Immune Responses Induced by Different COVID-19 Vaccine Platforms

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WHO Framework for Evaluating New COVID-19 Vaccines, Geneva, Switzerland
February 23, 2022
Differential Kinetics of Humoral Immune Responses Elicited by mRNA and Ad26 Vaccines

Live Virus nAb

Pseudovirus nAb

RBD IgG

Collier et al. NEJM, October 15, 2021
Differential Kinetics of Cellular Immune Responses Elicited by mRNA and Ad26 Vaccines

![Graph showing differential kinetics of CD4 and CD8 T cells elicited by mRNA and Ad26 vaccines.](image)

Collier et al. NEJM, October 15, 2021
Efficacy Wanes for mRNA Vaccines in US (N=17 Million)

Zheutlin et al. 2022 medRxiv
Heavily Mutated Omicron Spike

Omicron NAbs Minimal After Initial mRNA Vaccination, Increase with Boost, and Decline by 6 Months

Pajon et al. NEJM, January 26, 2022
Vaccine Protection Against SARS-CoV-2 Omicron

- Vaccine protection against acquisition of infection with Omicron appears to be relatively modest and transient, even with 3rd or 4th boosts.

- Vaccine protection against hospitalization with Omicron in South Africa remains robust, largely in absence of high titers of neutralizing antibodies:
  - 2-shot BNT162b2 efficacy: 70%
  - 2-shot Ad26.COV2.S efficacy: 85%

- These data suggest that immune mechanisms other than neutralizing antibodies may be critical for protection against severe disease.
Most CD8 T Cell Epitopes are Unaffected by Omicron

Grifoni et al. 2021 Cell Host & Microbe
Courtesy Alba Grifoni and Alex Sette
Accelerated Article Preview

Vaccines Elicit High Conserved Cellular Immunity to SARS-CoV-2 Omicron

Received: 28 December 2021
Accepted: 25 January 2022
Published online: 31 January 2022

Jayan Liu, Abhishek Chandran, Navneet Gellar, Julia Barrett, Katharine Ayers-Delan, Michelle Lutton, Katherine Mobah, Michele Scienza, Nathan Nersisyan, Conny Wu, Jingyu Yu, Alvin Y. Geiller & Dan H. Barouch

Accelerated Article Preview

T cell responses to SARS-CoV-2 spike cross-recognize Omicron

Received: 27 December 2021
Accepted: 20 January 2022
Published online: 31 January 2022


Accelerated Article Preview

CORONAVIRUS

Divergent SARS CoV-2 Omicron-reactive T- and B cell responses in COVID-19 vaccine recipients


SARS-CoV-2 vaccination induces immunological T cell memory ability to cross-recognize variants from Alpha to Omicron

Alison Tarke, Camila H. Coelho, Zei Zhang, Jennifer M. Dan, Esther Dawen Yu, Nils Methot, Nathaniel I. Bloom, Benjamin Goodwin, Elizabeth Phillips, Simon Mathal, John Sidney, Gilberto Filaci, Daniela Weiskopf, Ricardo da Silva Antunes, Shane Crotty, Alba Grittoni, Alessandro Sette

P1: S0002-867422(00)0073-3
DOI: https://doi.org/10.1016/j.cell.2022.01.015
Reference: CELL 12347

To appear in: Cell

GeurtsvanKessel et al. Sci Immunol, Feb 3, 2022
Tarke et al. Cell, in press
Vaccine-Elicited CD8 T Cell Responses are Highly Cross-Reactive to Omicron

Vaccine-Elicited CD8 T Cell Responses are Highly Cross- Reactive to Omicron

**Ad26.COV2.S**

- **Delta:**
  - $R=0.78$
  - $P<0.0001$
  - Slope=0.90

- **Omicron:**
  - $R=0.76$
  - $P<0.0001$
  - Slope=0.75

**BNT162b2**

- **Omicron:**
  - $R=0.56$
  - $P<0.0001$
  - Slope=0.81

Vaccine-Elicited CD4 T Cell Responses are Highly Cross-Reactive to Omicron

Ad26.COV2.S

BNT162b2

Time Following Immunization

Vaccine-Elicited CD4 T Cell Responses are Highly Cross-Reactive to Omicron

Time Following Boost Immunization

COVID-19 Breakthrough Cases During Omicron Surge in US

Rates of COVID-19 Cases by Vaccination Status and Vaccine Product

April 04 - January 22, 2022 (29 U.S. jurisdictions)

- Unvaccinated: 3230
- Janssen: 1144
- Pfizer - BioNTech: 1554
- Moderna: 1305
COVID-19 Breakthrough Cases During Omicron Surge in US

Rates of COVID-19 Cases by Vaccination Status, Booster Dose,** and Primary Series Vaccine Type

September 19 - January 01, 2022 (26 U.S. jurisdictions)

- **Unvaccinated**
- **Fully Vaccinated without booster dose***
- **Fully Vaccinated with booster dose***

### Moderna Peak
- Incidence per 100,000 population:
  - Nov 2021: 945
  - Jan 2022: 1558
  - Peak: 3244

### Pfizer - BioNTech Peak
- Incidence per 100,000 population:
  - Nov 2021: 1129
  - Jan 2022: 1711
  - Peak: 3244

### Janssen Peak
- Incidence per 100,000 population:
  - Nov 2021: 1083
  - Jan 2022: 1216
  - Peak: 3244

Positive specimen collection date by end of week

CDC 2/20/22
COVID-19 Vaccines: Looking Forward

• Short-term neutralizing antibody responses are important, but durability of antibody and CD8 T cell responses are likely critical for long-term protection, particularly against severe disease with viral variants.

• mRNA and Ad26 platforms exhibit different short-term vs long-term humoral and cellular immune responses.

• Boosts are useful and currently dominate much discussion, but the top priority should remain providing initial vaccines to unvaccinated people.

• A strategy of boosting the entire population every 3-6 months is likely not practical for the developed world and not possible for the developing world; vaccine platforms with improved durability desirable.
Acknowledgements

Beth Israel Deaconess
Ai-ris Collier
Jingyou Yu
Jinyan Liu
Abishek Chandrashekar
Erica Borducchi
Lisa H. Tostanoski
Katherine McMahan
Catherine Jacob-Dolan
Aiquan Chang
Tochi Anioke
Michelle Lifton
Joseph Nkolola
Kathryn Stephenson

Janssen / J&J
Mathieu Le Gars
Jerald Sadoff
Anne Marit de Groot
Dirk Heerwegh
Frank Struyf
Macaya Douoguih
Johan Van Hoof
Hanneke Schuitemaker
Mathai Mammen
Paul Stoffers

Ragon Institute
Galit Alter
Caroline Atyeo
Sally Shin

Funding
BARDA/J&J
Ragon Institute
MassCPR
NIAID

All Trial Volunteers