

Antibodies against SARS CoV 2 in convalescent plasma

C. Ellen van der Schoot

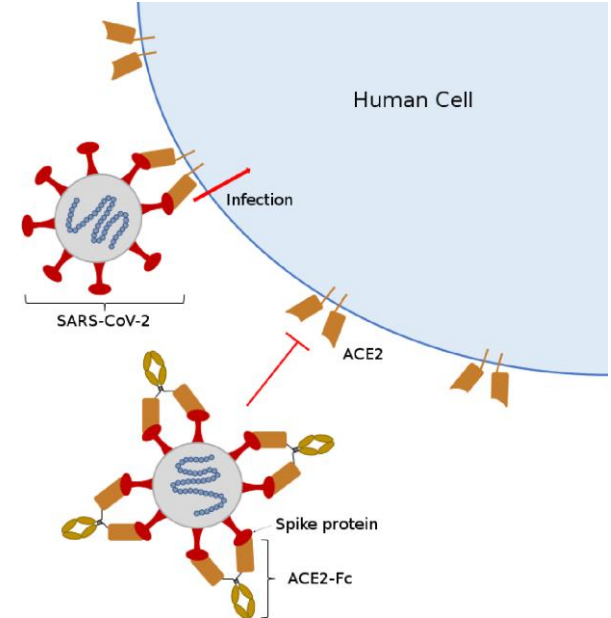
Department Experimental Immunohematology

Sanquin Research

Amsterdam, the Netherlands

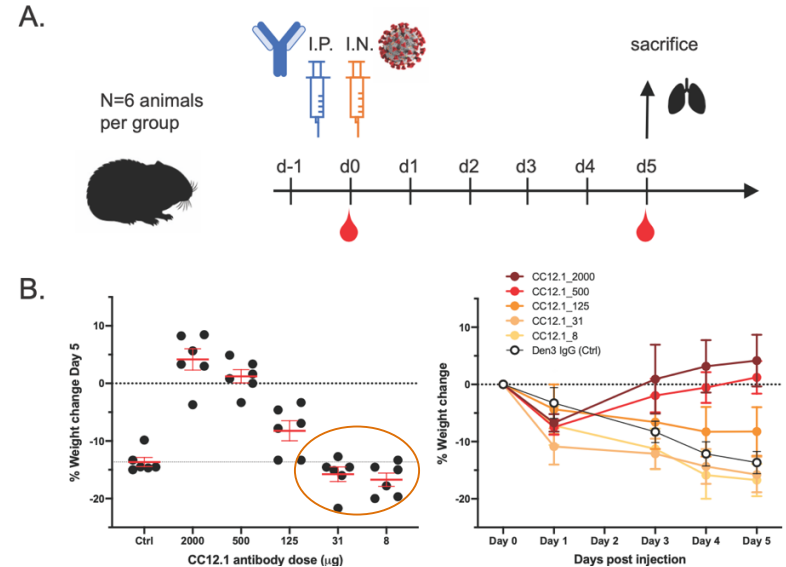
Working mechanisms of convalescent plasma

- Neutralizing activity:
 - **Inhibition of viral entry**
 - But also : ADCC, phagocytosis, complement ???
- Cave:
 - Antibody Dependent Enhancement (ADE)
 - increased infectivity by non-neutralising Abs
 - Immune activation in the donor by low-fucosylated IgG
 - Immune mediated side effects by plasma
 - TRALI
 - Autoantibodies against IFNa ?
 - Inhibiting immune response of the recipient



Effect of neutralising antibodies

- Experimental data on
 - Human plasma
 - Recombinant Moabs
- In syrian hamster models
- In macaque models
- In clinical trials
- Prevent disease progression before infection
- Clearance of virus in early infections
- Positive effect of Convalescent Plasma



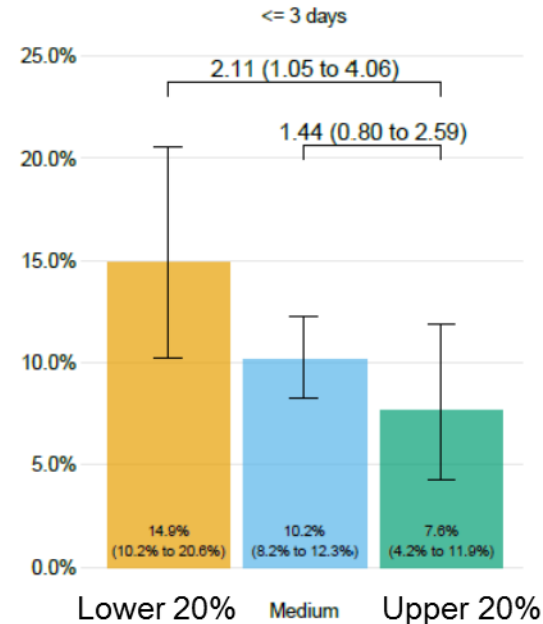
Rogers TF et al. (Scripps) Science

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-
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Dose -effect Clinical trial Mayo-clinic (n=3159)

7-Day Adjusted Mortality



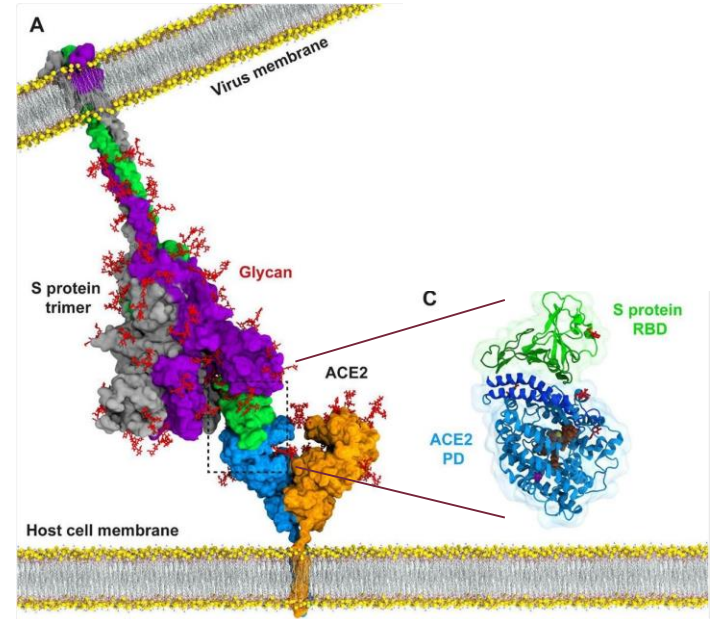
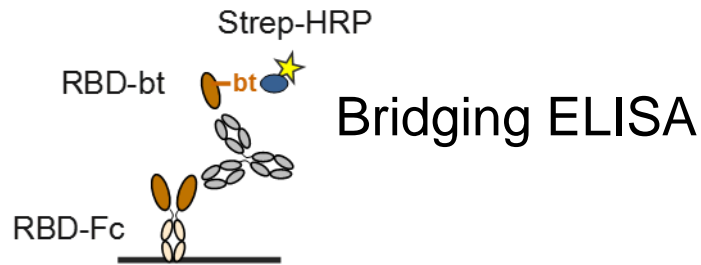
Measuring neutralisation activity in plasma

- plaque reduction neutralization test (PRNT)
 - microneutralization (MN) assay
- } BSL-3 biosafety level
- Low throughput assays using SARS CoV-2 virus strains

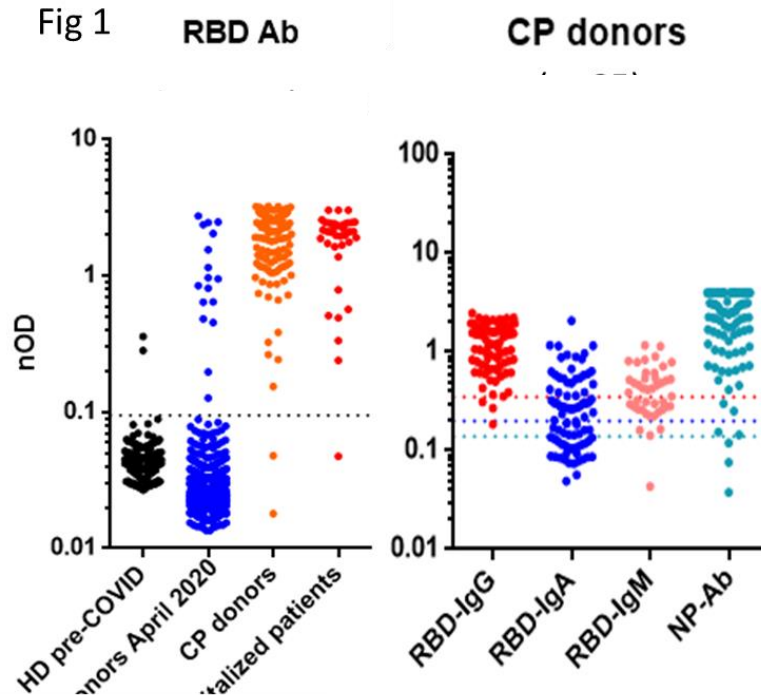


Need for high throughput ELISA assays,
correlating with virusneutralisation activity

Anti-Receptor Binding Domain ELISA



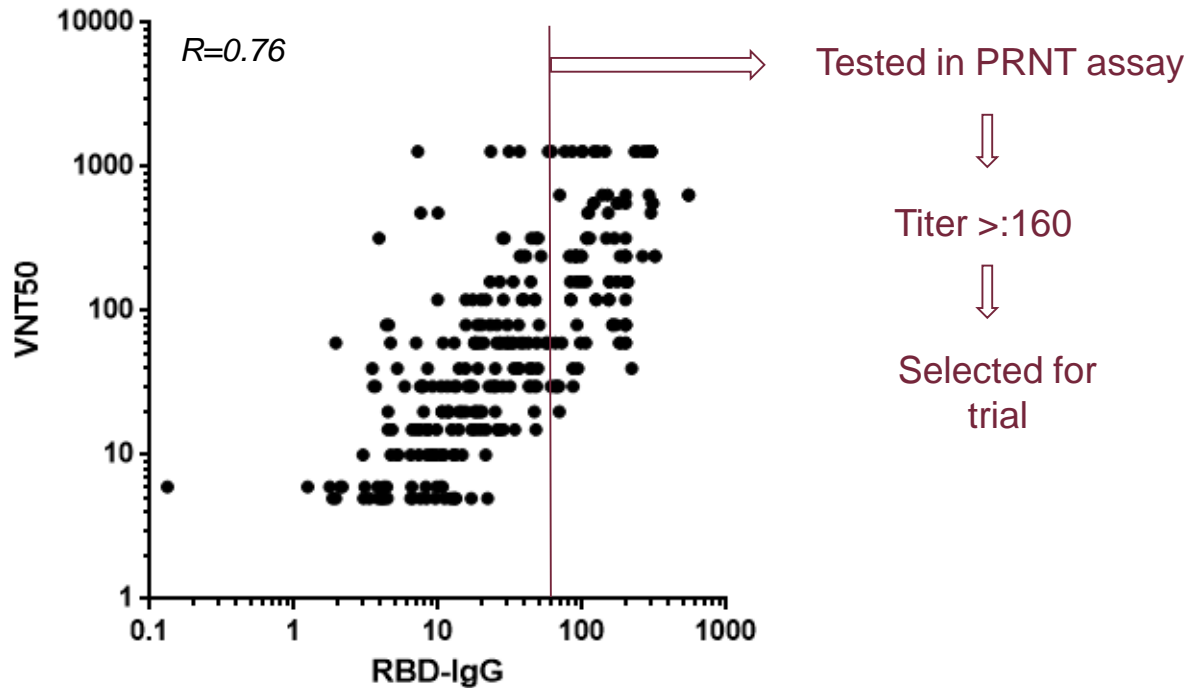
Highly variable levels of anti-RBD in Convalescent plasmadonors



Ab-levels correlate with:

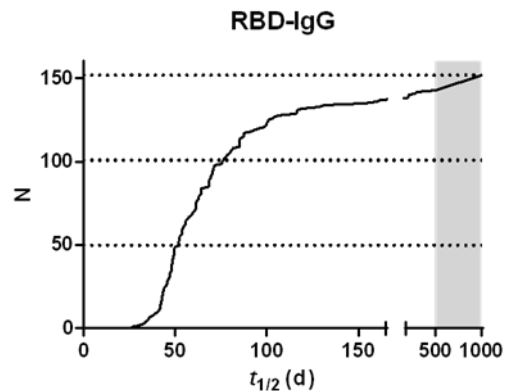
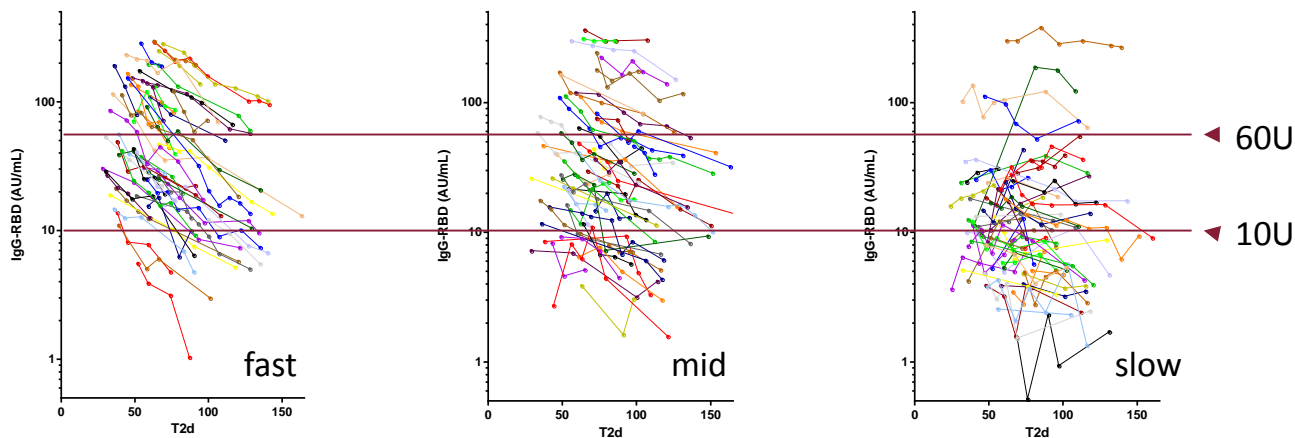
- Disease symptoms
- Age

Correlation between virus neutralisation and anti-RBD IgG



Longitudinal levels of anti-RBD in convalescent plasma donors

IgG stratified against fitted slopes in 3 groups (694 samples of 152 donors, analyzed by mixed effects model (log-linear in IgG; random intercept and slope, time as fixed variable))



Estimated half-life: 65 days

Conclusion

- Large program for the collection of convalescent plasma
- Stand op 27 oktober 2020

Aangemelde donors	20.965
Actieve donors	8.606
Aantal donaties	30.604
Voldoende titer	82%
Donatiefrekwentie	2.4

Sanquin Bloedbank
Francis Swaneveld
Hans Vrielink
Vera Novotny
Ron Kanbier
en vele anderen

Ongoing research projects within Sanquin

- Seroprevalence studies : Hans Zaaijer, Boris Hogema, Ed Slot
- SARS CoV2 specific B cell responses: Marieke van Ham
- SARS CoV2 specific T cell responses: Anja ten Brinke, Pleun Hombrink
- Characterization of antibody responses: Theo Rispens
- Fc-fucosylation of anti-SARS CoV2 antibodies : Gestur Vidarsson
- COVID-19 infections in patients with immune diseases: Taco Kuijpers, Gert Jan Wolbink
- Protective immunity : correlates of protection : Ellen van der Schoot, Katja van den Hurk



Will antibodies protect against re-infection??

- ZON MW grant:
 - PCR-tested individuals are asked whether they are blood donor
 - plasma samples from 300.000 blood donors stored at Sanquin
- PCR+ versus PCR- :
 - presence of anti-SARS CoV2 antibodies in plasma stored in the first wave (march-june 2020)
- => Correlates of protection