

Challenges to develop and assess variant-specific vaccines

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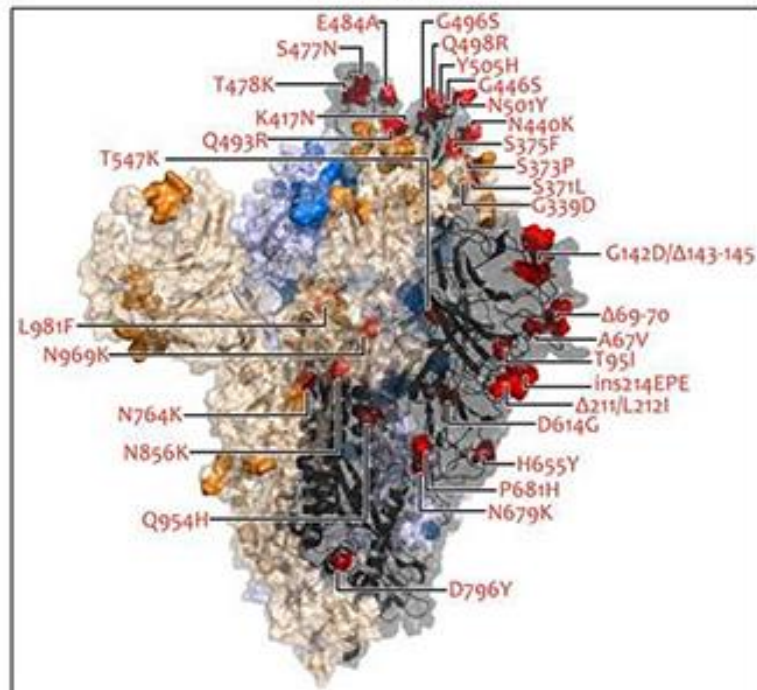
WHO meeting on COVID-19 Vaccines Research

December 6th 2021

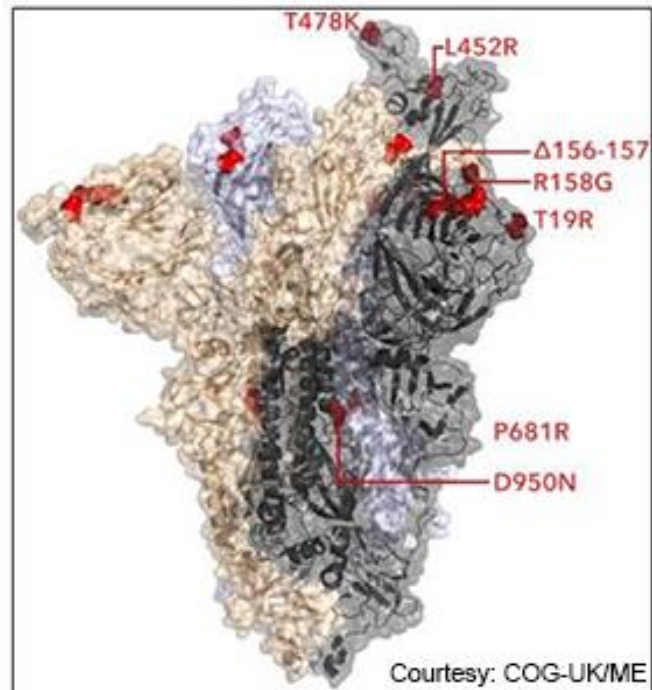


**Mount
Sinai**

Omicron



Delta



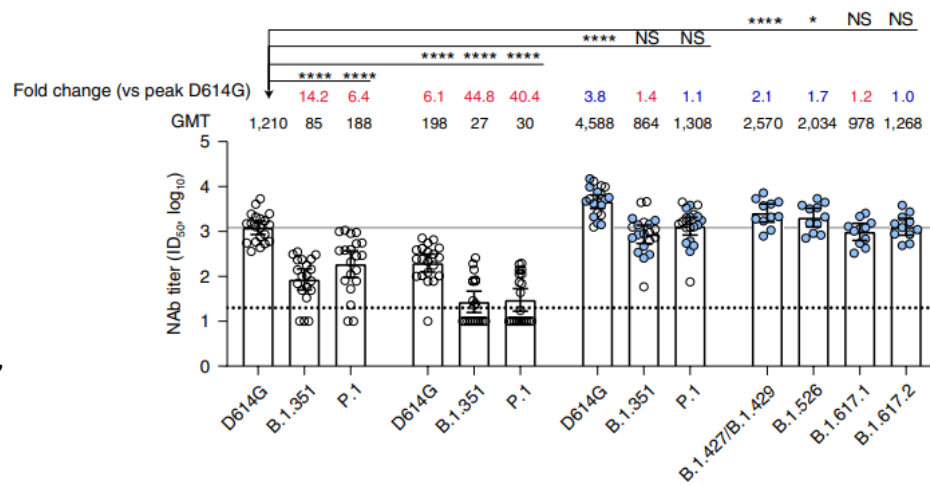
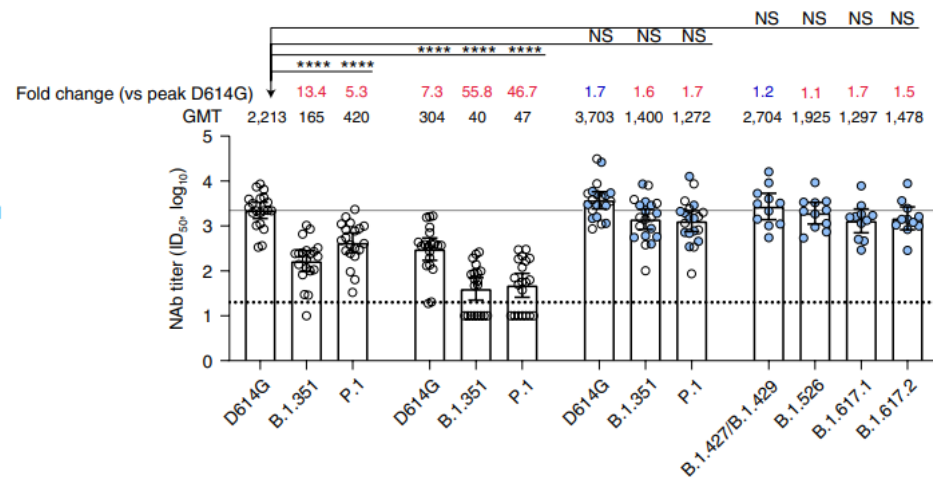
Courtesy: COG-UK/ME



OPEN

Safety and immunogenicity of SARS-CoV-2 variant mRNA vaccine boosters in healthy adults: an interim analysis

Angela Choi^{1,4}, Matthew Koch^{1,4}, Kai Wu^{1,4}, Laurence Chu², LingZhi Ma¹, Anna Hill¹, Naveen Nunna¹, Wenmei Huang¹, Judy Oestreicher¹, Tonya Colpitts¹, Hamilton Bennett¹, Holly Legault¹, Yamuna Paila¹, Biliiana Nestorova¹, Baoyu Ding¹, David Montefiori¹, Rolando Pajon¹, Jacqueline M. Miller¹, Brett Leav¹, Andrea Carfi¹, Roderick McPhee¹ and Darin K. Edwards^{1,5}

a**b**

'regular vaccine'

'regular vaccine'

'regular vaccine'

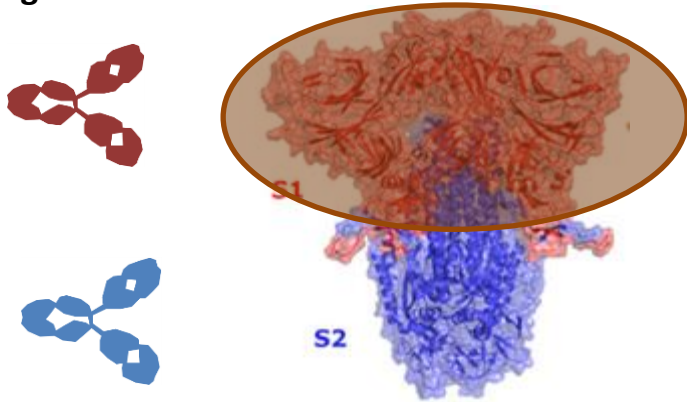
mRNA-1273
boostermRNA-1273.351
booster

'Beta/B.1.351 vaccine'

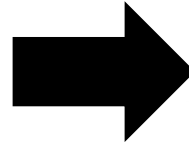
What will happen after a booster dose with an Omicron specific vaccine?

- Original Antigenic Sin?

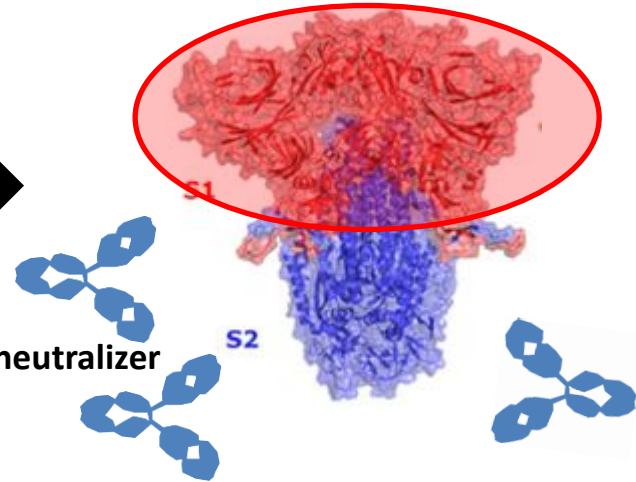
Strong neutralizer



Weak/non- neutralizer

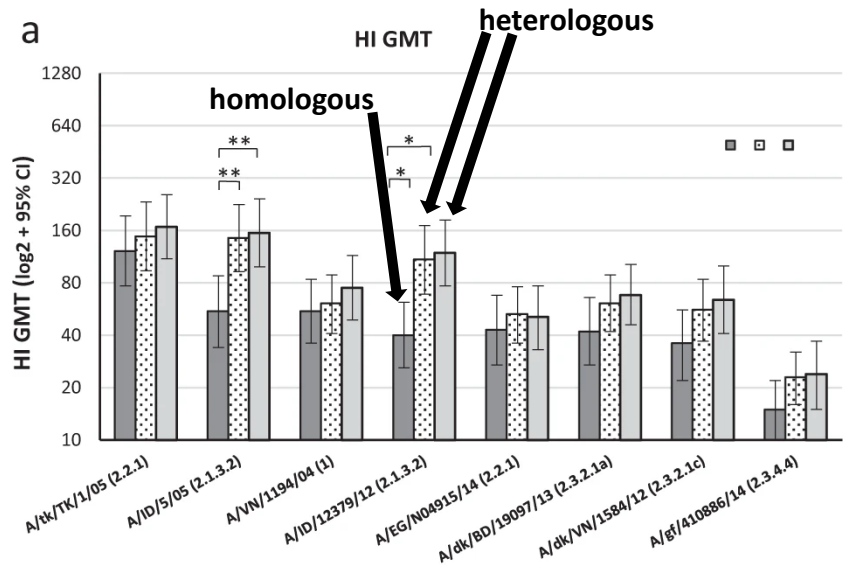
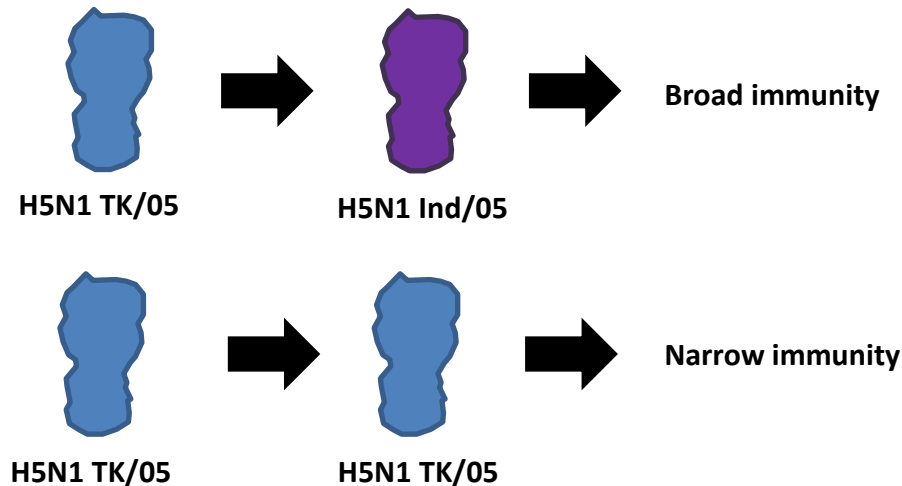


Weak/non- neutralizer



What will happen after a booster dose with an Omicron specific vaccine?

- Increase in breadth?
- Likely similar to heterologous H5N1 vaccination

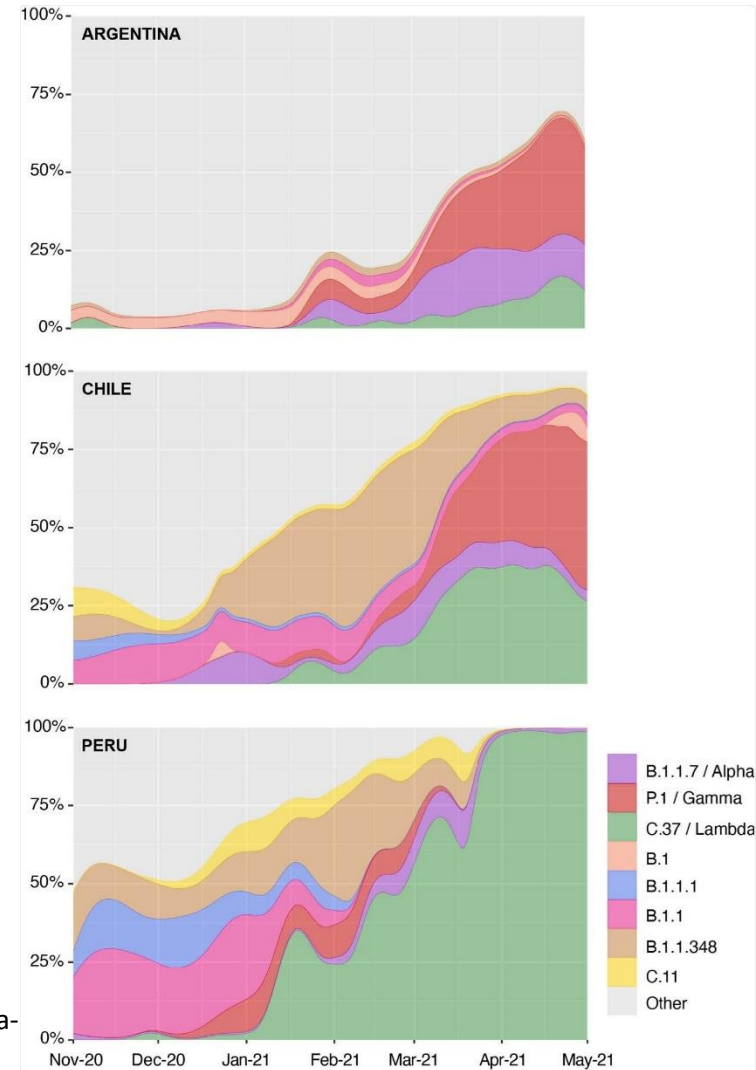


What is the strategy for individuals so far not vaccinated?

Especially when Omicron co-circulates with other variants?

- Local or temporal dynamics of different variants (e.g. Delta versus Omicron)
- Omicron only? Does it cross-protect well against other variants?
- ‘Regular’ vaccine followed by Omicron vaccine?
- Bivalent vaccines? (cost)
 - For vectored and mRNA vaccines – will heterotrimerization lead to problems in protein folding?

<https://www.news-medical.net/news/20210707/SARS-CoV-2-Lambda-variant-spreading-rapidly-in-South-America-report-reveals.aspx>



How easy is it to change the vaccines?

- **mRNA vaccines**
 - Probably easy, has already been shown
- **Vectored vaccines**
 - Probably easy
- **Inactivated vaccines**
 - How well does the new variant grow? Low yields could impact highly on number of doses to be produced.
 - How stable is the variant spike protein?
- **Recombinant protein vaccines**
 - How well does the new spike express? Wild type expression levels are already low. How does this impact on yields.
 - How stable is the variant spike protein in the process and over time?

What will be needed for regulatory approval?

- **Influenza: No clinical trials needed, strain changes are routinely performed**
- **Clinical trials in a 'booster' setting?**
- **Clinical trials in convalescent individuals?**
- **Clinical trials in naïve individuals?**
- **Will immune-bridging be sufficient?**
- **Will clinical trials need to be conducted before roll-out or in parallel?**