Preclinical development update of a mRNA candidate vaccine to block transmission of *P. vivax*

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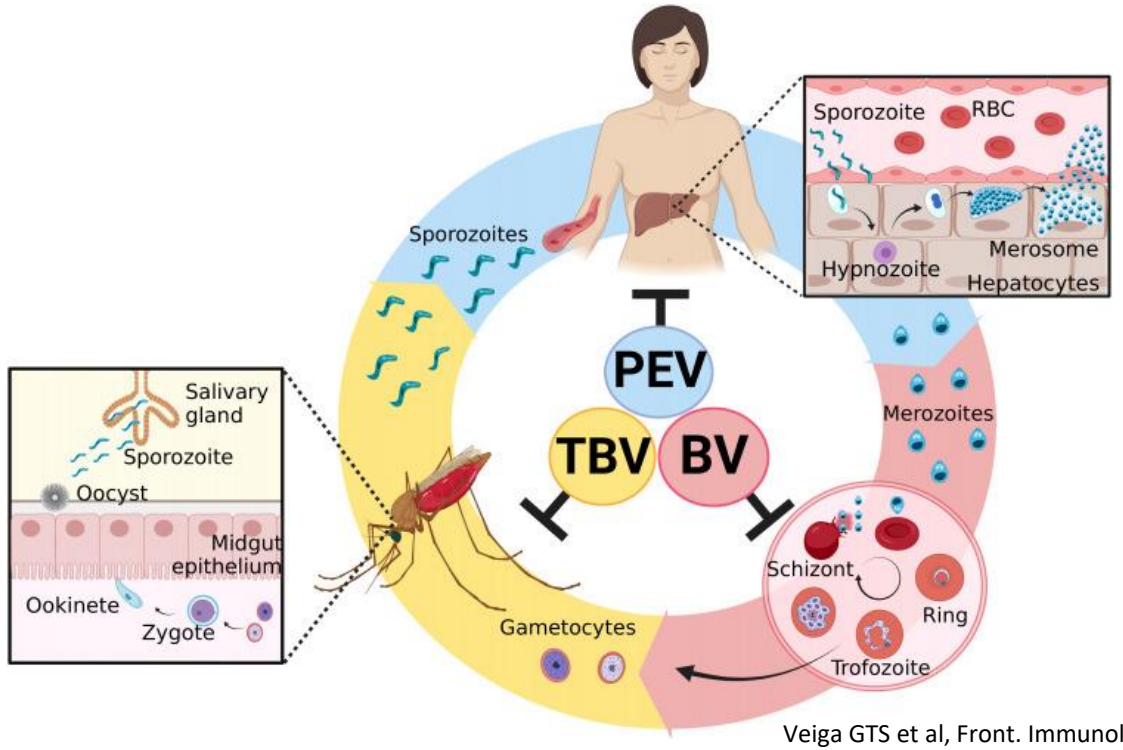
Slow progress towards the development of *P. vivax* vaccine

Pre-erythrocytic vaccines (PEV)
- PvCSP

Transmission-blocking vaccines (TBV)
- Pvs25



Veiga GTS et al, Front. Immunol (2023)

Blood-stage vaccines (BV)
- PvDBPII

Few vaccine candidates in clinical trials

- Pvs25
- PvCSP
- PvDBPII

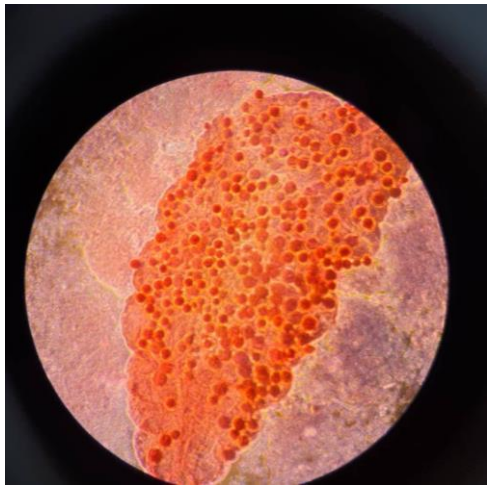
Main technical challenges

- The lack of in vitro culture
- Limited access to experimental models

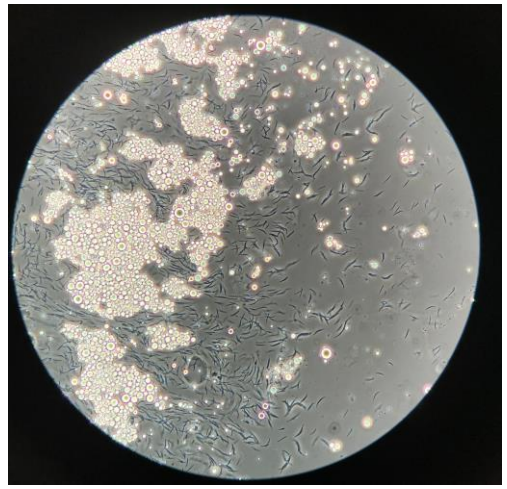
Stable accessibility of *P. vivax* clinical isolates

Field sites

Insectary



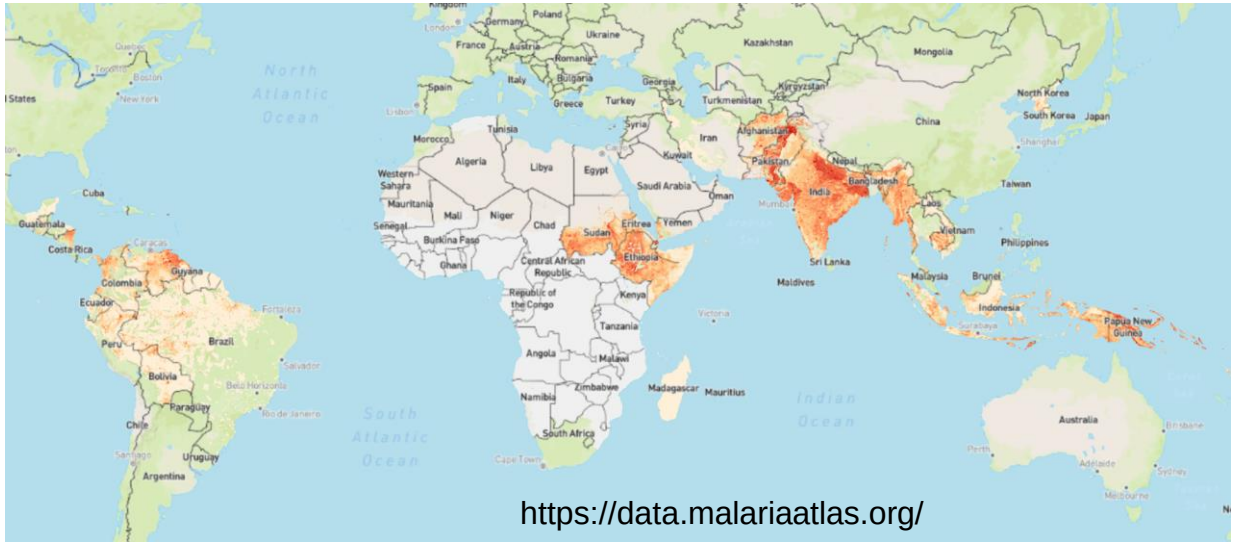
Oocysts
1 week post feeding



Sporozoites
2 week post feeding

A need for transmission blocking vaccines for *Plasmodium vivax*

Global distribution of P. vivax 2020



Malaria Vaccine Technology ROADMAP (WHO) Strategic Goals towards malaria eradication (by 2030)

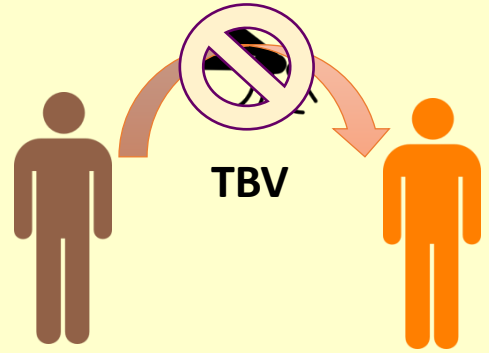
- Malaria vaccines that reduce transmission of the parasite

***P. vivax* Facts: Challenges for elimination**

- Latent hypnozoites cause relapses.
- Large number of asymptomatic carriers
- Highly efficient transmission

Transmission Blocking Vaccines (TBV) : A tool for malaria elimination

- Inhibit malaria development in mosquitoes
- Block parasite transmission from one person to the others
- Reduce spread/reintroduction of parasite
- Decrease reservoir of hypnozoites
- Surrogate assays to test vaccine efficacy available



Transmission-blocking assay

Serum

Pv infected Blood

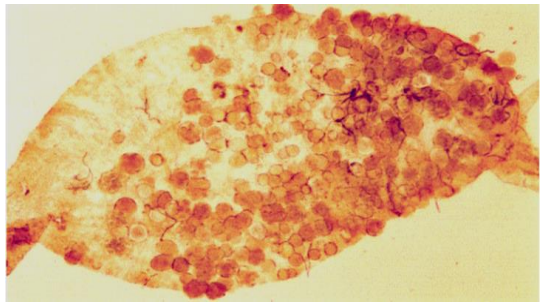
incubate for 30min

Anopheles dirus

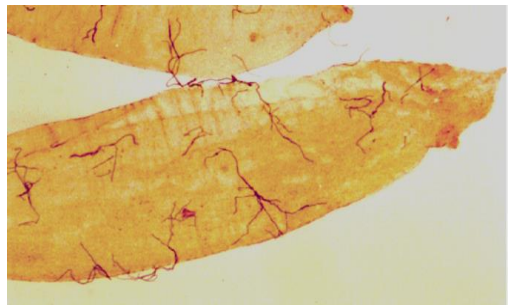
membrane-feeding apparatus

1 week 26˚C

Oocyst in mosquito midgut



control

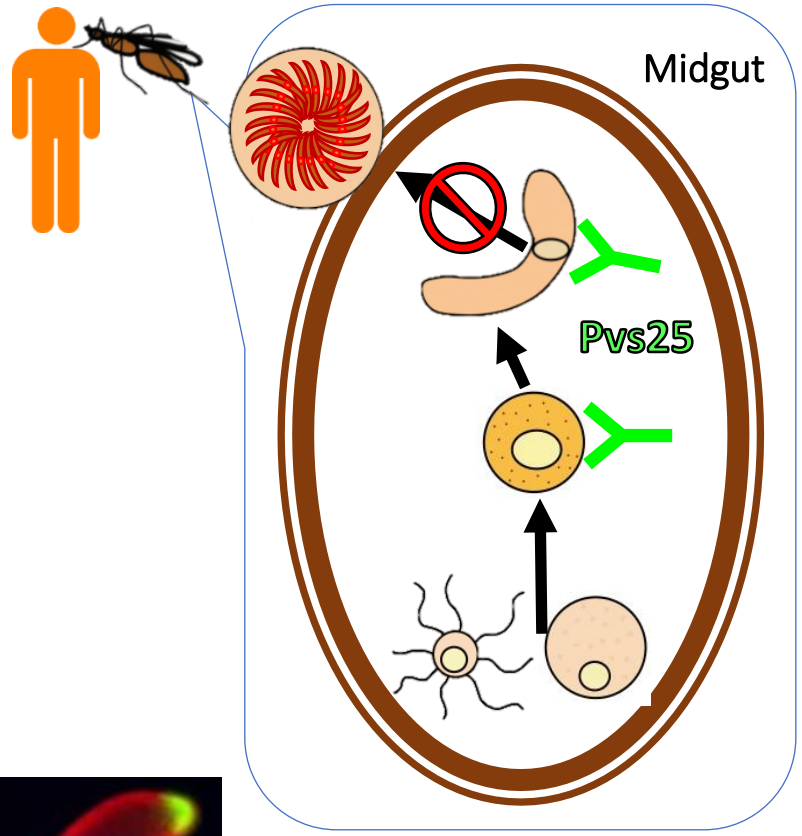


Transmission blocked

- % inhibition in oocyst density (transmission-reducing activity, or **%TRA**)
- % inhibition in prevalence of infected mosquitoes (transmission-blocking activity, or **%TBA**)

Development of Pvs25-based transmission blocking vaccine

Pvs25, most advanced candidate for *P. vivax* TBV



2004 DNA vaccine in mice

2005 Protein/ Montanide ISA720 in monkeys

2010 Baculo-virus in mice

2016 Plant based protein/adjuvant in mice

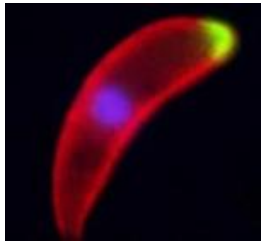
2019 The chimeric PvMSP1-Pvs25 protein

2005 Phase I: protein/Alum (safe, but low Ab)

2008 Phase I: protein/Montanide ISA51 (low Ab and **severe skin reaction**)

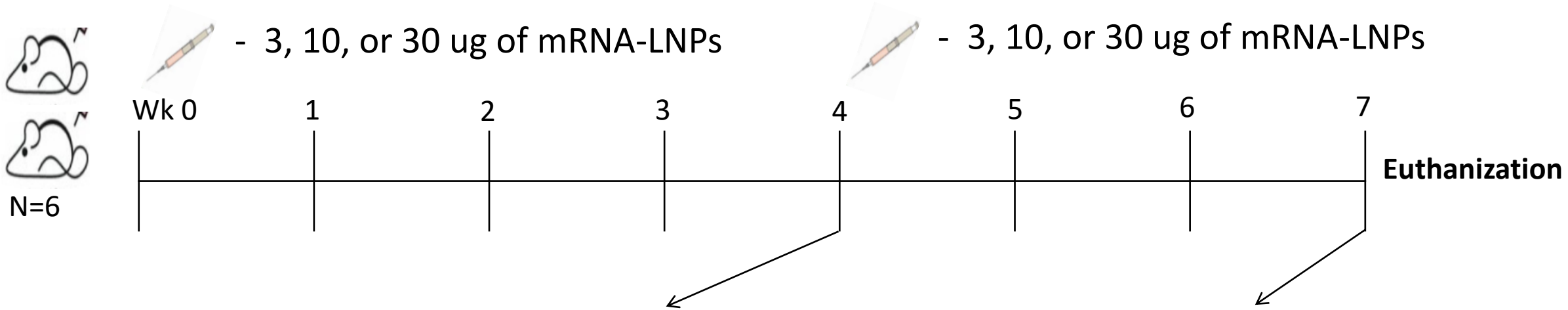
Protein/adjuvant → Strong reactogenicity
DNA/viral vectors → Low Ab, safety issue, pre-existing Ab to viral vector

Novel vaccine platforms are needed !!



Pvs25 on ookinete surface

Mouse immunization of Pvs25 mRNA-LNP vaccines

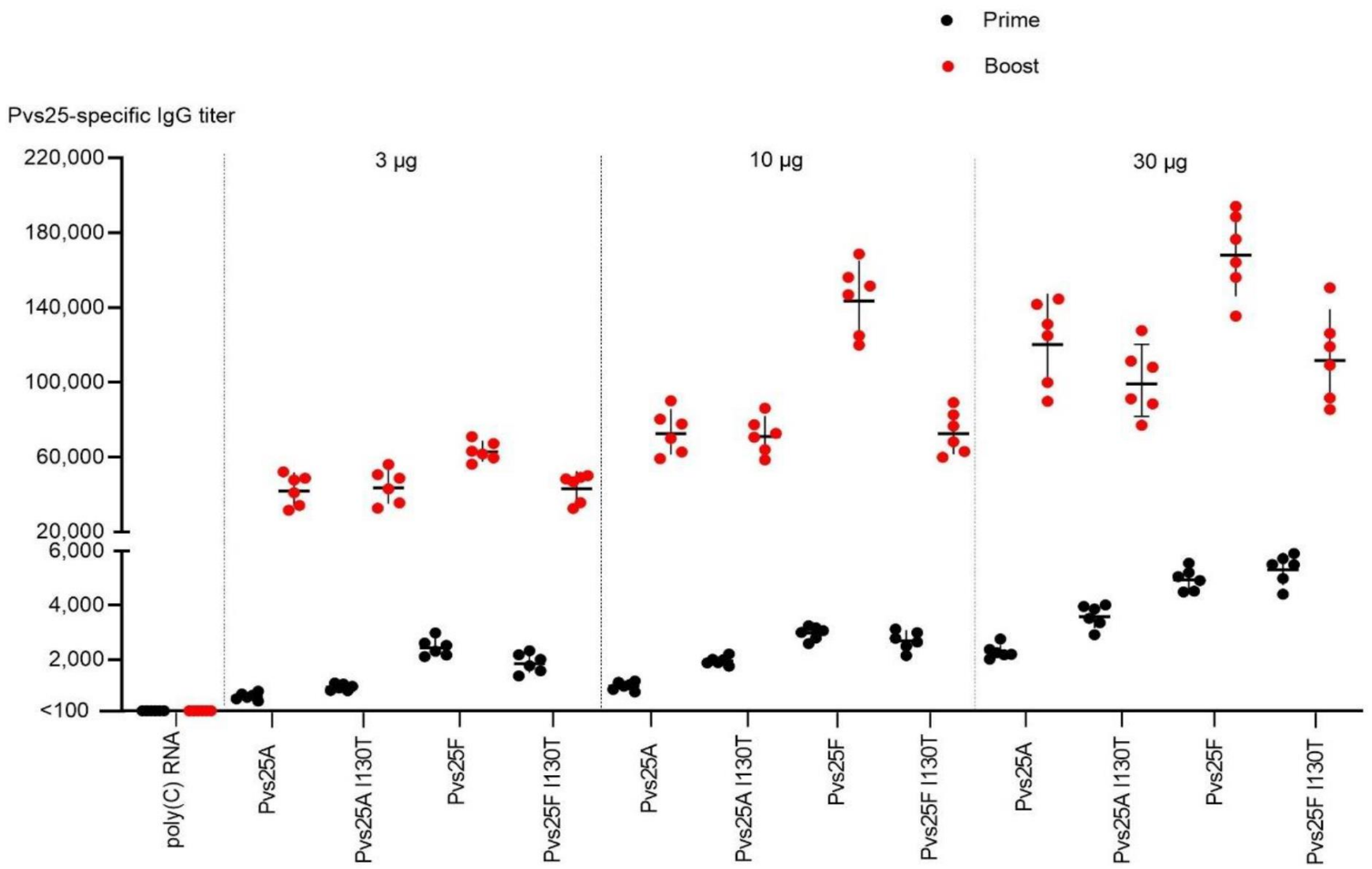


Blood collection
- ELISA

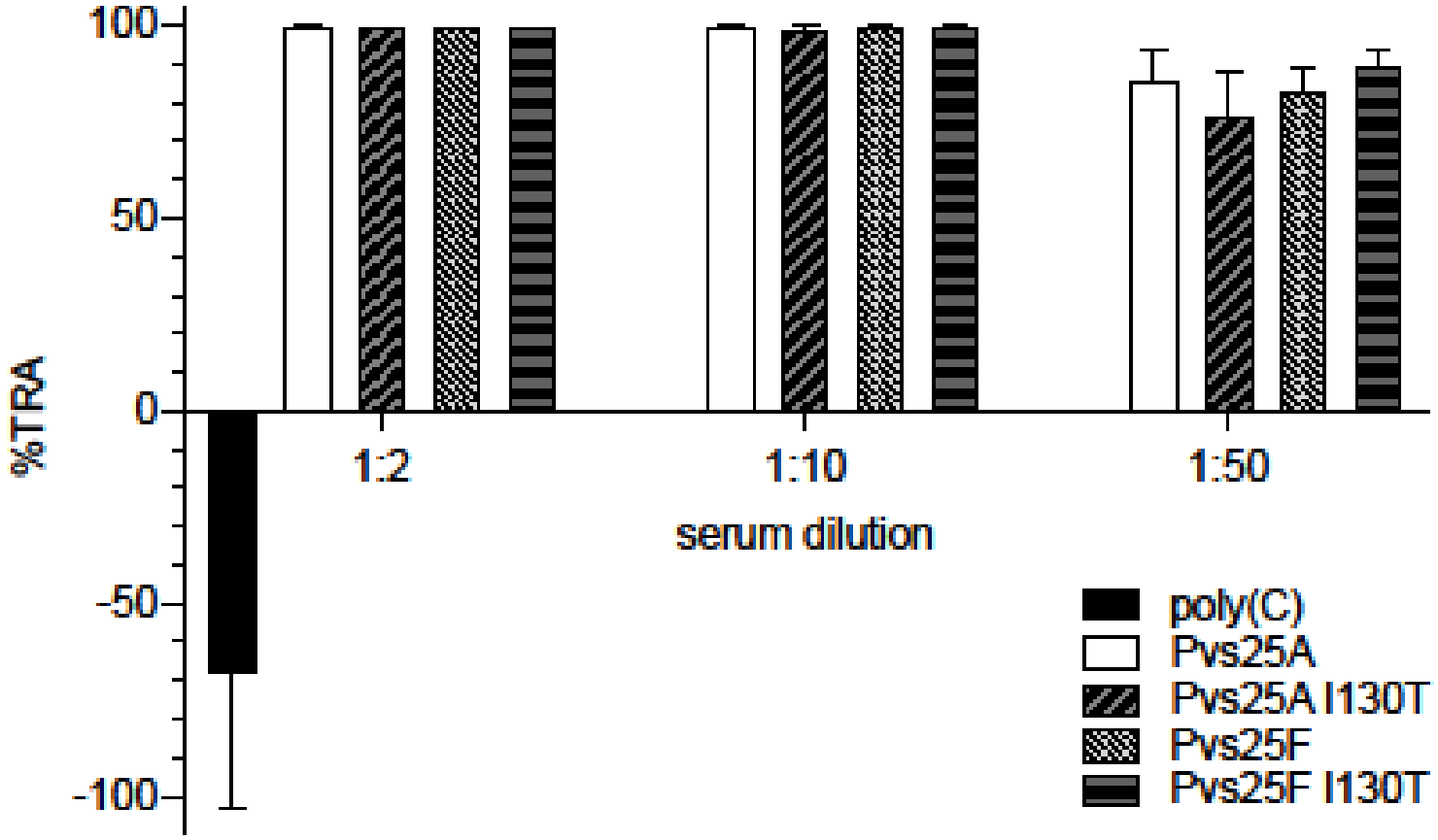
Assessment of Pvs25 antigen-specific immune response

-ELISA
-Memory B cell response
-T cell response
-Transmission blocking activity

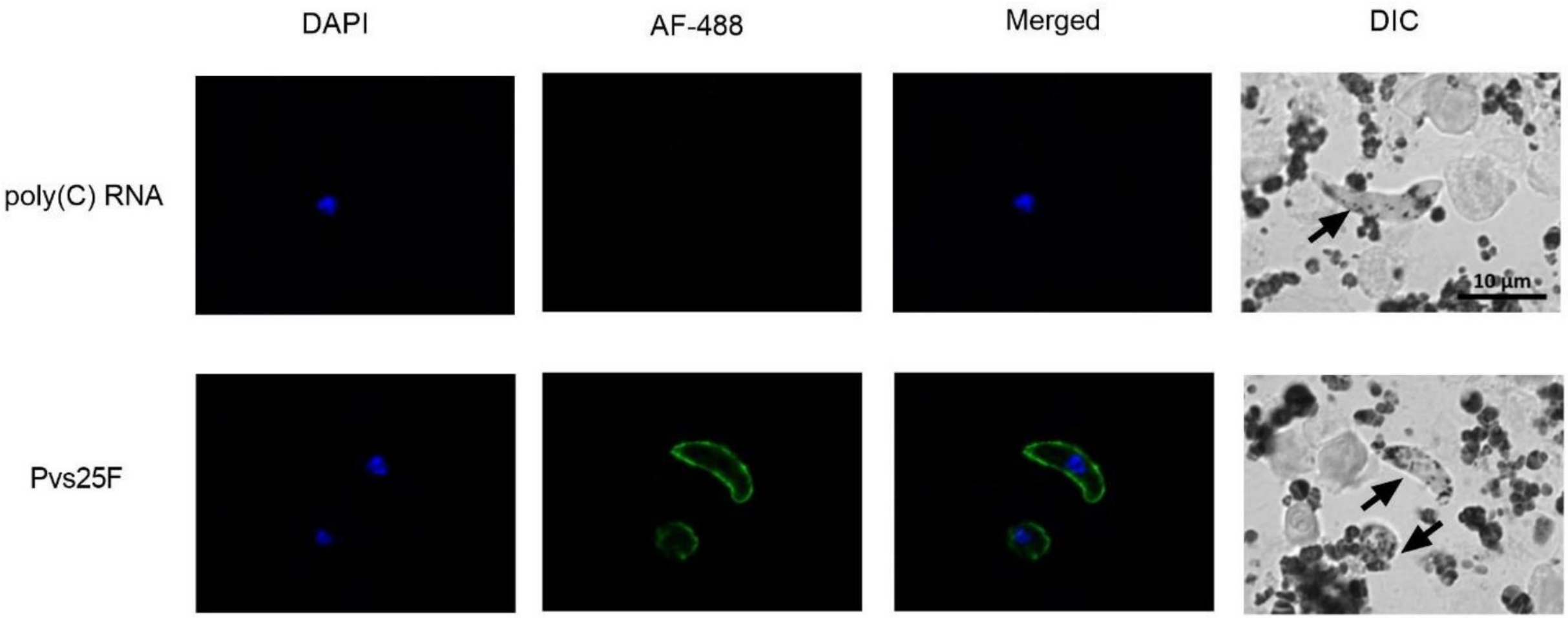
Antibodies induced by Pvs25 mRNA-LNP vaccines



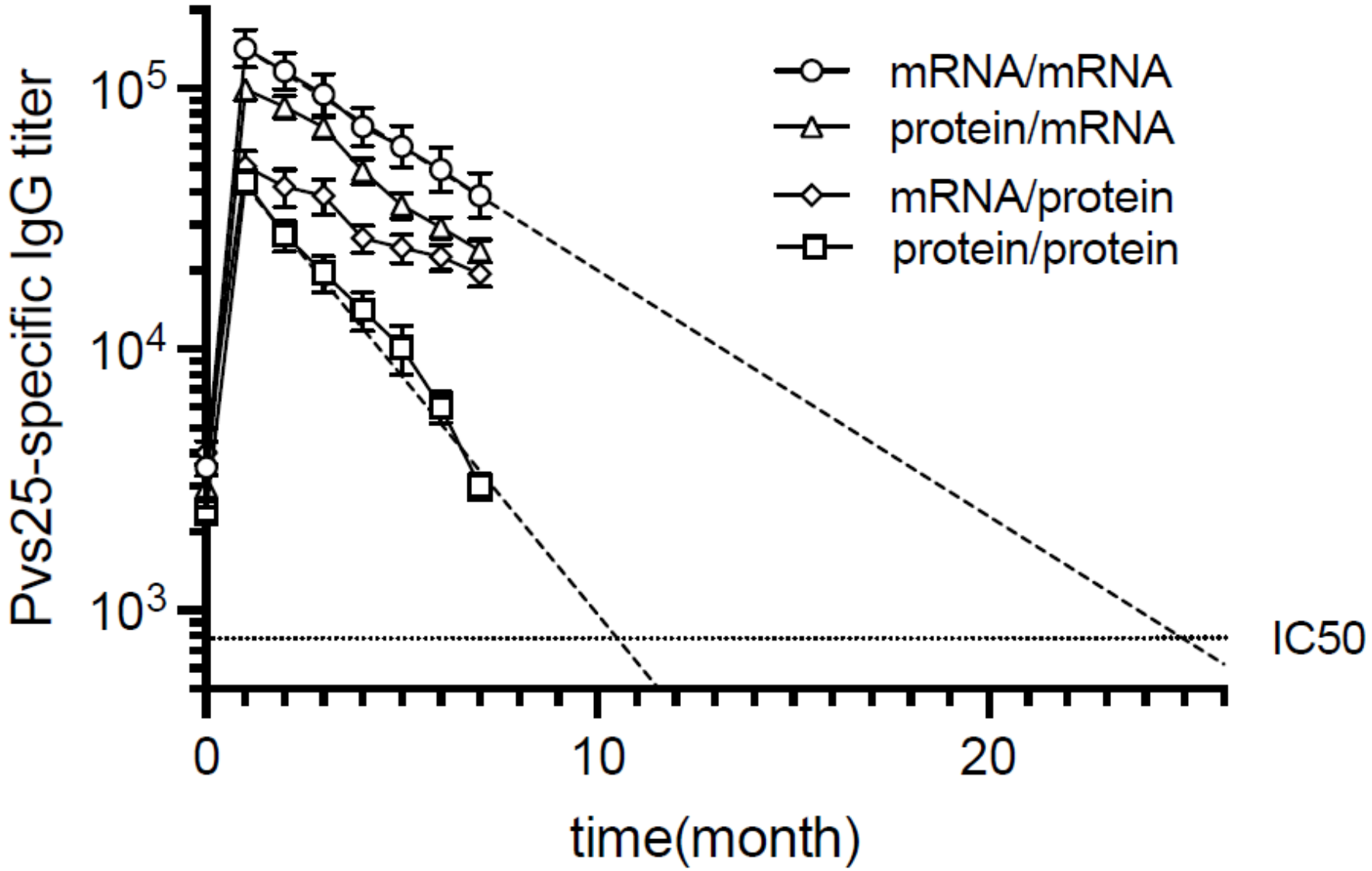
Transmission reducing activity (%TRA) of induced antibodies



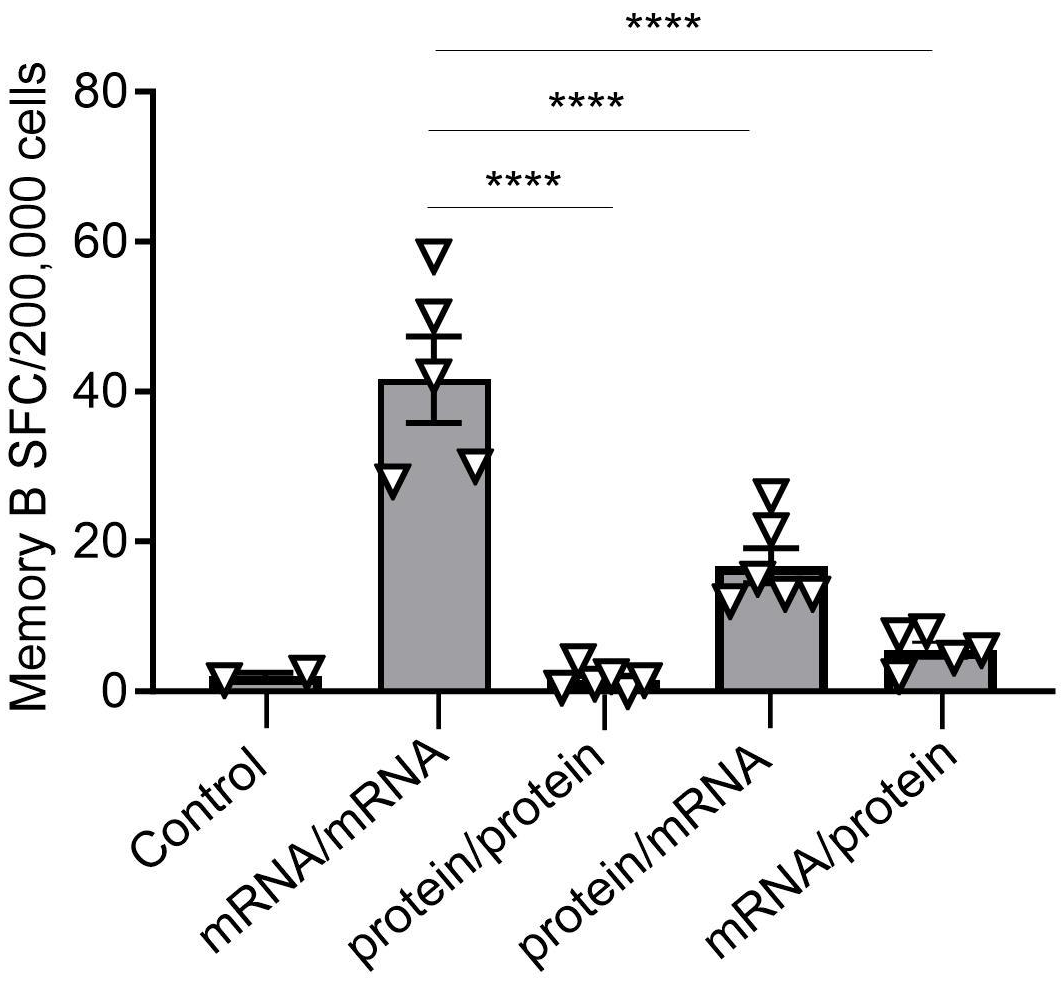
Native antigen recognition by induced antibodies



Durable antibody response induced by a Pvs25 mRNA vaccine



Cellular immune responses elicited by a Pvs25 mRNA vaccine



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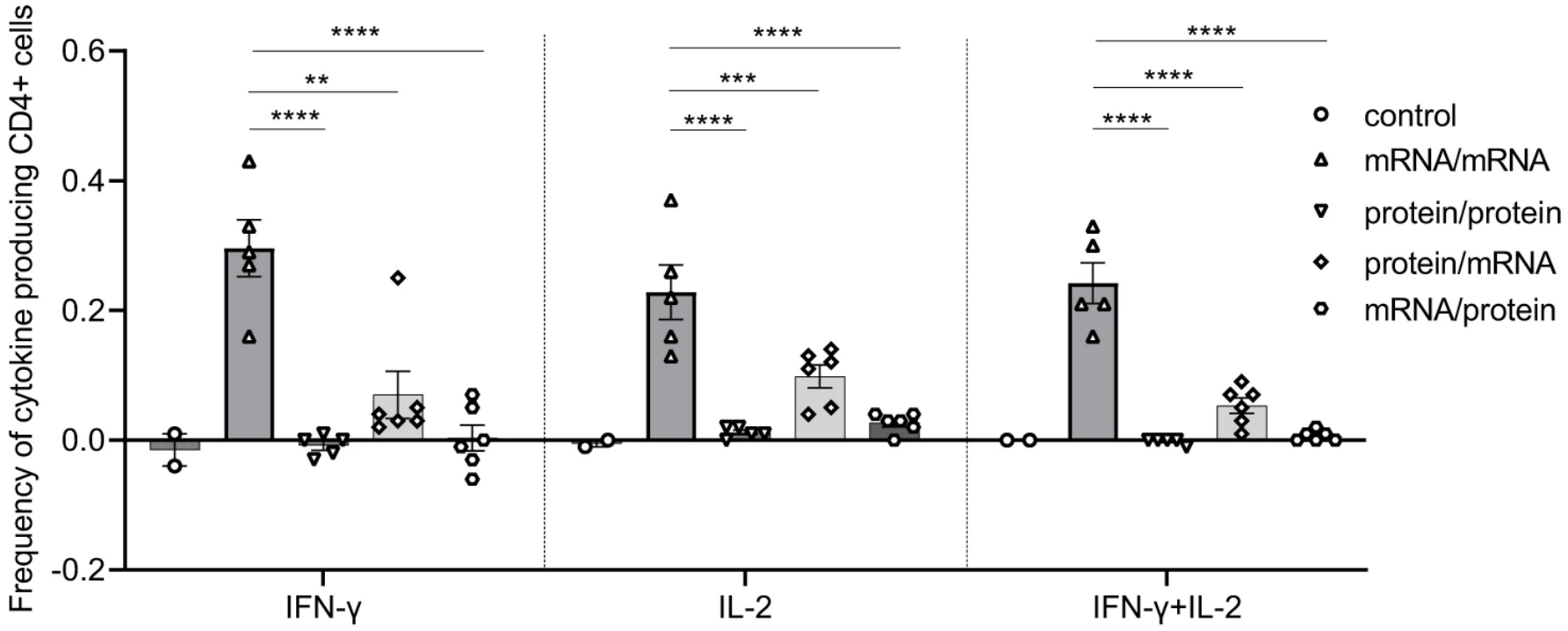
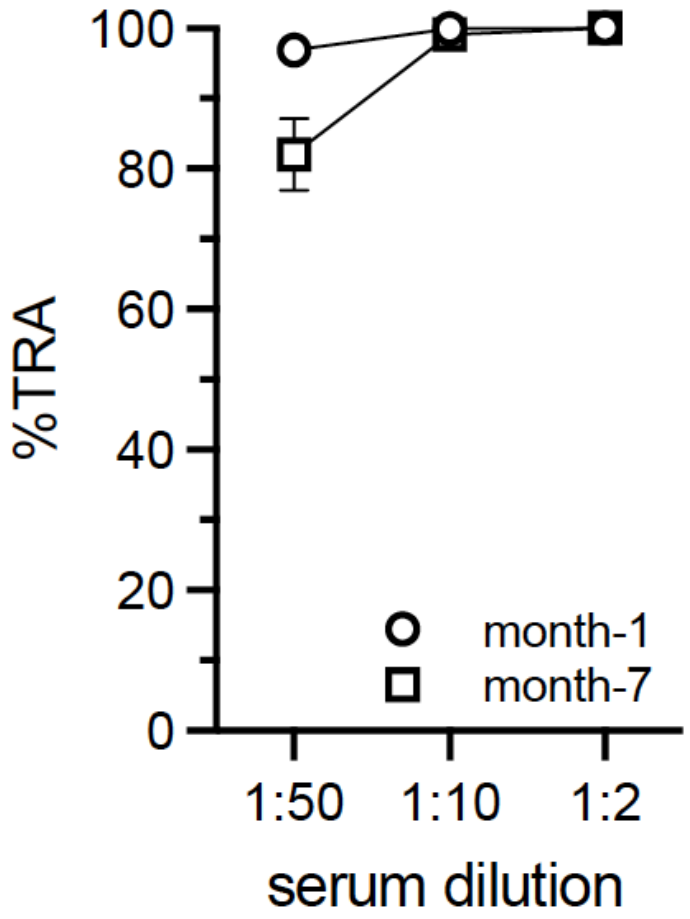
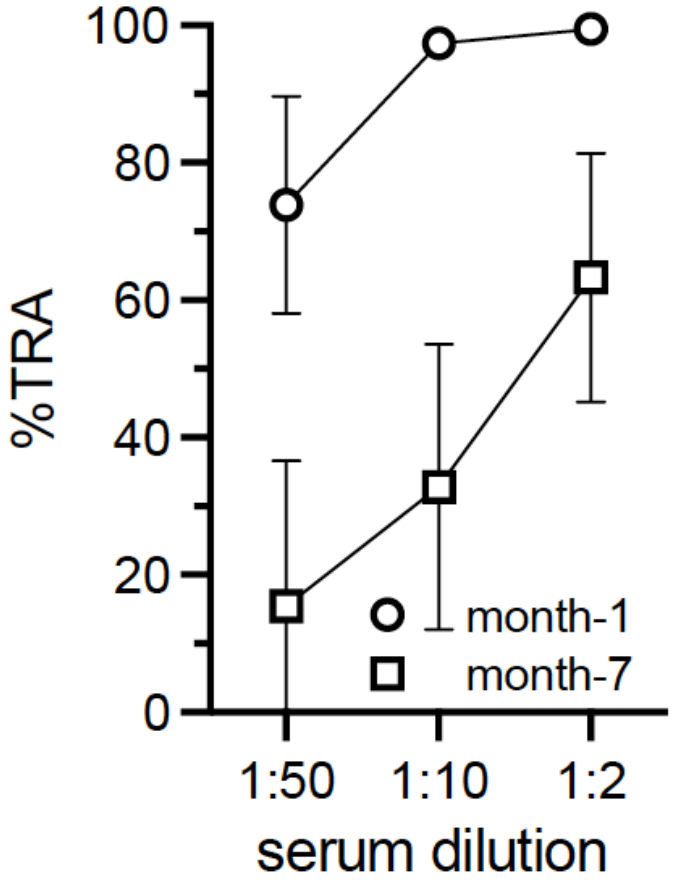


mRNA vaccine outperforms protein vaccine

Pvs25F mRNA/LNP vaccine



Protein / ISA51 vaccine



Ongoing mRNA vaccine validation

Construct optimization

- PvCSP and Pvs230

Circular RNA vaccine technology

- Pvs25 and Pvs230

Chula VRC formulation, Chula Vaccine Research Center, Chulalongkorn University

- Pvs25, PvCSP, and Pvs230
- Multistage vaccines
- Pvs25 is ready for non-human primate testing
- National Primate Research Center of Thailand (Chulalongkorn University)

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