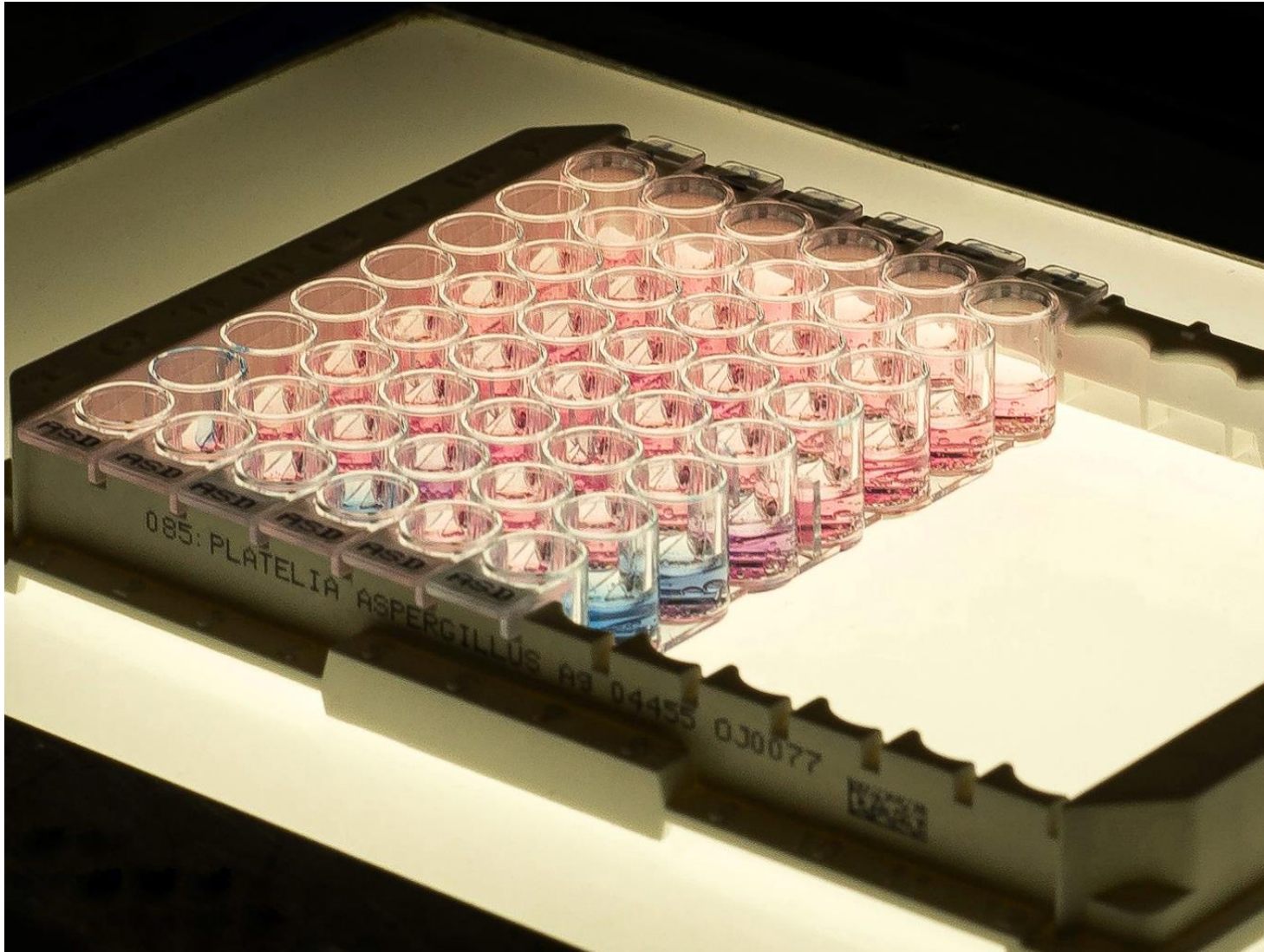


A microscopic image showing a large, spherical virus particle with a textured surface, likely a coronavirus, against a green background. The particle is the central focus, with other smaller particles visible in the background.

SARS CoV-2 immunity from a clinical perspective

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The use of SARS CoV-2 serology in clinical practice



The use of SARS CoV-2 serology in clinical practice

1. How good is SARS CoV-2 serology?
2. Use of IgG binding as correlate of protection in HC?

The use of SARS CoV-2 serology in clinical practice

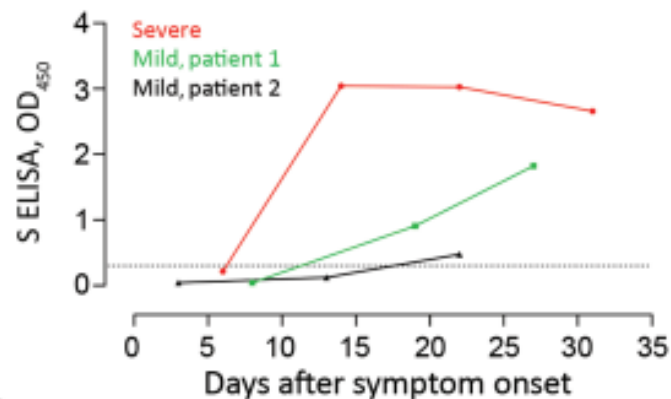
1. How good is SARS CoV-2 serology?
2. Use of IgG binding as correlate of protection?

Validation of SARS CoV-2 serology...this was just the start

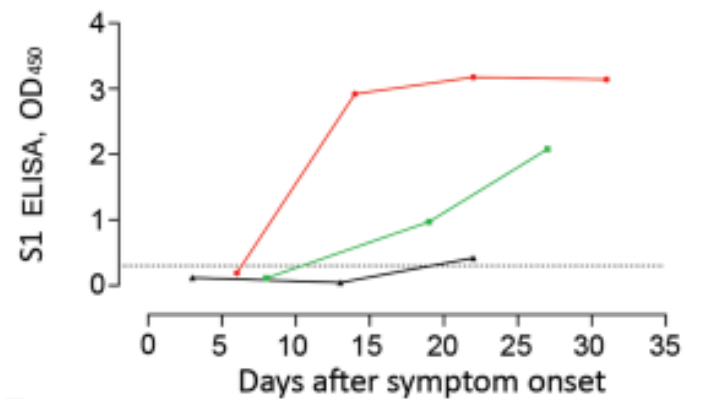
Table 1. Cohorts used to validate specificity and sensitivity of assays for SARS-CoV-2*

Cohort	Country	Sample source	Infection	No. samples	Postdiagnosis range or time
A	The Netherlands	Healthy blood donors (negative cohort)	NA	45	NA
B	The Netherlands	Non-CoV respiratory infections†	Adenovirus	5	2-4 wk
			Bocavirus	2	2-4 wk
			Enterovirus	2	2-4 wk
			HMPV	9	2-4 wk
			Influenza A	13	2-4 wk
			Influenza B	6	2-4 wk
			Rhinovirus	9	2-4 wk
			RSV	9	2-4 wk
			PIV-1	4	2-4 wk
			PIV-3	4	2-4 wk
			<i>Mycoplasma pneumoniae</i>	1	2-4 wk
			CMV	5	2-4 wk
			ERV	7	2-4 wk
C	The Netherlands	HCoV infections†	α-1 α-2 β-1		
D	The Netherlands South Korea	Zoonotic CoV infections†			
E	Hong Kong, China	Zoonotic CoV infection†			
F	France	RT-PCR confirmed SARS-CoV-2 infections			

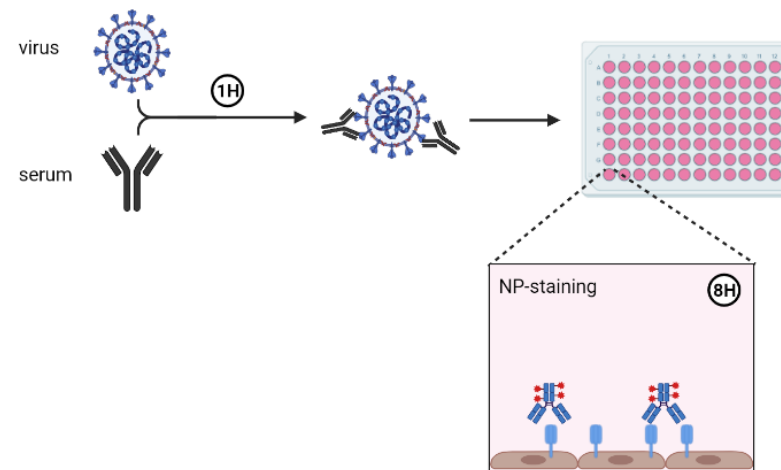
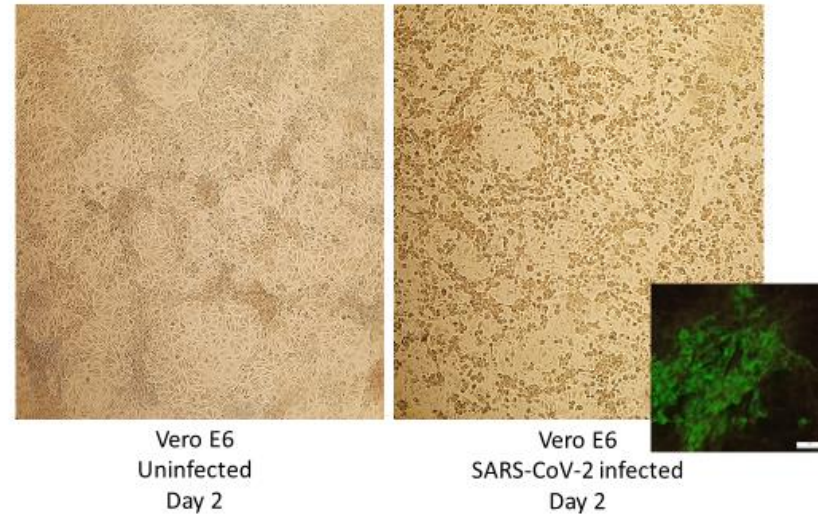
A



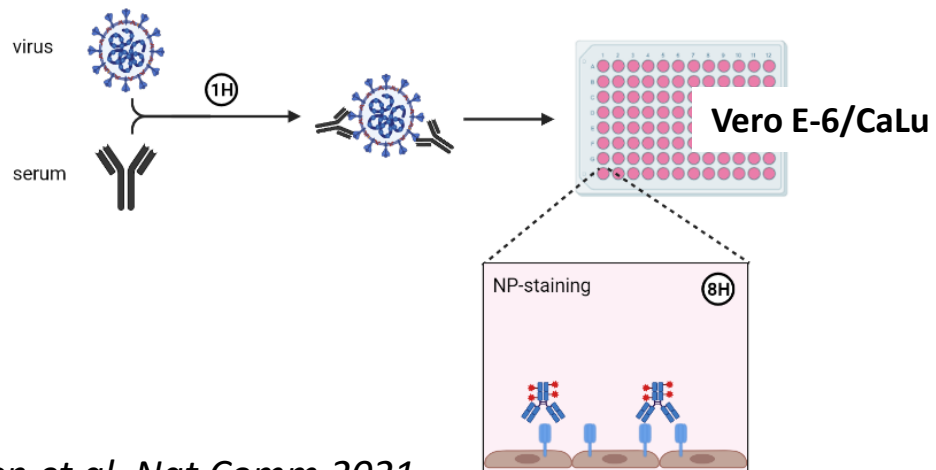
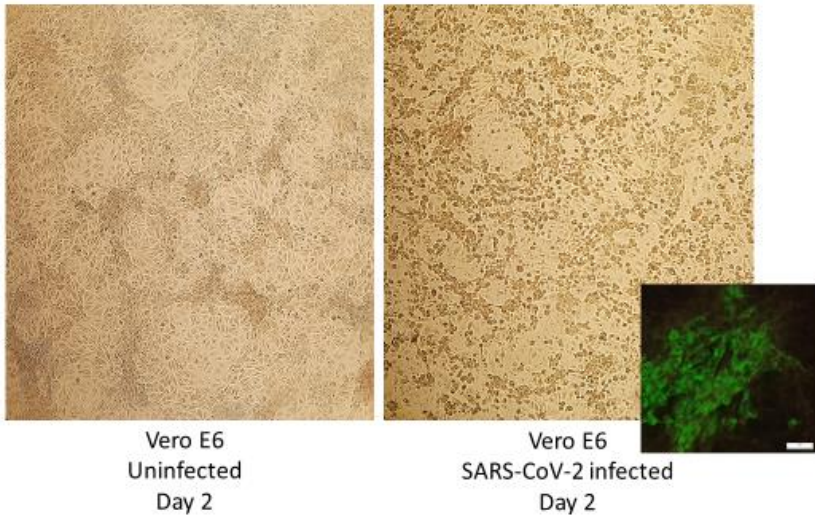
B



Validation of SARS CoV-2 serology: virus neutralization



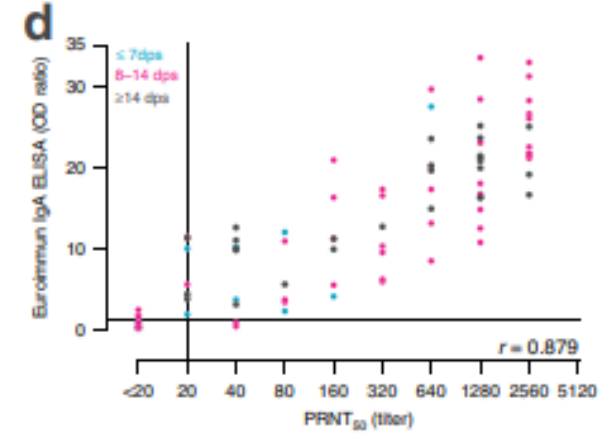
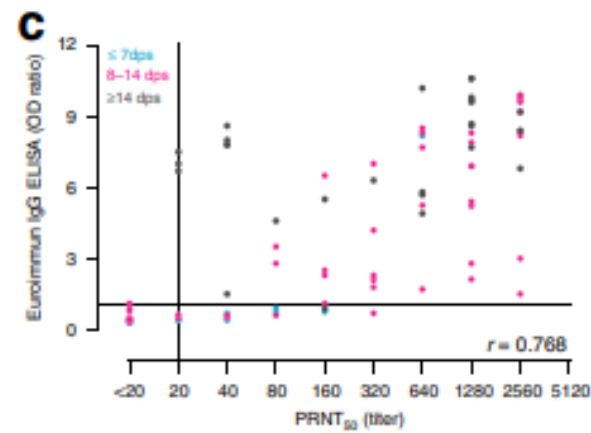
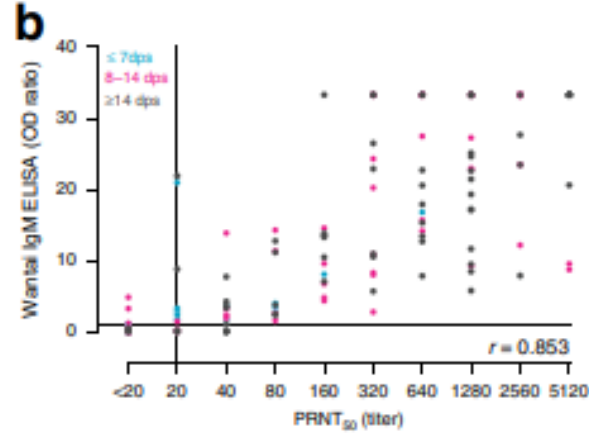
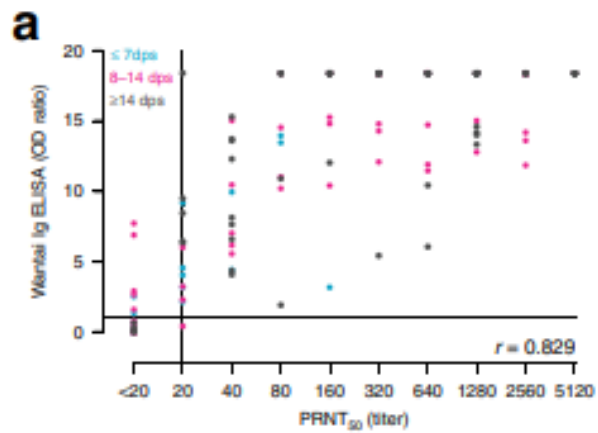
Determining functionality of antibodies by virus neutralization



titer	n	POS	NEG
< 1:20	31	27 (87%)	4 (13%)
1:20	10	4 (40%)	6 (60%)
1:40	7	2 (29%)	5 (71%)
1:80	2	0 (0%)	2 (100%)
1:160	4	0 (0%)	4 (100%)
1:320	11	0 (0%)	11 (100%)
1:640	9	0 (0%)	9 (100%)
1:1280	14	0 (0%)	14 (100%)
1:2560	16		

Probability <5% when PRNT is at least 1:80

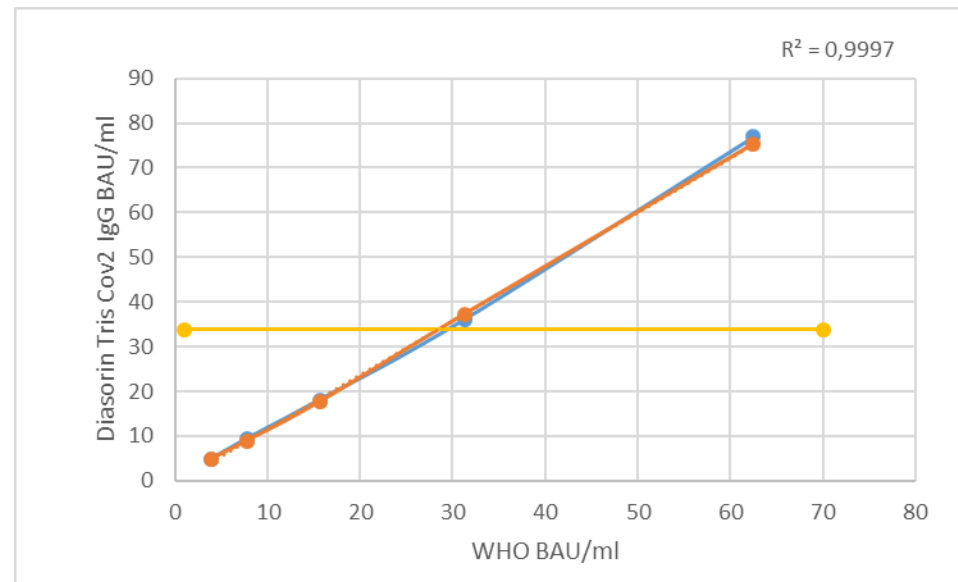
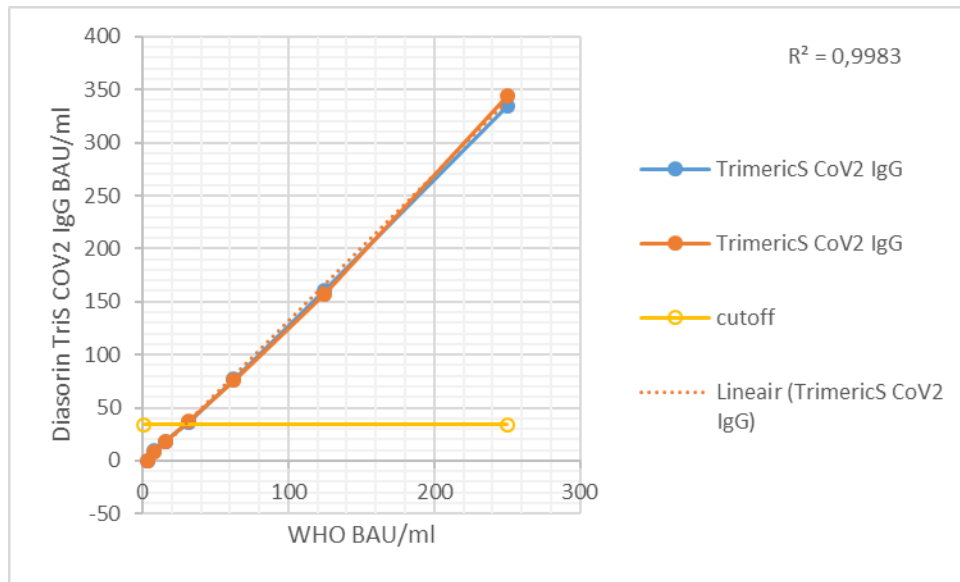
Validation of SARS CoV-2 serology: assay comparison



Timing
Severity of disease
Used antigen

Validation of SARS CoV-2 serology: assay comparison

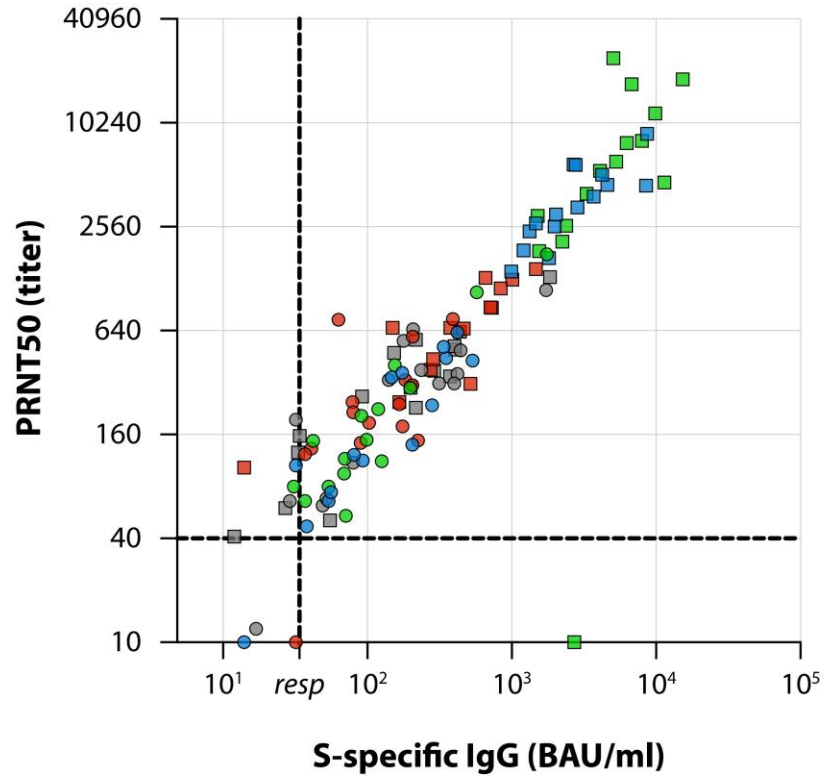
DiaSorin Trimeric SARS CoV-2 IgG anti Spike



DiaSorin TrimericS CoV2 IgG : 7.8125-250 BAU/ml

Validation of SARS CoV-2 serology: current situation

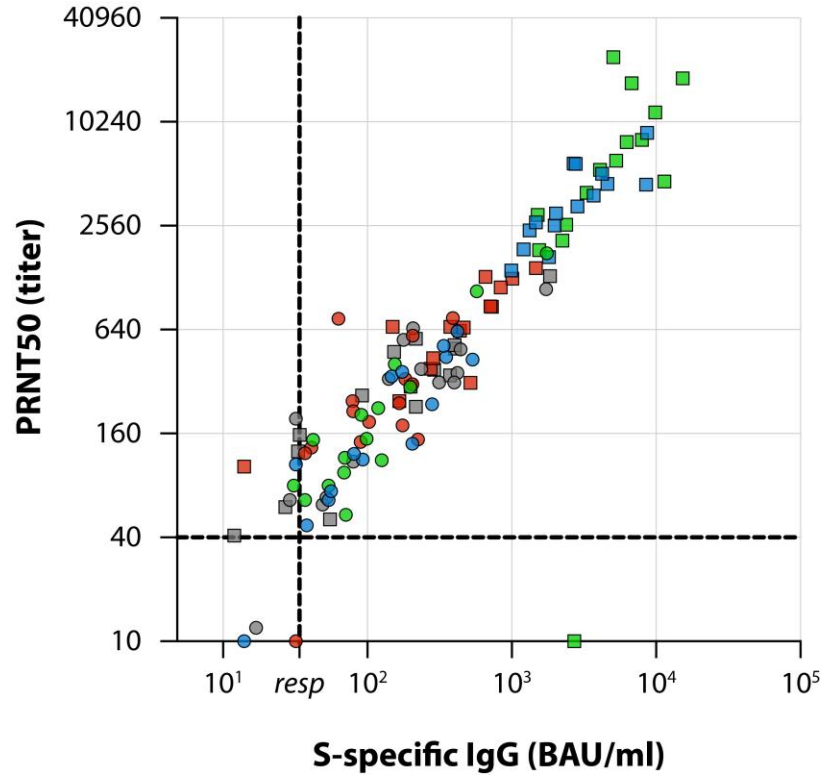
Wild type virus



Liaison Trimeric S

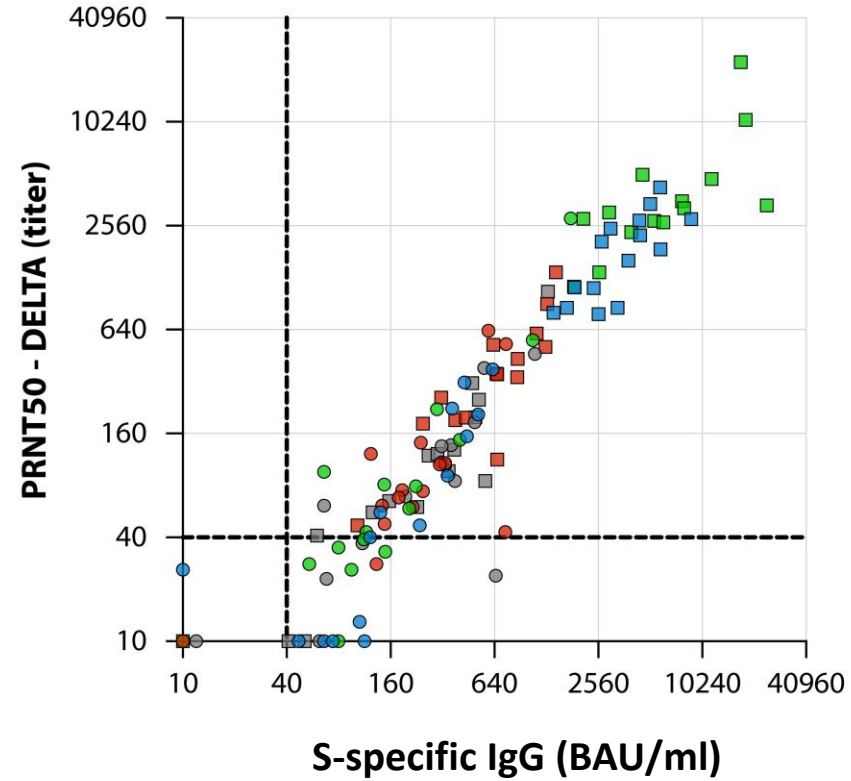
Validation of SARS CoV-2 serology: current situation

Wild type virus



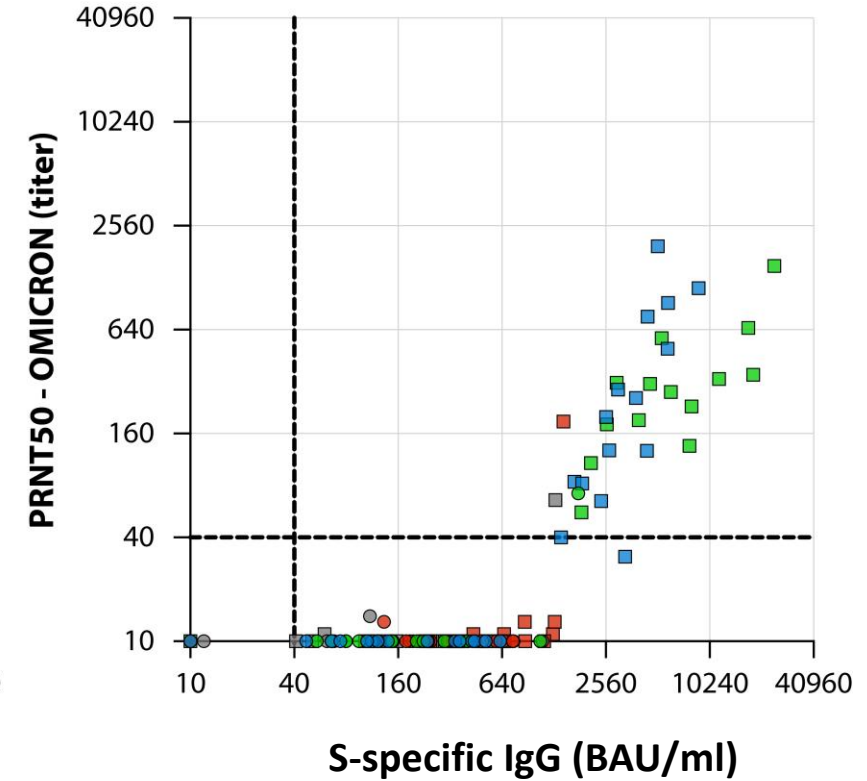
Liaison Trimeric S

Delta



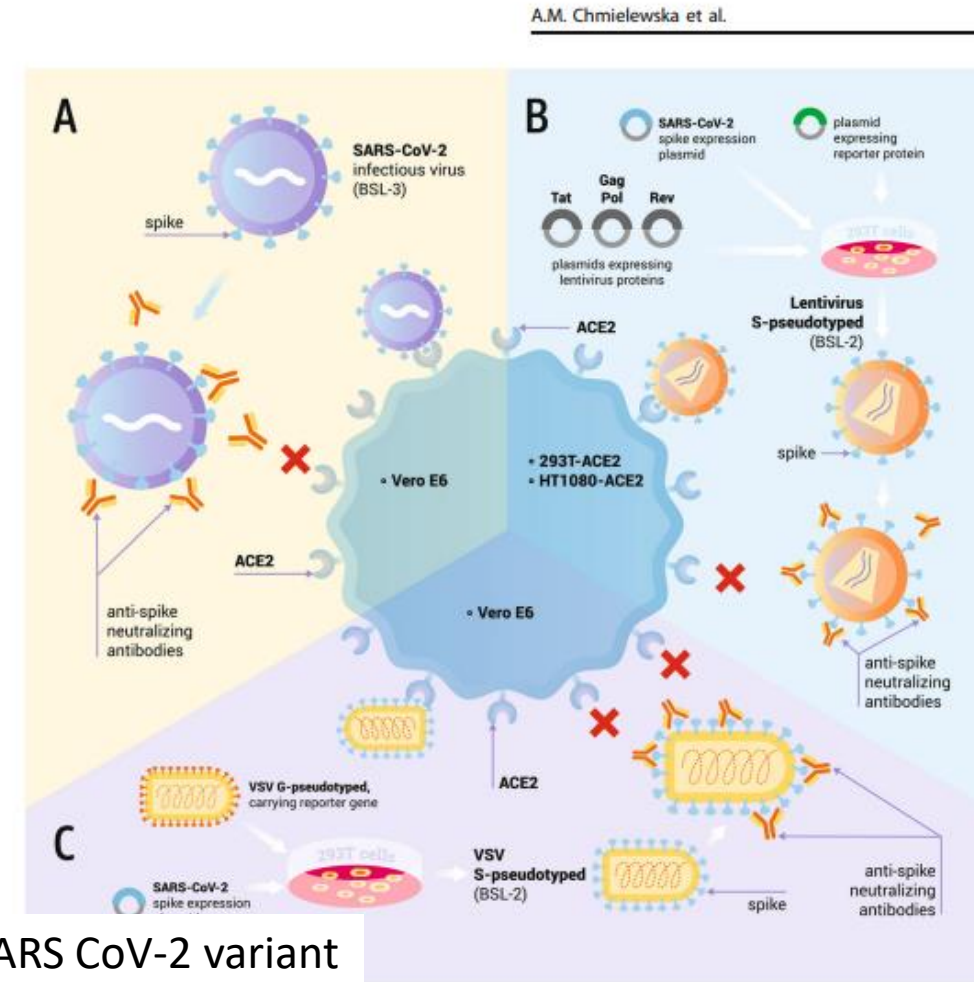
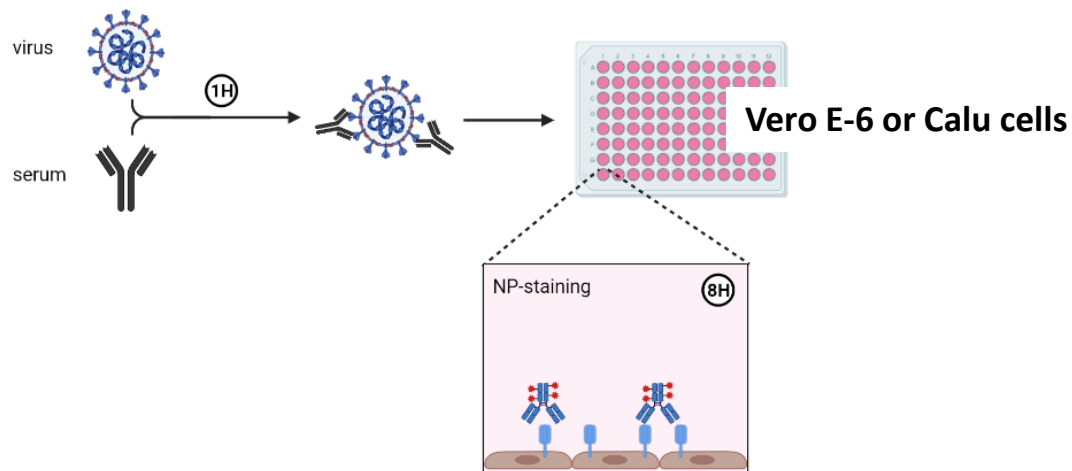
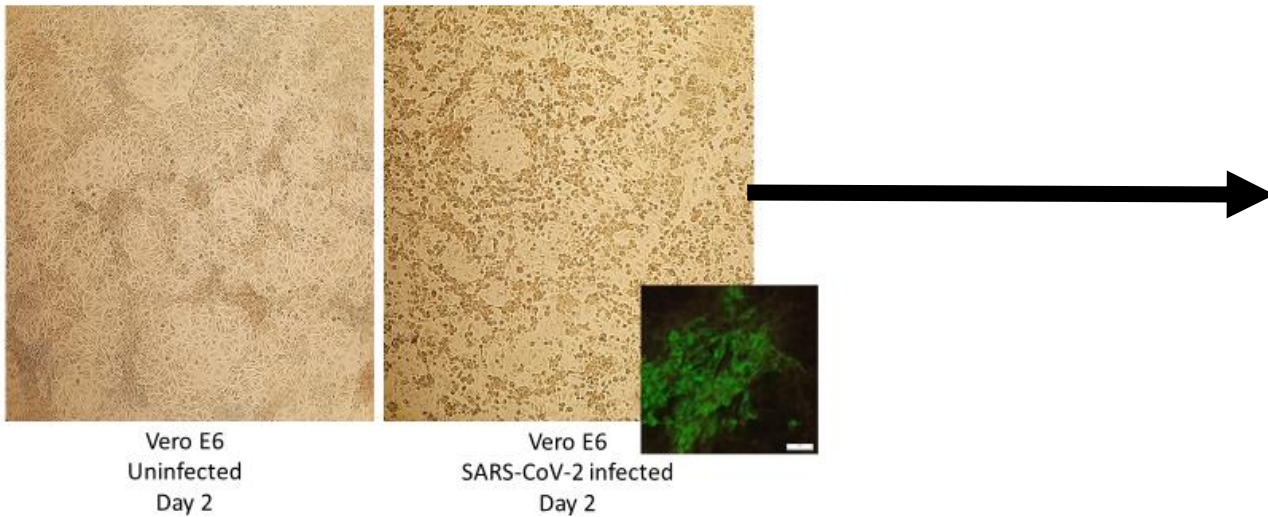
Liaison Trimeric S

Omicron



Liaison Trimeric S **MC**
Amsterdam
2afms

Determining functionality of antibodies by virus neutralization



- Type of SARS CoV-2 variant
- Type of cells
- Incubation
- Live virus or pseudotyped

The use of SARS CoV-2 serology in clinical practice

1. How good is SARS CoV-2 serology?
2. Use of IgG binding as correlate of protection?



- **Correlates of protection:**

Measurable signs that a person is immune, in the sense of being protected against becoming infected and/or developing disease

- **Antibodies**

- SARS-CoV-2-specific antibodies bind to the virus, and can prevent infection of cells



- **T-cells**

- SARS-CoV-2-specific T-cells recognize infected cells, leading to viral clearance





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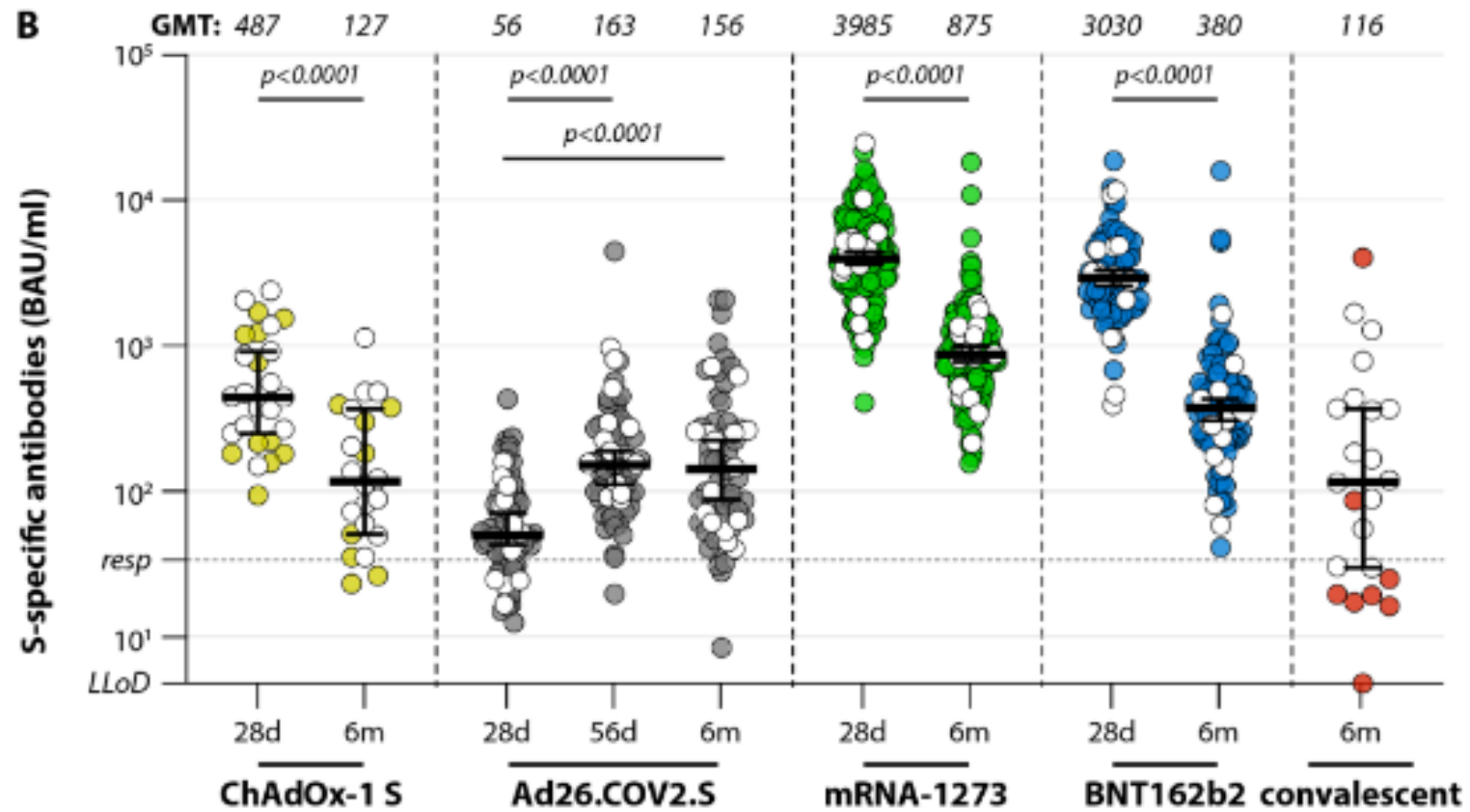
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Interpretation of serological results

- **Kinetics** of antibody levels in time, stratified by **vaccine** platform
- **Functionality** of antibodies (binding versus neutralizing antibodies)
- Comparison of methods and **standardization**
- **Patient characteristics** : immune suppression/ COVID treatment

Kinetics of binding antibody responses in healthy individuals



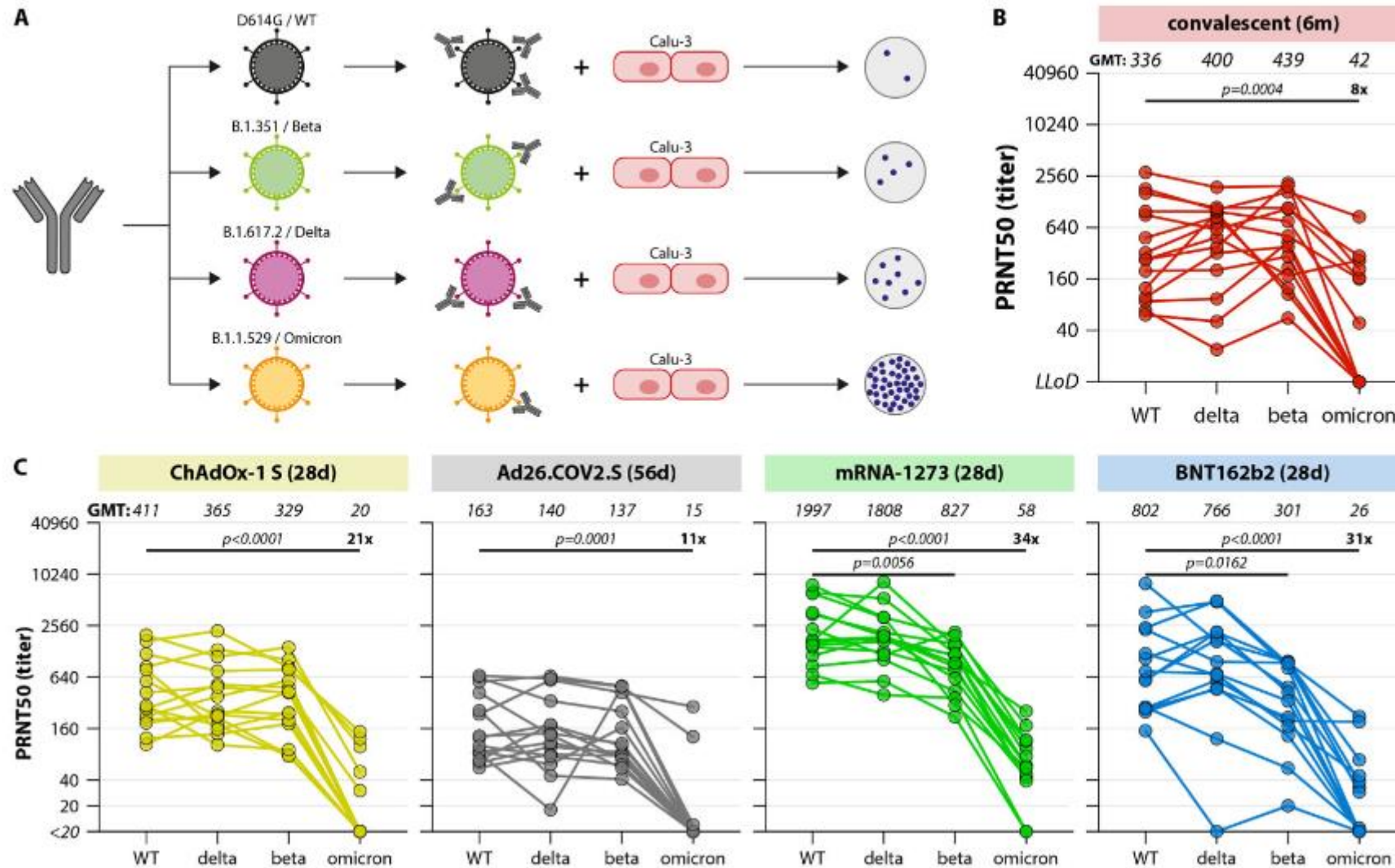
AZ

Janssen

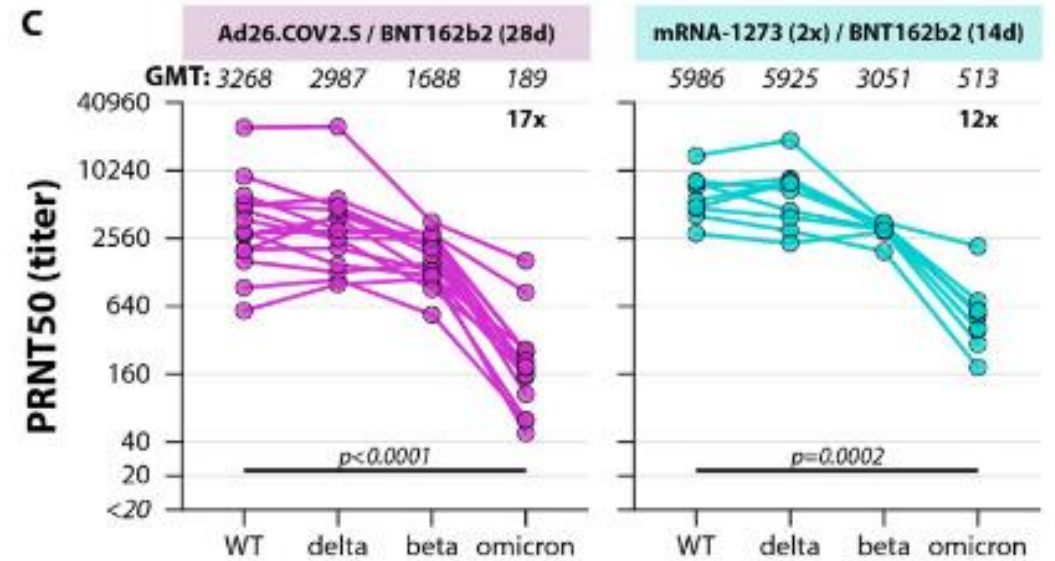
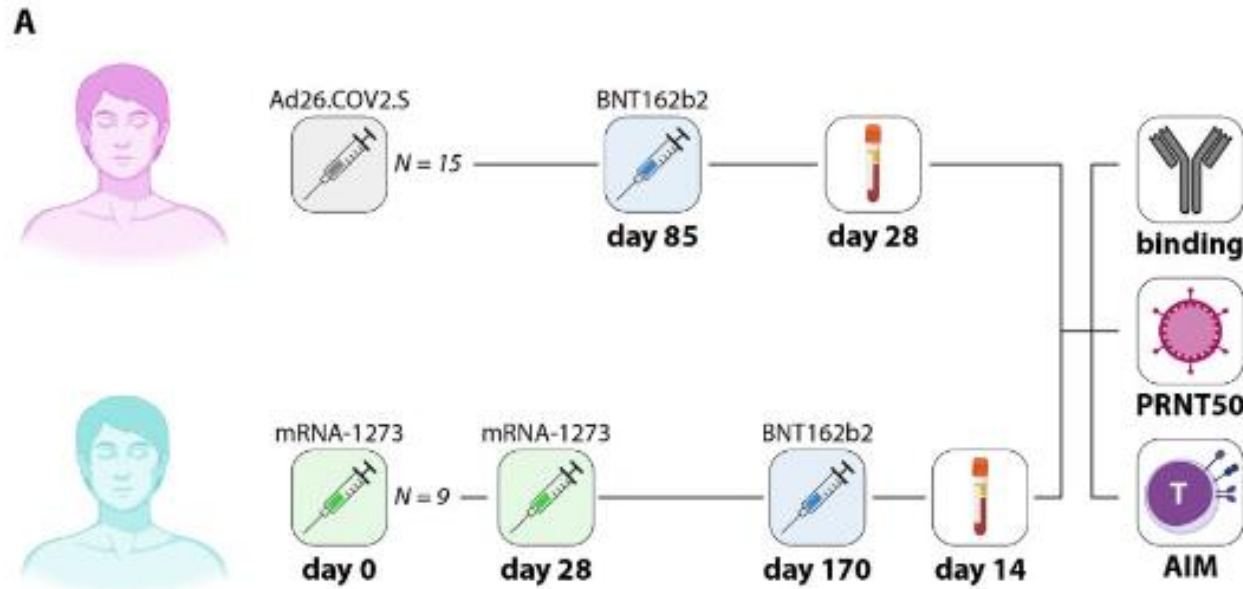
Moderna

Pfizer

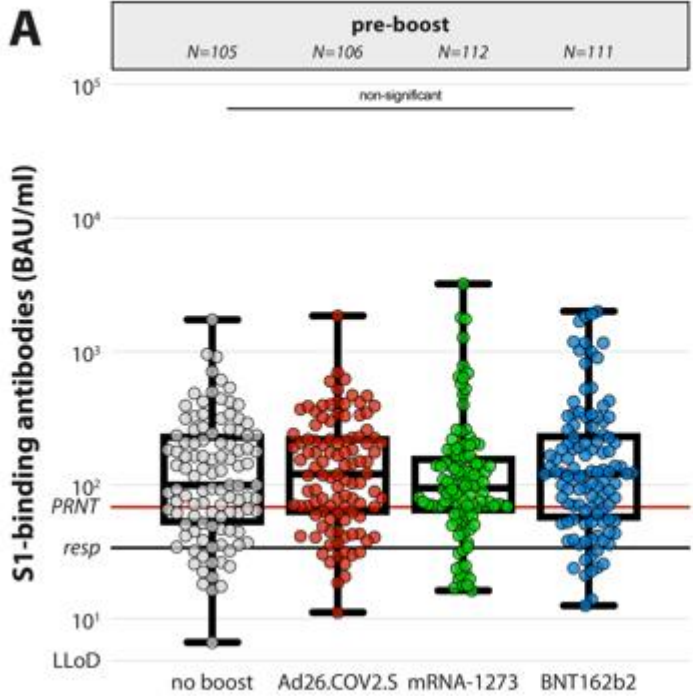
Determining functionality of antibodies by virus neutralization



Booster response in healthy individuals

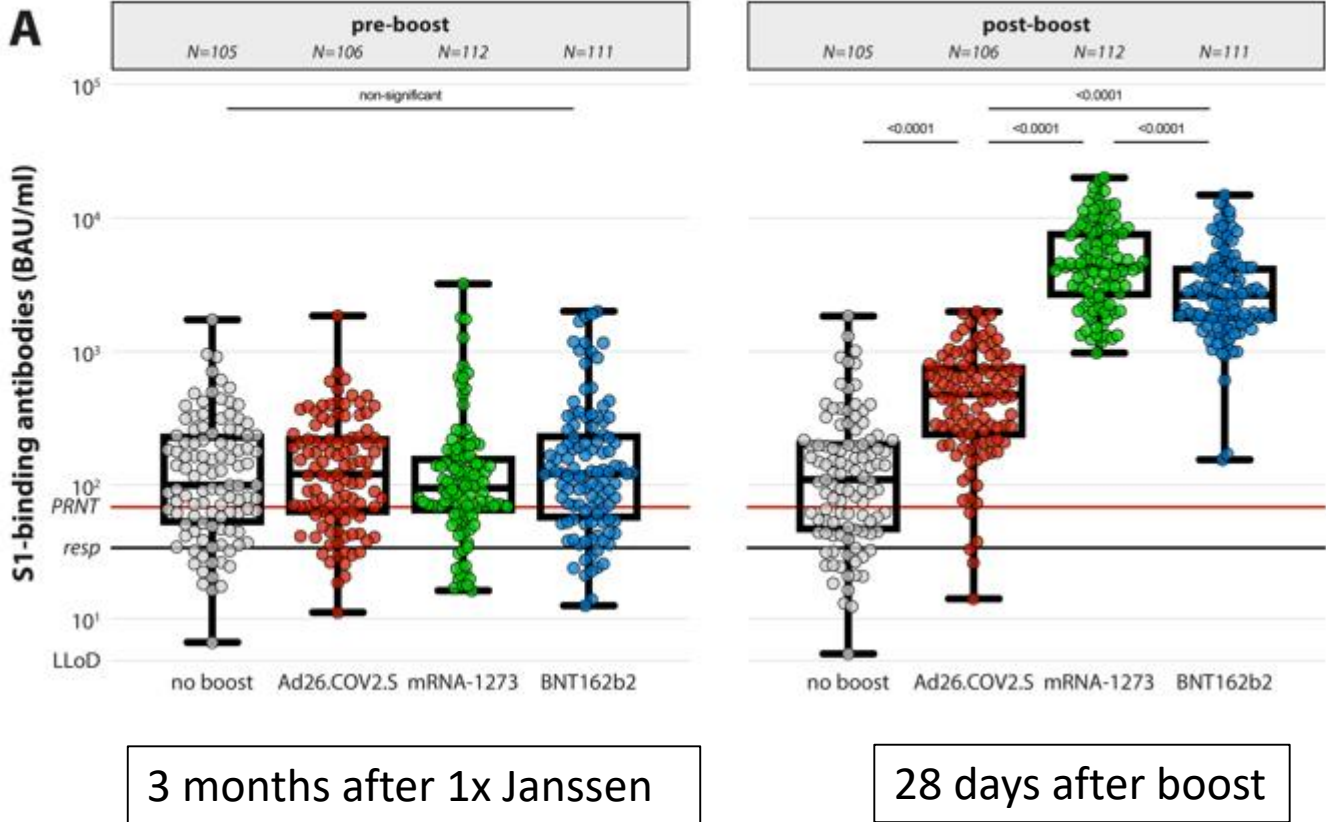


Binding antibodies upon heterologous boosting of Janssen vaccinees

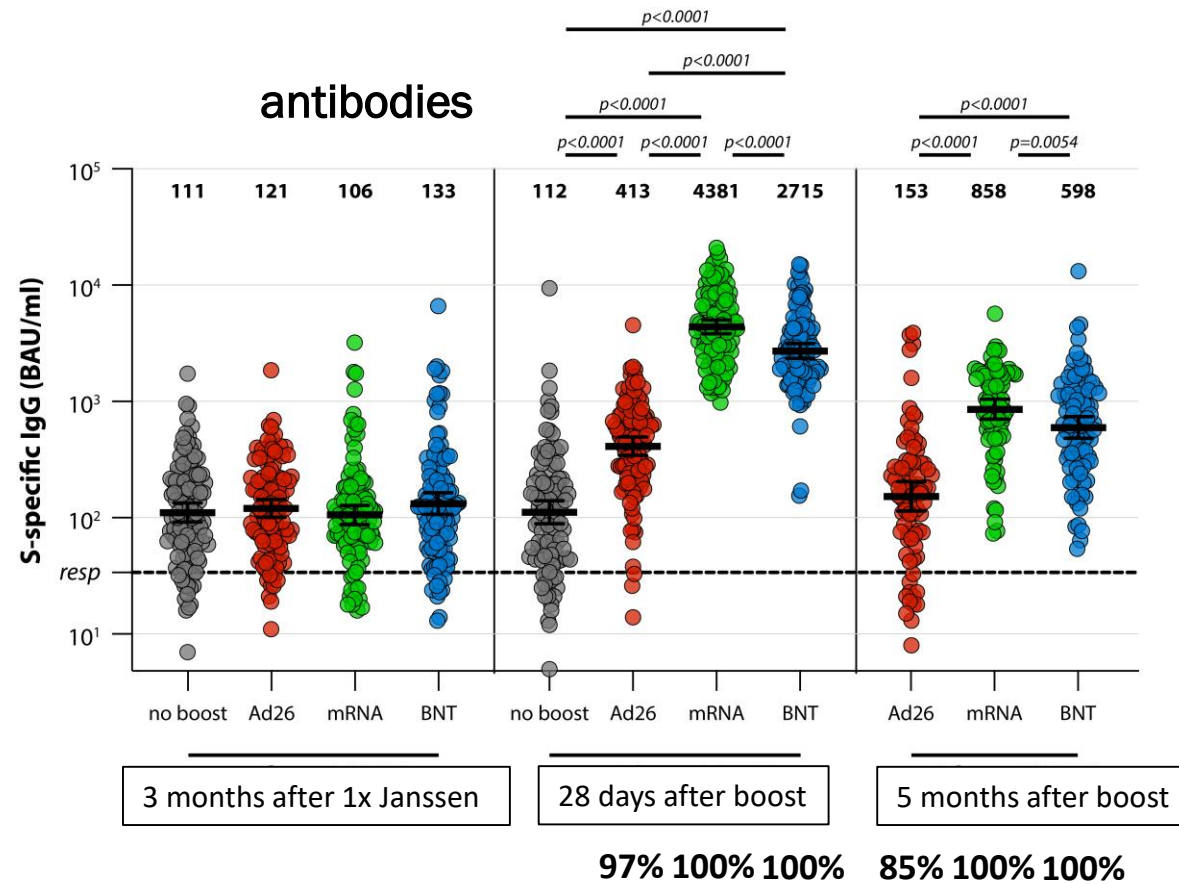


3 months after 1x Janssen

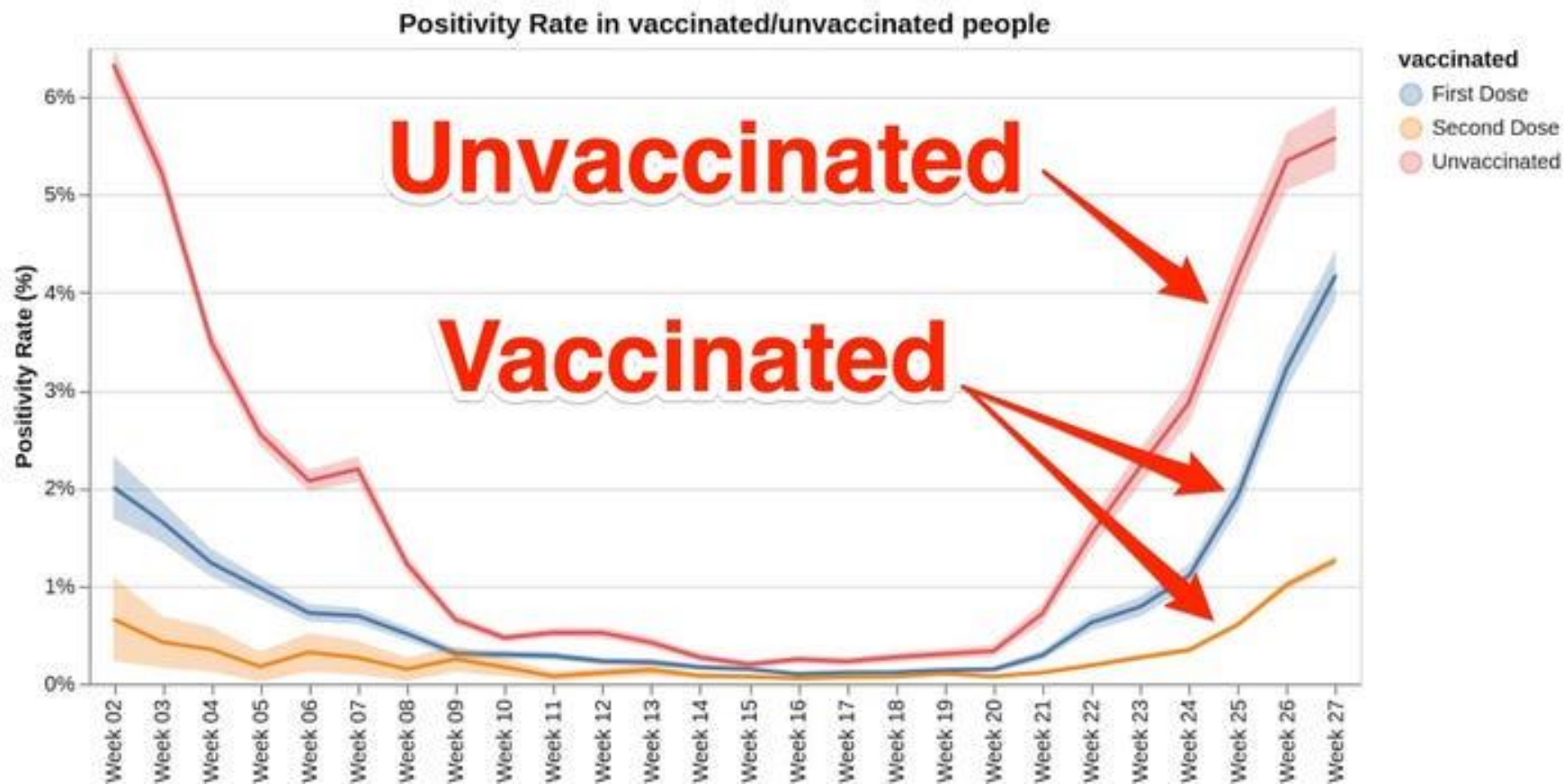
Binding antibodies upon heterologous boosting of Janssen vaccinees



5 months upon booster vaccination



Breakthrough infections



Immune responses in risk populations

- Department of Viroscience directly involved in multiple vaccination studies:



- Healthy individuals

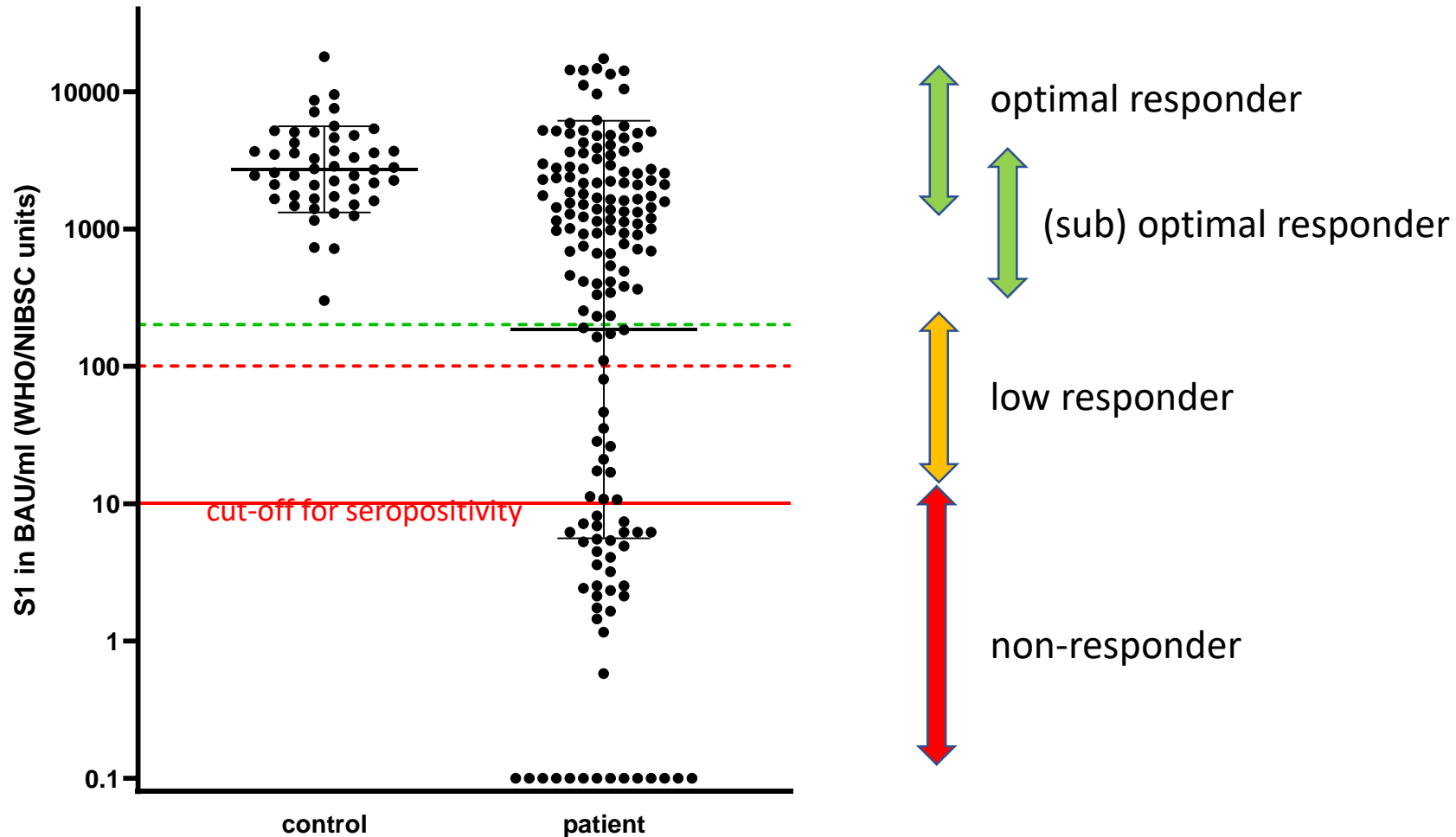
- *HCW*: follow-up of healthcare workers vaccinated with different vaccines
- *HCW boost*: follow-up of healthcare workers boosted with Pfizer
- *SWITCH*: improving immune responses in Janssen vaccinated individuals

- Immunocompromised patients

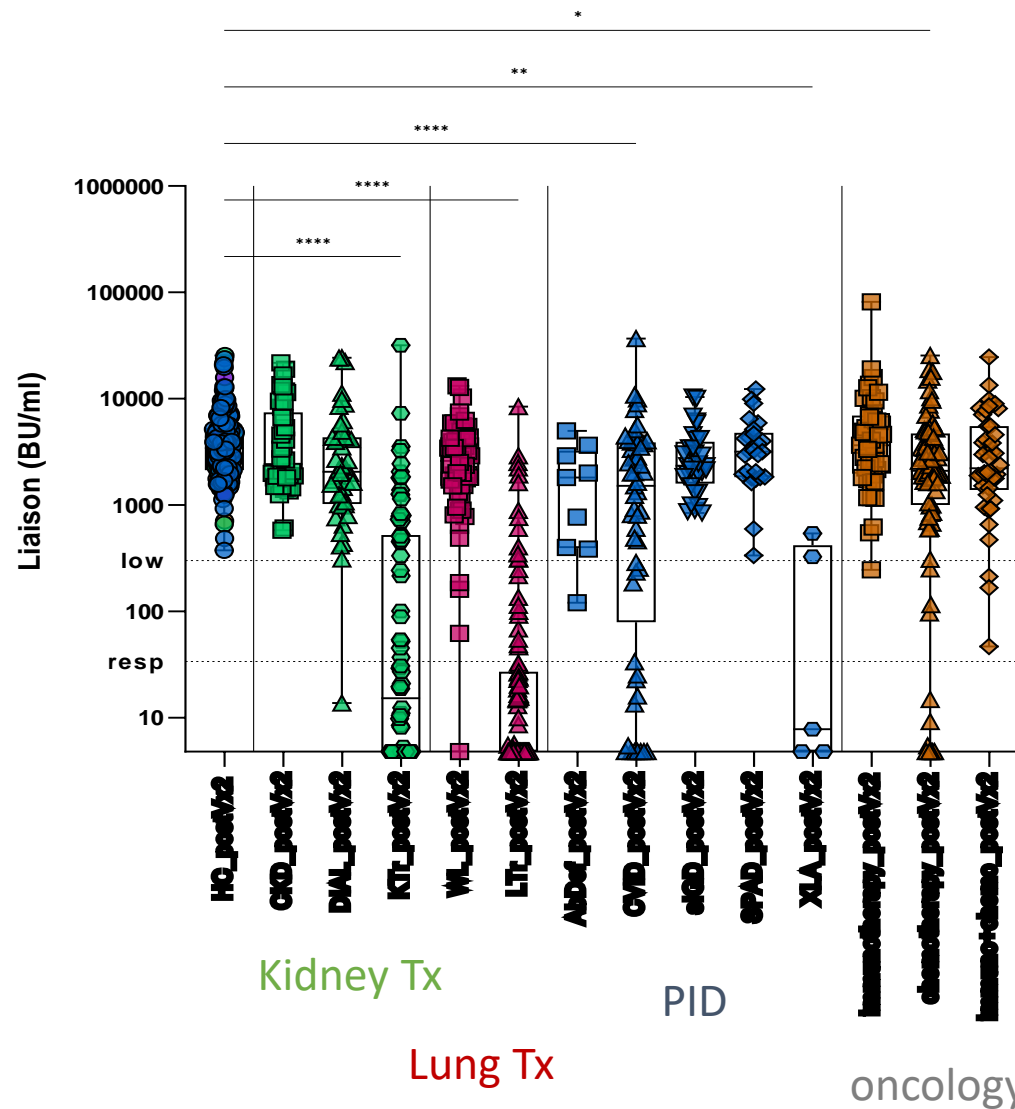
- *RECOVAC*: immune responses after vaccination in kidney disease patients
- *COVALENT*: immune responses after vaccination in lung transplant recipients
- *VACOPID*: immune responses after vaccination in patients with primary immunodeficiencies
- *VOICE*: immune responses after vaccination in cancer patients
- *COVIH*: immune responses after vaccination in HIV patients

Serological cut off based on virus neutralization

Moderna vaccinated at 28 days post 2nd vaccination

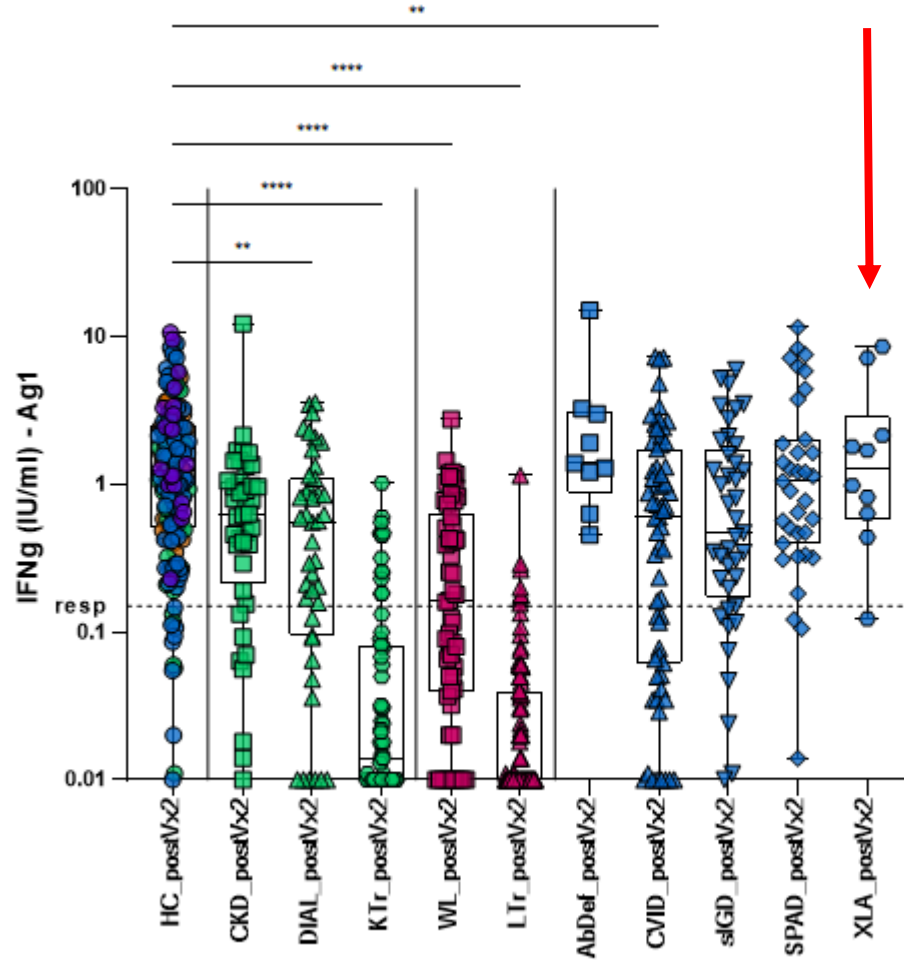


Comparative serology 28 days after Moderna vaccination



XLA :failure of B-lymphocyte precursors to mature into B-lymphocytesinfo-icon and ultimately plasma cells

Comparative T cell immunology 28 days after Moderna (IGRA)



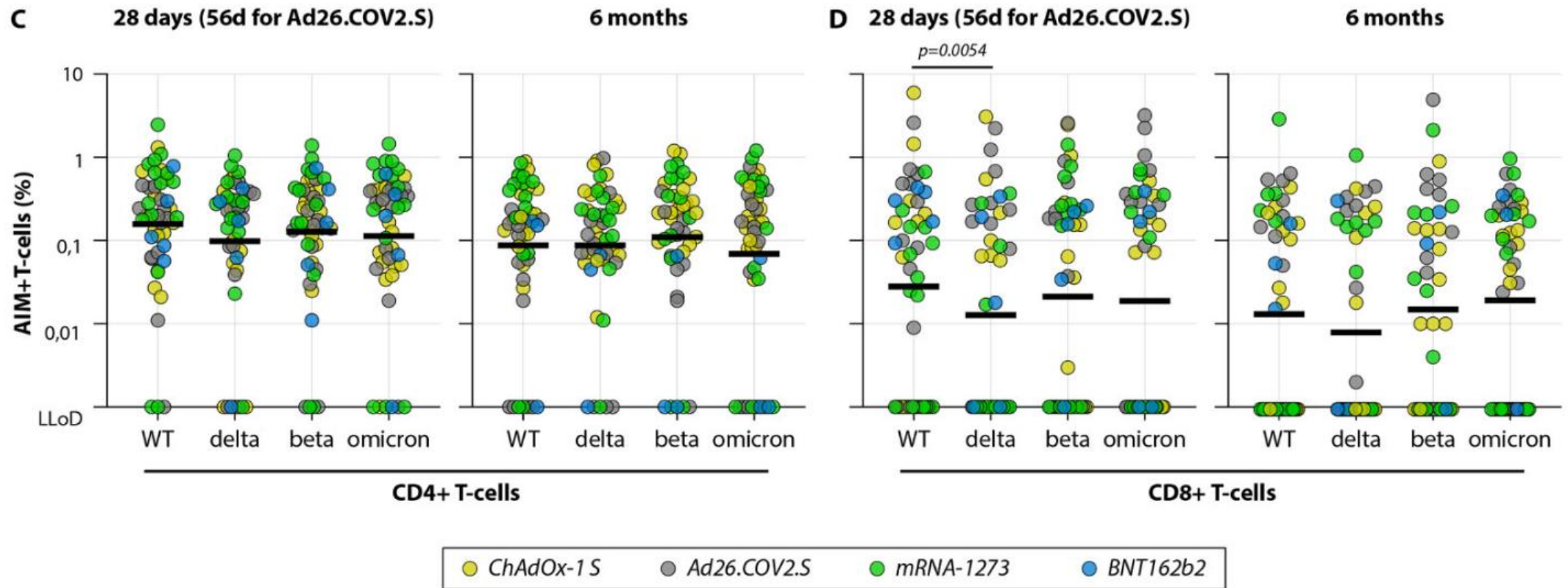
Kidney Tx

Lung Tx

PID

XLA :failure of B-lymphocyte precursors to mature into B-lymphocytesinfo-icon and ultimately plasma cells

Vaccination-induced S-specific T-cells equally recognized VOC including Omicron



The use of serology in clinical practice

1. Use of IgG binding as correlate of protection in HC?
2. Use of IgG binding as correlate of protection in immune compromised patients

Requirements:

1. Standardised quantitative assay (calibrated with NIBSC)
2. Fixed timing → 28 days post vaccination?
3. Analysis based on type of vaccine
4. Definition of risk groups?

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ZonMw

Health~Holland
SHARED CHALLENGES, SMART SOLUTIONS



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BILL & MELINDA
GATES foundation

