Challenges to develop and assess variant-specific vaccines

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WHO meeting on COVID-19 Vaccines Research
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Safety and immunogenicity of SARS-CoV-2 variant mRNA vaccine boosters in healthy adults: an interim analysis

Angela Choi, Matthew Koch, Kai Wei, Laurence Chu, Ling Zhi Ma, Anna Hill, Naveen Nunnari, Wenmei Huang, Judy Oestreicher, Tonya Colpitts, Hamilton Bennett, Holly Legault, Yamuna Palli, Biliana Nestorova, Basuyu Ding, David Montefiori, Rolando Pajon, Jacqueline M. Miller, Brett Loav, Andrea Carfi, Roderick McPhree and Darin K. Edwards

'b regular vaccine' 'Beta/B.1.351 vaccine'
What will happen after a booster dose with an Omicron specific vaccine?

• **Original Antigenic Sin?**

[Image showing Strong and Weak neutralizers]

https://www.science.org/doi/10.1126/sciadv.abf3671
What will happen after a booster dose with an Omicron specific vaccine?

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

![Diagram showing breadth and immunity](https://www.nature.com/articles/s41541-019-0114-8)
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?

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?