Vaccine Protection Against the SARS-CoV-2 Omicron Variant in Macaques

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Vaccine Protection Against SARS-CoV-2 Omicron in Macaques

• Goal: To evaluate the protective efficacy and immune correlates of mRNA and adenovirus vaccines against Omicron

• 30 cynomolgus macaques (N=6/group)
  • BNTx3: BNT162b2 (week 0, 3, 14)
  • BNTx2/Ad26: BNT162b2 (weeks 0, 3), Ad26.COV2.S (week 14)
  • Ad26/BNT: Ad26.COV2.S (week 0), BNT162b2 (week 14)
  • Ad26x2: Ad26.COV2.S (week 0, 14)
  • Sham: Sham (weeks 0, 3, 14)

• High-dose $10^6$ PFU SARS-CoV-2 Omicron challenge at week 19 by the IN+IT routes (challenge stock provided by Mehul Suthar, Emory)
# Study Outline

<table>
<thead>
<tr>
<th>Week</th>
<th>Prime</th>
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<th>Boost</th>
<th>SARS-CoV-2 Omicron</th>
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<tbody>
<tr>
<td>0</td>
<td>BNT</td>
<td>BNT</td>
<td>14</td>
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<td>3</td>
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<td>Ad26</td>
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<td>Ad26x2</td>
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<td>Sham</td>
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1. BNTx3
2. BNTx2/Ad26
3. Ad26/BNT
4. Ad26x2
5. Sham
CD4+ T Cell Responses

Week 14

Week 16

Log IFN+ / CD4+ T Cells


BNTx3 BNTx2 Ad26 Ad26x2 Sham

BNTx3 BNTx2 Ad26 Ad26x2 Sham
Viral Loads (sgRNA) in BAL

Days Following Challenge

Log sgRNA Copies / ml

Sham

BNTx3

Ad26/BNT

BNTx2/Ad26

Ad26x2
Peak and Day 4 Viral Loads (sgRNA) in BAL
Viral Loads (sgRNA) in Nasal Swabs

Days Following Challenge
Peak and Day 4 Viral Loads (sgRNA) in Nasal Swabs
Day 2 Infectious Virus Titers (TCID50)

- **BAL**
  - Log TCID50 / ml
  - BNTx3, BNTx2/Ad26, Ad26/BNT, Ad26x2, Sham

- **Nasal Swab**
  - Log TCID50 / Swab
  - BNTx3, BNTx2/Ad26, Ad26/BNT, Ad26x2, Sham
Immunologic Profile of Vaccine Failures

**NAb**

**CD8**

Log NAb Titer

Log IFN+ / CD8+ T Cells

- BNTx3
- BNTx2/Ad26
- Ad26/BNT
- A26x2
- Sham

- BNTx3
- BNTx2/Ad26
- Ad26/BNT
- A26x2
- Sham
Immunologic Profile of Vaccine Failures Suggests Role of Antibodies and CD8 T Cells in Protection

![Graph showing the relationship between Log NAb Titer and Log IFN+ / CD8+ T Cells. The graph illustrates a negative correlation with red and black data points, indicating a decrease in Log IFN+ / CD8+ T Cells as Log NAb Titer increases.]
Antibody Correlates of Protection

**Peak**
- \( R = -0.6315 \)
- \( P = 0.0002 \)

**Day 4**
- \( R = -0.6917 \)
- \( P < 0.0001 \)

**Log sgRNA Copies / ml** vs. **Log NAb Titer**

**Log sgRNA Copies / ml** vs. **Log ELISA Titer**

**Log sgRNA Copies / ml** vs. **Log NAb Titer**

**Log sgRNA Copies / ml** vs. **Log ELISA Titer**
T Cell Correlates of Protection

Peak

Day 4

Log sgRNA Copies / ml vs Log IFN+ / CD8+ T Cells

R=-0.4586
P=0.0108

R=-0.3149
P=0.0901

Log sgRNA Copies / ml vs Log IFN+ / CD4+ T Cells

R=-0.6994
P<0.0001

R=-0.5075
P=0.0042
Vaccine Protection Against SARS-CoV-2 Omicron in Macaques

• Rapid virologic control in vaccinated macaques in lower respiratory tract following SARS-CoV-2 Omicron challenge

• Significant virologic control by heterologous vaccine regimens (BNT/Ad26, Ad26/BNT) in upper respiratory tract

• BNT162b2 induced higher antibody responses; Ad26.COV2.S induced higher CD8 T cell responses

• Both antibody and CD8 T cell responses correlated with virologic control; virologic failure in upper respiratory tract associated with moderate NAb titers and low CD8 T cell responses
# Acknowledgements

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<th>CVVR, Beth Israel Deaconess</th>
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