Variable loss of antibody potency against Omicron

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Pseudovirus neutralization assay
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

![Graph showing neutralization percentage against dilution for WT and Omicron strains.]

WHO IS (20/136)

Neutralization (%) vs. dilution

40x drop

WT

Omicron
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.

<table>
<thead>
<tr>
<th>Mab</th>
<th>D614G IC50 (ug/ml)</th>
<th>Omicron IC50 (ug/ml)</th>
<th>Fold Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>IH_REGN-10933</td>
<td>0.009</td>
<td>&gt;10</td>
<td>&gt;1100</td>
</tr>
<tr>
<td>IH_REGN-10987</td>
<td>0.008</td>
<td>&gt;10</td>
<td>&gt;1200</td>
</tr>
<tr>
<td>IH_LY-CoV555</td>
<td>0.007</td>
<td>&gt;10</td>
<td>&gt;1400</td>
</tr>
<tr>
<td>IH_LY-CoV16</td>
<td>0.037</td>
<td>&gt;10</td>
<td>&gt;270</td>
</tr>
<tr>
<td>IH_S309</td>
<td>0.104</td>
<td>0.2</td>
<td>2</td>
</tr>
</tbody>
</table>

Regeneron
Eli Lilly
Vir (sotrovimab)
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

![Graphs showing PSV Neutralization (ID50 titer) for Blood Donor and Hospital Worker cohorts.](image)
Assay or Cohort?

Convalescent

Blood Donor

Hospital Worker

PSV Neutralization (ID₅₀ titer)

WT  Omicron

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WT  Omicron

WT  Omicron
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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