Moderna mRNA vaccine-mediated protection in mice against emerging SARS-CoV-2 variants

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Immunogenicity and challenge analysis of preclinical Moderna mRNA vaccines in mice

Primary series: two doses
High dose = 5 μg
Low dose = 0.1 or 0.25 μg (more like human response)
How does a primary (two-dose) series of mRNA-1273 perform against B.1.1.529 (Omicron)?

Day 42: Bleed
Day 0: 1st dose
5 or 0.1 mg
Day 22: 2nd dose
5 or 0.1 mg
Day 56/57: Challenge
WA1/2020 or B.1.1.529
High-dose mRNA-1273 vaccine generates neutralizing antibodies against B.1.1.529 (Omicron) but low-dose loses this activity

Ying et al, unpublished
Low-dose mRNA-1273 vaccine results in substantial breakthrough infection by B.1.1.529 (Omicron) in lungs

Ying et al, unpublished
Low-dose **mRNA-1273** vaccine results in B.1.1.529 (Omicron) breakthrough infection with lung inflammation

![Heatmap of cytokine expression](image)

- **0.1 µg mRNA Vaccine**
- **WA1/2020 D614G**
- **B.1.1.529**

*Ying et al, unpublished*
Low-dose mRNA-1273 vaccine results in B.1.1.529 (Omicron) breakthrough infection with mild pneumonia

Ying et al, unpublished
How does a **mRNA-1273** booster (3rd dose) perform against B.1.1.529 (Omicron)?

Day 139/155: Bleed

Pre-boost

Day 0: 1st dose
5 or 0.25 mg

Day 21/22: 2nd dose
5 or 0.25 mg

Day 168/184: Challenge

B.1.1.529

3 weeks  4 weeks  17/19 weeks

Day 140/156: booster
1 mg

Day 166/182: Bleed
Post-boost

K18-hACE2 Tg
A **mRNA-1273** booster (3rd dose) generates a 5-fold higher neutralizing antibody response against B.1.1.529 (Omicron)

Ying et al, unpublished
A mRNA-1273 booster (3rd dose) results in substantial protection for a low-dose primary series against B.1.1.529 (Omicron) in lungs

Ying et al, unpublished
How does a **mRNA-1273.529** vaccine (two-dose) primary series perform?

**Day 0:** 1st dose
- 1 mg or 0.1 mg

**Day 21:** 2nd dose
- 1 mg or 0.1 mg

3 weeks later:

**Day 21:** Bleed

2 weeks later:

**Day 36:** Bleed

**BALB/c**
mRNA-1273.529 vaccine generates high neutralizing antibody responses against B.1.1.529 (Omicron), but not against other VOC
How does a mRNA-1273.529 booster (3\textsuperscript{rd} dose) perform against B.1.1.529 (Omicron)?

Day 97/98: Bleed
Pre-boost
Day 0: 1\textsuperscript{st} dose
5 or 0.25 g
Day 21: 2\textsuperscript{nd} dose
5 or 0.25 g
Day 124/126: Challenge
WA1/2020 N501Y/D614G B.1.1.529

Day 98/99: booster
1 g

Day 121/122: Bleed
Post-boost
Day 124/126: Challenge
WA1/2020 N501Y/D614G B.1.1.529

3 weeks
3-4 weeks
10-11 weeks
A mRNA-1273.529 booster (3rd dose) generates 42-fold higher neutralizing antibody responses against B.1.1.529 (Omicron)

Note: mRNA-1273 booster generates 5-fold higher neutralizing antibody responses

Ying et al, unpublished
A mRNA-1273.529 booster (3rd dose) results in substantial protection for a low-dose primary series against B.1.1.529 (Omicron) in lungs.

Note: mRNA-1273 booster also results in significant protection against B.1.1.529.
A mRNA-1273.529 booster (3rd dose) results in less lung inflammation for a low-dose primary series against B.1.1.529 (Omicron)

Note: mRNA-1273 booster also results in less lung inflammation

Ying et al, unpublished
• High-dose primary (two-dose) series of vaccines protect against B.1.1.529

• Low-dose primary (two-dose) series of vaccines (more like human responses?) shows virological breakthrough, inflammation and mild pneumonia in the lung with B.1.1.529

• Boosting with the current ‘unmatched’ vaccine shows protection against B.1.1.529

• A primary (two-dose) series with B.1.1.529-targeted vaccine shows immunogenicity against B.1.1.529, but not against other variants of concern

• Boosting with a ‘matched’ B.1.1.529-targeted vaccine shows some increased protection compared to the ‘unmatched’ vaccine against B.1.1.529

• Testing sera from mice boosted with ’unmatched’ and ‘matched’ B.1.1.529-targeted vaccines for immunogenicity to B.1.1.529 BA.2 lineage underway
Acknowledgements

Diamond Lab
Baoling Ying
Bradley Whitener
Suzanne Schaefer
Brett Case
Ahmed Hassan
Natasha Kafai
Alex Wessel
Sharmila Nair
Roseanne Zhao
Chris Bullock
Autumn Holmes
Saran Raju

Pritesh Desai
Hongming Ma
Ofer Zimmerman
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John Errico
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Lucas Adams

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