SARS-CoV-2 Spike Ferritin Nanoparticle Vaccine

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World Health Organization Pan-Sarbecovirus Vaccine Consultation

28 January 2022
We know what is awaiting us on the horizon
Parallel Pursuits

Universal Coronavirus Vaccines — An Urgent Need
David M. Morens, M.D., Jeffery K. Taubenberger, M.D., Ph.D., and Anthony S. Fauci, M.D.

AS Fauci, White House Briefing, 26 January 2022
Self-assembling influenza nanoparticle vaccines elicit broadly neutralizing H1N1 antibodies

Hadi M Yassine1,6, Jeffrey C Boyington1,6, Patrick M McTamney1,5,6, Chih-Jen Wei1,5,6, Masaru Kanekiyo1, Wing-Pui Kong1, John R Gallagher2, Lingshu Wang1, Yi Zhang1, M Gordon Joyce1, Daniel Lingwood1,5, Syed M Moin1, Hanne Andersen3, Yoshinobu Okuno4, Srinivas S Rao1,5, Audray K Harris2, Peter D Kwong1, John R Mascola1, Gary J Nabel1,5 & Barney S Graham1

Hemagglutinin-stem nanoparticles generate heterosubtypic influenza protection

Masaru Kanekiyo1, Chih-Jen Wei1, Hadi M Yassine1, Patrick M McTamney4, Jeffrey C Boyington1, James R. R. Whittle1, Srinivas R. Rao5, Wing-Pui Kong1, Lingshu Wang1 & Gary J. Nabel1,5

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Gordon Joyce, Masaru Kanekiyo, Yi Zhang, M Gordon Joyce, Daniel Lingwood, Syed M Moin, Hanne Andersen, Yoshinobu Okuno, Srinivas S Rao, Audray K Harris, Peter D Kwong, John R Mascola, Gary J Nabel & Barney S Graham
Immunogen Designs – 4 Categories, 215 Candidates

- **SARS-CoV-2 Spike-Ferritin Nanoparticle**
  - pCoV1B-01 – 02
    - (12-1137)
  - pCoV1B-03 – 04
    - (12-1208)
  - pCoV1B-05 – 10
    - (12-1158)

- **SARS-CoV-2 RBD-Ferritin Nanoparticle**
  - pCoV29 – pCoV31
    - RBD linker sequence variations
  - pCoV1A-01 – 06
    - Increase distance of RBD from ferritin
  - pCoV49 – pCoV63
    - Individual mutations to reduce surface hydrophobicity

- **Combinations of mutations**
  - pCoV127 – 132
    - pCoV127: F490A + NAG 518
    - pCoV128: F490R + L518R
    - pCoV129: Y449K, L455R, F490R + NAG 518
    - pCoV130: Y449K, L455R, F490R + L518R
    - pCoV132: Y453R + L518R

- **SARS-CoV-2 RBD-NTD-Ferritin Nanoparticle**
  - pCoV122
  - pCoV123 – pCoV126
    - Individual mutations to reduce surface hydrophobicity
  - pCoV146
    - RFN
      - pCoV131
        - Y453R + NAG 518

- **SARS-CoV-2 S1-Ferritin Nanoparticle**
  - pCoV02 (16-676)
  - pCoV11 – pCoV120
    - Surface mutations to reduce hydrophobicity
  - Addition of S2 region
  - pCoV108
    - (12-655)
  - pCoV109
    - (12-696)
  - pCoV111
    - (12-676–689-696)

- **Combinations of mutations**
  - pCoV123 – pCoV126
    - Individual mutations to reduce surface hydrophobicity
  - pCoV127: F490R
  - pCoV124: F490A
  - pCoV125: NAG 518
  - pCoV126: L518R

- **RFN**
  - Y453R + NAG 518

- **G. Joyce...K. Modjarrad. Cell Reports 2021.**
SARS-CoV-2 Spike Ferritin Nanoparticle (SpFN) with ALFQ Adjuvant

Figure 5. Theoretical formation of a “sugar lawn” of ten sugars on the surface of ALFQ by interaction of QS21 with ALF liposomes containing a ratio of 55 mol% cholesterol compared to phospholipid.

M Rao, K Peachman, C Alving

G. Joyce…K. Modjarrad. Cell Reports 2021
Lung & Nasal Viral Load Post Challenge in SGH

K Wuertz....K Modjarrad NPJ Vaccines 202
Potent neutralizing activity (peak) against all VOCs in NHPs

<table>
<thead>
<tr>
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</table>

G. Joyce...K. Modjarrad. Science Translational Medicine 2021
SpFN Elicits a Neutralizing Activity against SARS-CoV-1 (Urbani)


**Mice**

**C57BL6**

- Week 2
- Week 5
- Week 8

**Balb/c**

- Week 2
- Week 5
- Week 8

*10ug with ALFQ

**NHPs**

**Live Virus**

SARS1: week 6 sera

**Pseudovirus**

SARS-1


What’s Next?