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ORIGINAL ARTICLE

An mRNA Vaccine against SARS-CoV-2 — Preliminary Report

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Journal Club

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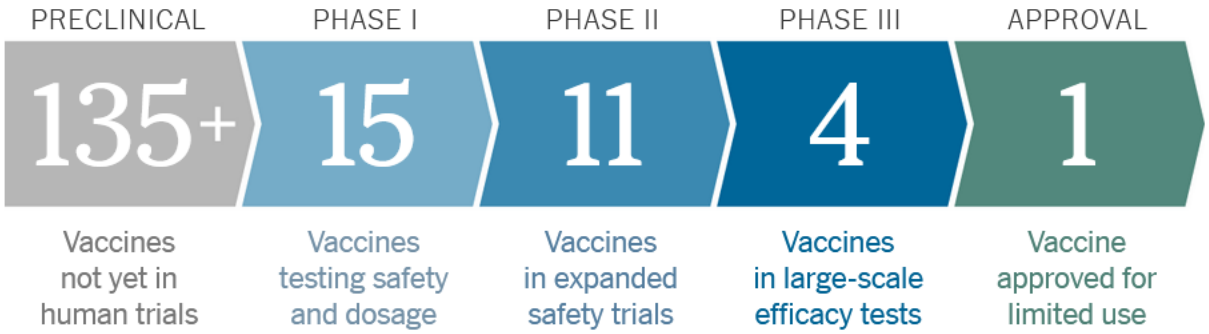
Sabine Kuster

Background

The New York Times

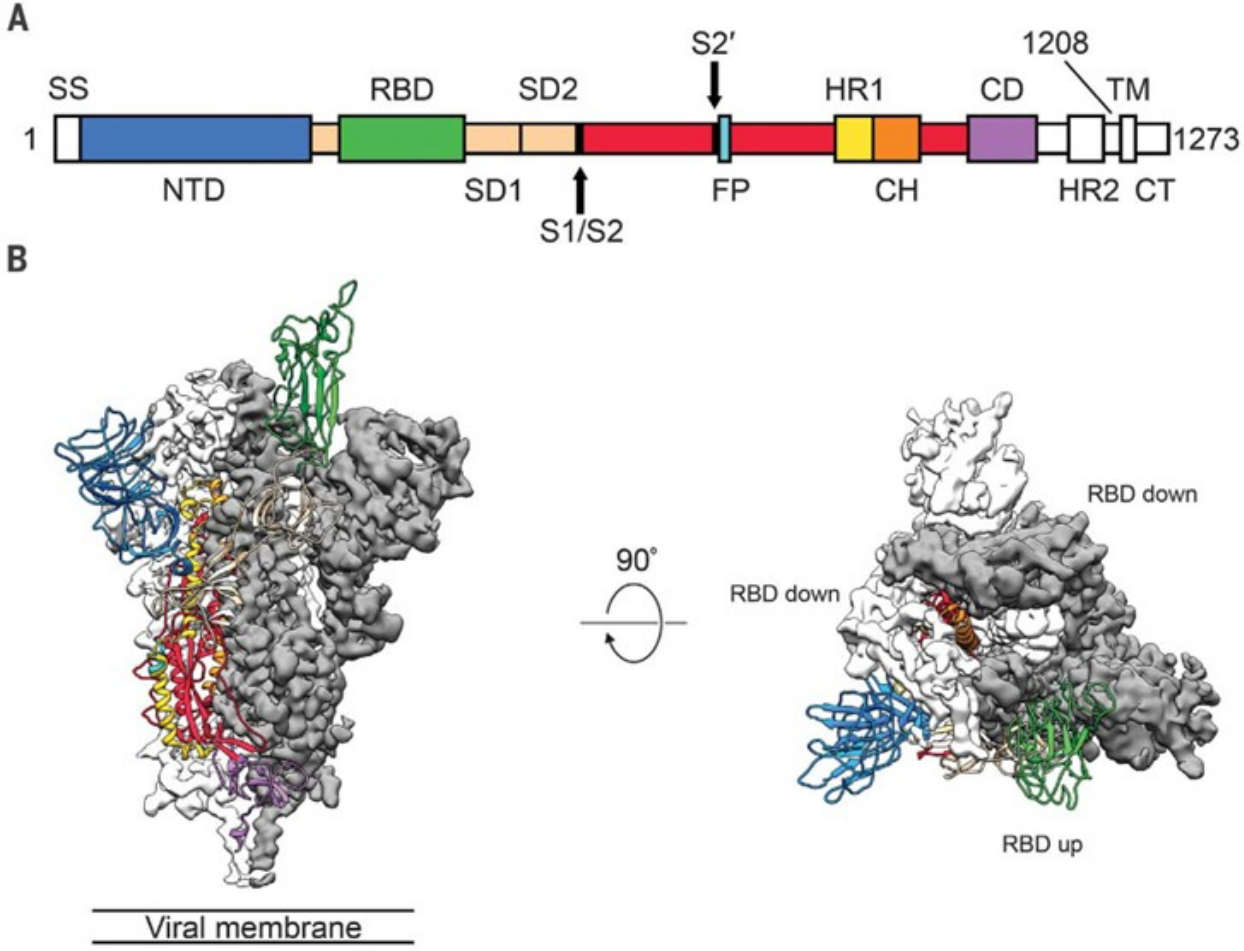
Coronavirus Vaccine Tracker

By Jonathan Corum, Denise Grady, Sui-Lee Wee and Carl Zimmer Updated July 16, 2020



Researchers around the world are developing more than 155 vaccines against the coronavirus, and **23 vaccines** are in human trials. Vaccines typically require years of research and testing

SARS-CoV-2 Spike Protein



Wrapp D, Wang N, Corbett KS et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion confirmation. Science 2020;367:1260-3

Trial design and praticipants

- Phase 1 dose-escalation, open-lable trial
- Healthy adults 18 – 55 years of age
- Two injections 28 days apart
- Dose: 25µg, 100µg and 250µg
- No screening for SARS-CoV-2 infection before enrollment
- Developed by NIAID and Moderna

Vaccine

- mRNA-1273 encodes the S-2P antigen
  - SARS-CoV-2 glycoprotein with transmembran anchor and intact S1-S2 cleavage site
- S-2P is stabilized in prefusion conformation
- Nanoparticle capsule of four lipids

Trial procedures

- 0.5ml injection on day 1 and day 29
- Follow-up visits: day 7 and day 14 after each vaccination, days 57, 119, 209 and 394
- 4 sentinel participants in each group
- Recording of local and systemic reactions

Assessment of immunoresponses

- ELISA to asses binding antibody responses to S-2P and the isolated receptor-binding-domain
- Neutralizig activity was assessed using pseudotyped lentivirus (PsVNA) and live wild-type virus (PRNT)
- Comparison with 41 convalescent serum specimens
- Intracellular cytokine-staining of T-cells

Results

Table 1. Characteristics of the Participants in the mRNA-1273 Trial at Enrollment.*

Characteristic	25-μg Group (N=15)	100-μg Group (N=15)	250-μg Group (N=15)	Overall (N=45)
Sex — no. (%)				
Male	9 (60)	7 (47)	6 (40)	22 (49)
Female	6 (40)	8 (53)	9 (60)	23 (51)
Age — yr	36.7±7.9	31.3±8.7	31.0±8.0	33.0±8.5
Race or ethnic group — no. (%)†				
American Indian or Alaska Native	0	1 (7)	0	1 (2)
Asian	0	0	1 (7)	1 (2)
Black	0	2 (13)	0	2 (4)
White	15 (100)	11 (73)	14 (93)	40 (89)
Unknown	0	1 (7)	0	1 (2)
Hispanic or Latino — no. (%)	1 (7)	3 (20)	2 (13)‡	6 (13)
Body-mass index§	24.6±3.4	26.7±2.6	24.7±3.1	25.3±3.2

* Plus–minus values are means ±SD.
† Race or ethnic group was reported by the participants.
‡ One participant did not report ethnic group.
§ The body-mass index is the weight in kilograms divided by the square of the height in meters. This calculation was based on the weight and height measured at the time of screening.

Adverse events

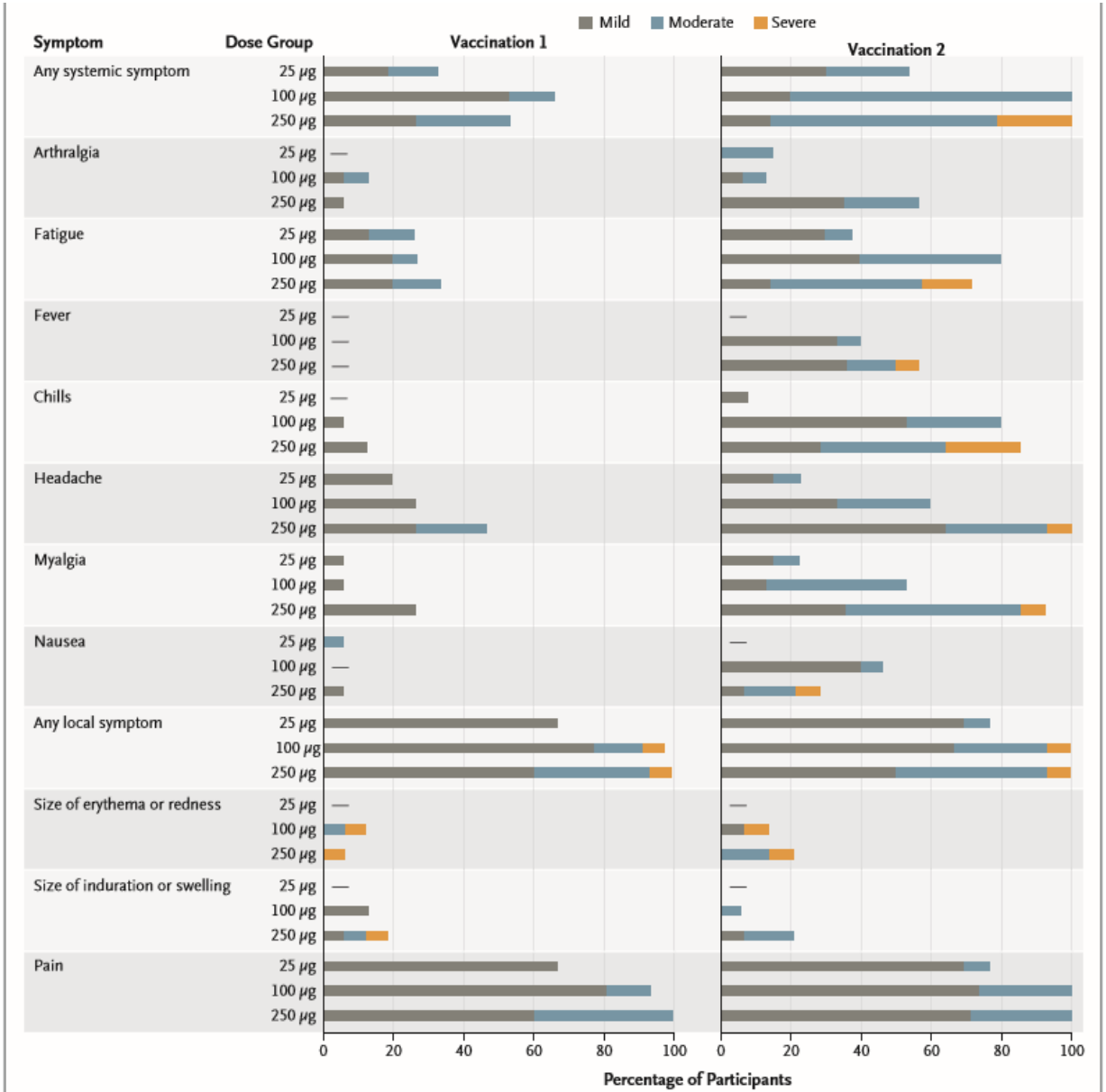
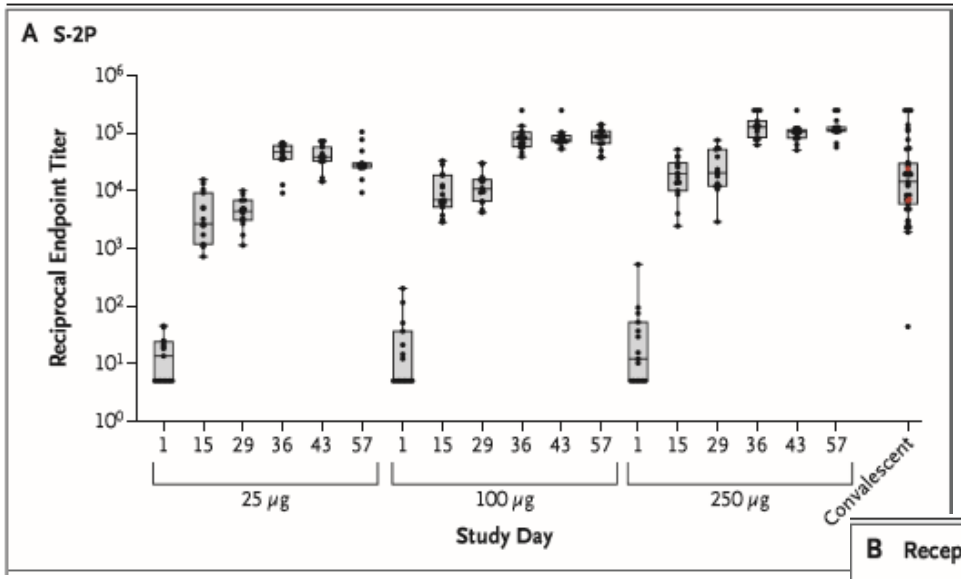
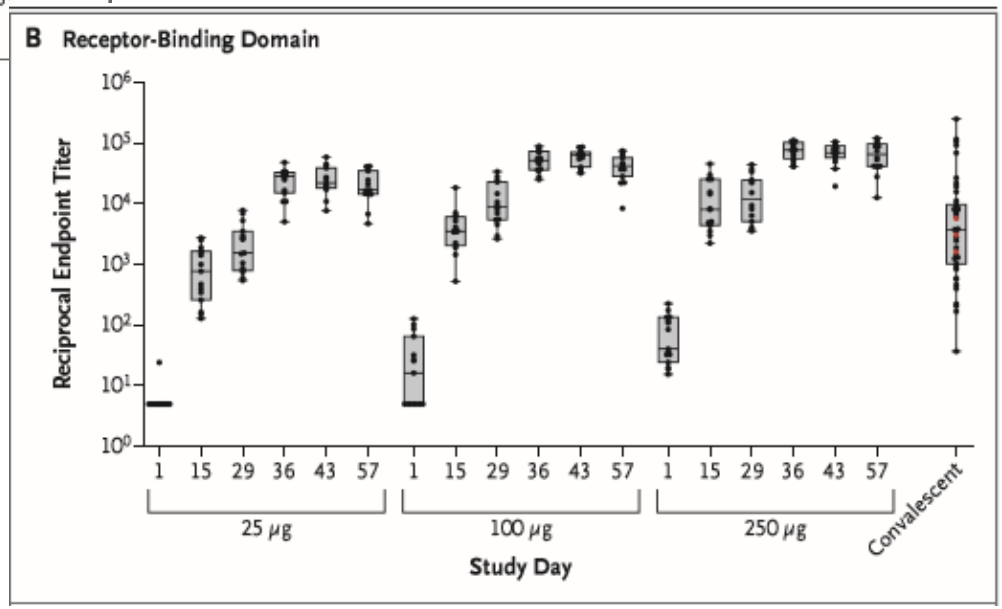


Figure 1. Systemic and Local Adverse Events.

The severity of solicited adverse events was graded as mild, moderate, or severe (see Table S1).

Antibody Respones





Neutralization respones

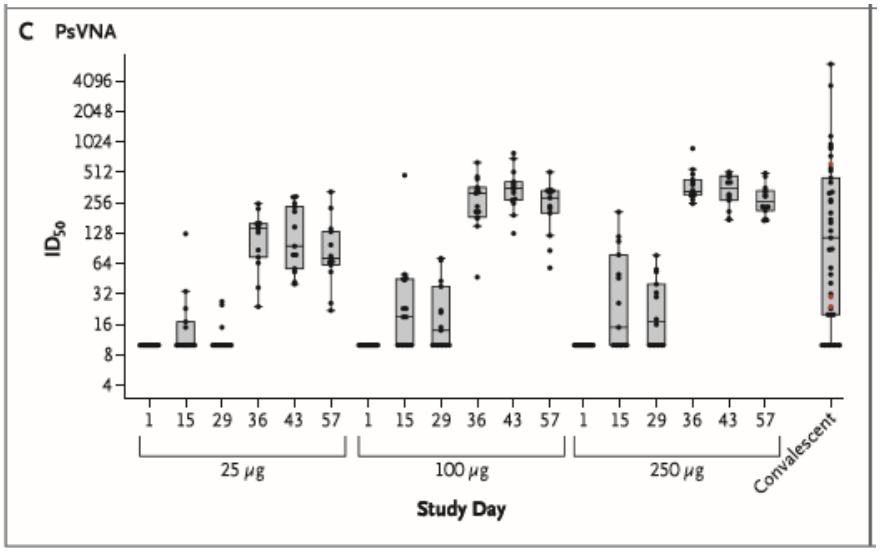
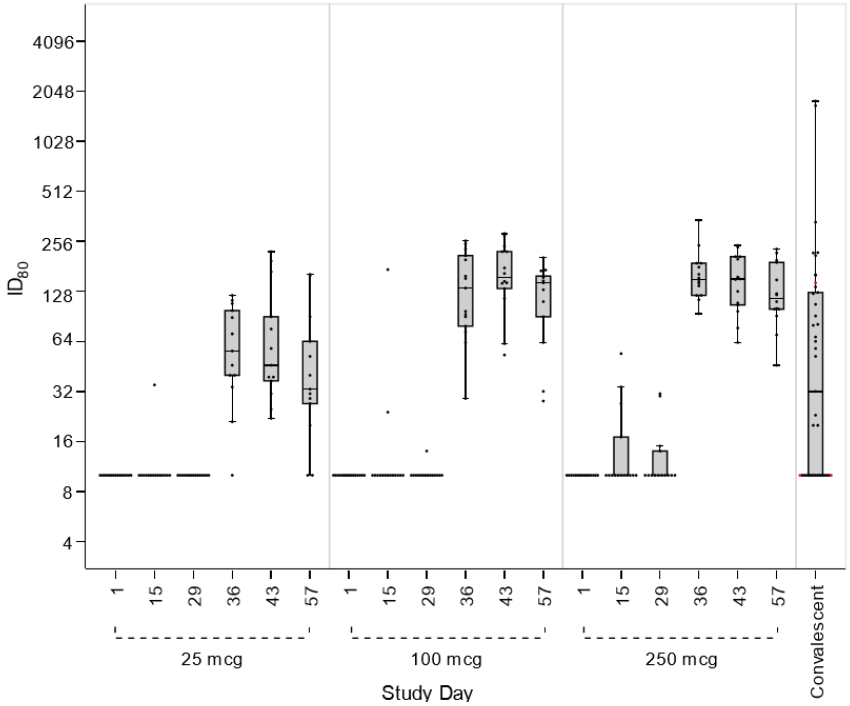


Figure S2. Pseudovirus neutralization assay responses by time point and vaccination group - ID80.



Neutralization responses (2)

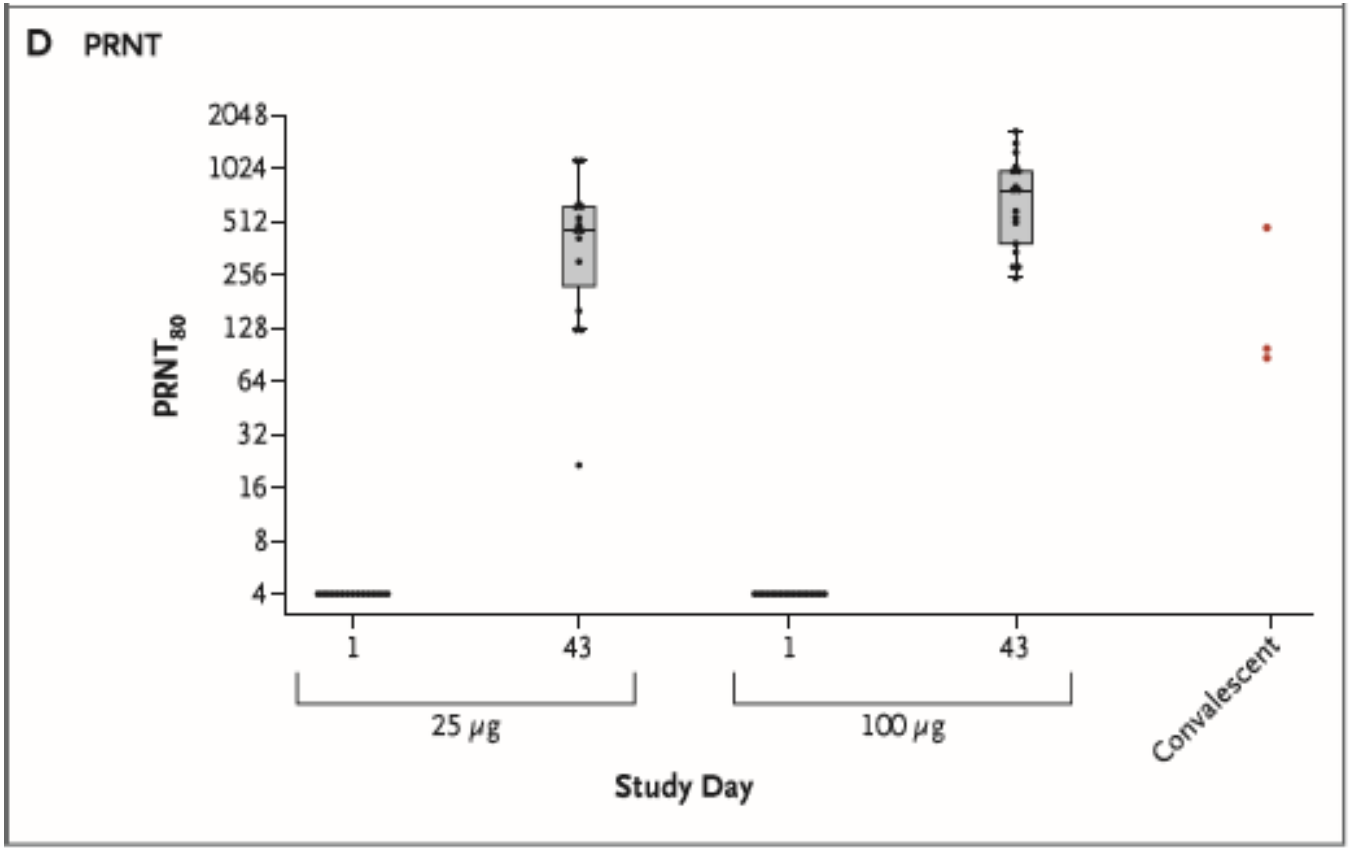


Figure S5. Pseudovirus neutralization correlates with binding in ELISA.

A, vaccinee sera pseudovirus neutralization (ID50) vs S-2P binding (AUC). **B**, vaccinee sera pseudovirus neutralization ID80 vs S-2P AUC. **C**, convalescent sera ID50 vs S-2P AUC. **D**, convalescent sera ID80 vs S-2P AUC.

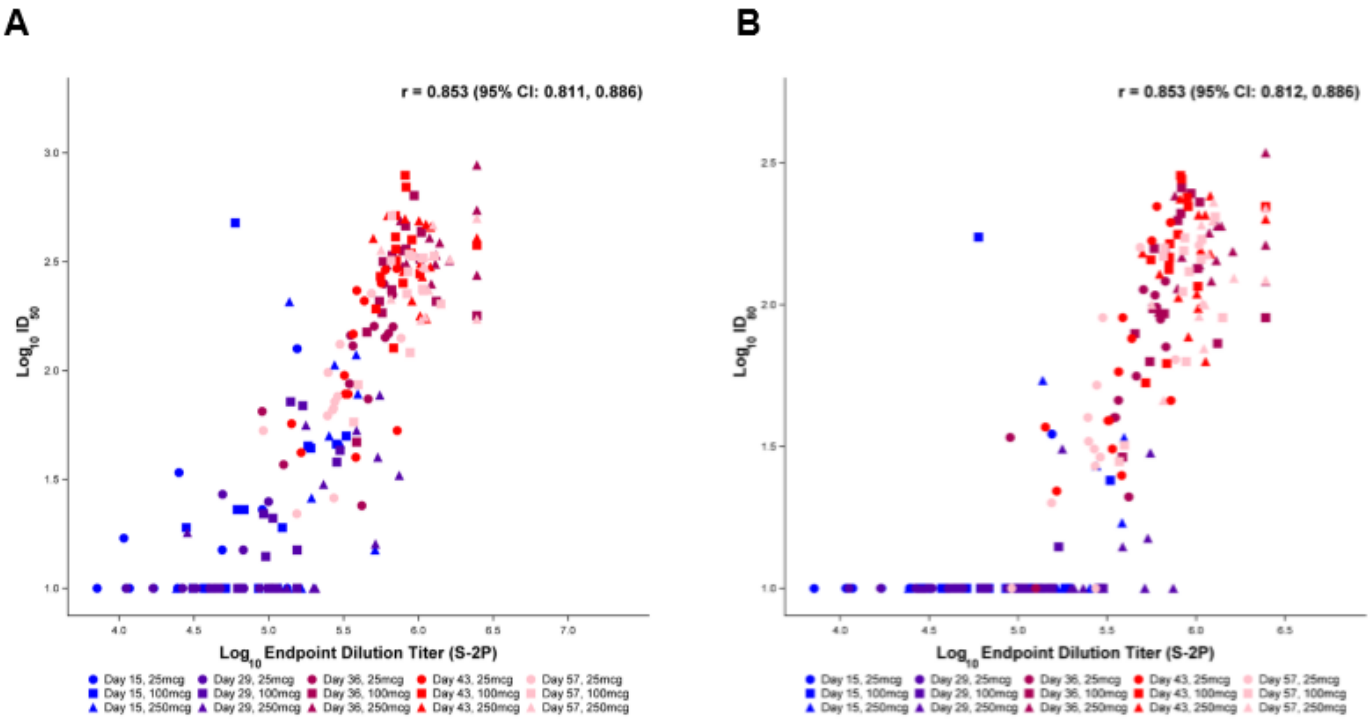
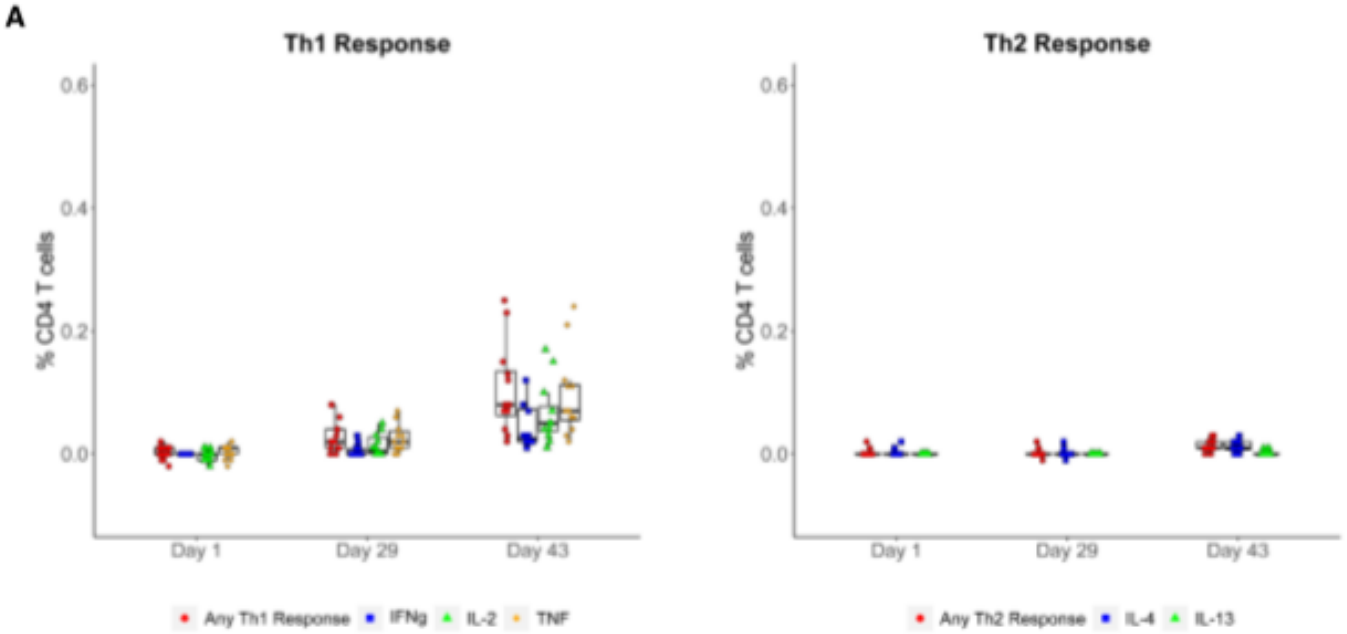


Fig S9. mRNA-1273-specific CD4 T cell responses (S1 peptide pool).

Frequencies of CD4 T cells producing the indicated cytokines from 25mcg (**A**) or 100mcg (**B**) dose groups following stimulation with SARS-CoV-2 S1 peptide pool. For Th1 responses (left) red circles indicate any combination of IFN-γ, IL-2 and TNF, blue squares indicate IFN-γ, green triangles indicate IL-2, and orange diamonds indicate TNF. For Th2 cytokine responses (right), red circles indicate any combination of IL-4 and IL-13, blue squares indicate IL-4, and green triangles indicate IL-13.



Discussion

- Generally without serious toxicity
- Vaccine is immunogenic
- Antibody titers were similar to those in convalescent serum
- Serum neutralizing activity is a mechanistic correlate of protection for other respiratory viruses

Discussion (2)

- Durability of the immune responses are unknown
- Robust immunogenicity profile due to innovative structure-based vaccine antigen design

Conclusion

- Safety and immunogenicity findings support advancement of the mRNA-1273 vaccine to later-stage clinical trials

Outlook

- Phase I trial results with 7 additional groups
- Phase II trial results (600 healthy adults, placebo controlled, dose-confirmation study 50µg vs. 100µg)
- Phase III trial (1:1 placebo vs. 100µg)