Interpreting NAb Assays and Animal Models

Dan H. Barouch, M.D., Ph.D.
Director, Center for Virology and Vaccine Research
Beth Israel Deaconess Medical Center
William Bosworth Castle Professor of Medicine
Harvard Medical School
Ragon Institute of MGH, MIT, and Harvard

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Omicron: BA.1 and BA.2 South Africa

Enabled by data from the South African contributions to GISAID and cov.lanl.gov

Update 12/13  Bette Korber
Omicron vs. Delta Spike Mutations

Omicron:
- E484A
- S477N
- T478K
- K417N
- T547K
- Q493R
- G496S
- Q498R
- Y505H
- S4946S
- N501Y
- N440K
- S375F
- S373P
- L371F
- G339D
- G142D/G143-145
- L981F
- N969K
- N647K
- N856K
- Q954H
- D796Y

Delta:
- T478K
- L452R
- Δ156-157
- Δ156-157
- R158K
- T19R
- P681R
- D950N

Courtesy: COG-UK/ME
Select Key Questions for the Omicron Variant

• Severity of illness?

• Transmissibility?

• Evasion of immune responses?
  • Natural immunity
  • Vaccines
  • mAbs
To What Extent Does the Omicron Variant Escape from Current Vaccines?

• Many groups have now reported decreased NAb titers to the Omicron variant, and partial restoration with boosting

• Less data available for binding and other functional antibodies and T cell responses to the Omicron variant

• At least two studies have reported preliminary vaccine effectiveness against the Omicron variant (UK, RSA)
Pseudovirus NAbs Correlate with Protection Against SARS-CoV-2 WA1/2020 Challenge in Rhesus Macaques

Mercado et al. Nature July 30, 2020
Dose-Dependent Adoptive Transfer of Purified IgG Protects Against SARS-CoV-2 in Rhesus Macaques

Days Following Challenge

Log sgRNA Copies / ml

250 mg/kg (N=3)

25 mg/kg (N=3)

2.5 mg/kg (N=3)

0 mg/kg (N=3)

McMahan et al. Nature Dec 4, 2020
CD8 Depletion Partially Abrogates Protection of Natural Immunity Against SARS-CoV-2 in Rhesus Macaques

McMahan et al. Nature Dec 4, 2020
IgG Adoptive Transfer and CD8 Depletion Studies

• Purified IgG protects macaques against SARS-CoV-2 challenge in a dose-dependent fashion

• CD8 depletion reduced protection against re-challenge in convalescent macaques with waning Ab titers

• These data suggest that Abs alone can protect, but cellular immune responses contribute when Ab titers are borderline or subprotective

McMahan et al. Nature Dec 4, 2020
Immunogenicity of Ad26.COV2.S Against SARS-CoV-2 Variants: Neutralizing Antibody Responses

Alter et al. Nature, June 9, 2021
Immunogenicity of Ad26.COV2.S Against SARS-CoV-2 Variants: Fc Functional Antibody Responses

After et al. Nature, June 9, 2021
Immunogenicity of Ad26.COV2.S against SARS-CoV-2 Variants: CD8 and CD4 T Cell Responses

Alter et al. Nature, June 9, 2021
Immunogenicity of Ad26.COV2.S Against SARS-CoV-2 Variants

- Substantial impact of variants on NAb responses
- Less impact of variants on binding and Fc functional antibodies
- No impact of variants on CD8 T cell responses
- Cellular immune responses may be more preserved than NAb responses against Omicron

Alter et al. Nature, June 9, 2021
Setting the Stage for Omicron Studies

- Neutralizing antibody responses, if present at high titers, will likely protect against infection.

- However, the magnitude and durability of neutralizing antibody responses against Omicron with current vaccines may be reduced.

- Other antibody functions and cellular immune responses may show greater cross-reactivity against Omicron and may contribute to protection against severe disease.

- Correlates of protection in humans against variants remain unclear.
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