

¿Las vacunas del SARS-CoV-2 llegarán a tiempo?

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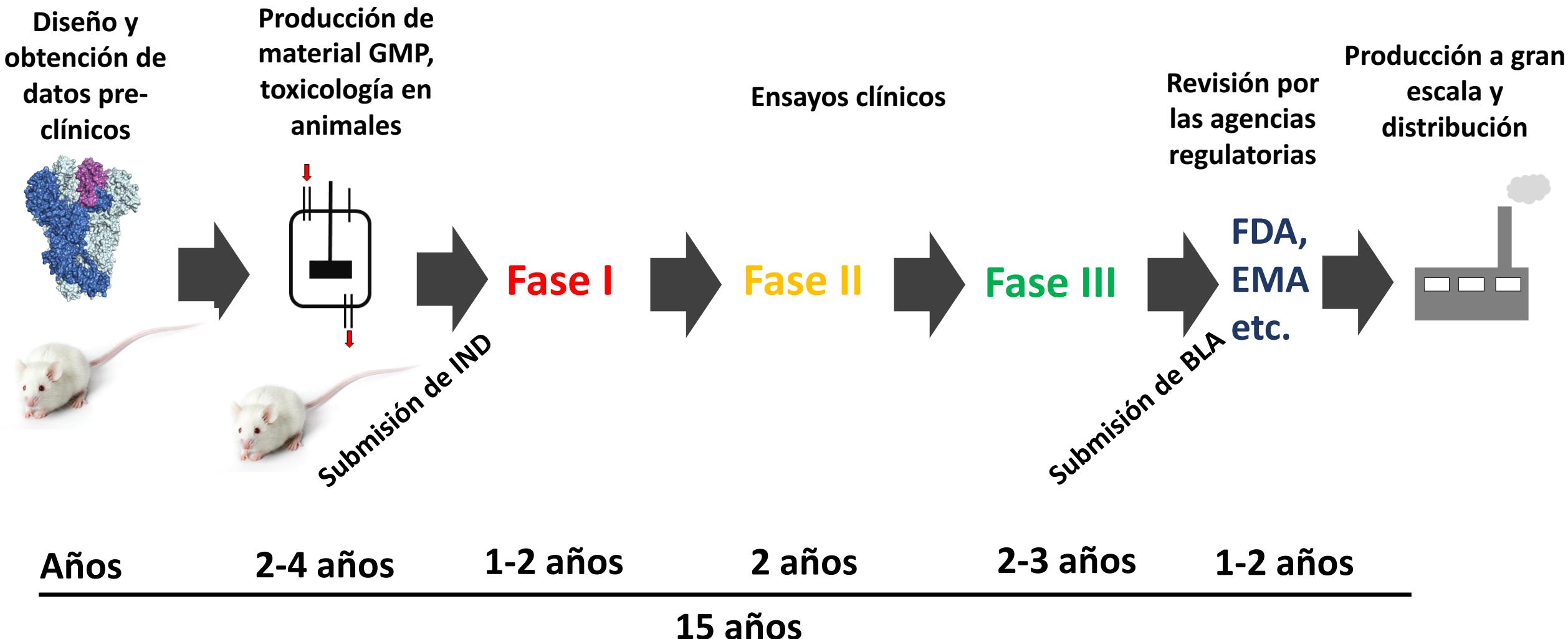
Vacuna ideal

Una sola administración proporciona protección por largo tiempo contra la infección y la enfermedad en todos los grupos.

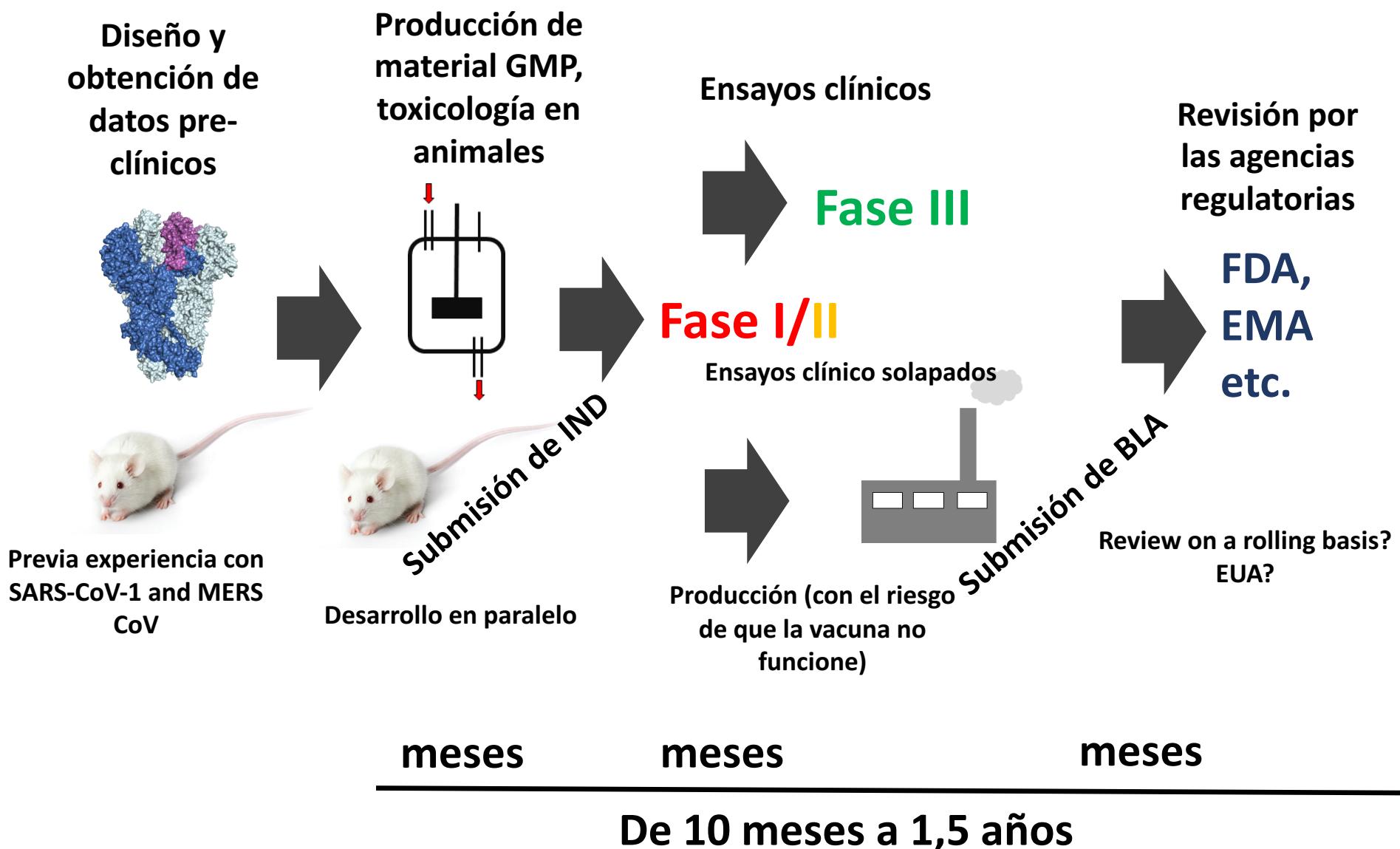
Pero incluso una vacuna que proporcione protección parcial por un año contra la enfermedad después de varias dosis ayudaría mucho en este momento.

Las vacunas son en general poco inmunogénicas en personas de edad avanzada. Sin embargo, todavía se podrían beneficiar de una vacuna por la protección de rebaño.

Tiempo habitual de desarrollo de una nueva vacuna antes de la pandemia de COVID-19



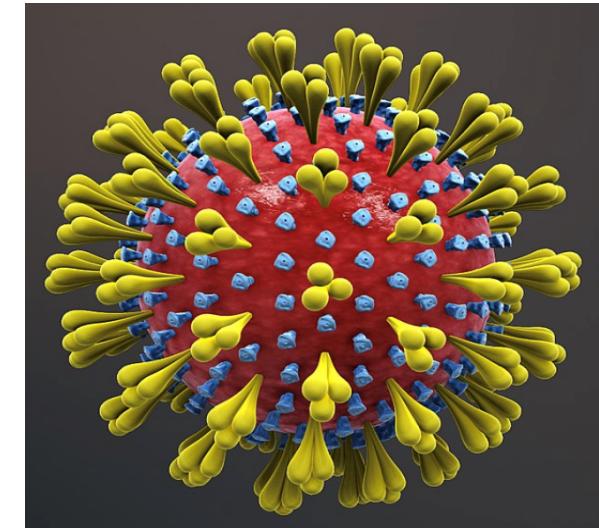
Tiempo para el desarrollo de una vacuna para COVID-19



Vacunas de COVID-19

Estrategias

- Inactivadas
- Atenuadas
- Proteína recombinante
- Vectorizada
- DNA
- RNA



Otras consideraciones

Adyuvantes

Nano partículas

Ruta de administración

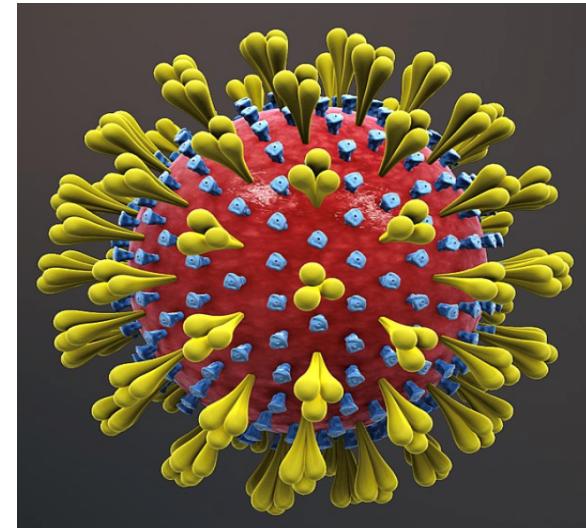
Antígeno

Spike (S)

Antígenos víricos adicionales

Vacunas de COVID-19

- Las vacunas se están produciendo en un tiempo record
- Más de 100 candidatos
- Unos pocos están ya en Fase 3 de pruebas clínicas
- Los resultados en modelos animales y los de Fase 1/2 son prometedores
- Pero quedan todavía muchas preguntas sin resolver:
 - ¿Cuáles son los niveles de anticuerpos en sangre que correlaciona con protección (infección, enfermedad)?
 - ¿Se requiere inmunidad mucosal para la efectividad?
 - ¿Cuánto dura la inmunidad?
 - ¿Cuándo conoceremos los resultados de los ensayos de Fase 3?
 - ¿Cómo y dónde producir las dosis requeridas, cómo administrarlas rápidamente?
 - ¿A qué grupos administrar la vacuna primero?
 - ¿Se va a vacunar todo el mundo si se disponen de las dosis necesarias?



Se necesitan 16,000 millones de dosis

Uso de NDV como vacuna para COVID-19

Posibles ventajas

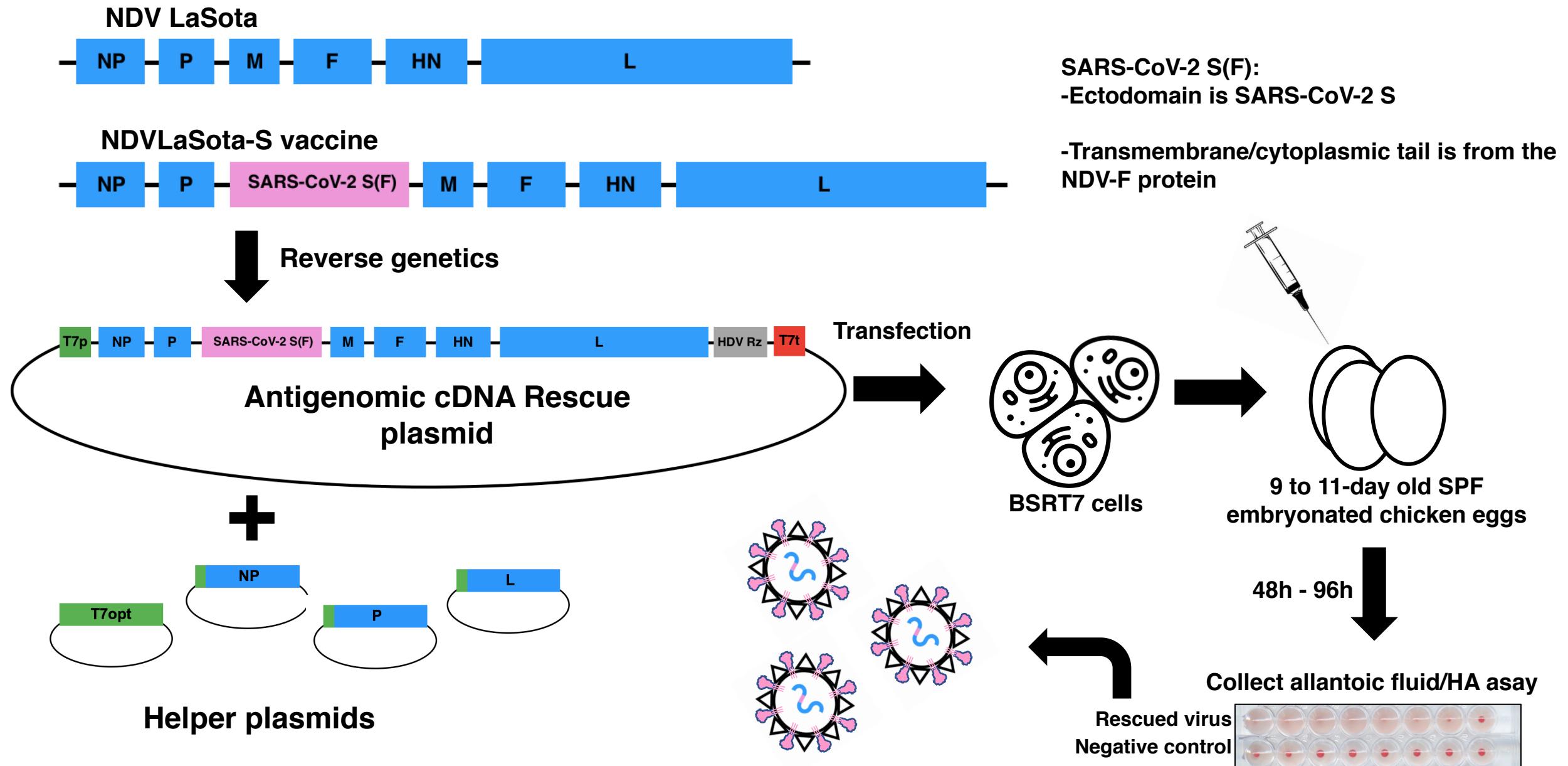
No existen inmunidad pre-existente en humanos contra el vector NDV.

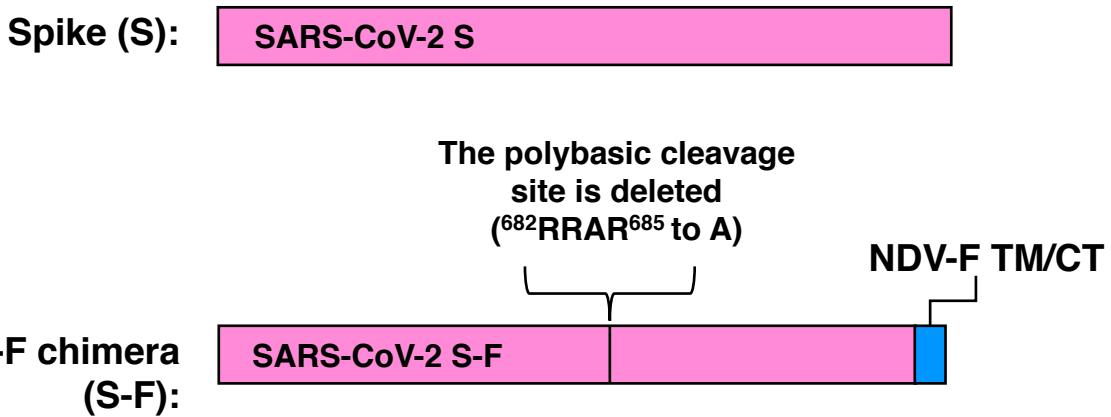
Se pueden producir usando la misma tecnología que se usa para producir las vacunas de gripe.

NDV se ha probado en pacientes con cáncer y no produce efectos adversos severos.

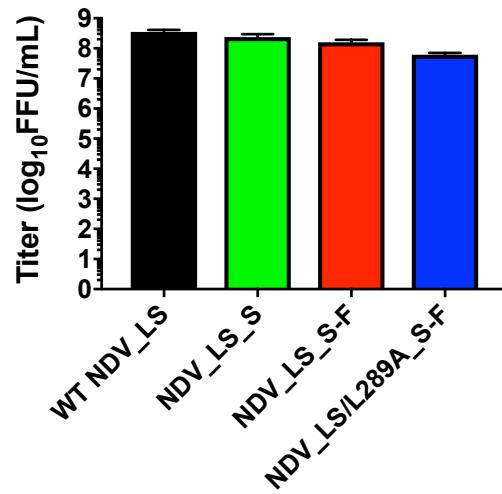
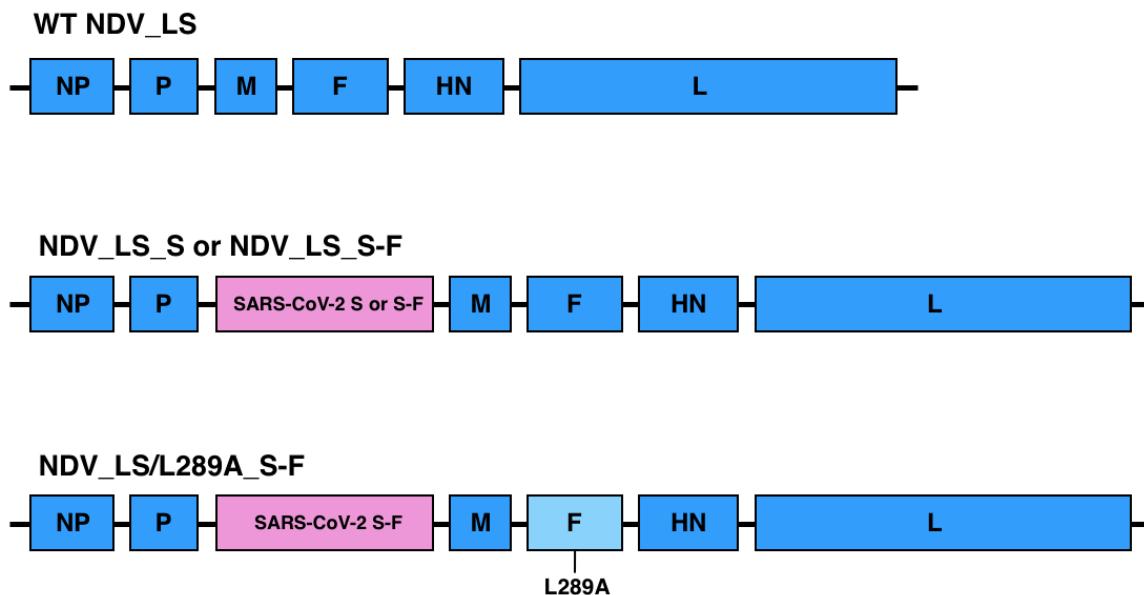
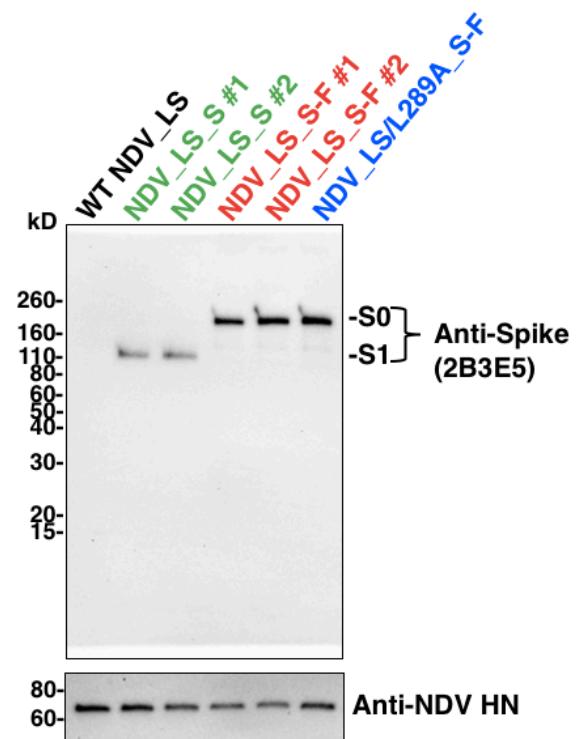
Peter Palese, Weina Sun, Adolfo García-Sastre and Florian Krammer
Icahn School of Medicine at Mount Sinai

Rescue of NDV expressing the SARS-CoV-2 S(F) protein



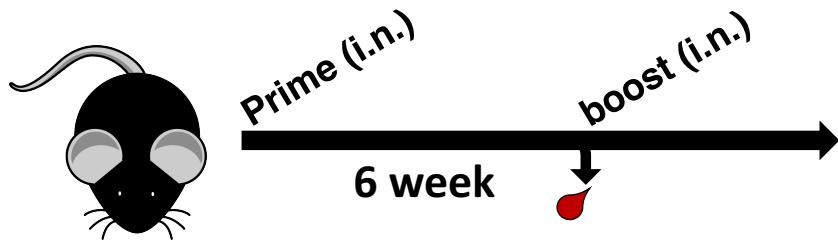
A**C**

Virus grown in embryonated chicken eggs

**B****D**

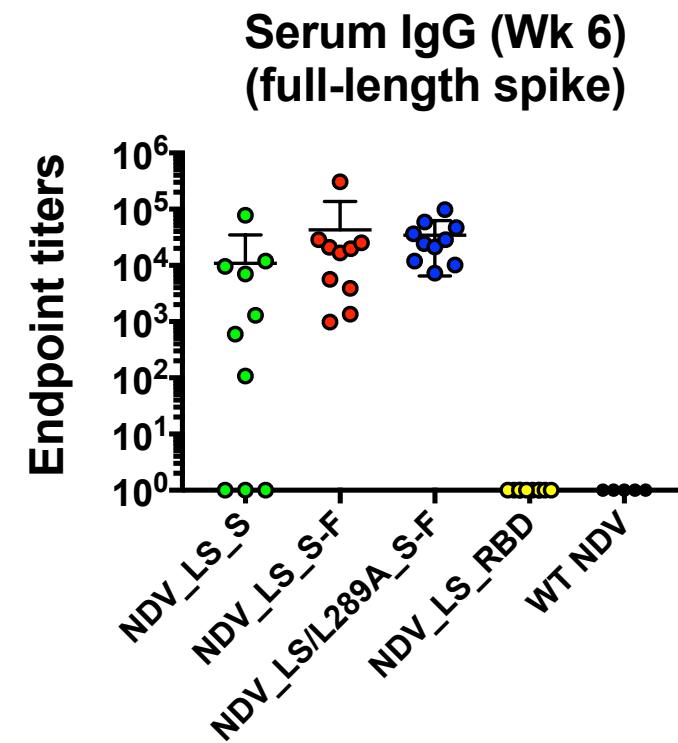
A pilot intranasal vaccination experiment

A



Groups	Prime	Boost
1	NDV_LS_S	NDV_LS_S
2	NDV_LS_S-F	NDV_LS_S-F
3	NDV_LS/L289A_S-F	NDV_LS/L289A_S-F
4	NDV_LS_RBD	NDV_LS_RBD
5	WT NDV_LS	NDV_LS_S-F WT

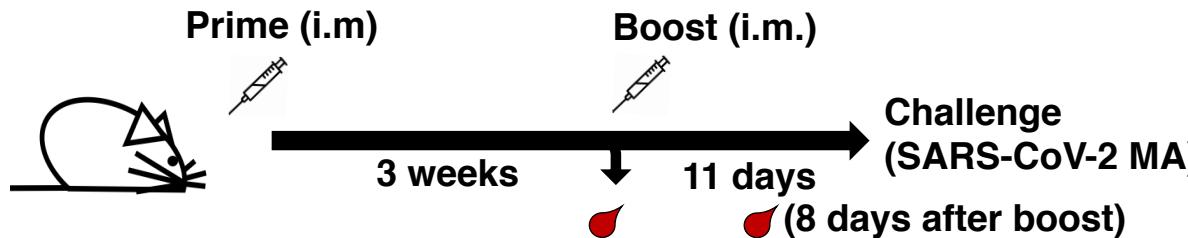
B



(A) Immunization groups and regimen. C57BL/6 mice were vaccinated with 10^5 ffu/mouse of NDV_LS_S, NDV_LS_S-F, NDV_LS/L289A_S-F or NDV_LS_RBD (secreted RBD was expressed as the transgene) intranasally (i.n.). Wild type NDV_LS was given to a group of mice at 10^5 ffu/mouse as negative controls. Six weeks after the prime, each group of mice were bled and then boosted with the same virus at the same dose (10^5 ffu/mouse). **(B)** Serum IgG titers. Pre-boost (6 weeks after prime) serum IgG toward the full-length spike was measured by ELISAs.

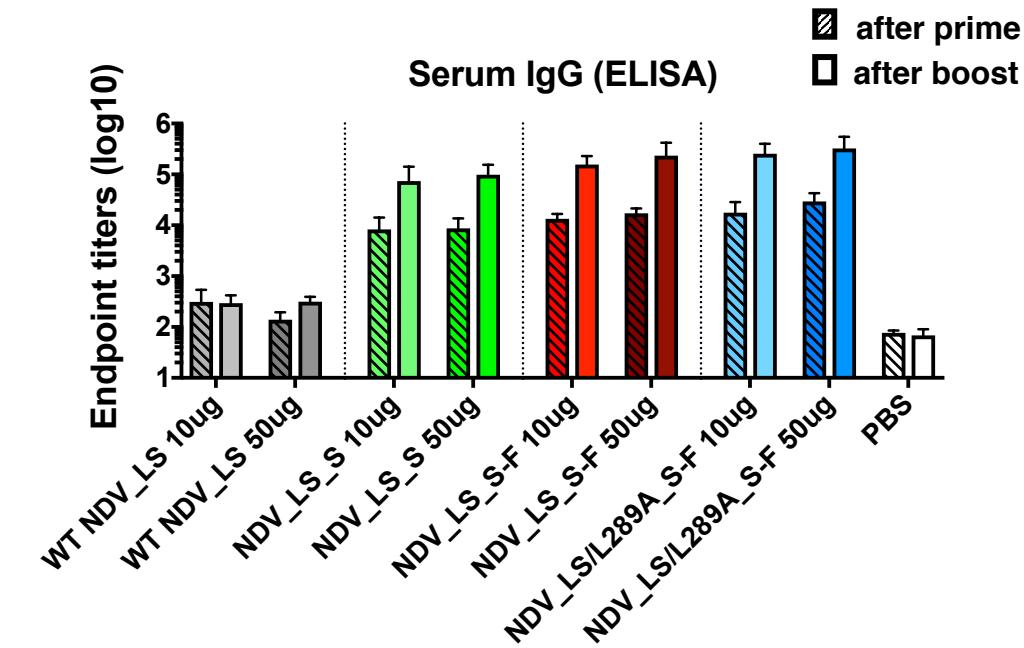
The NDV-S live vaccine induced high spike-specific serum IgG in mice

A

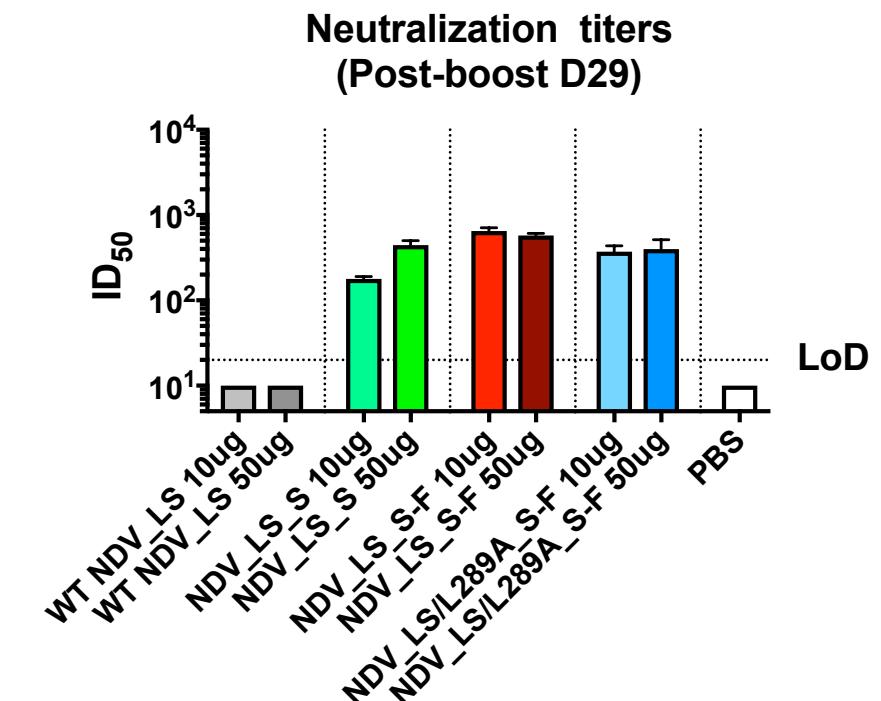


Groups (n=5)	Prime	Boost
1	WT NDV_LS 10ug	WT NDV_LS 10ug
2	WT NDV_LS 50ug	WT NDV_LS 50ug
3	NDV_LS_S 10ug	NDV_LS_S 10ug
4	NDV_LS_S 50ug	NDV_LS_S 50ug
5	NDV_LS_S-F 10ug	NDV_LS_S-F 10ug
6	NDV_LS_S-F 50ug	NDV_LS_S-F 50ug
7	NDV_LS/L289A_S-F 10ug	NDV_LS/L289A_S-F 10ug
8	NDV_LS/L289A_S-F 50ug	NDV_LS/L289A_S-F 50ug
9	PBS	PBS
10	Healthy control	

B

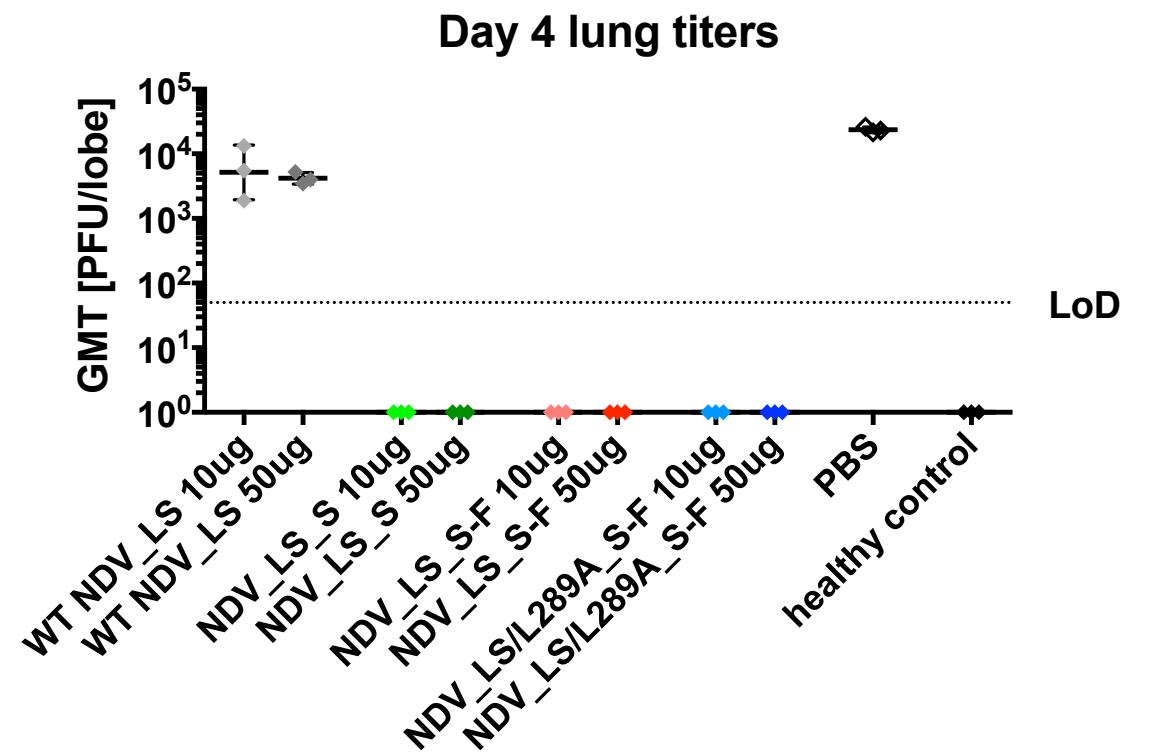
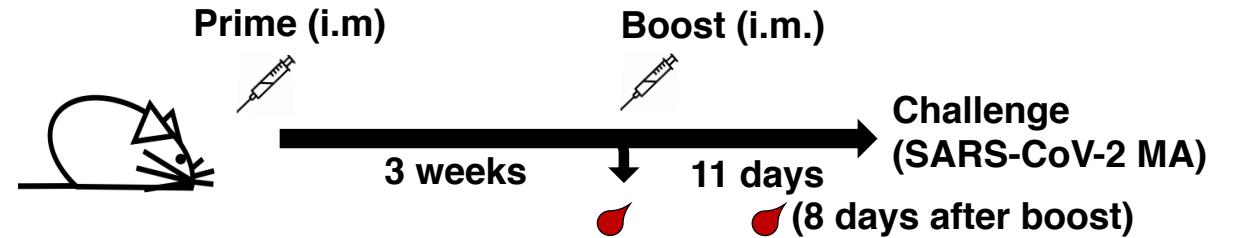


C

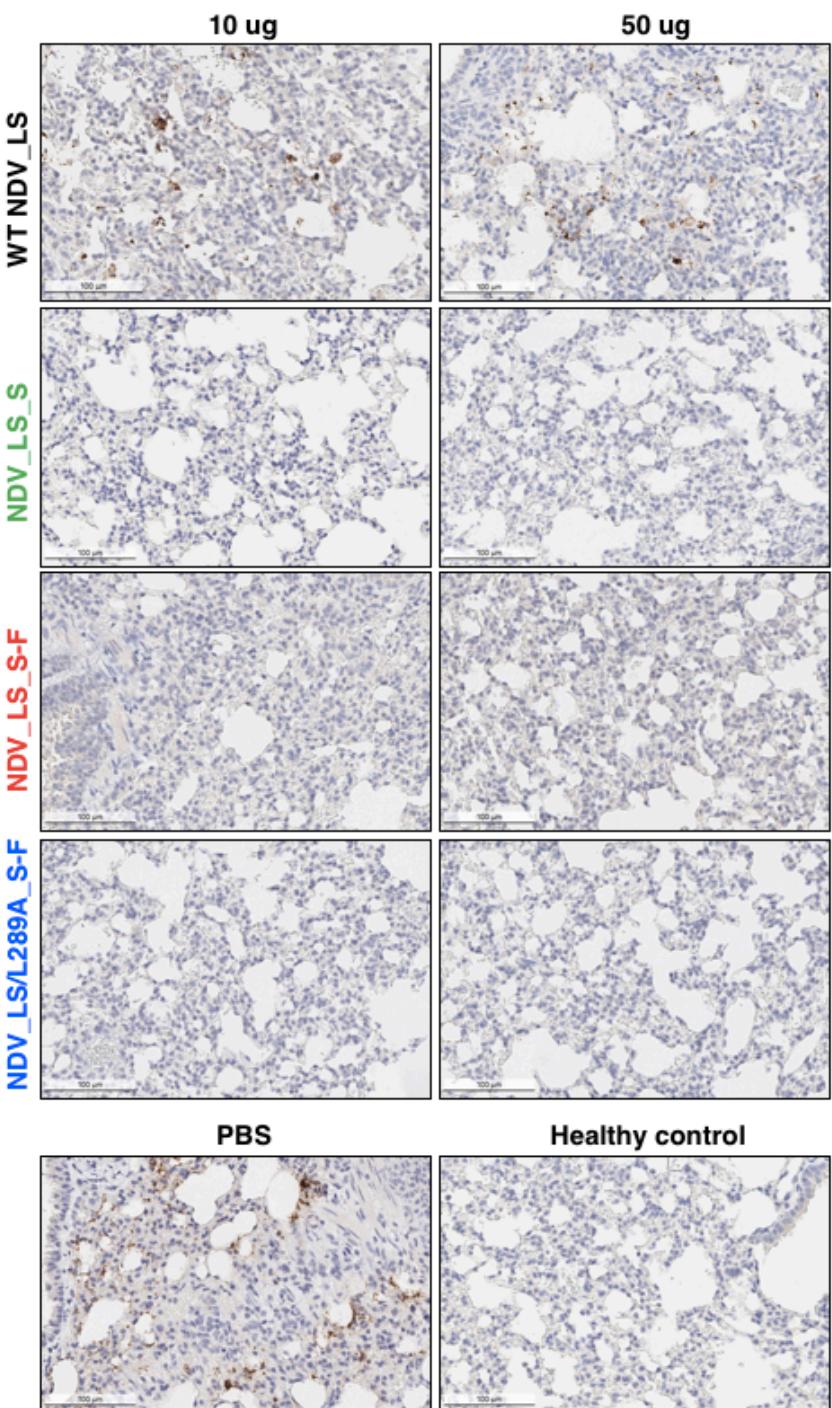


The NDV-S live vaccine protects mice from SARS-CoV-2 infections

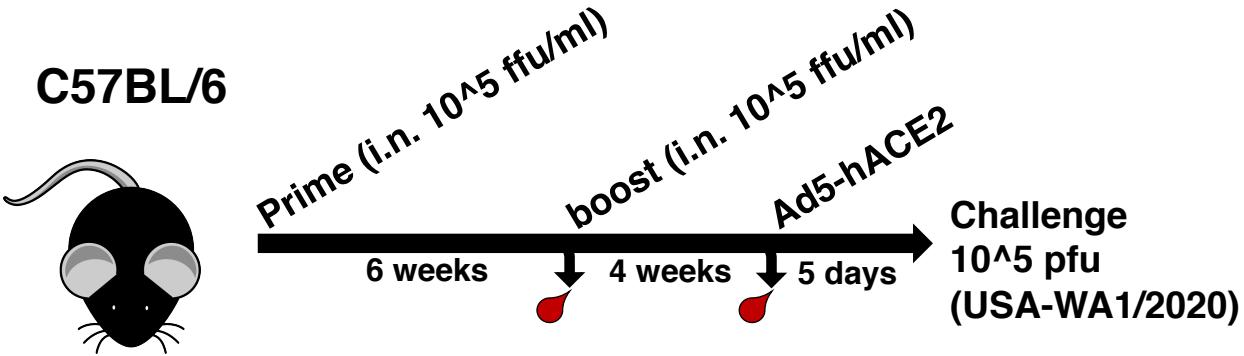
A



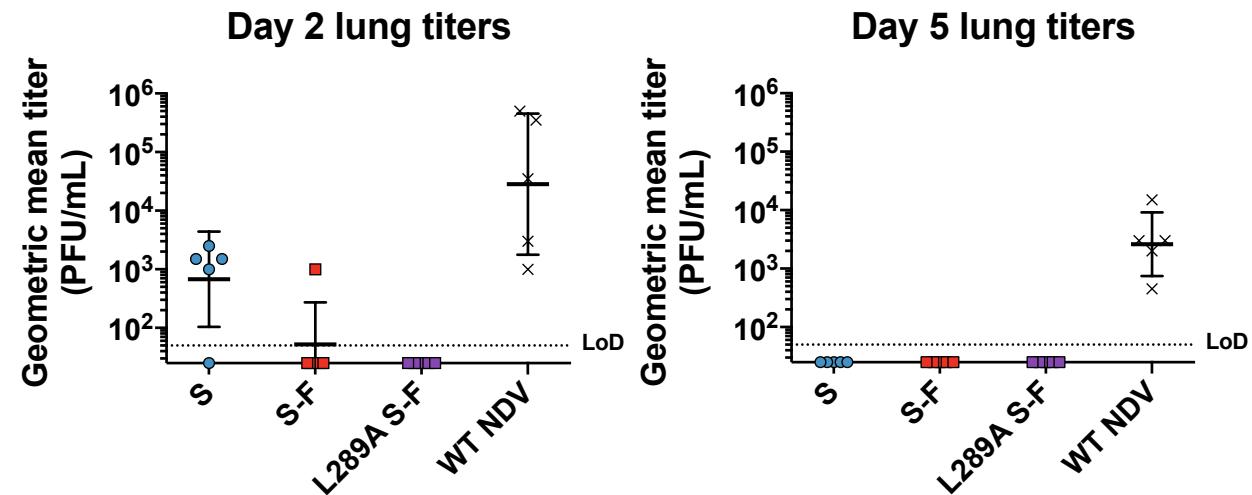
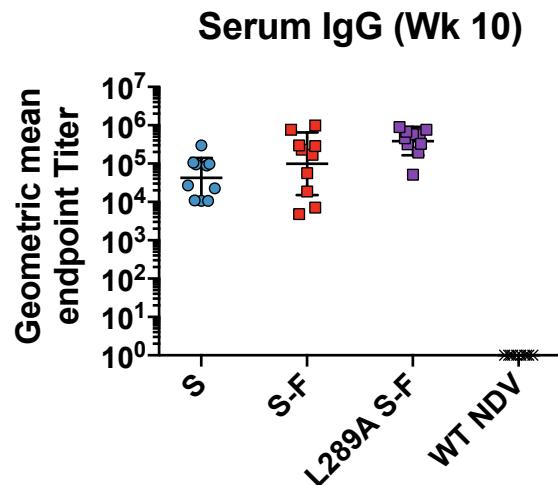
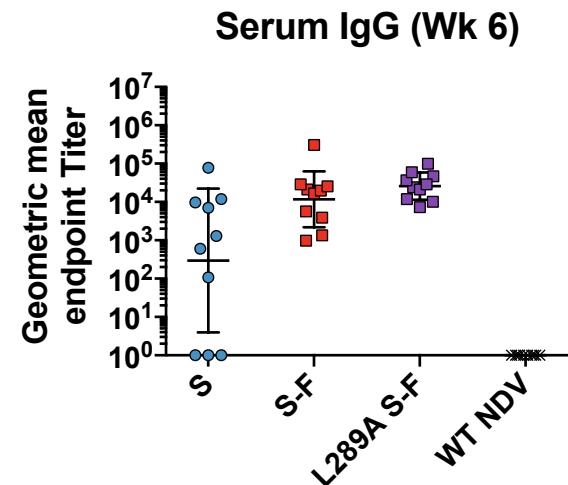
B



Intranasal immunization of mice with NDV vectors expressing the spike protein of SARS-CoV-2



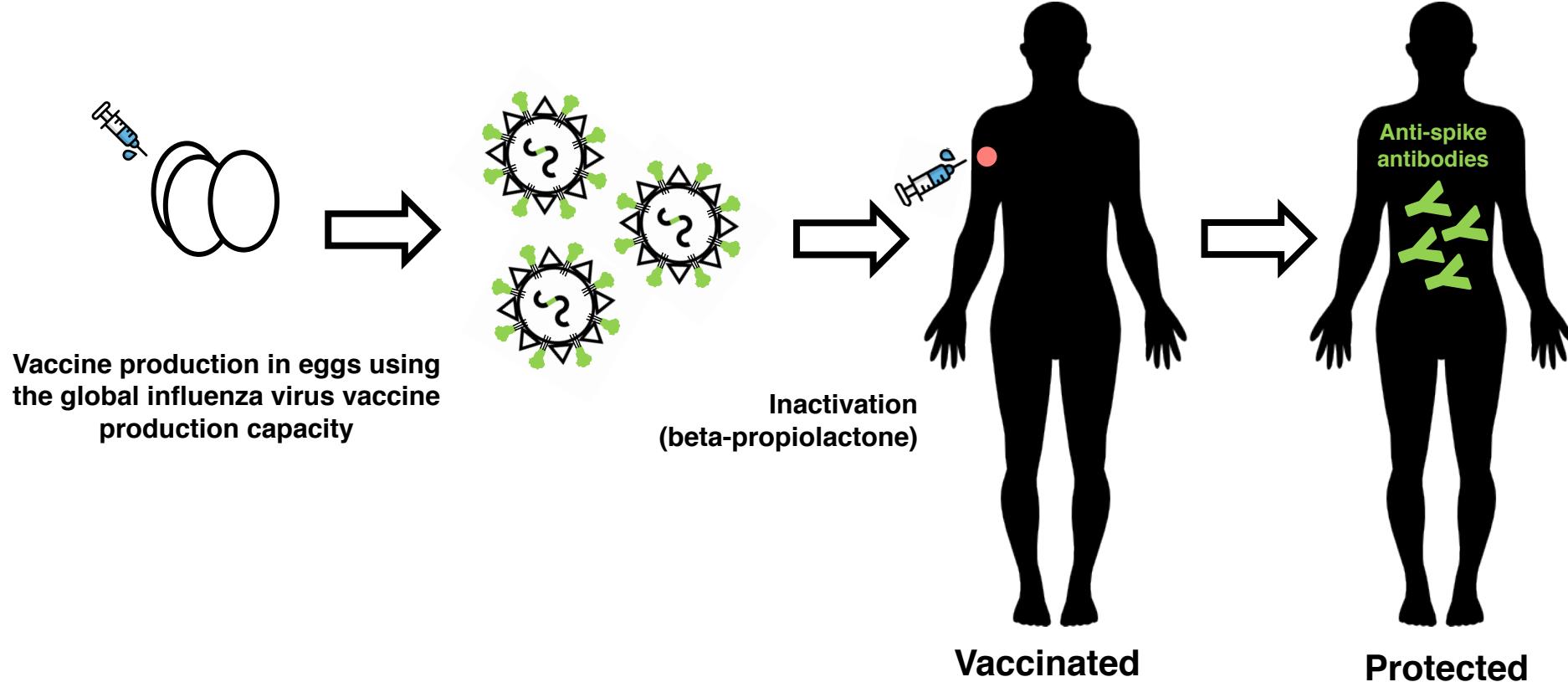
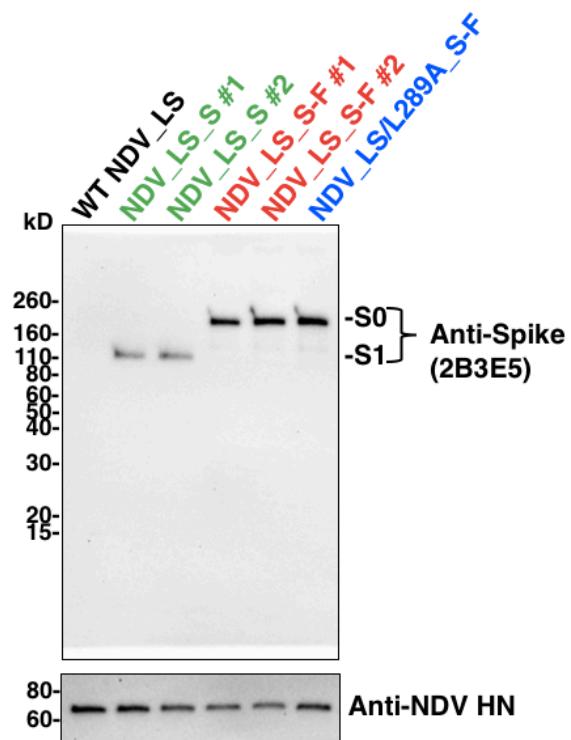
Groups	Prime	Boost
1	NDV_LS_S	NDV_LS_S
2	NDV_LS_S-F	NDV_LS_S-F
3	NDV_LS/L289A_S-F	NDV_LS/L289A_S-F
4	WT NDV_LS	WT NDV_LS



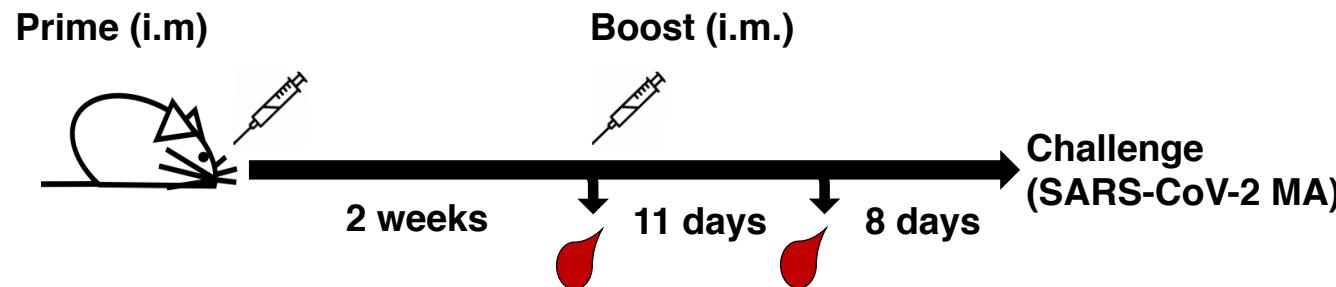
The challenge was performed by Dr. Ralph S. Baric's group at University of North Carolina at Chapel Hill

Concept overview of using the NDV vector expressing the membrane-anchored spike as an inactivated SARS-CoV-2 vaccine

NDV_LS/L289A_S-F (NDV-S)



The inactivated NDV-S vaccine induced high spike-specific serum IgG in mice

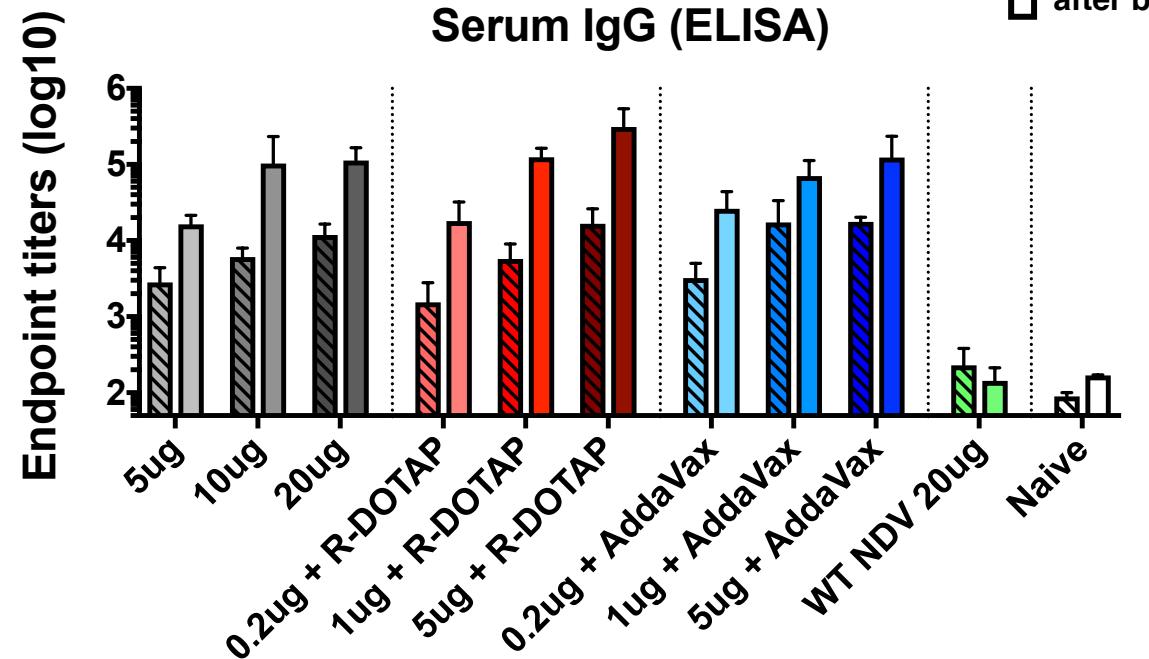


Groups (n=5)	Prime	Boost
1	5 ug	5 ug
2	10 ug	10 ug
3	20 ug	20 ug
4	0.2 ug + R-DOTAP	0.2 ug + R-DOTAP
5	1 ug + R-DOTAP	1 ug + R-DOTAP
6	5 ug + R-DOTAP	5 ug + R-DOTAP
7	0.2 ug + AddaVax	0.2 ug + AddaVax
8	1 ug + AddaVax	1 ug + AddaVax
9	5 ug + AddaVax	5 ug + AddaVax
10	WT NDV 20 ug	WT NDV 20 ug

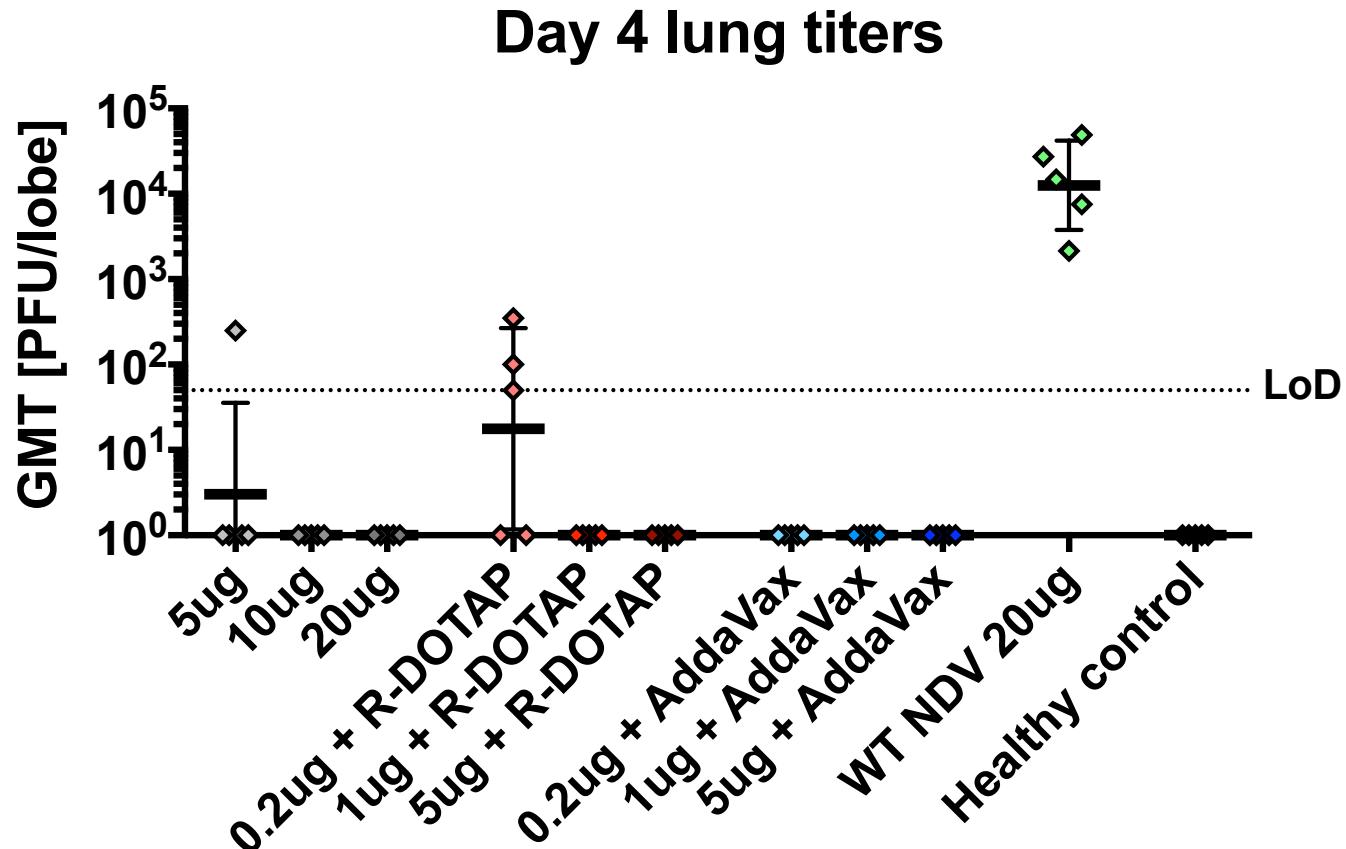
R-DOTAP: a clinical-stage liposomal suspension adjuvant (R-enantiomer of the cationic lipid DOTAP)

AddaVax: MF-59 like squalene-based oil-in-water nano-emulsion

▨ after prime
□ after boost



The inactivated NDV-S vaccine protects mice from SARS-CoV-2 infections



Summary

- Intranasal and intramuscular immunizations of mice with live NDV vector and intramuscular immunizations with inactivated adjuvanted NDV vector expressing the spike protein of the SARS-CoV-2 induced high titers of serum IgG and reduced viral titers in the lung in a mouse model
- NDV vectors expressing the S-F chimera induced higher spike-specific antibodies and conferred better protection than NDV vector expressing the WT S

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