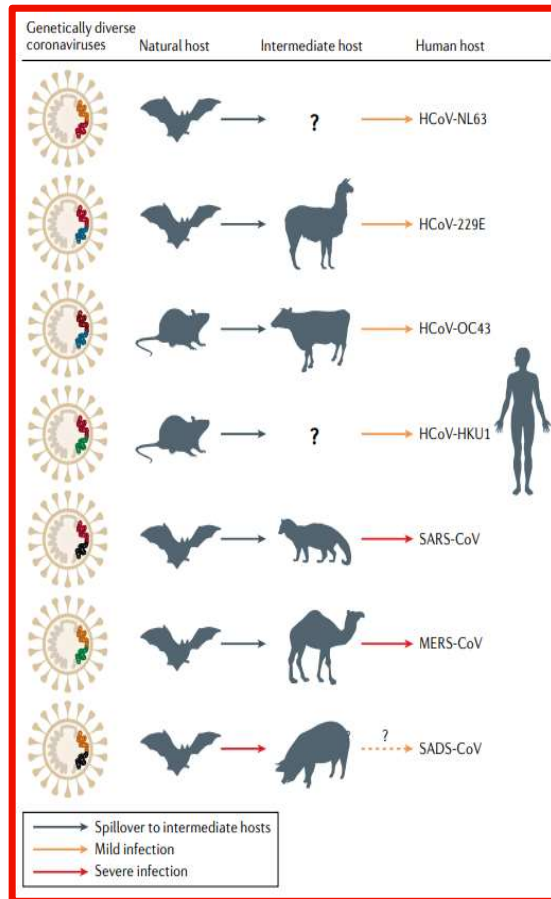
- Virus **infectivity**, rather than presence of nucleic acids
- Virus **neutralization**, rather binding of virus
- Basis: cell culture work, under biocontainment

Virus	Infectivity test	Nucleic acid test (e.g. PCR)
Antibody	Neutralization test, gold standard reference	Binding-assay (e.g. ELISA), unclear cross-reactivity
	 <ul style="list-style-type: none"><li>• <b>Biocontainment laboratory, BSL 3</b></li><li>• Cell culture</li><li>• Sterile work bench</li></ul>	 <ul style="list-style-type: none"><li>• More simple diagnostic lab</li><li>• PoC (?)</li></ul>

# 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

| Origin and Evolution of Pathogenic Coronaviruses, Nature Reviews [2019] 17:181

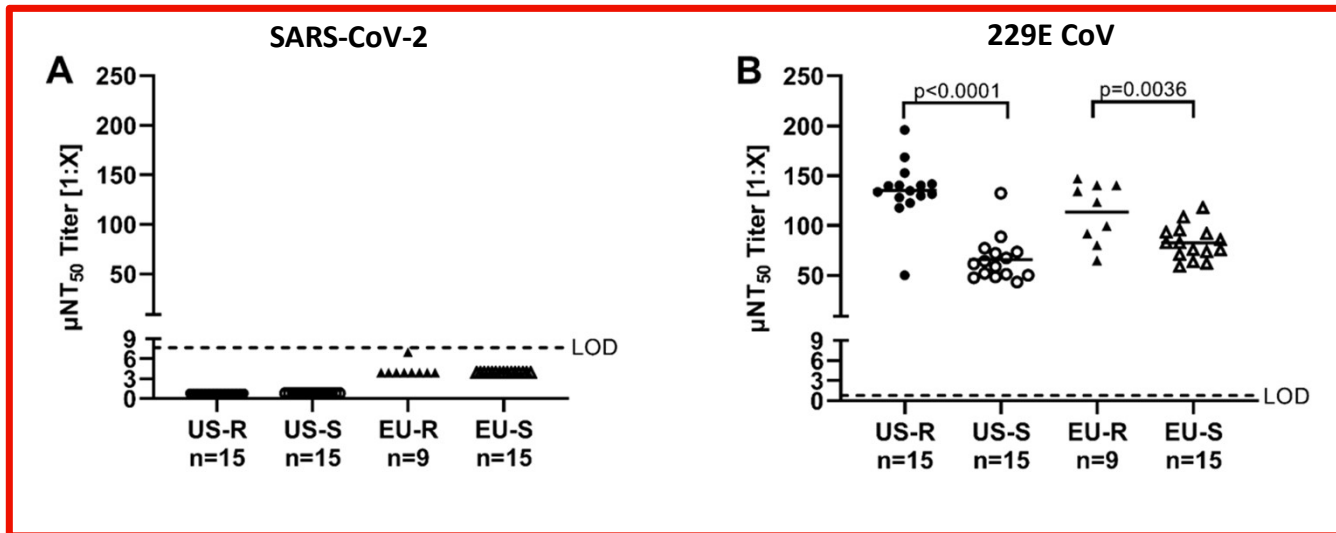
1 | Novel **Canine** Coronavirus Isolated from a Hospitalized Pneumonia Patient, East Malaysia, Clin Inf Dis [2022] 74:446

| Independent infections of **porcine deltacoronavirus** among Haitian children, Nature [2021] 600:133

# 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**

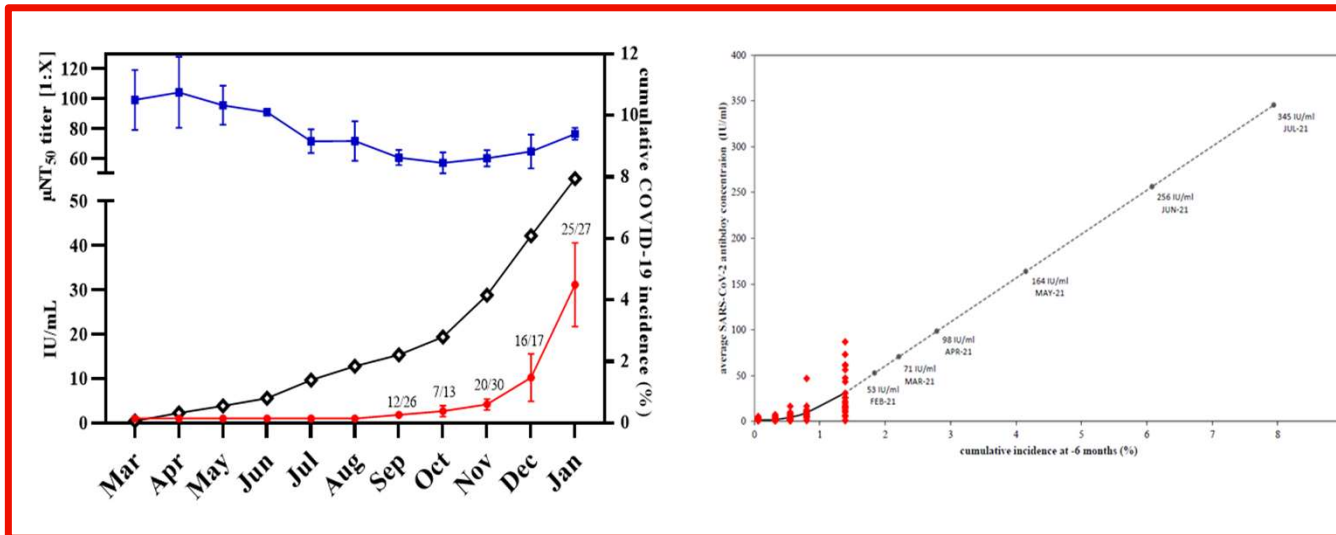
No SARS-CoV-2 Neutralization by Intravenous Immunoglobulins Produced From Plasma Collected Before the 2020 Pandemic

Julia Schwaiger,<sup>1</sup> Michael Karbiener,<sup>1</sup> Claudia Aberham,<sup>2</sup> Maria R. Farcet,<sup>1</sup> and Thomas R. Kreil<sup>1</sup>

# 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,<sup>1</sup> Michael Karbiener,<sup>1</sup> Julia Schwaiger,<sup>1</sup> Reinhard Ilk,<sup>2</sup> and Thomas R. Kreil<sup>1</sup>

The scatter plot shows a positive correlation between cumulative incidence at -6 months (%) on the x-axis (0-9) and average SARS-CoV-2 antibody concentration (IU/ml) on the y-axis (0-400). A dashed diagonal line represents the trend. Data points are labeled with dates and antibody concentrations: 53 IU/ml FEB-21, 71 IU/ml MAR-21, 98 IU/ml APR-21, 164 IU/ml MAY-21, 256 IU/ml JUN-21, and 345 IU/ml JUL-21.

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



### 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

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



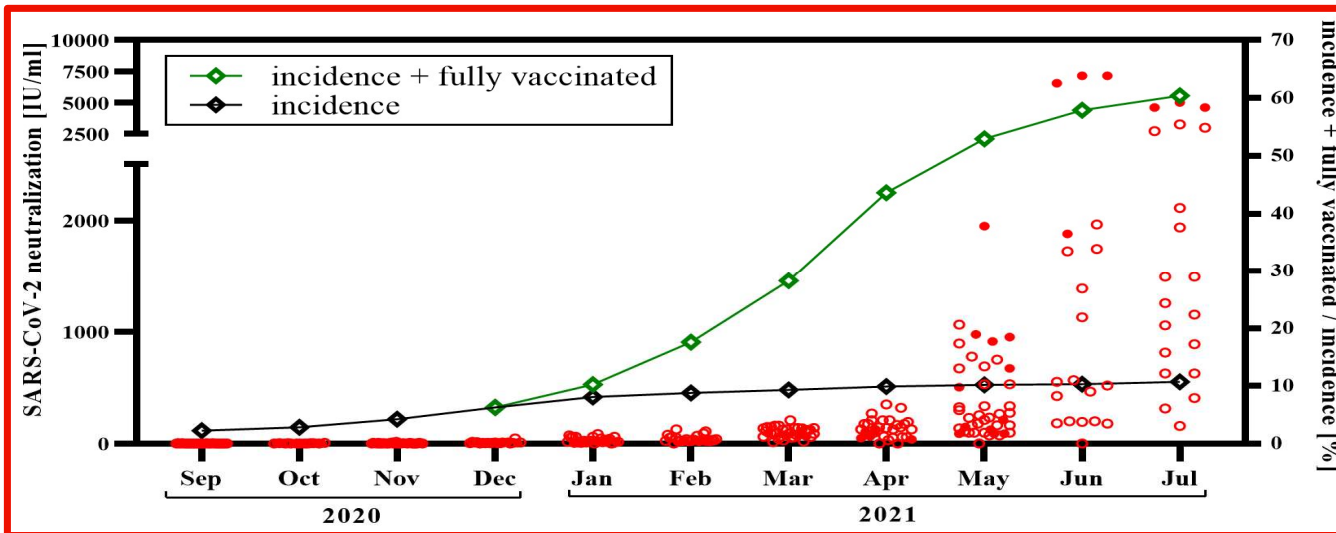
## July 2021

- 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**

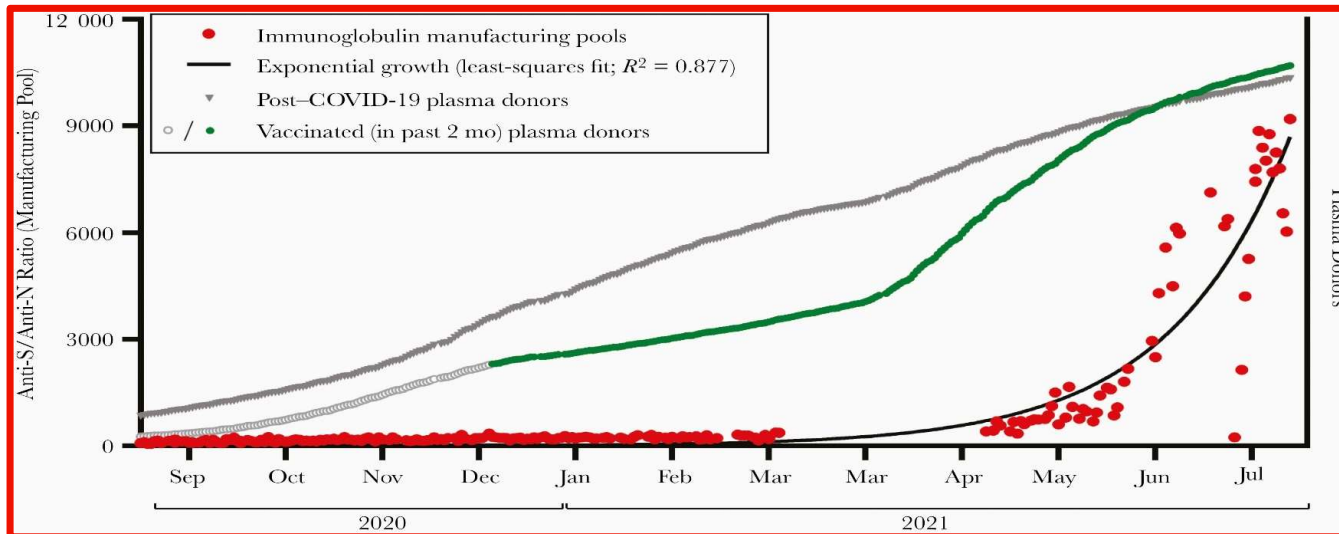
Michael Karbiener,<sup>1,2</sup> Maria R. Farcet,<sup>1,2</sup> Julia Schwaiger,<sup>1</sup> Nicholas Powers,<sup>2</sup> James Lenart,<sup>2</sup> Joseph M. Stewart,<sup>2</sup> Hema Tallman,<sup>2</sup> and Thomas R. Kreil<sup>1</sup>



# 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**



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**BRIEF REPORT**

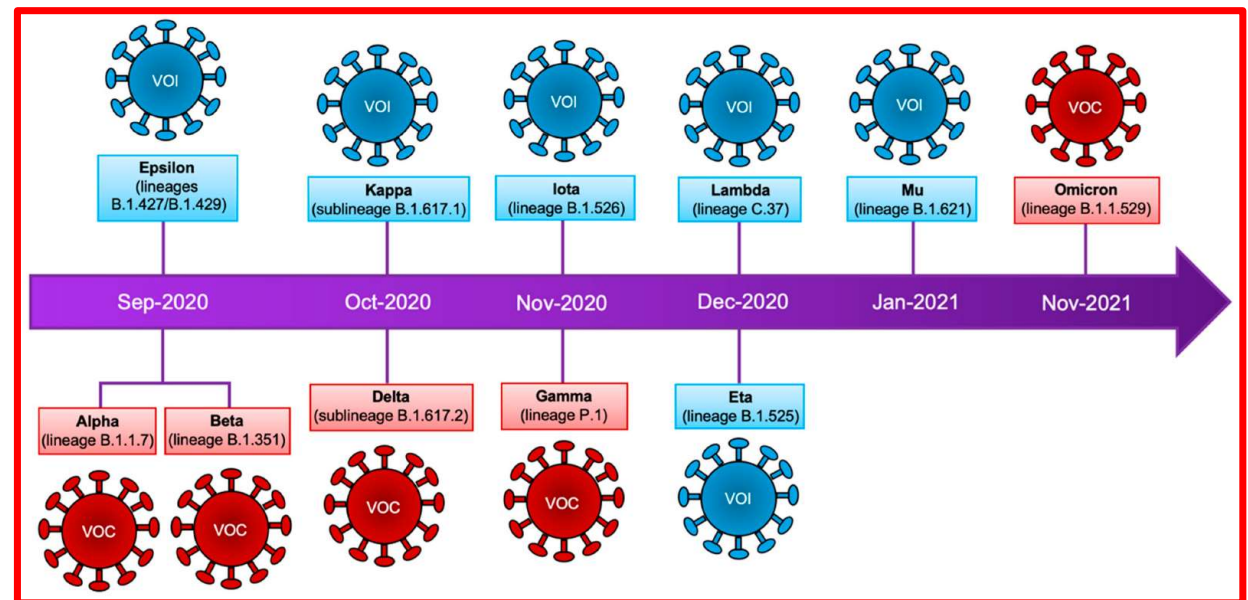
**Highly Potent SARS-CoV-2 Neutralization by Intravenous Immunoglobulins manufactured from Post-COVID-19 and COVID-19-Vaccinated Plasma Donations**

Michael Karbiener,<sup>1,2</sup> Maria R. Farcet,<sup>1,2</sup> Julia Schwaiger,<sup>1</sup> Nicholas Powers,<sup>2</sup> James Lenart,<sup>2</sup> Joseph M. Stewart,<sup>2</sup> Hema Tallman,<sup>2</sup> and Thomas R. Kreil<sup>1</sup>

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



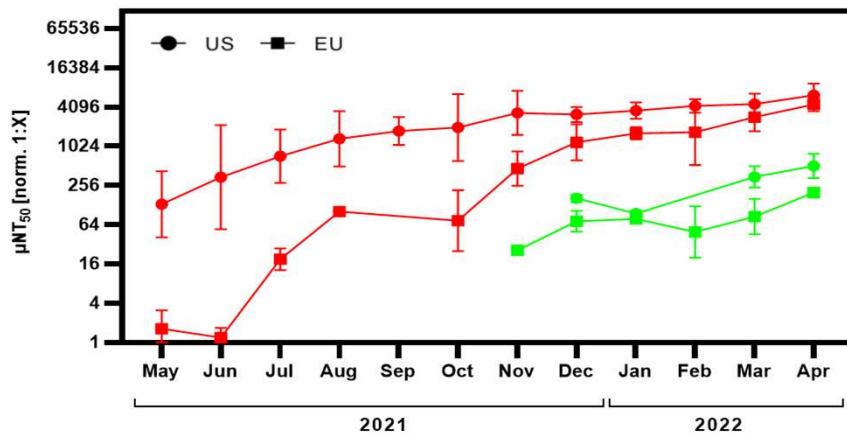
- „Highly potent “ → against the Wuhan SARS-CoV-2 prototype
- Virus variants ? Immune escape ?



# SARS-CoV-2 Omicron, and Antibodies in IG



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



JOURNAL ARTICLE ACCEPTED MANUSCRIPT

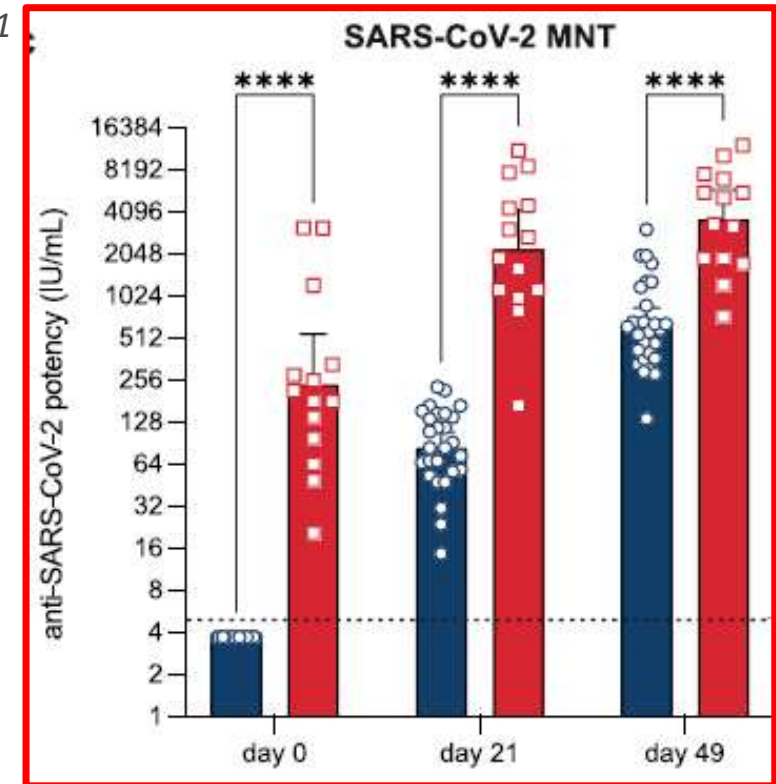
## Omicron SARS-CoV-2 Neutralization by Immunoglobulin Preparations Manufactured from Plasma Collected in the US and Europe

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).<sup>1</sup>
- **Naive and convalescent + 2x vaccinated plasma**
  - 633 and 3,600 IU/ml GMT <sup>2</sup>
- **IGs, April 2022**
  - Wuhan: US 11.226 and EU 8.146 IU/ml mean  
Omicron: approx. 10 to 20-fold lower <sup>3</sup>



| 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>

# Cross-Coronavirus Antibodies



- **CVID**

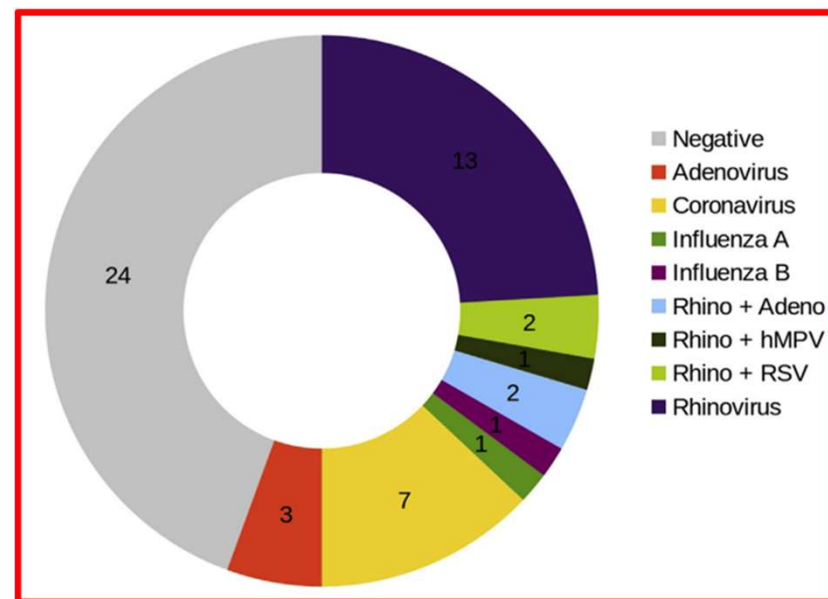
- *Even with immunoglobulin replacement, respiratory tract infections remain the commonest clinical feature in common variable immunodeficiency (CVID) and impair quality of life.*

- 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

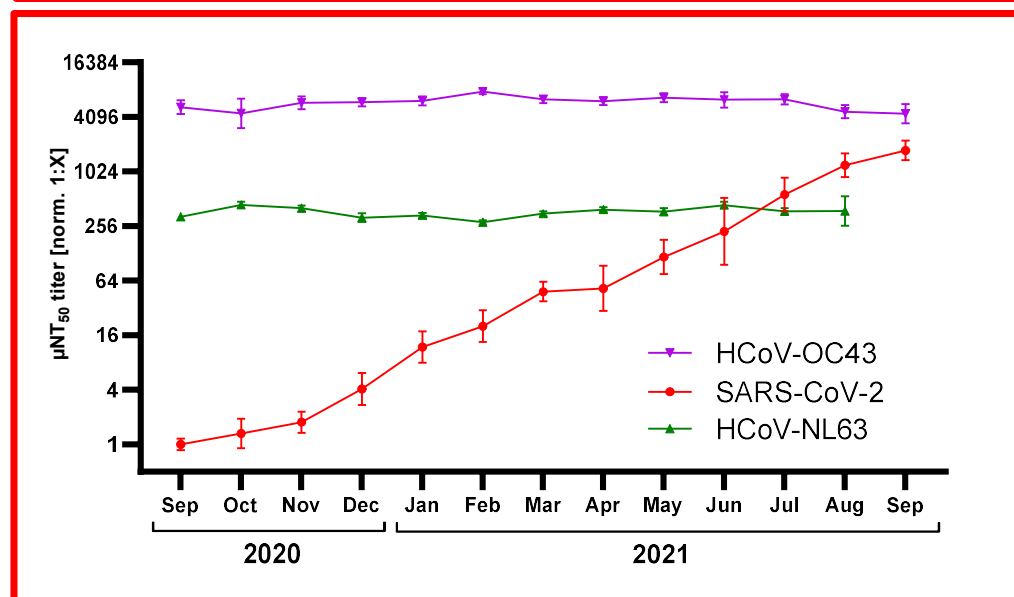
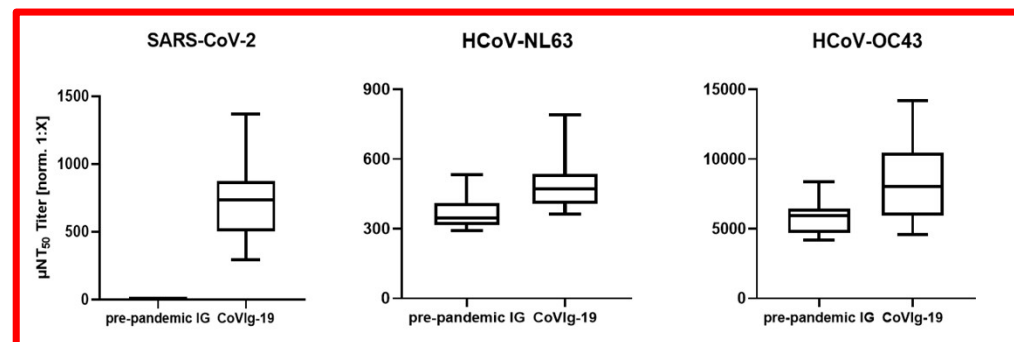
- protection against seasonal coronavirus ?



# Cross-Coronavirus antibodies



- **Binding – YES** <sup>1</sup>
- **Neutralizing – NO** <sup>2</sup>
  - 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



13 | 1) Kaplonek P et al., Science Immunology [2021] 6/64: September 9, 2021; Early cross-coronavirus reactive signatures of humoral immunity against COVID-19  
| 2) Farcet MR, Schwaiger J, Karbiener M, Kreil TR, Front Med [2022] 9: 924426 - August 2, 2022; Function matters: Coronavirus cross-binding antibodies do not cross-neutralize

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



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

THANK YOU !



## Global Pathogen Safety

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

