PLACCINE Nucleic Acid Vaccine Platform

PLACCINE: A Novel DNA Vaccine Platform with Potential to Create Next Generation Vaccines

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PLACCINE – A Novel DNA Vaccine Platform

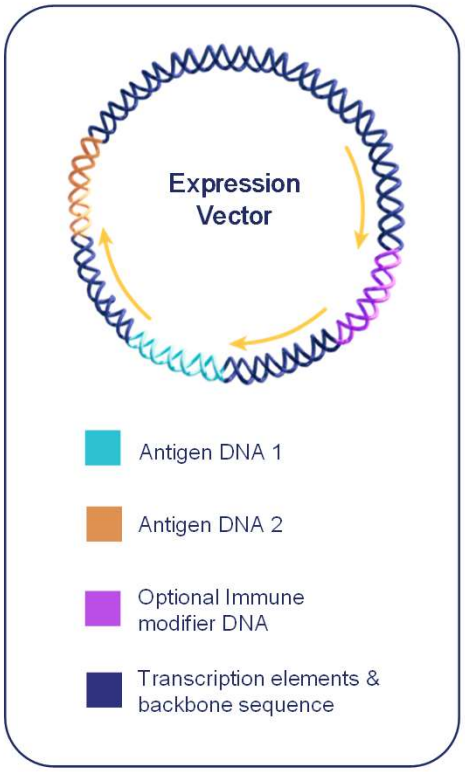
Key Attributes

Multi-valent	• Multiple antigens in a single plasmid DNA • Breadth of Immune Responses
Durable	• Durable antigen expression/nAB & T-cell responses
Novel Formulation	• Independent of virus, device, or LNPs
Flexible Design	• "Plug & Play", rapid Manufacturing
Stable at Workable Temp	• > 9 months stability at $\geq$ 4° C

Broad-spectrum immunity, durable nAB and T-cell responses, protection, longer shelf-life at workable temperatures, and flexible manufacturing warrants PLACCINE as a potential alternative to current vaccines

PLACCINE Technology Platform

Multicistronic or Single Antigen Vector Formulations Independent of Virus or Device



Up to 4 genes have been successfully incorporated and expressed

PLACCINE pDNA Constructs

PLACCINE Delivery Systems

-Synthetic Delivery Systems
- Non-viral
- Non-device

Numerous vectors and delivery systems tested for optimization studies

Nanoparticles/Complexes

PLACCINE Vaccines

Intramuscular (IM) Administration

Humoral & Cell Mediated Immune Response

Potential Administration Routes
- Subcutaneous (SC)
- Intradermal (ID)
- Intranasal (IN)

Current Vaccines Despite Some Success Have Significant Limitations

PLACCINE Technology to Potentially Address These Limitations

mRNA

- Short-lived responses requiring frequent boosts
- Poor stability at working temperatures

Protein

- Manufacturing challenges
- Poor cytolytic T-cell responses

pDNA Well-suited to overcome these Limitations

- Longer duration of antigen expression/exposure
- Strong T-cell responses
- Stability at $\geq 4^{O}$ C

pDNA limitation: Insufficient delivery relying on viruses or devices (e.g., electroporation, jet)

PLACCINE Approach

- Leveraging the DNA advantages (multi-cistronic, durability, CD8 response, shelf-life)
- Delivery without virus or device to achieve better safety and compliance

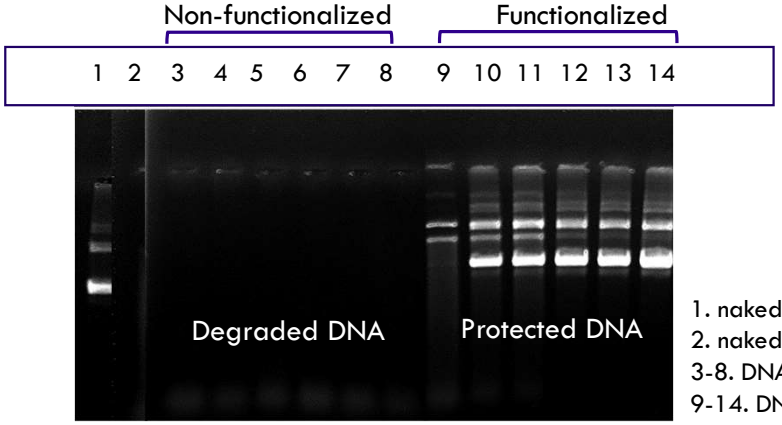
A Synthetic PLACCINE Delivery System for Intramuscular Delivery

DNA Protection, Enhanced Antigen Expression and Muscle Distribution in Mice

PLACCINE Delivery System

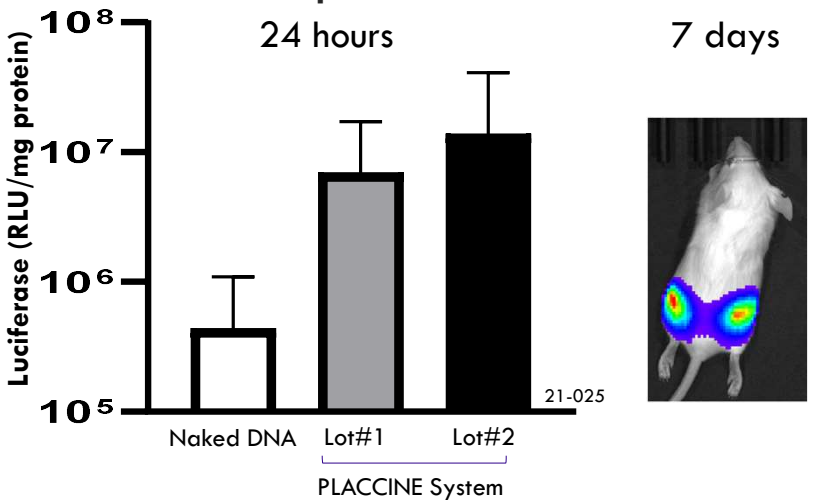
- An amphiphilic polymer that promotes DNA bioavailability, uptake, and distribution
- Covalently functionalized to improve function

Functionalized Polymer Protects DNA from Degradation by DNAse

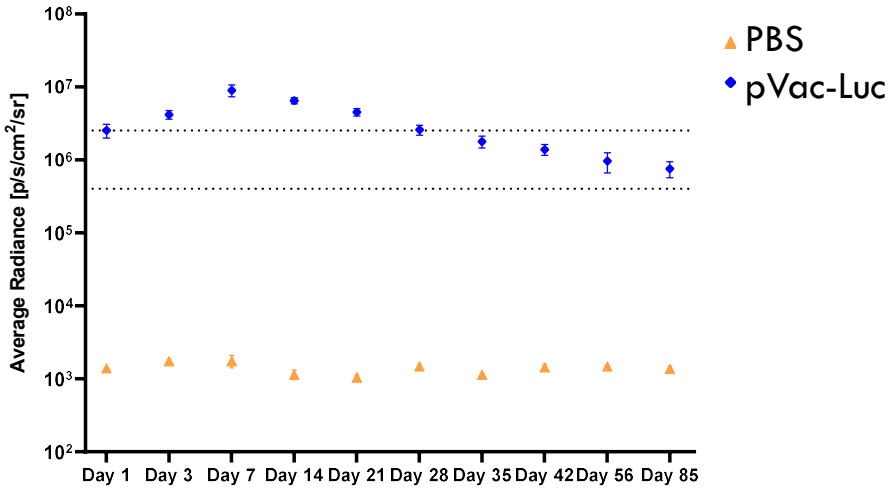


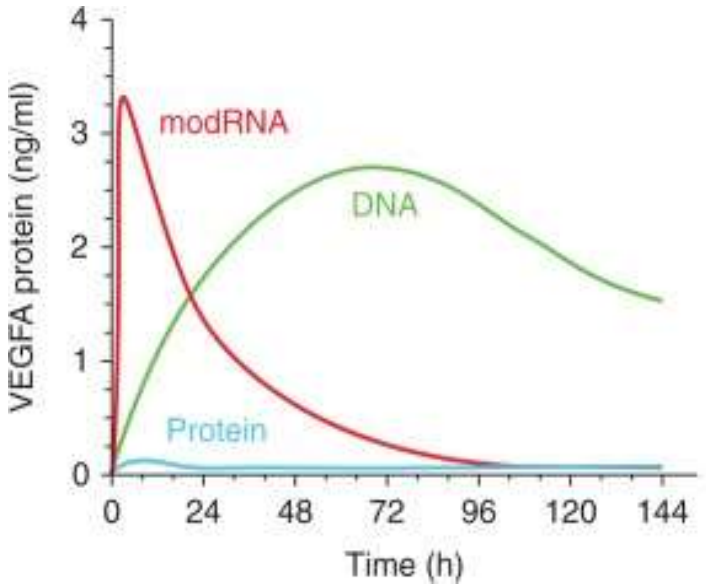
1. naked DNA, no DNAse
2. naked DNA + DNAse
3-8. DNA formulation in increasing concentrations of non-functionalized polymer
9-14. DNA formulated in increasing concentrations of functionalized polymer

PLACCINE Formulation Yields 10-15-fold Higher Gene Expression than Naked DNA



pDNA Yields More Durable Antigen Expression than the Protein or Modified mRNA

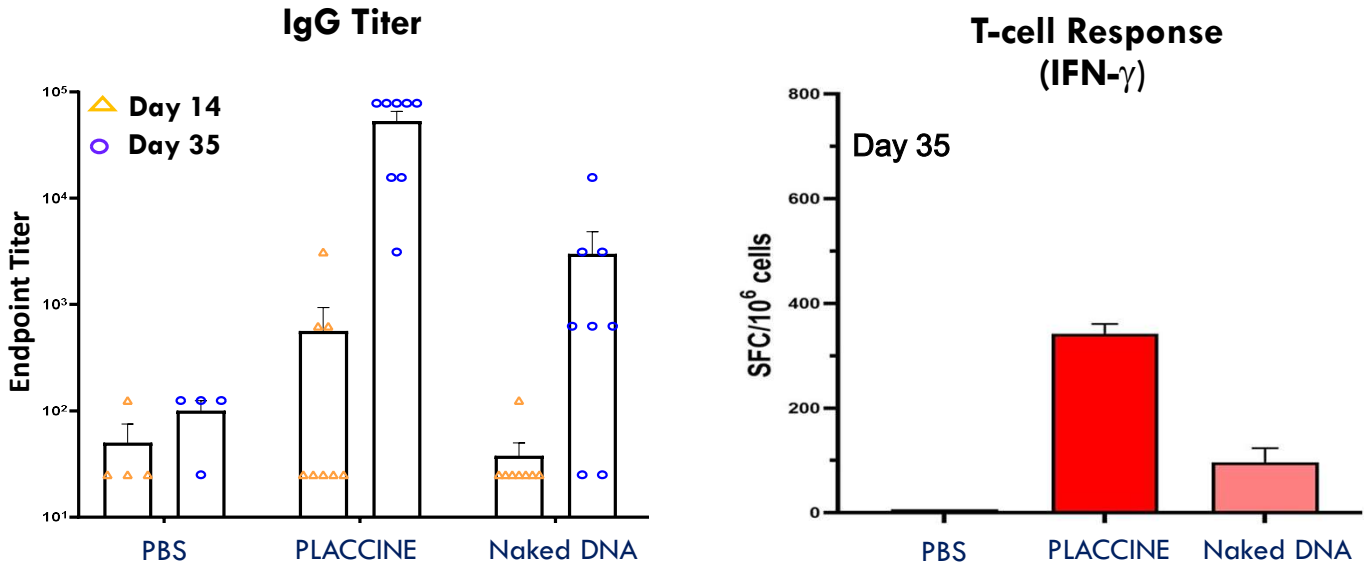




Chien KR Cold Spring Harb Perspect Med 2015;5:a014035

PLACCINE Formulation Yields Higher Immunogenicity than Naked pDNA

- DNA vector **pVac-9 (Spike-D614G)**
- Formulation PLACCINE
- 125 µg DNA

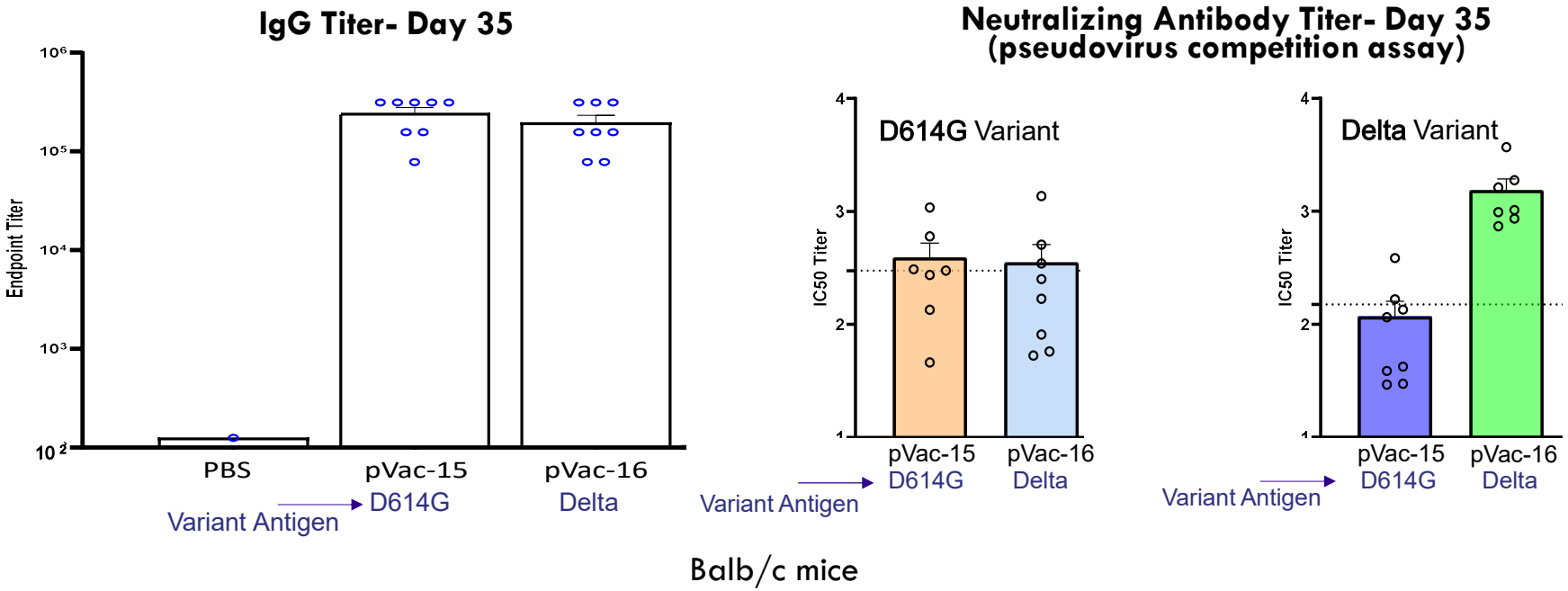


Balb/c mice

Immunogenicity of Single Antigen PLACCINE Vectors - IgG and nAB titers

Viral Mutation Warrants Vaccine Effectiveness Against Multiple Variants

- Optimized vectors **pVac-15 (D614G), pVac-16 (Delta)**
- Formulation: PLACCINE including an adjuvant
- 125 µg DNA

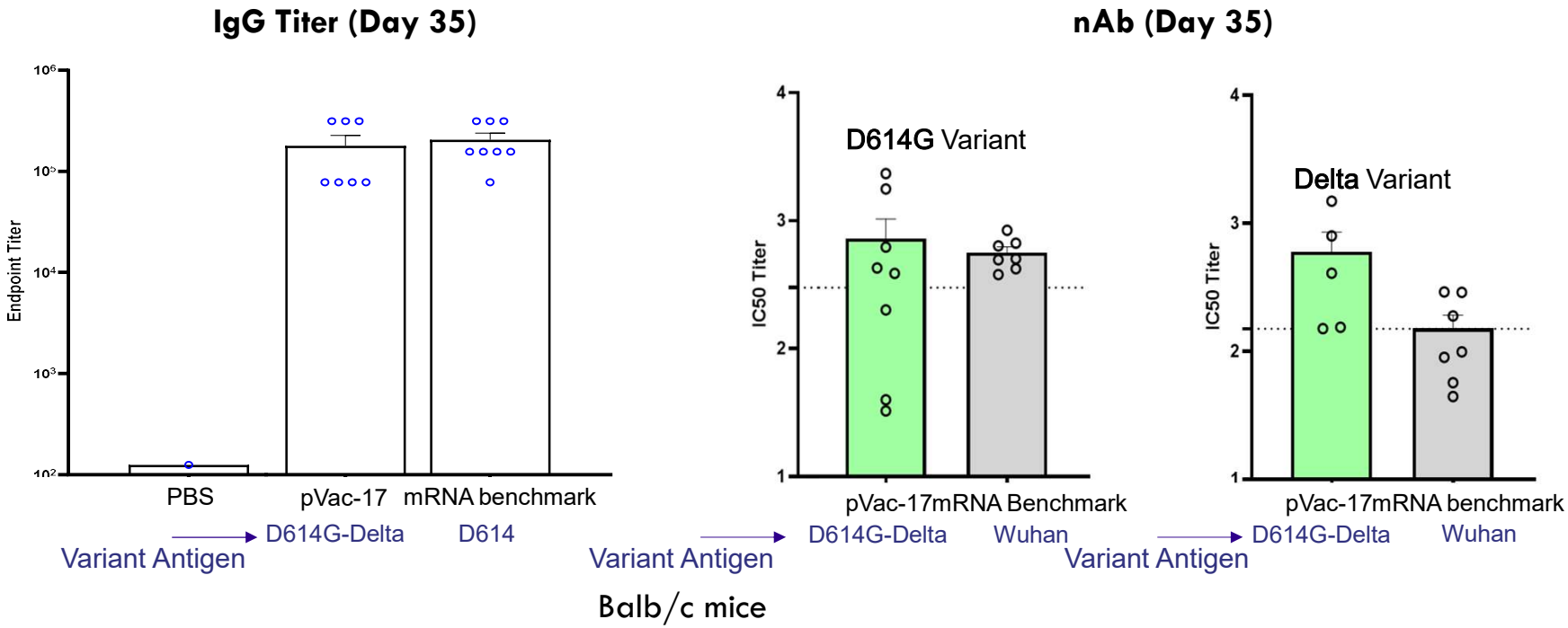


Balb/c mice

Immunogenicity of a Multi-variant PLACCINE Vaccine

A Bivalent Vaccine is Well Suited for a Mutating Virus

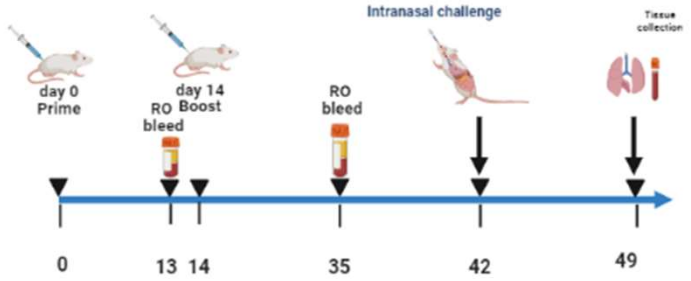
- Multicistronic vector **pVac-17 (D614G-Delta)**
- Formulation: PLACCINE including an adjuvant
- 125 µg DNA

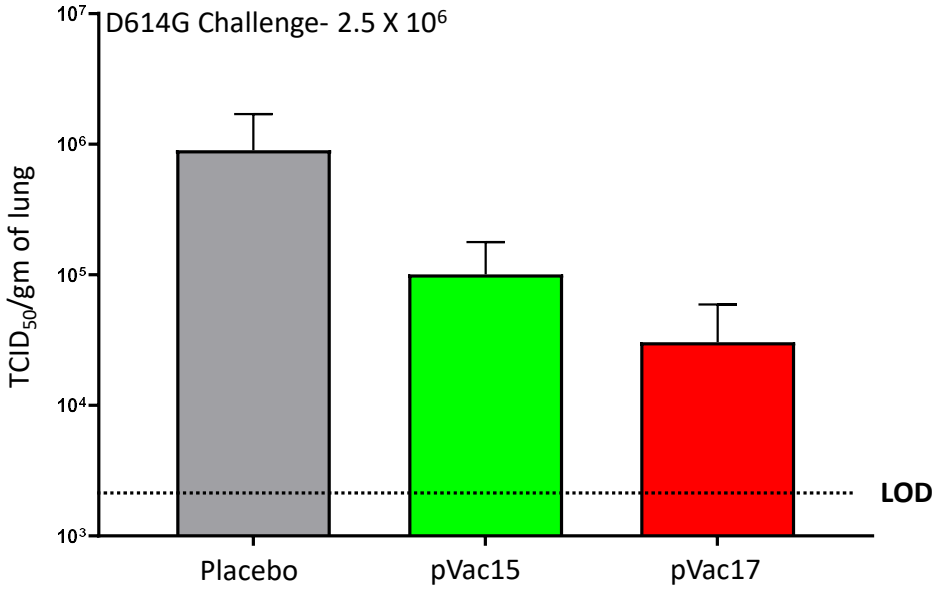


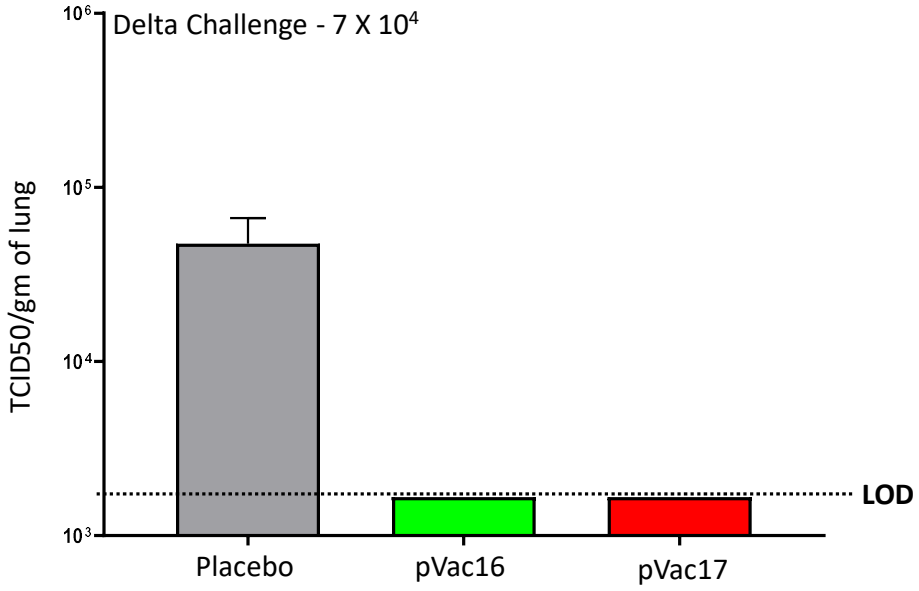
PLACCINE Vaccines Provide Protection Against Viral Challenge

hACE2:K18 Mouse Model

- **pVac-15 (D614G), pVac-16 (Delta), pVac-17 (D614G-Delta)**
- Formulation: PLACCINE including an adjuvant
- Dose - 125 µg DNA, Day-1, 21
  7 days post challenge

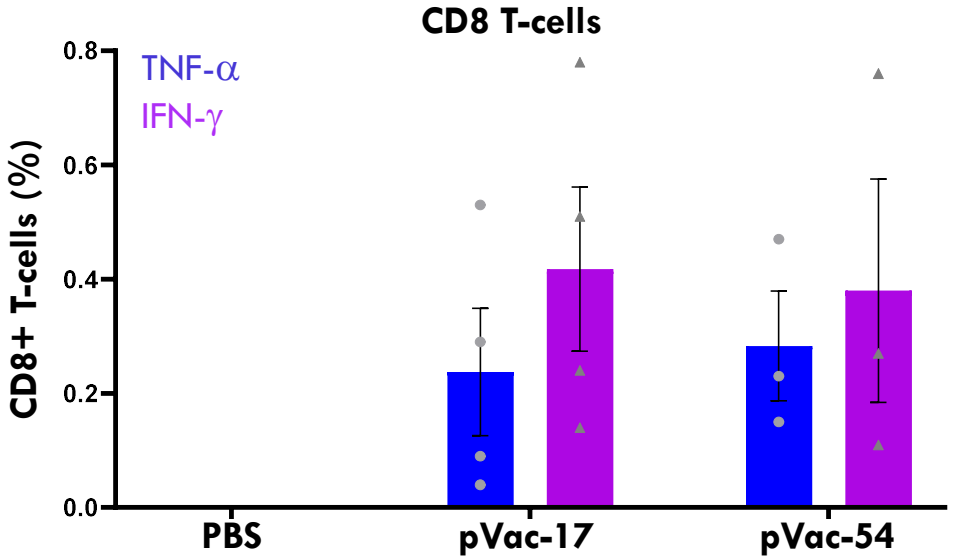


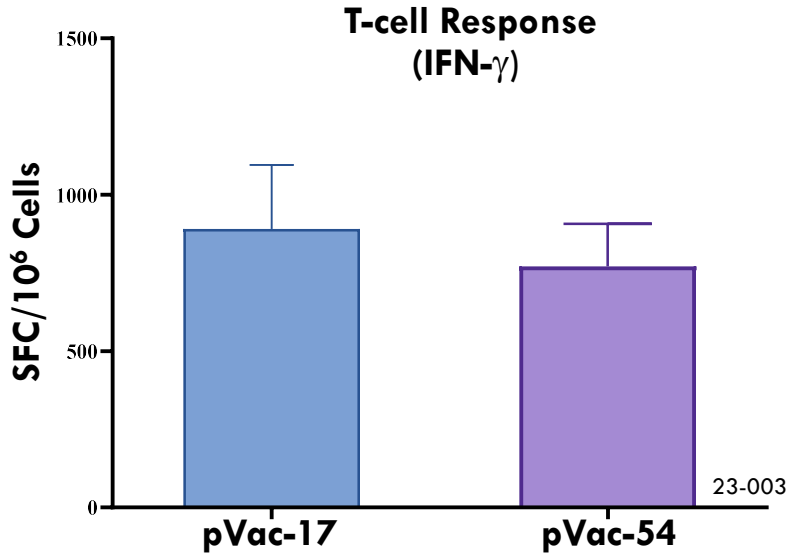




PLACCINE-induced T-cell Responses are Associated with Increases in CD8+ Cells Population in Spleenocytes

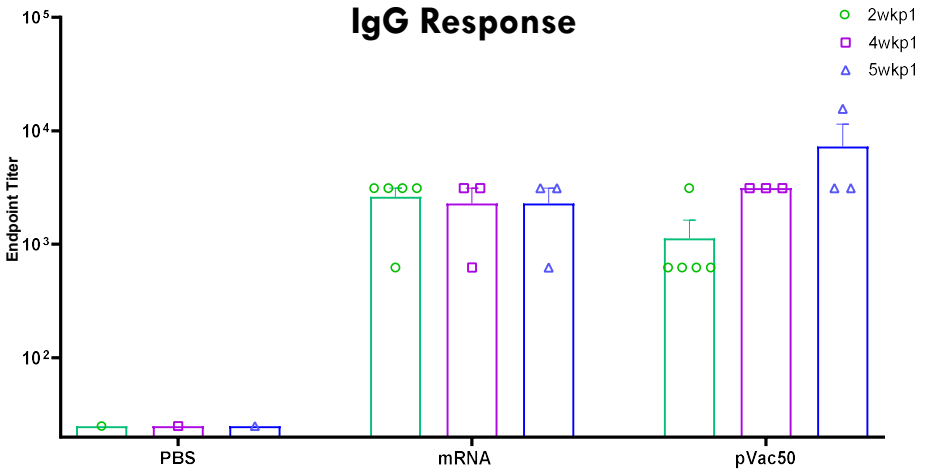
- Vectors: **pVac-16** (Delta), **pVac-17** (D614G+Delta)
- Formulation: PLACCINE
- 125 μg DNA
- Pseudo-typed lentivirus assay

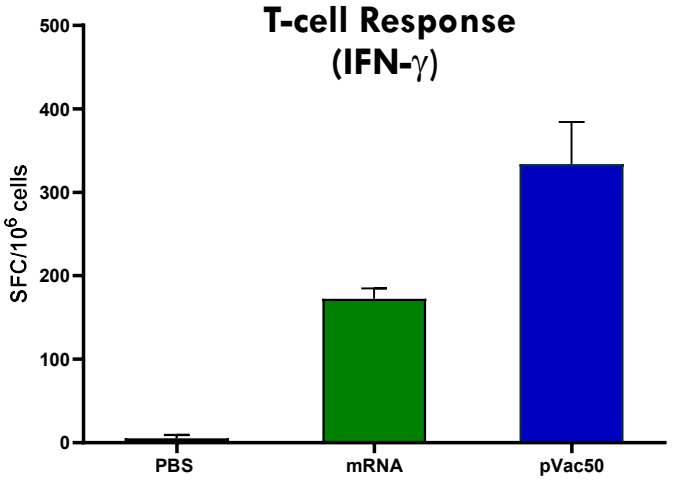




Single Dose PLACCINE Vs mRNA Vaccine

Better Immune Quality with PLACCINE



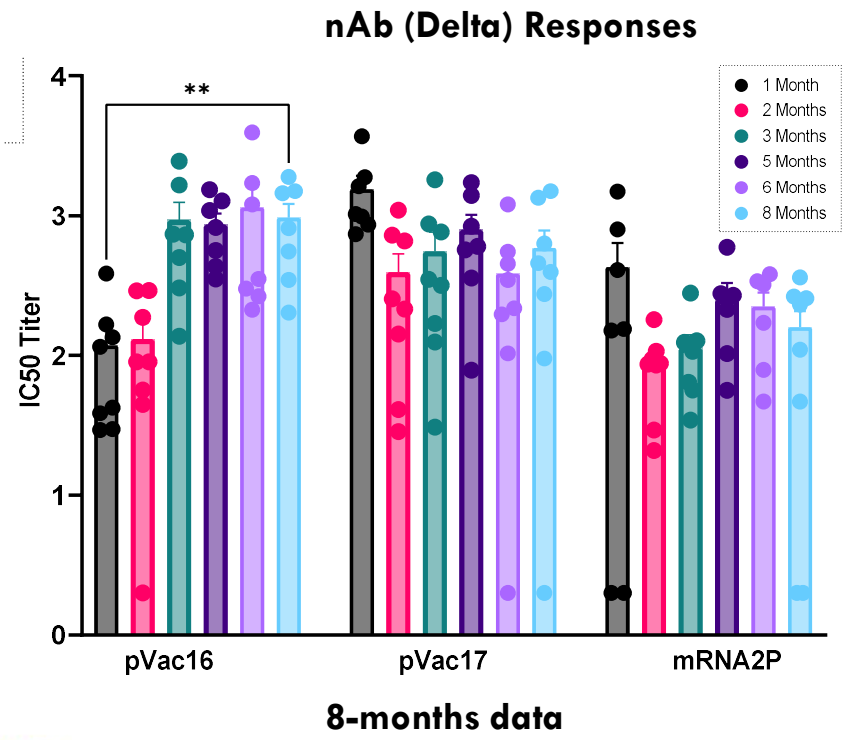


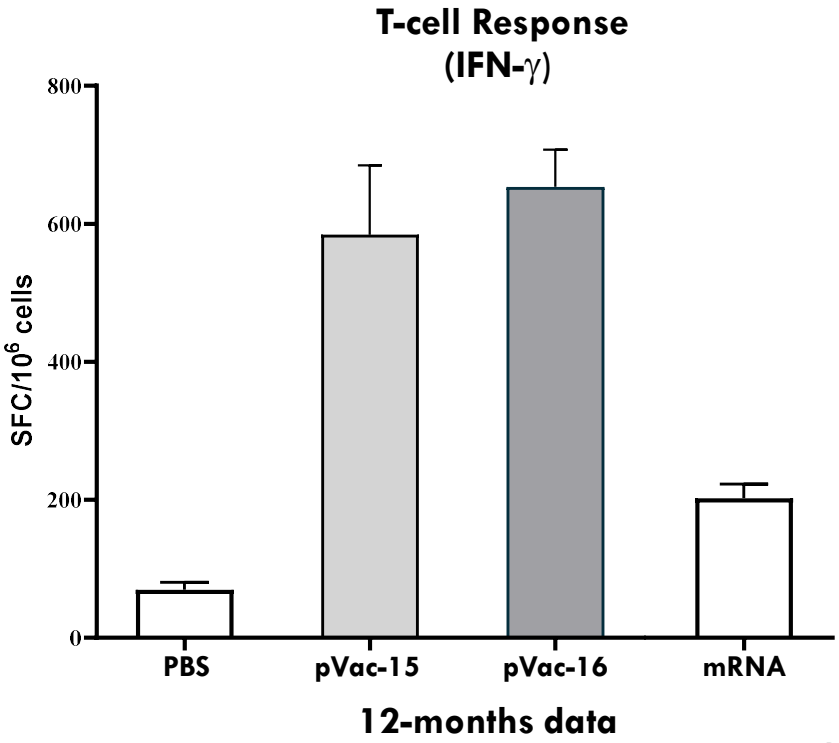
Additional Studies on Immune Quality Comparison are in Progress

PLACCINE Vaccines Provide Durable Neutralizing Antibody Response

>12-months Durability in Mice

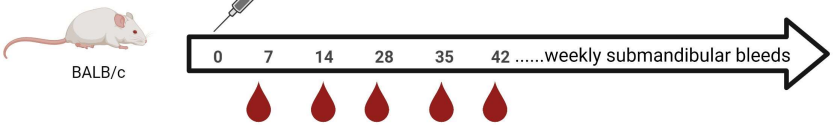
- Vectors: **pVac-16** (Delta), **pVac-17** (D614G+Delta)
- Formulation: PLACCINE including an adjuvant
- 125 µg DNA
- Pseudo-typed lentivirus assay for nAb



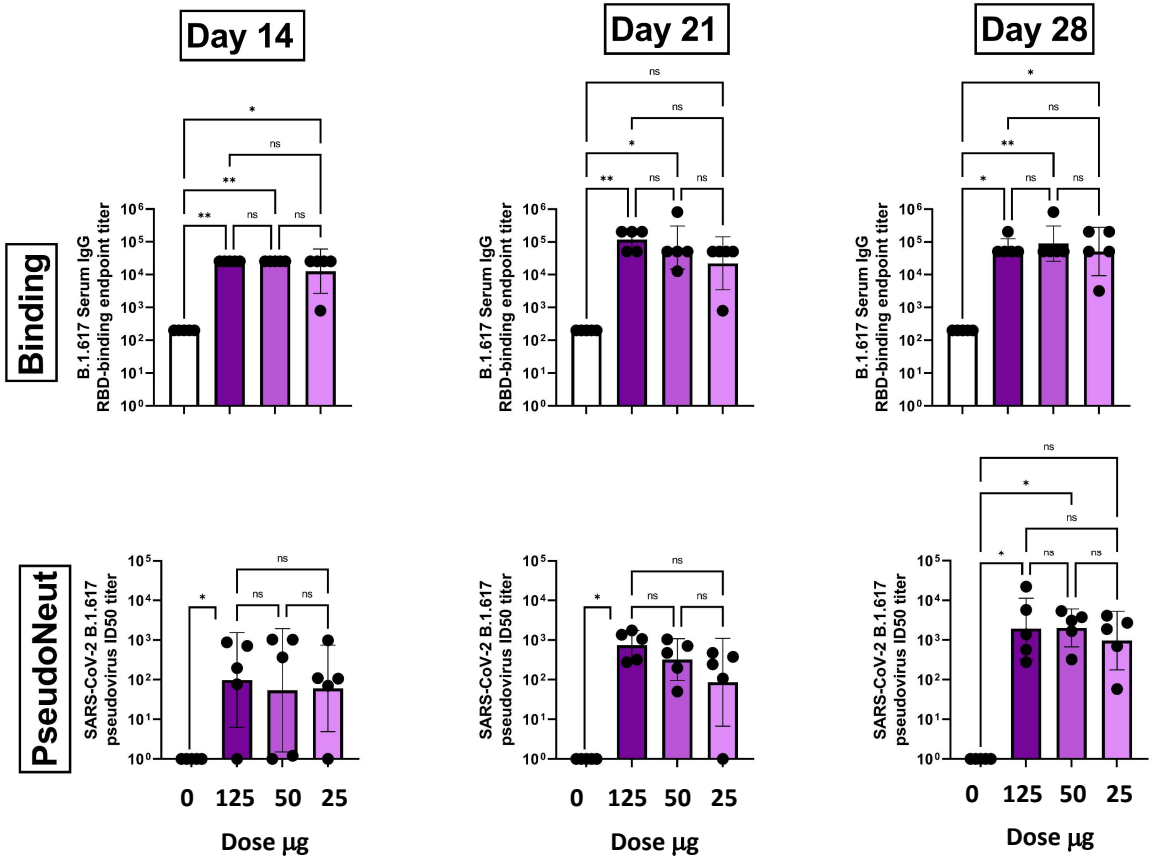


PLACCINE Induces Robust Immune Response after a Single Injection

Wistar Institute Collaboration



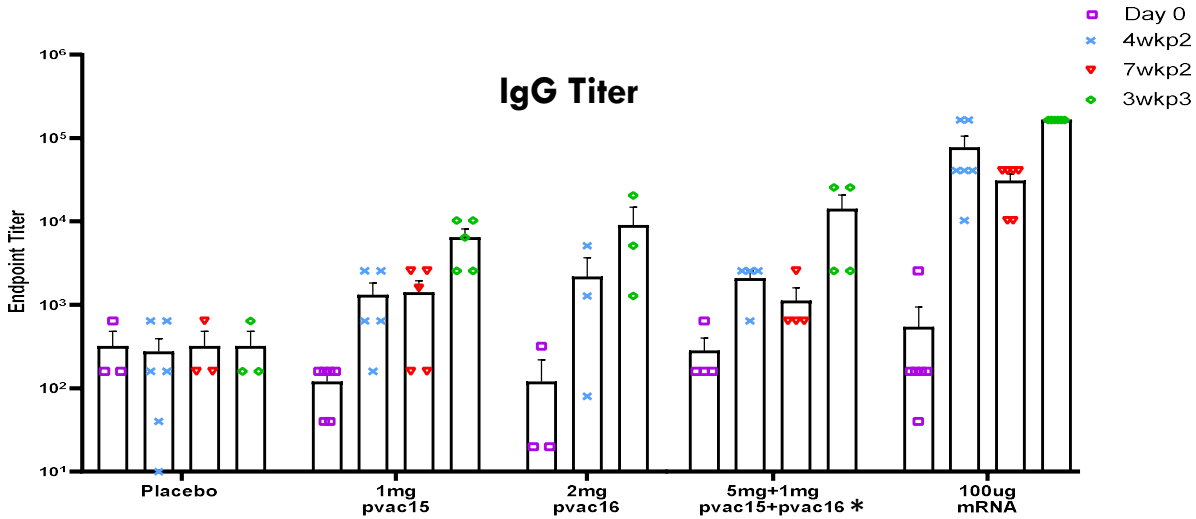
Group	Antigen
pVax	N/A
pVAC50 (125ug)	Delta spike-Imunon
pVAC50 (50ug)	Delta spike-Imunon
pVAC50 (25ug)	Delta spike-Imunon



PLACCINE Vaccines are Immunogenic in Cynomolgus Monkeys

PLACCINE Subjects Showed IgG and Neutralizing Antibody Response

- Single antigen vector: **pVac-15 (D614G) or pVac-16 (DELTA)**
- Comparator mRNA: **Commercial mRNA Vaccine** (LNP)
- Formulation: PLACCINE including an adjuvant
- Dosing schedule: Day 1, 28, 84

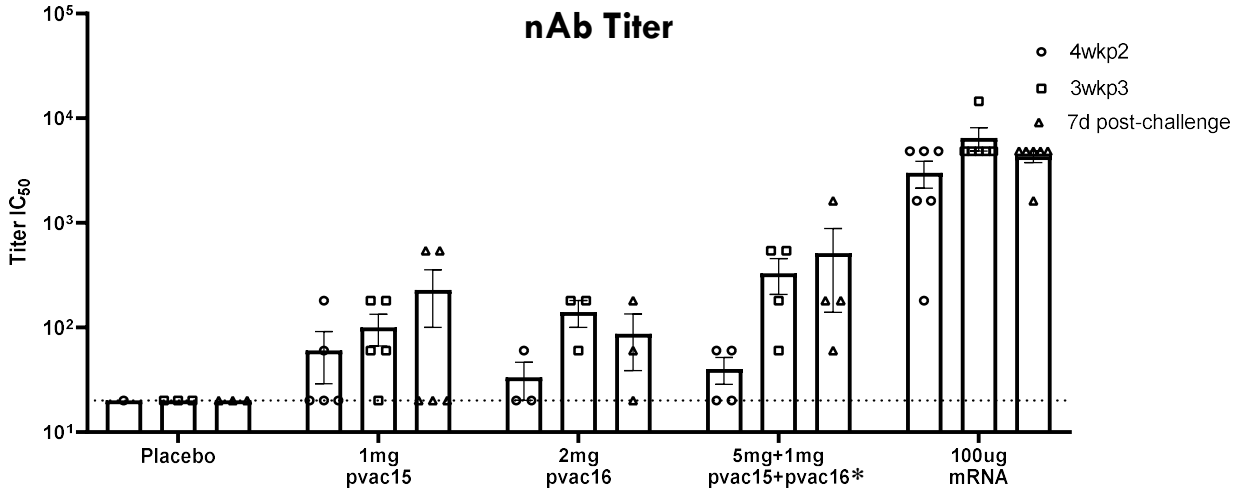


* The second booster was pVac-16 at 2 mg dose

Neutralizing Antibody Titers in PLACCINE-Vaccinated Cynomolgus Monkeys

90% of PLACCINE Subjects Showed Neutralizing Ab Response

- Single antigen vector — **pVac-15** (D614G) in PLACCINE
- Comparator mRNA — Commercial mRNA Vaccine (LNP)
- Dosing schedule — Day 1, 28, 84
- nAB titer — Day 105 (21 days after 3rd dose)



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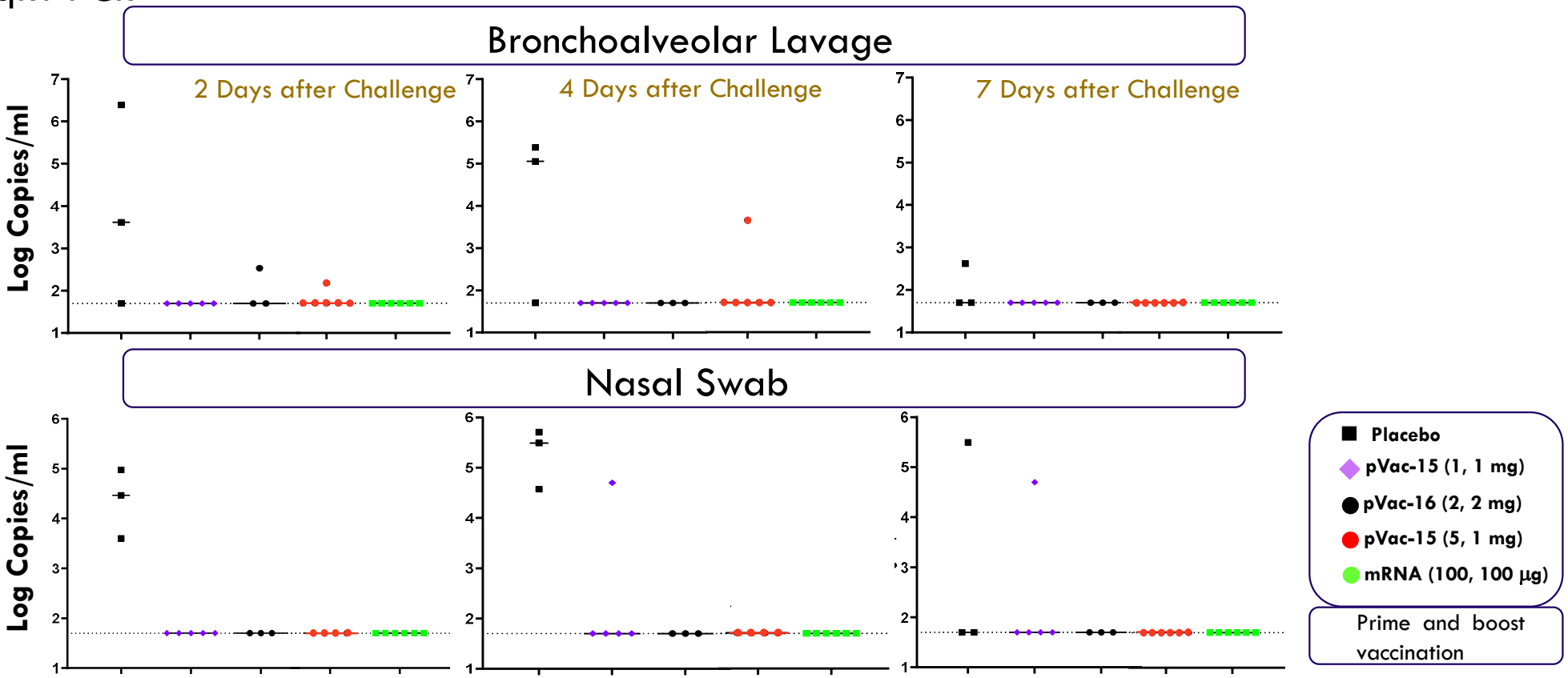
PLACCINE Vaccines Provide Complete Protection Against Viral Challenge

Comparable Efficacy to a Commercial mRNA Vaccine- Challenge dose: 1 x 10^6 $TCID_{50}$

qRT-PCR



PLACCINE Vaccines Provide Complete Protection Against Viral Challenge

Comparable Efficacy to a Commercial mRNA Vaccine- Challenge dose: 1 x 10^6 $TCID_{50}$

$TCID_{50}$ Assay

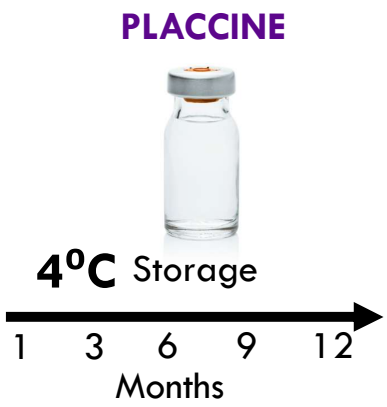
Vaccine	Bronchoalveolar lavage			Nasal swab		
	Day-2	Day-4	Day -7	Day-2	Day-4	Day -7
Placebo	6.20 3.20 5.20	4.37 4.37 <2.7	3.70 <2.7 <2.7	5.37 6.37 5.20	4.70 5.20 5.70	4.20 3.70 3.37
pVac 15 (1mg)	<2.7 <2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 4.70 <2.7	<2.7 <2.7 4.20 5.37 <2.7	<2.7 <2.7 <2.7 <2.7 <2.7
pVAC16 (2 mg)	<2.7 <2.7 <2.7	<2.7 <2.7 <2.7	<2.7 <2.7 <2.7	<2.7 <2.7 <2.7	<2.7 <2.7 <2.7	<2.7 <2.7 <2.7
pVac-15/pVac-16 (5mg, 1mg)	<2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7
mRNA (100ug)	<2.7 <2.7 <2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7 <2.7 <2.7	<2.7 <2.7 <2.7 <2.7 <2.7 <2.7

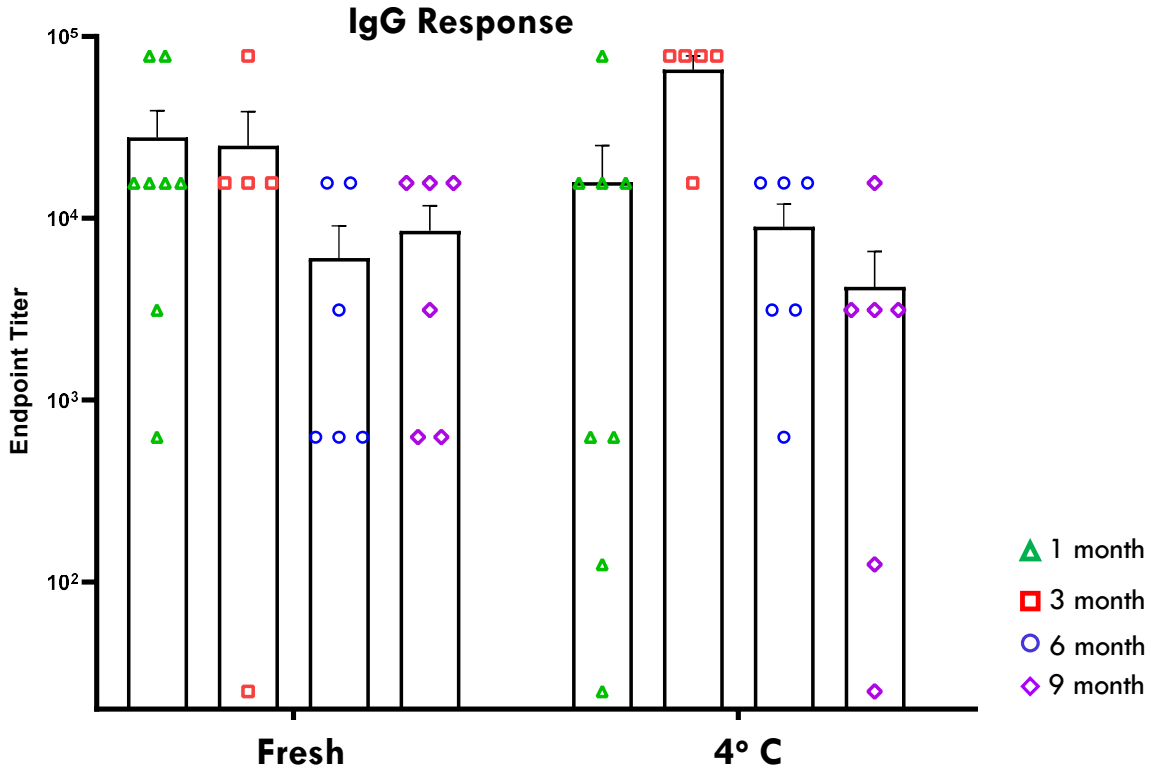
<2.7 means below the lower limit of detection

PLACCINE is Stable at 4°C for at Least 9 Months

Immunogenicity Studies in Mice

- Vector: pVac-17 (D614G-Delta)
- Formulation: PLACCINE





A Phase 1 / 2 Clinical Trial of a PLACCINE COVID-19 Booster Vaccine

Omicron XBB1.5 + A Highly Conserved Antigen

Phase 1

- **Total subjects:** 60
- **Age:** 18-55 years initially; expand into elderly population after 3-6 month of data review
- **Dose levels:** 0.5 mg, 1.0 mg, 2.0 mg
- **Dosing schedule:** Single or two doses (28 days apart)
- **Study period:** 12 months

Phase 2 Expansion
(potentially 3-6 months into Phase 1, based on the data)

- **Total subjects:** 100
- **Dose levels:** From phase 1
- **Dosing schedule:** From phase 1

Primary safety & immunogenicity objectives

- Reactogenicity assessment for 7 days, AES throughout the 1-year nAb against XBB1.5 and selected VOCs at baseline and at different time points over 1 year

Secondary immunogenicity objectives

- Seroresponse rate, T-cell response

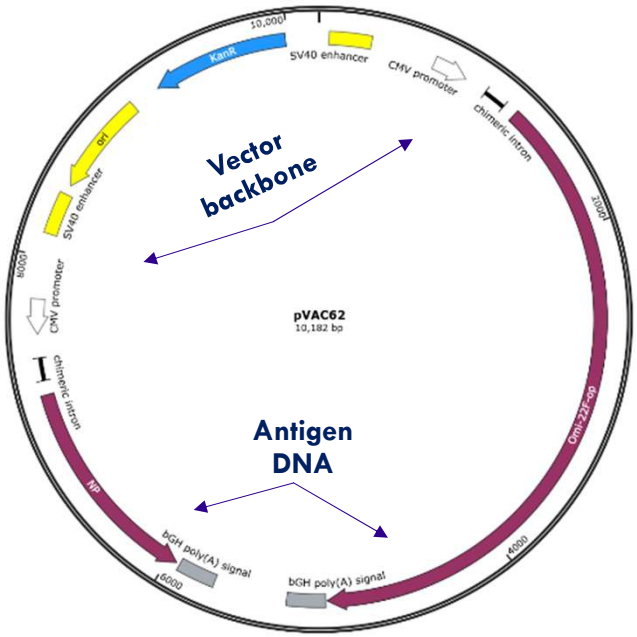
Exploratory immunogenicity objectives

- Immune cell populations over 1-year period

Flexible Design Allows for a Rapid Response to Changing Pathogen

"Plug & Play" Design and Leveraging Existing Preclinical Toxicology

"Plug & Play" Design



Clinical Vector with Standard Backbone

Summary

PLACCINE - A Potential Alternative to Current Vaccine Approaches

- Robust nAb & T-cell responses
- Durable & broad-spectrum Immunity
- Longer shelf-life at workable temperature
- Flexible design for rapid production

Thank You