Variable loss of antibody potency against Omicron

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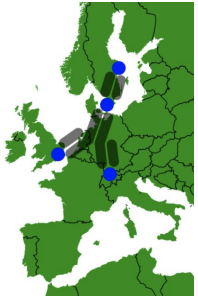
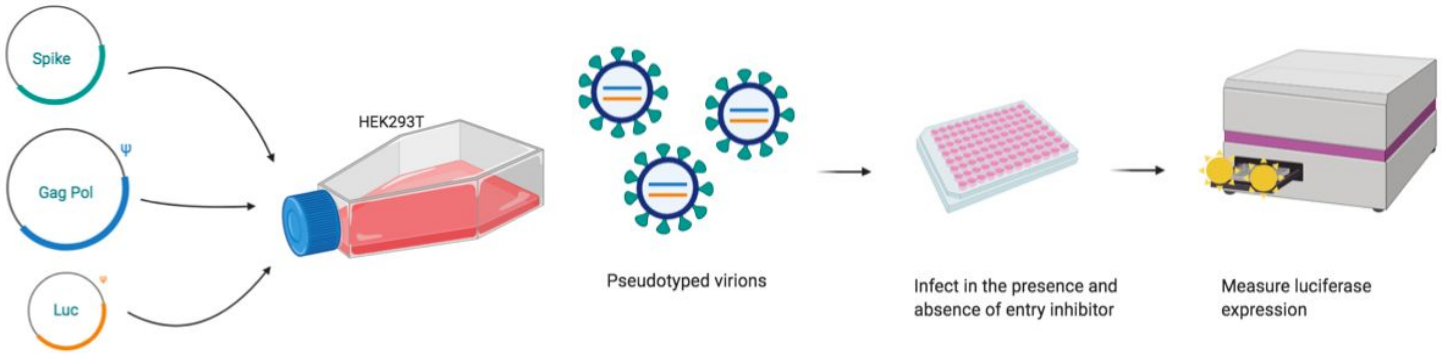


Pseudovirus neutralization assay



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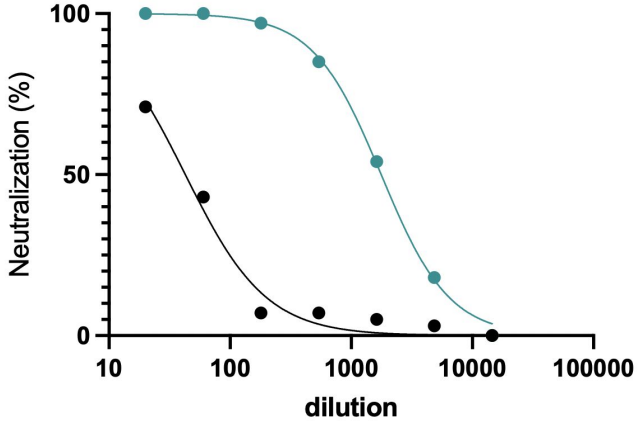
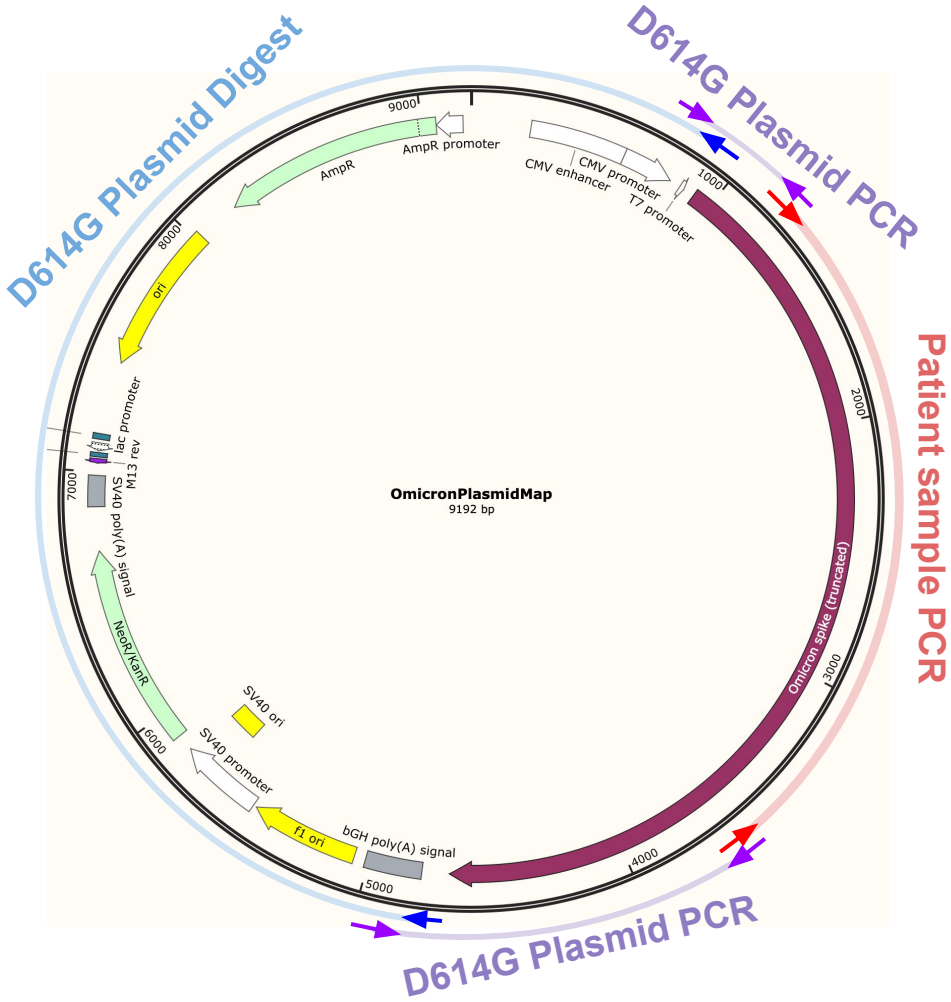


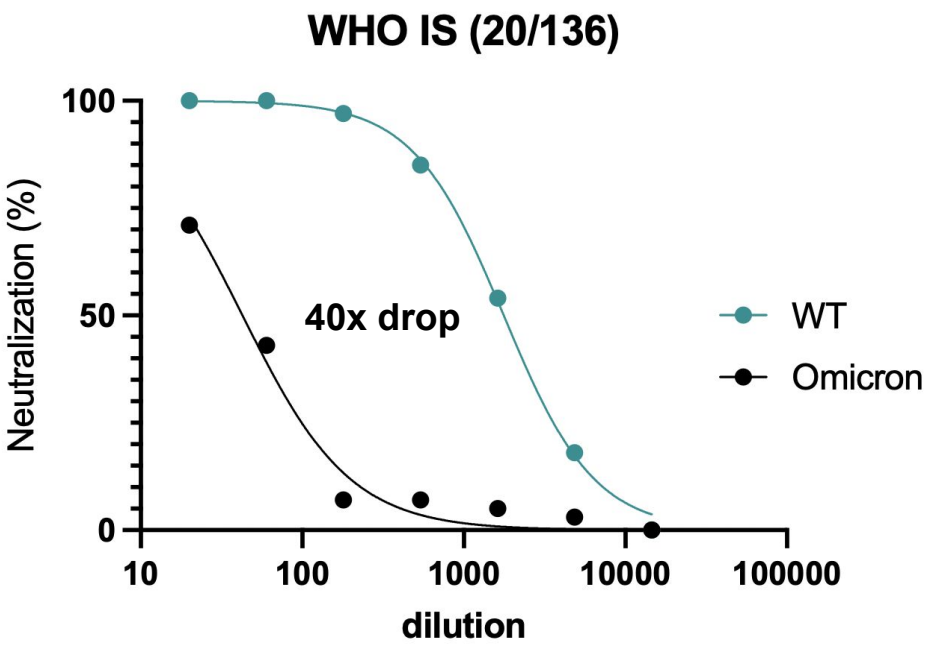
Spike from Sample

- Received suspected (due to SGTF) Omicron samples
- Use long-read spike PCR protocols to clone patient spike into codon optimized D614G
    - Our Omicron spike plasmid thus has native codons from AAs 43 to 1000, but is codon optimized outside of this.
- All AAs identical to the Omicron consensus

Timeline: 8 days from receiving Omicron samples to sharing neutralization results



WHO International Standard



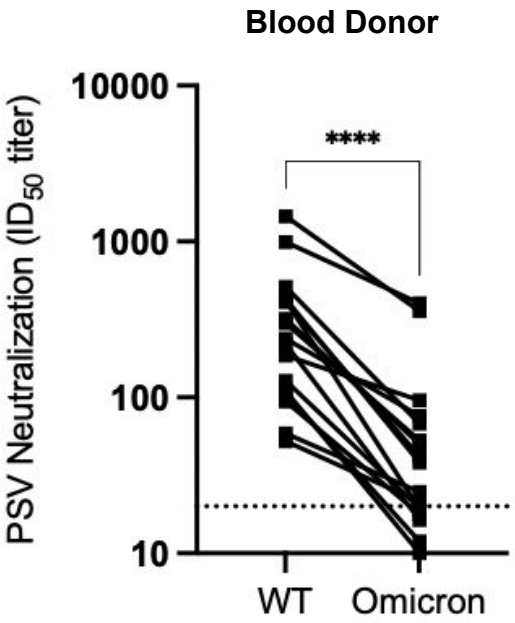
Monoclonal Antibodies (Preliminary)

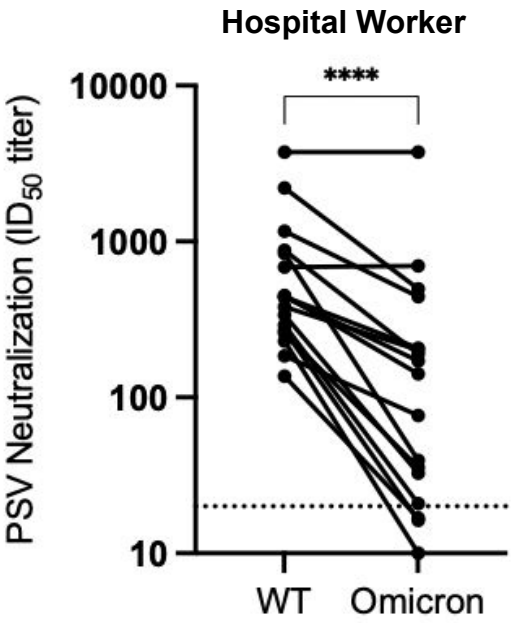
Mab	D614G IC50 (ug/ml)	Omicron IC50 (ug/ml)	Fold Loss	
IH_REGN-10933	0.009	>10	>1100	Regeneron
IH_REGN-10987	0.008	>10	>1200	
IH_LY-CoV555	0.007	>10	>1400	Eli Lilly
IH_LY-CoV16	0.037	>10	>270	
IH_S309	0.104	0.2	2	Vir (sotrovimab)

- Mabs produced “in house” by Sai Reddy’s lab (ETH Zurich)
- Sequences are the same as the clinical versions, but production and Fc modifications differ.

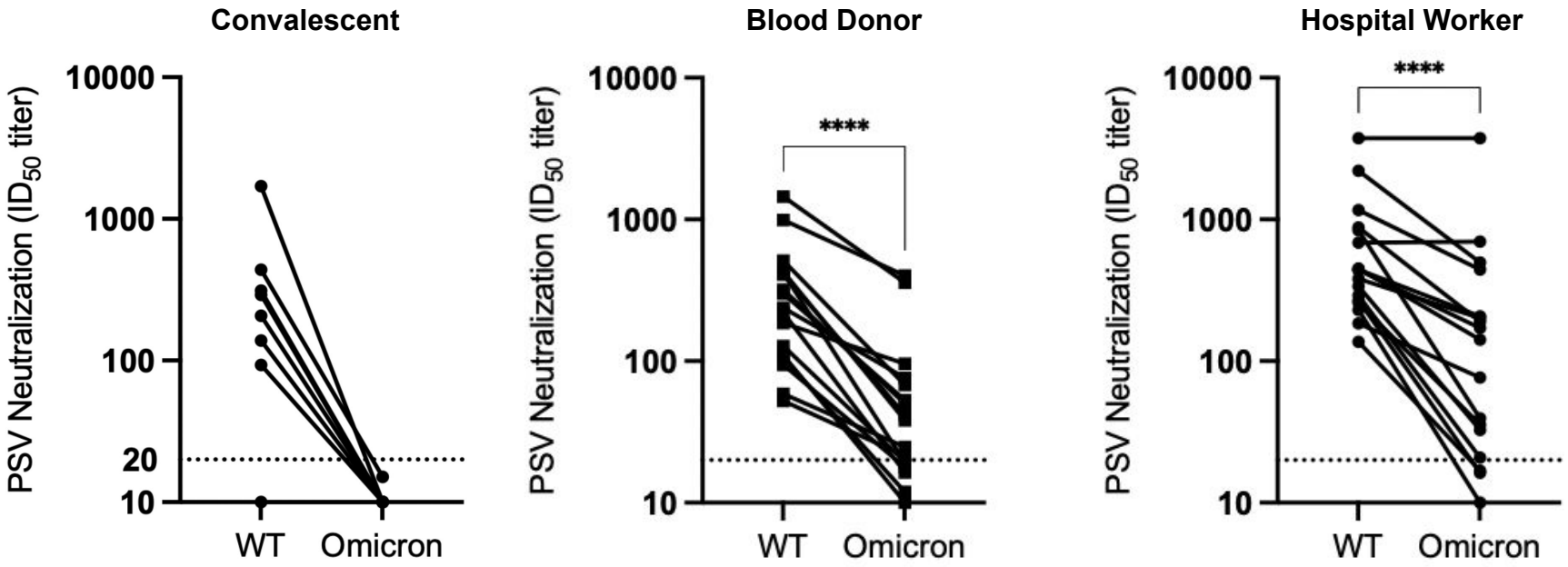
Cohorts

- 17 recent (week 48) Blood Donor samples.
  - No information.
- 17 previously-infected Hospital Workers.
  - Confirmed PCR+ in early 2020.
  - Varied subsequent vaccination histories.
    - 2xPfizer
    - 2xAZ
    - AZ+Pfizer





Assay or Cohort?



Conclusions

- Large differences in fold change between cohorts.
- In a Hospital Worker cohort with high exposure levels, but also in a random sample of *recent* blood donors, loss of neutralization was less extreme than expected.
- Given expected cohort differences, and uncertainty about assays, standardization across labs is critical.

- **Big picture:** In our cohorts, existing boosters may suffice (even without a booster broadening effect), and perhaps the situation is not as dire as would have been initially expected.

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