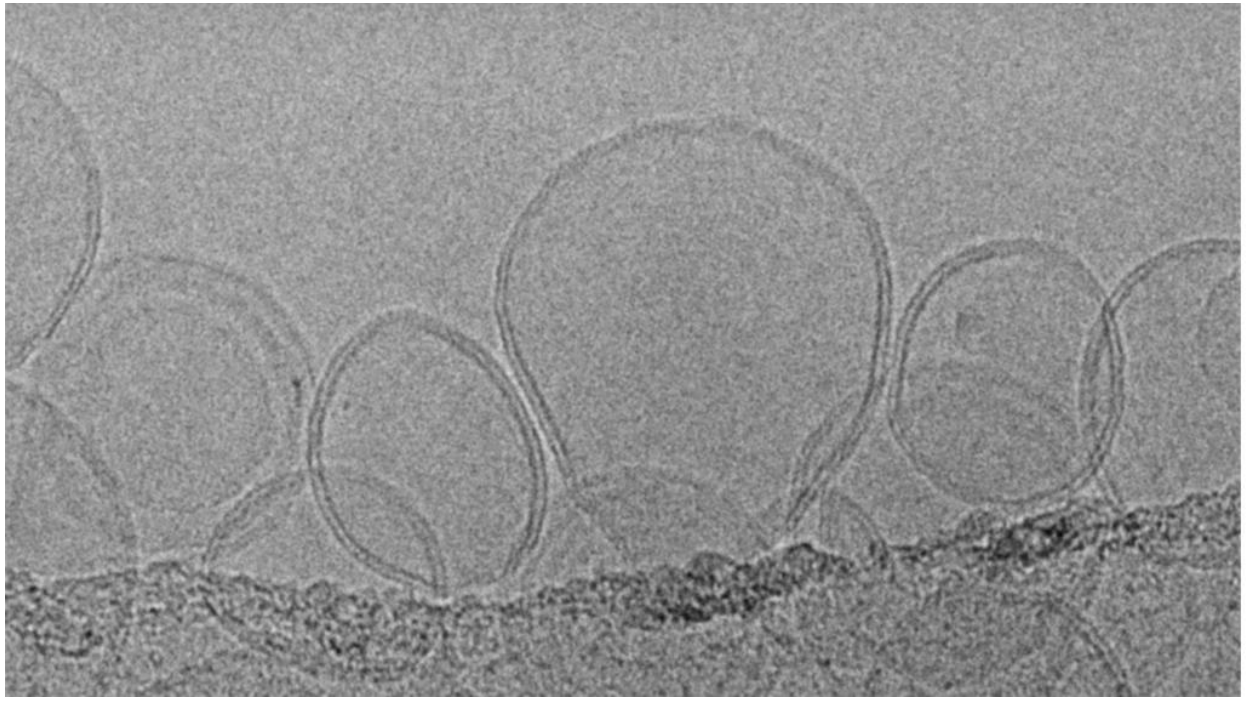
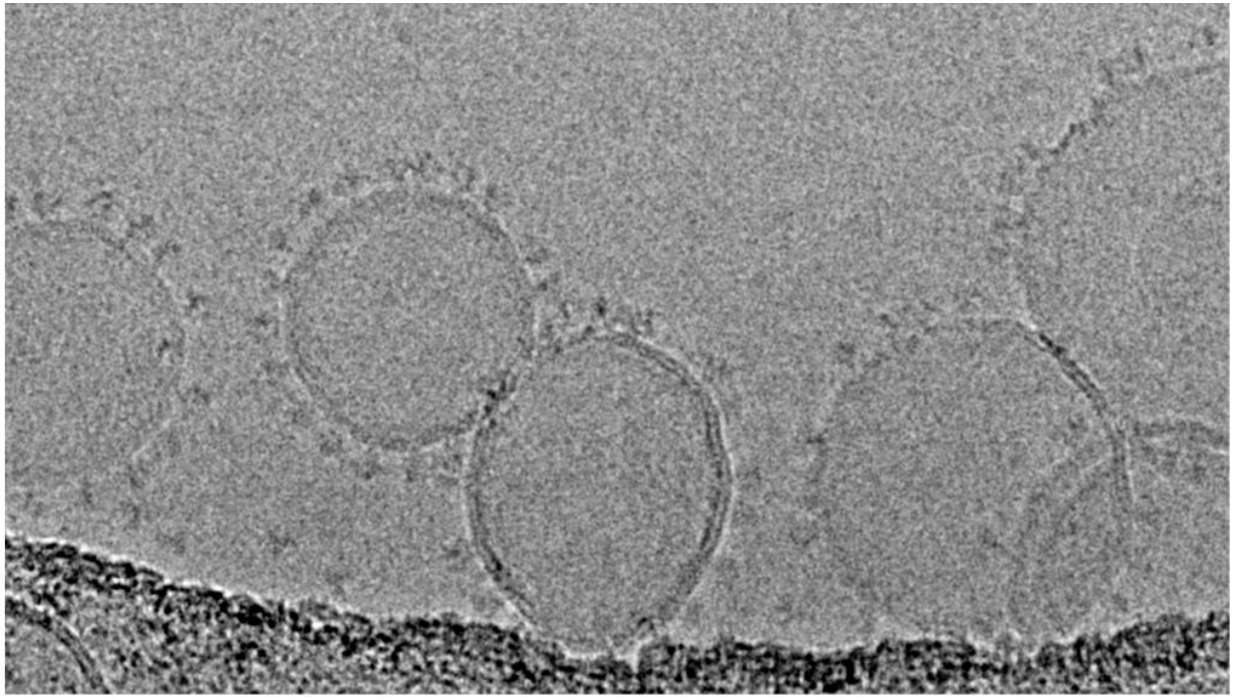
Liposome-Display of Antigens: A Versatile Approach for Vaccine Development





Jonathan Lovell, PhD

Empire Innovation Prof. BME, State University of New York at Buffalo

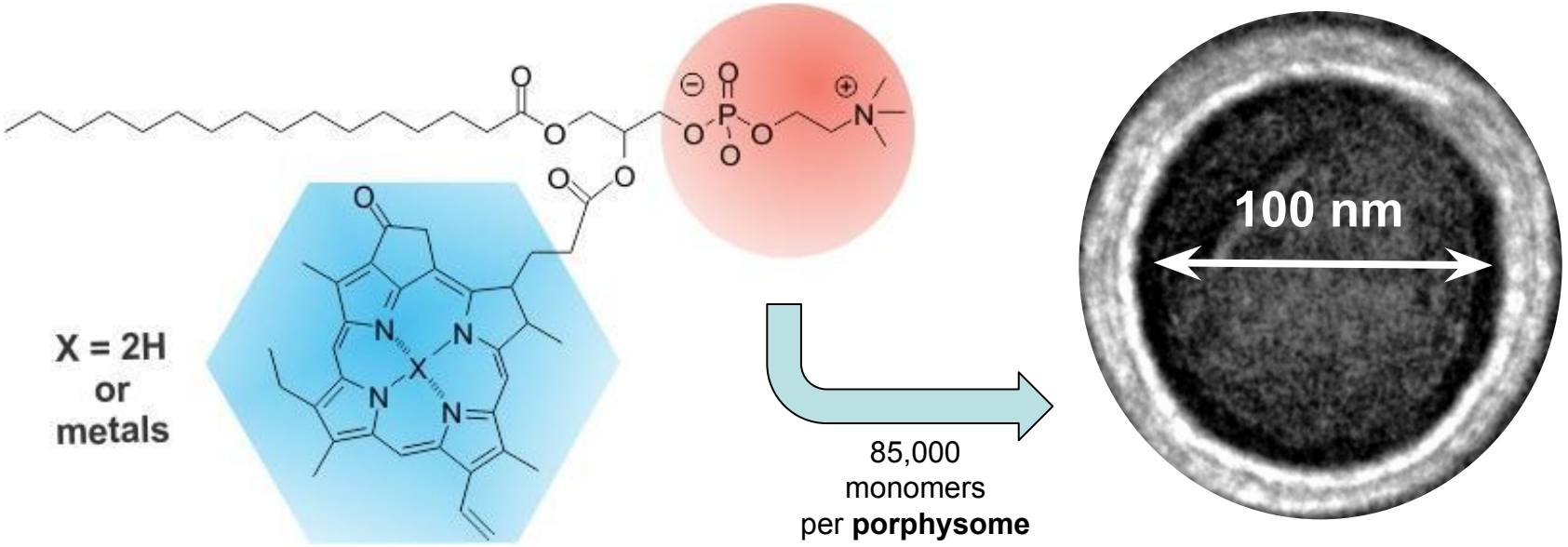
July 14 2022

Controlled Release Society 2022, Montreal, Canada

Conflict of Interest Statement

POPBIOTECH

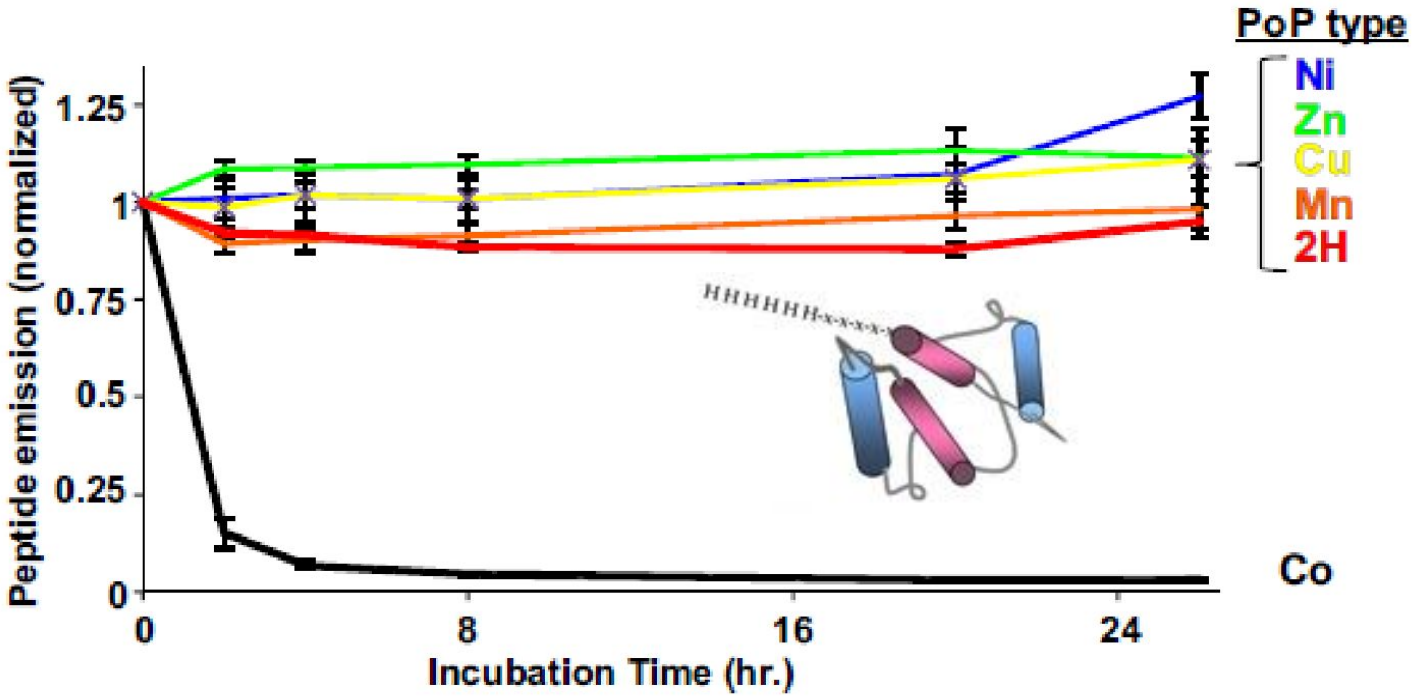
Porphyrin-phospholipid (PoP)

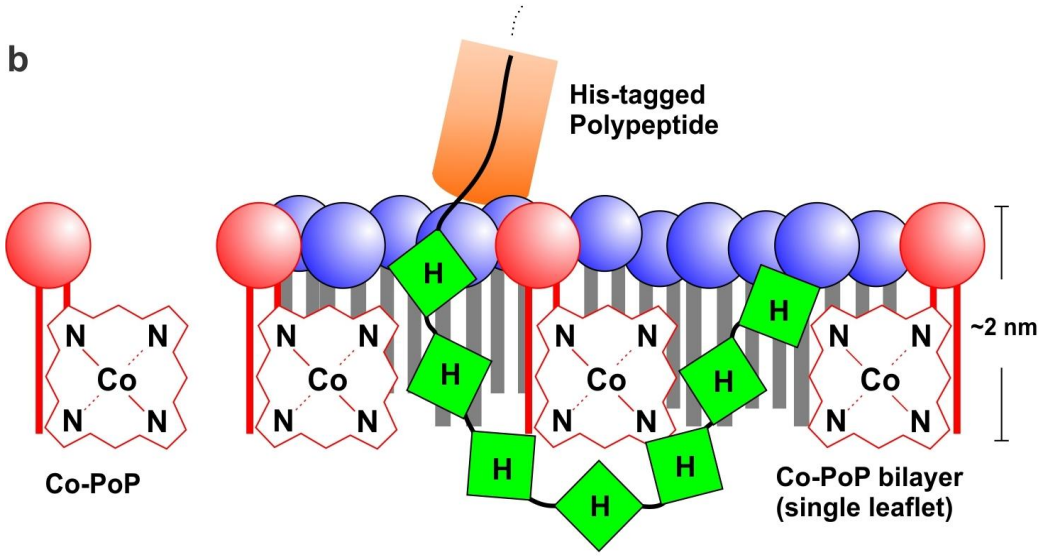


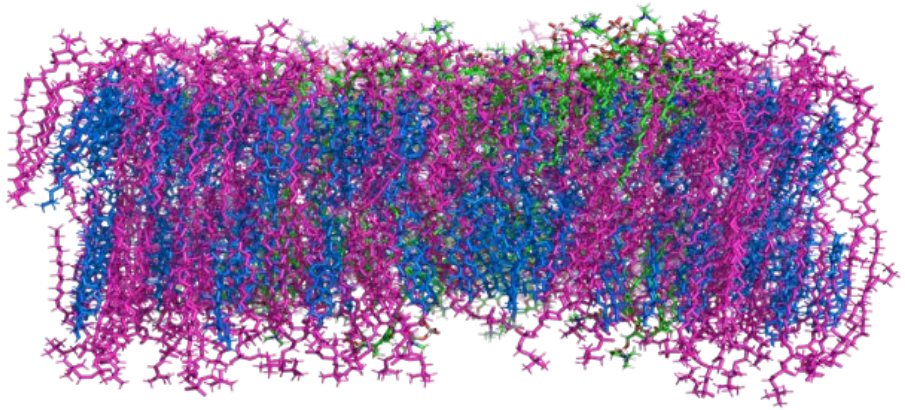
- Stable, simple liposome incorporation

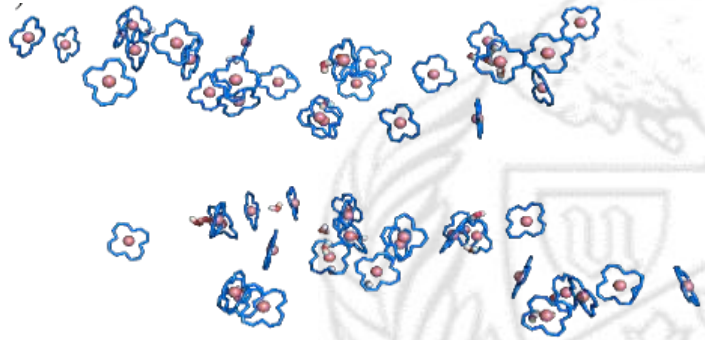
Lovell et al., Nature Materials, 20-324, 2011

Cobalt PoP liposomes bind his-tagged polypeptides



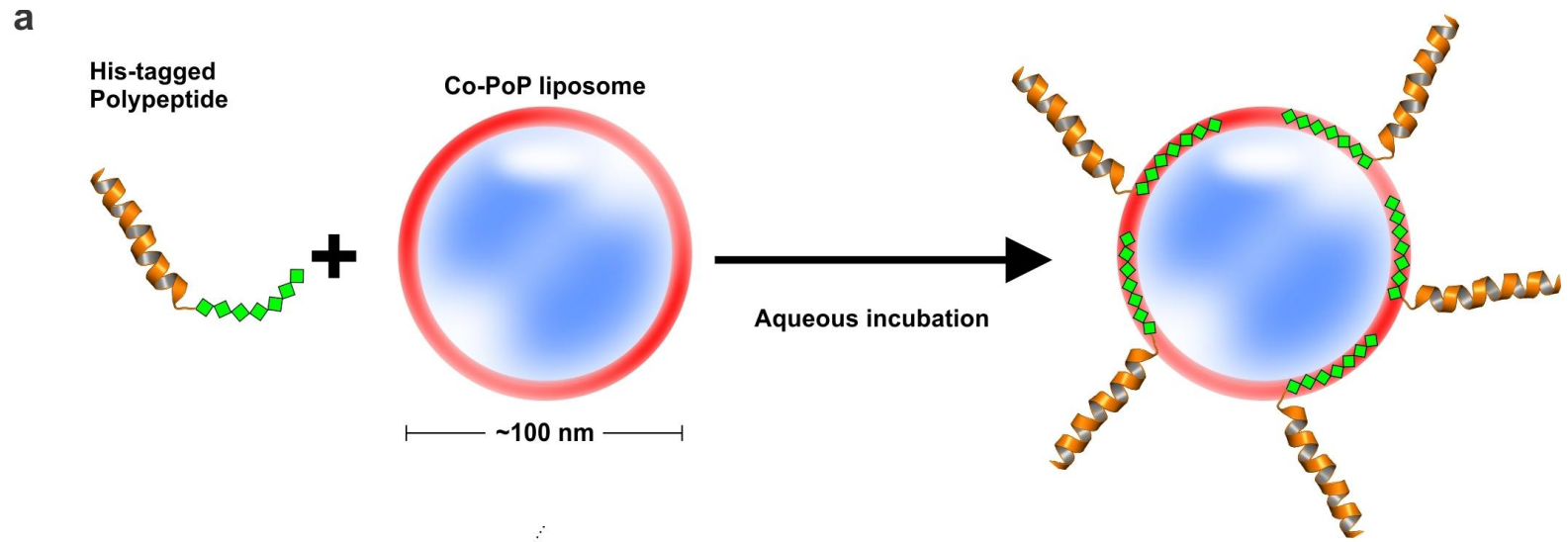


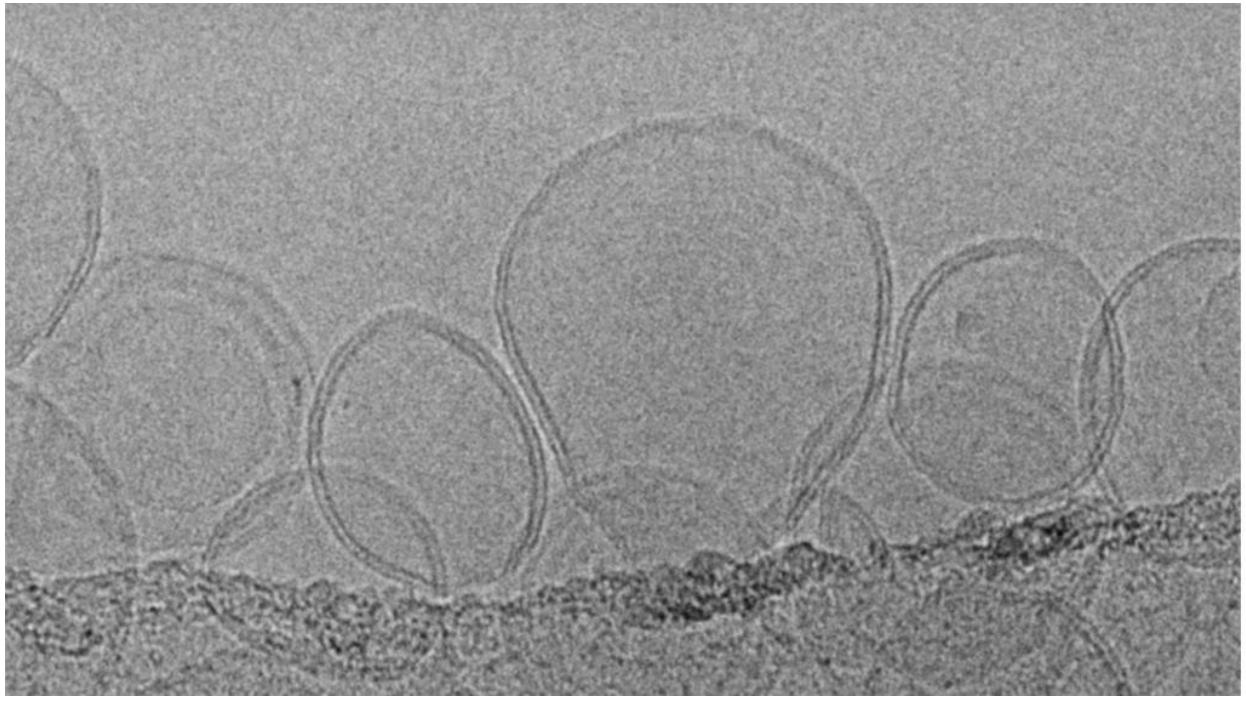


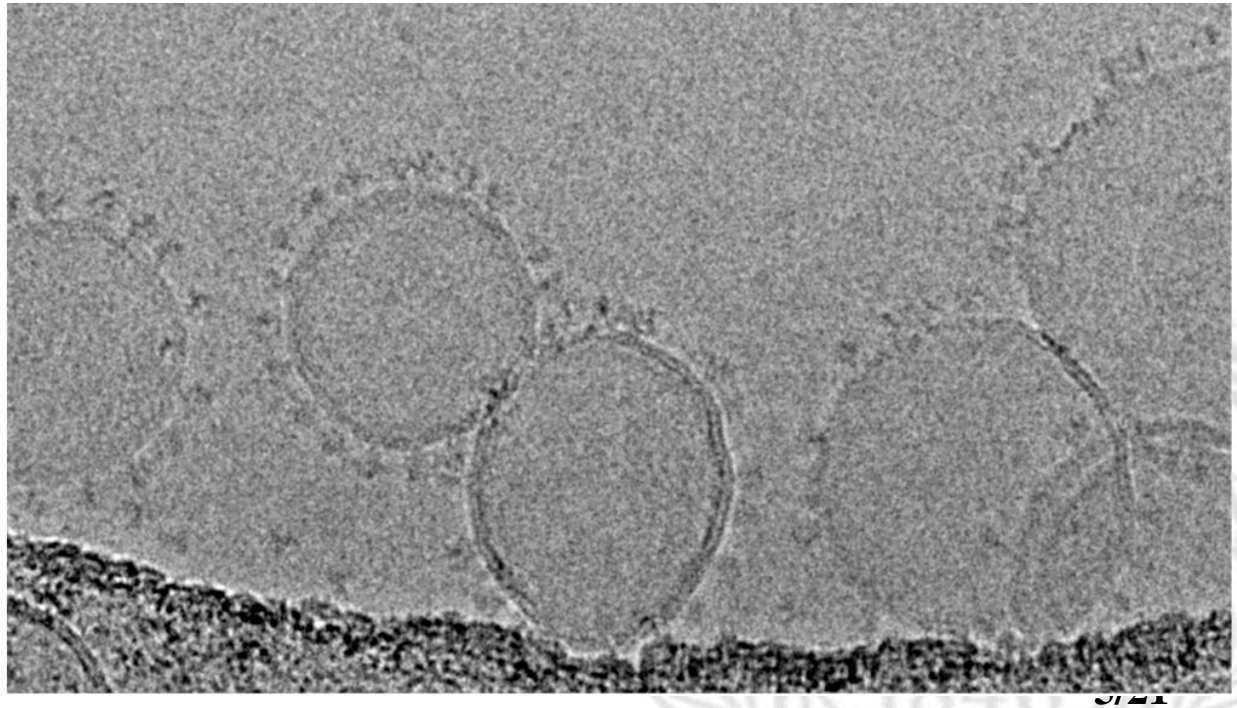


Shao et al., Nature Chemistry, 7-438, 2015

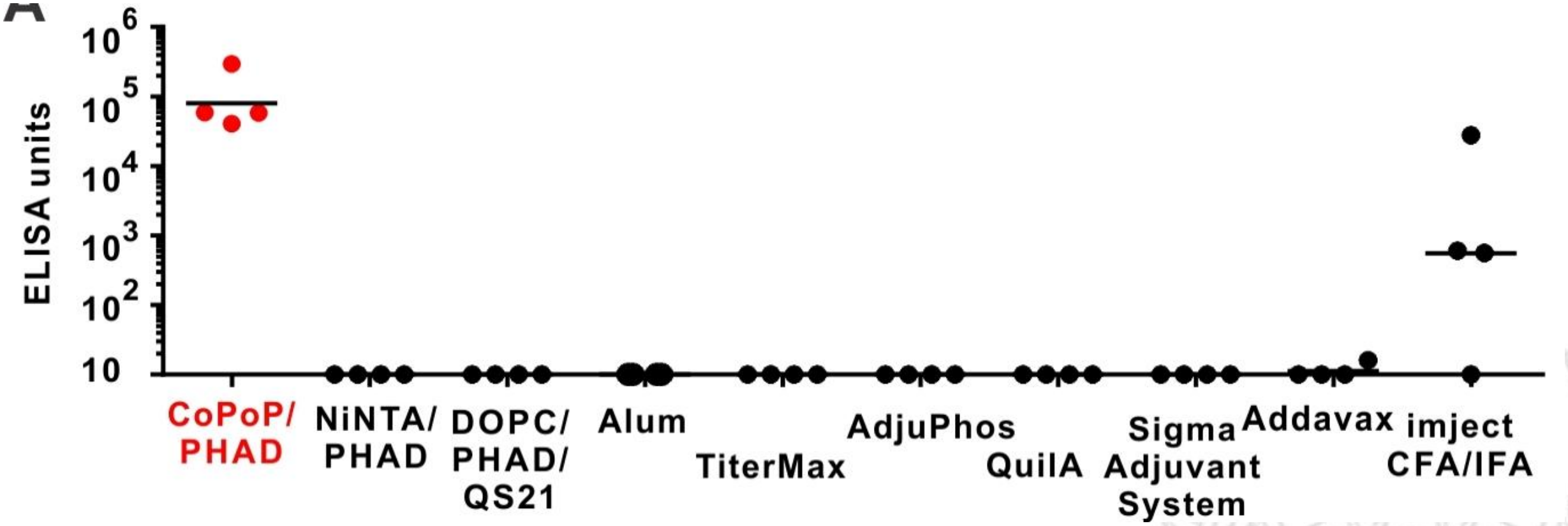
Simple formation of particle based vaccines







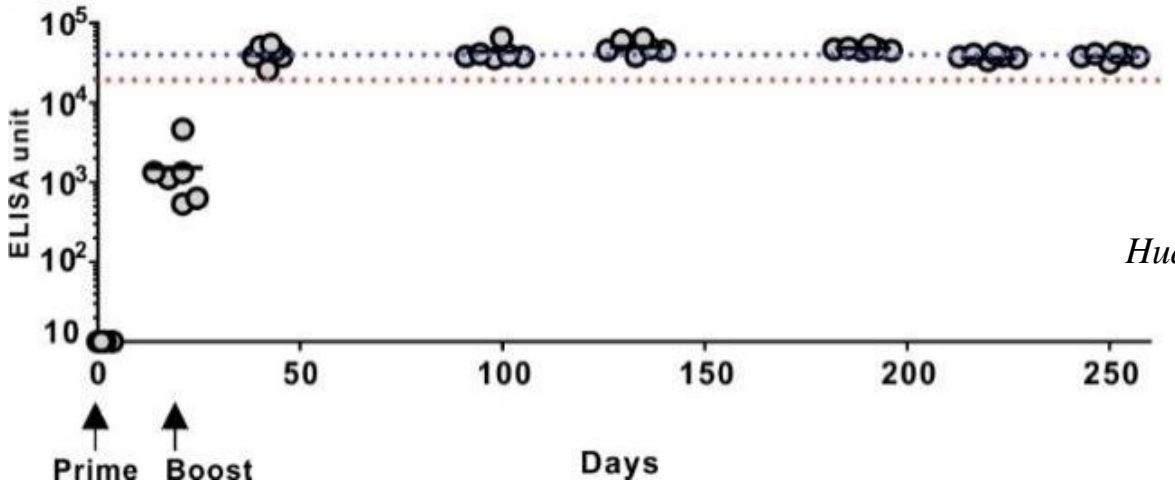
Particleization of a malaria antigen



Huang et al., Nature Nanotechnology, 13-1174, 2018

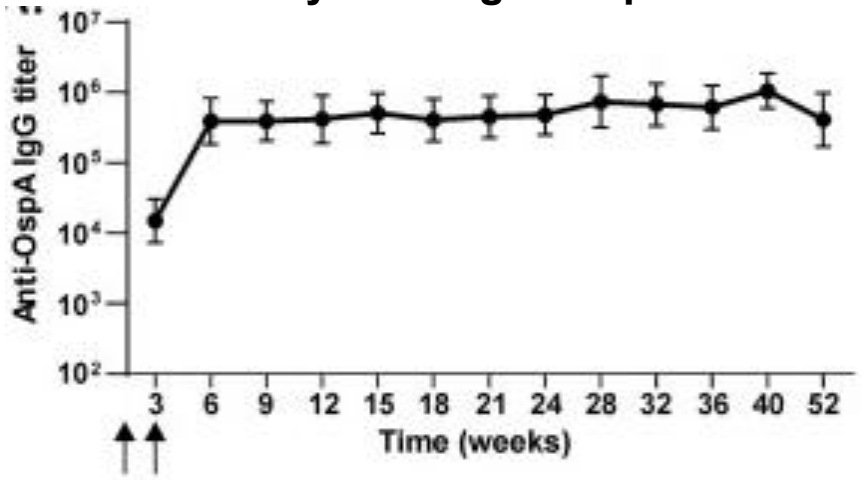
Durable antibody responses

Malaria antigen: Pfs25



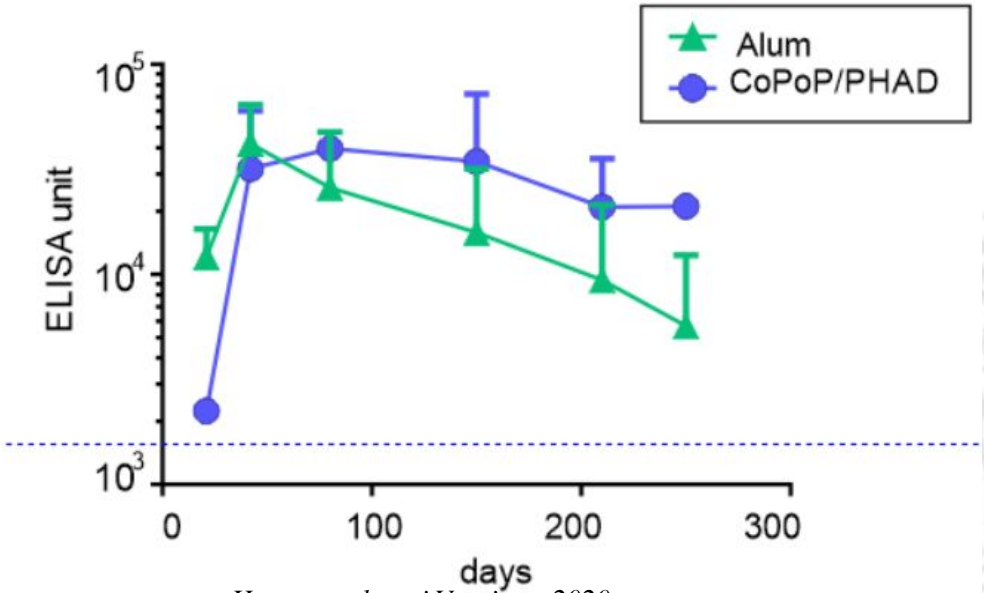
*Huang et al., Nature Nanotechnology, **13**, 1174–1181 (2018)*

Lyme antigen OspA



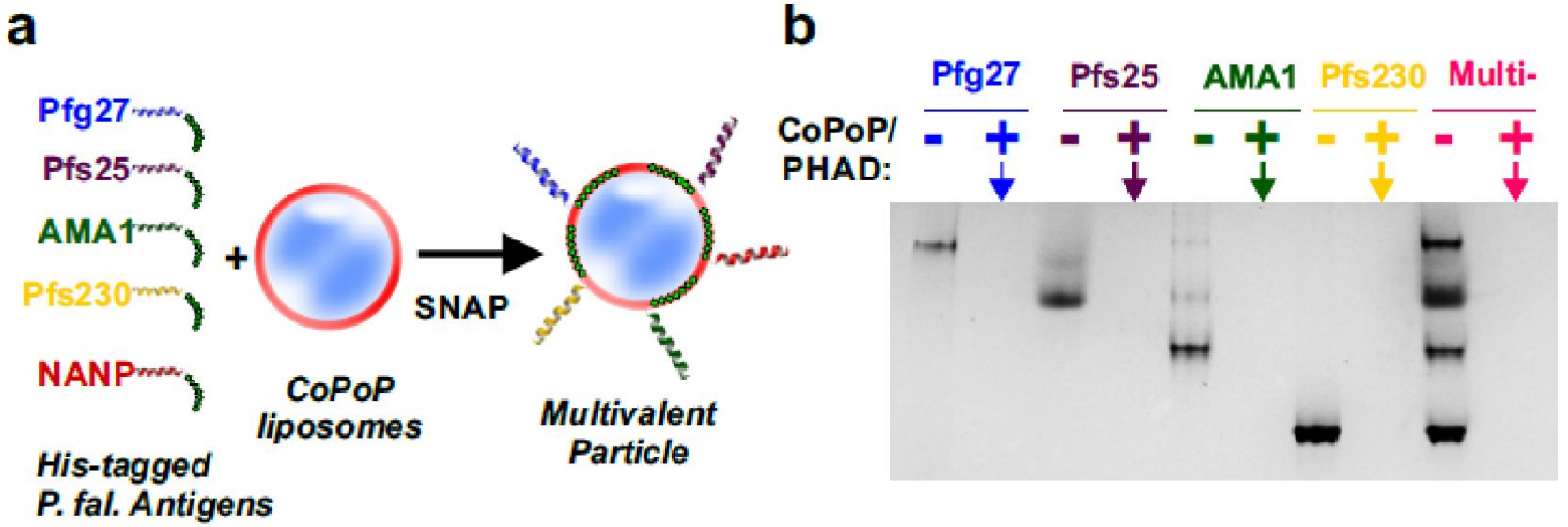
Federizon et al., Vaccine, 38-942 (2020)

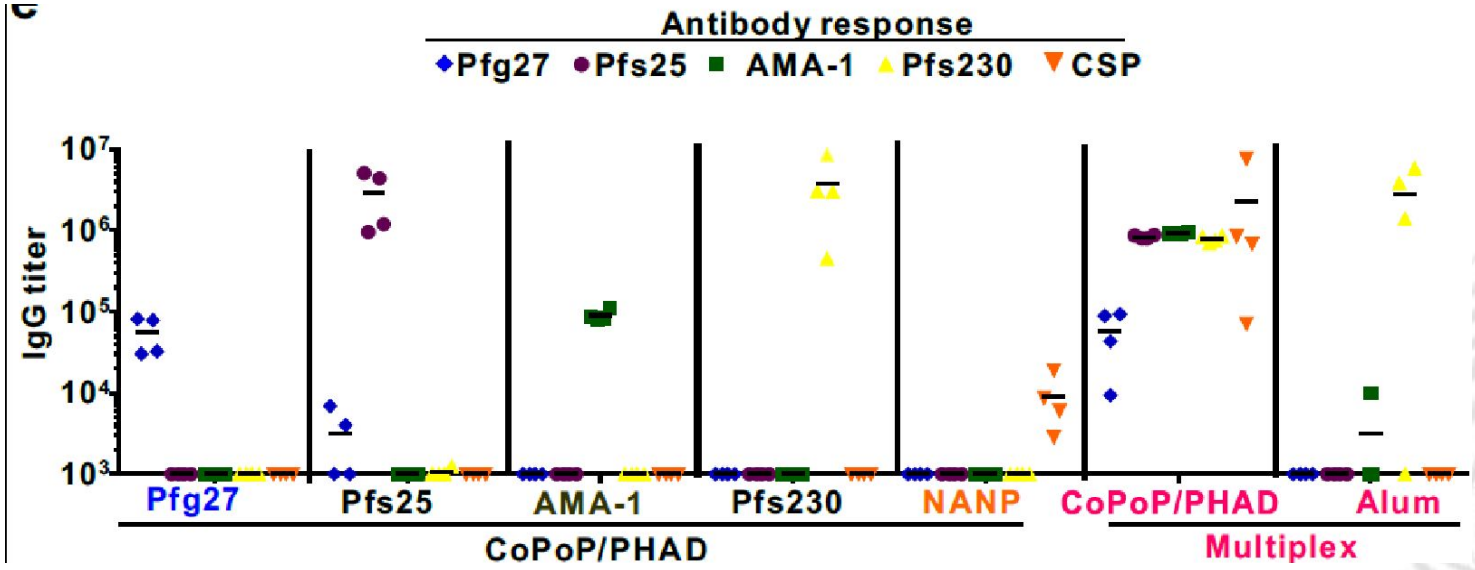
Malaria antigen: Pfs230C1



Huang et al., npj Vaccines, 2020

Simple antigen multiplexing

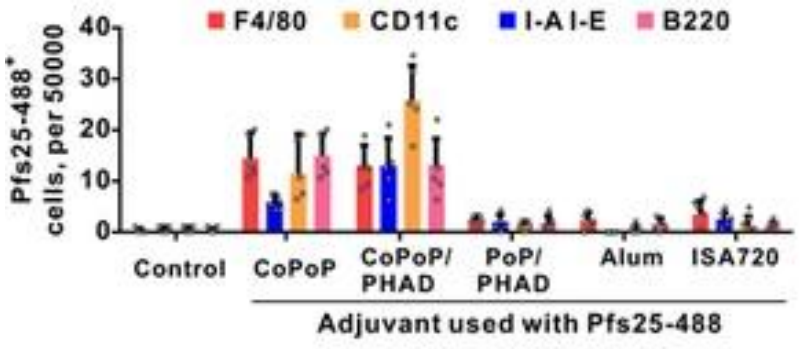




Huang et al., Nature Nanotechnology, 13-1174, 2018

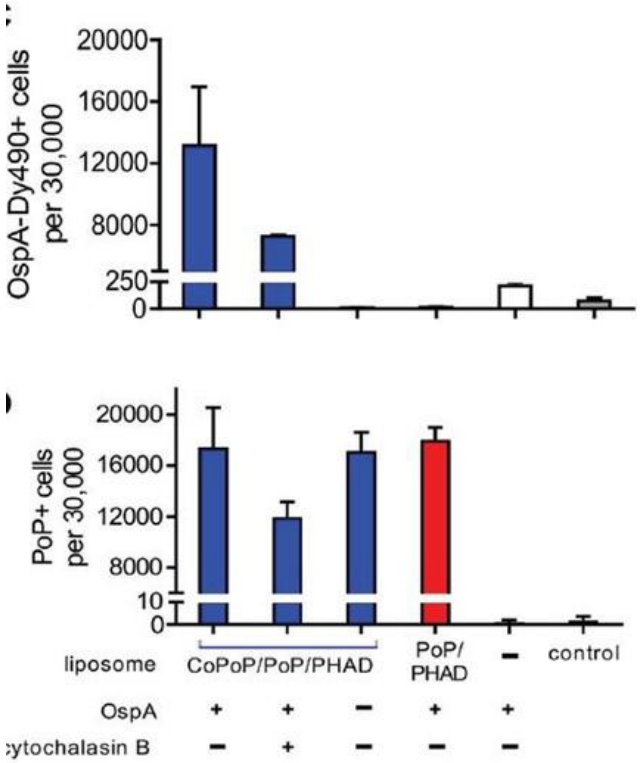
Enhancing antigen uptake in APC

Pfs25 uptake in mouse draining lymph nodes



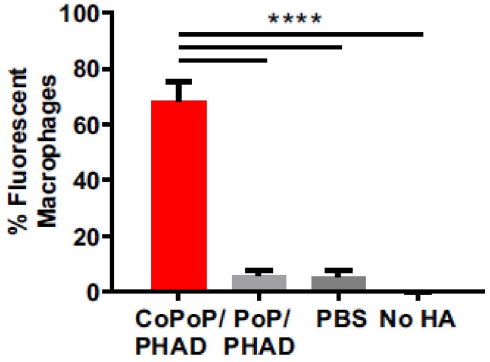
Huang et al., Nature Nanotechnology

OspA uptake in murine macrophages (in vitro)



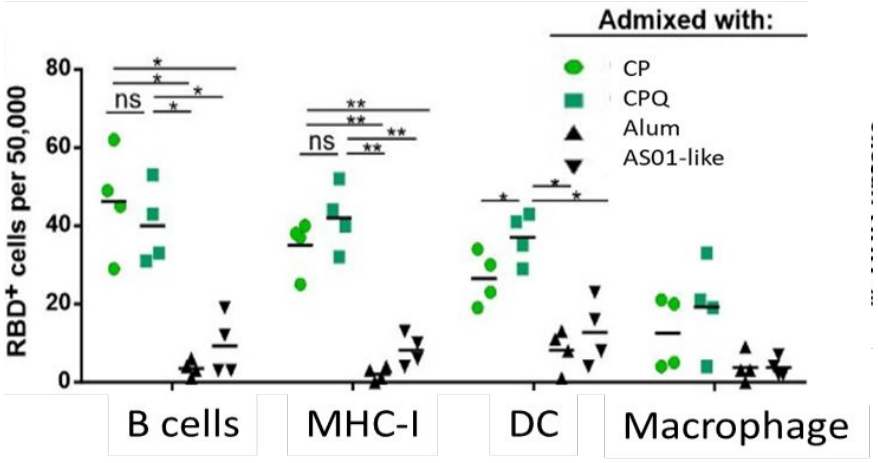
Federizon et al., Vaccine (2020)

HA uptake in murine macrophages



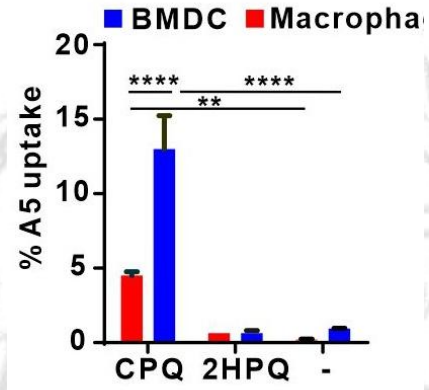
Sia et al., PNAS (2021)

RBD uptake in mouse draining lymph nodes



Huang et al., Advanced Materials (2020)

Peptide uptake in murine macrophages

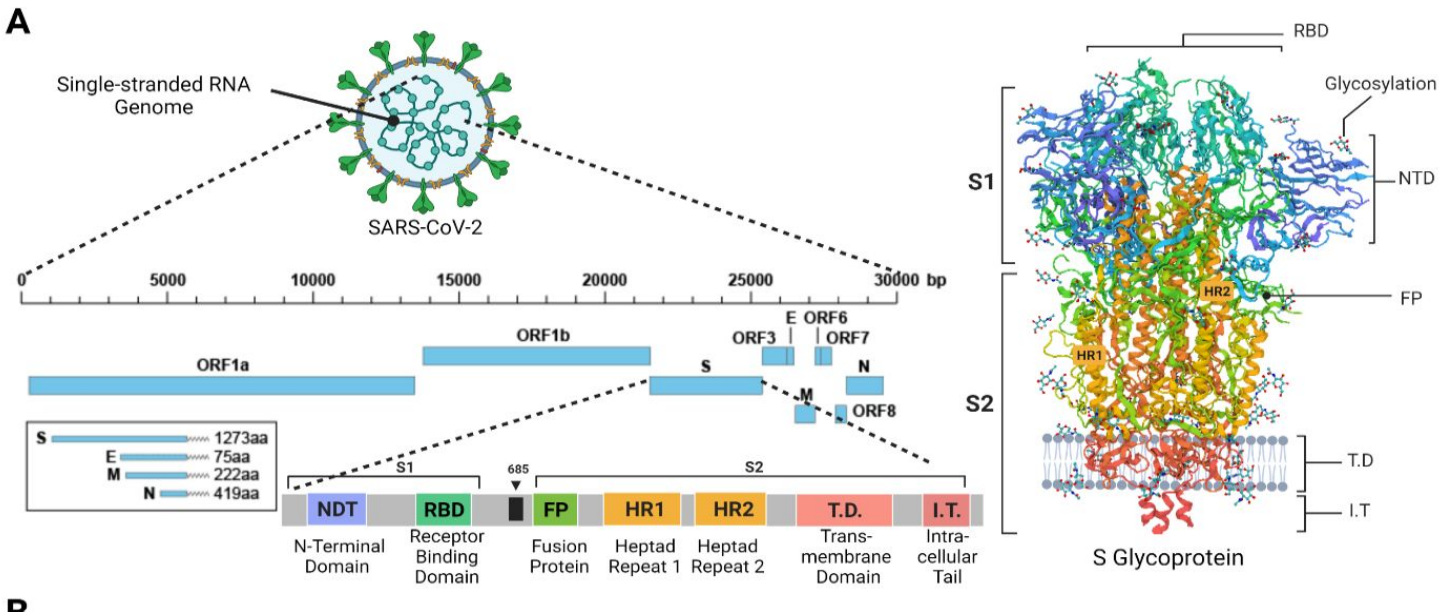


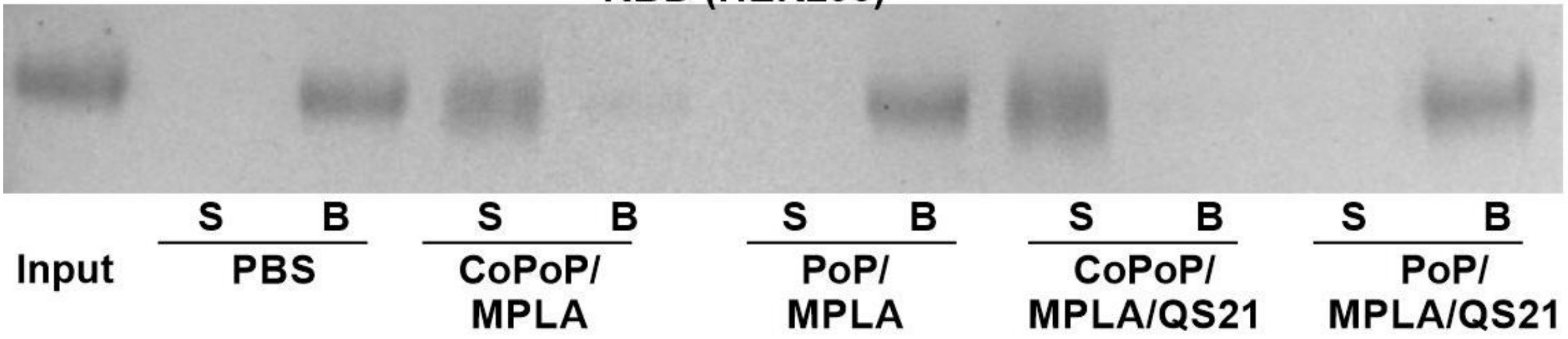
He et al., ACS Nano (2021)

The CoPoP Virus-like Particle

	CoPoP	Typical competitors
Scaffold material	Liposome-display	Protein-display
Exogenous protein content	None	Substantial (e.g. scaffold >> 50% total protein)
Off-target immune response	None	Substantial
Requirement of fusion antigens or chemical conjugation	No	Yes
Use of adjuvants	Incorporated and co-*delivered* to APCs	Co-*administered*
Antigen density	Tunable	Tunable or fixed (depends on platform)
Antigen 3D spatial orientation	Uniform	Uniform or random (depends on platform)
Cost per human dose	< $ 0.04	Depends on platform
Generating multivalent particles with controlled stoichiometry	Simple	Challenging

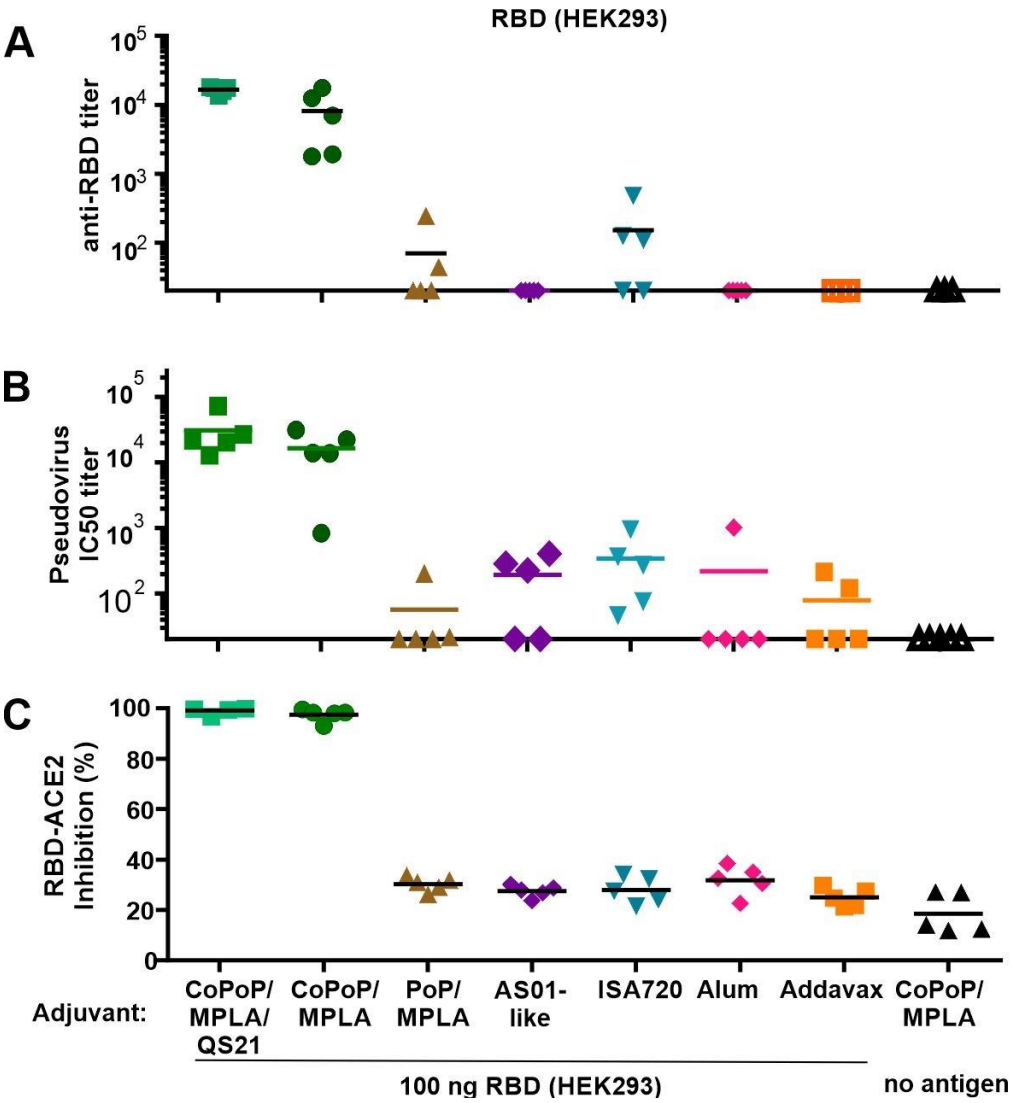
Making a particle based RBD SARS-CoV-2 vaccine



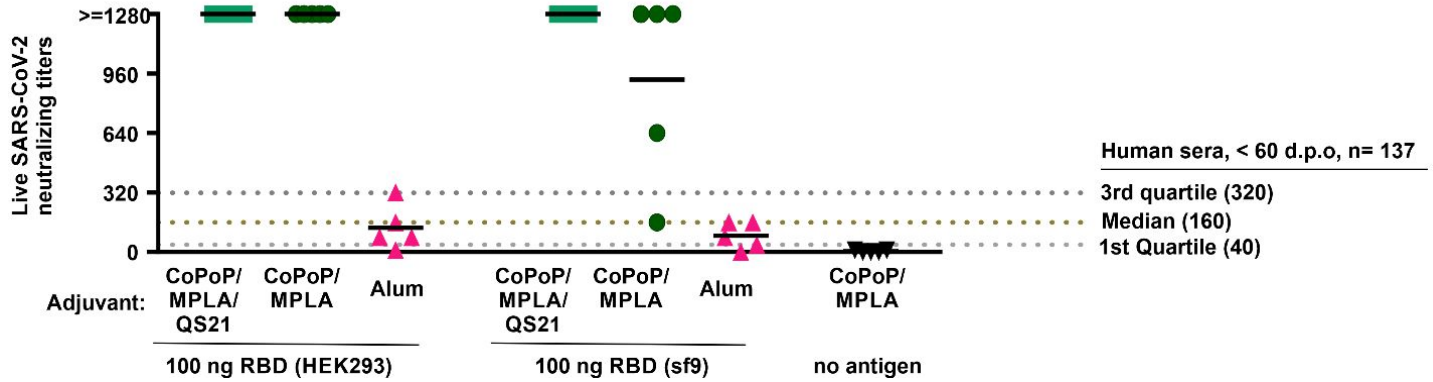


Mabrouk et al., Advanced Materials (2020, 2021)

The SARS-CoV-2 RBD benefits from particle presentation with CoPoP

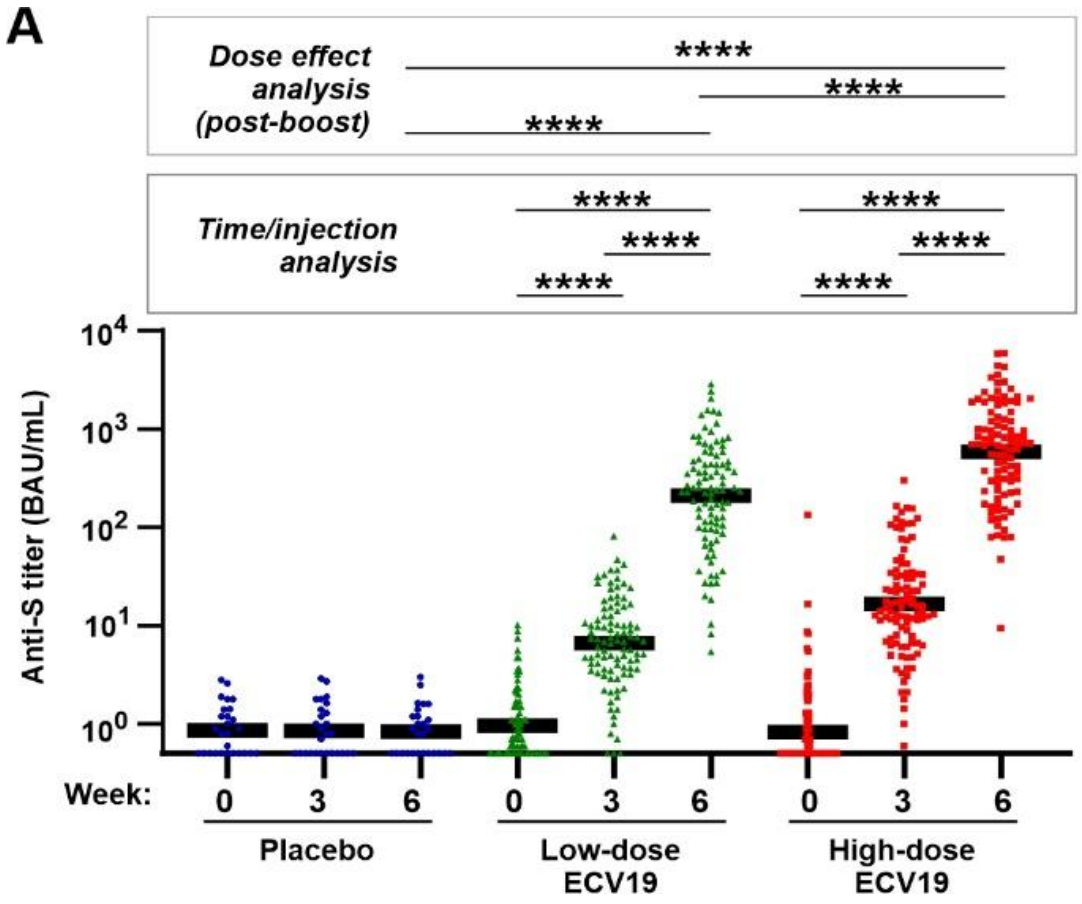


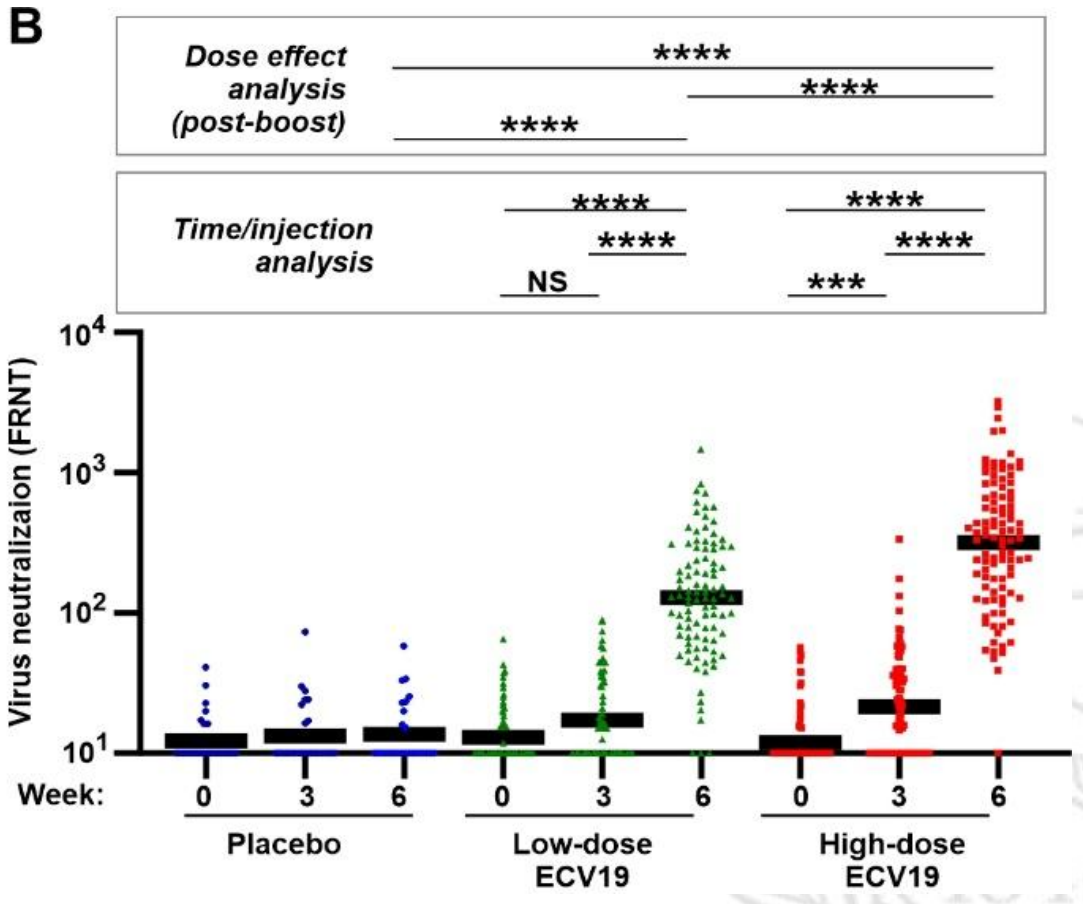
Mouse immunization with 100 ng RBD antigen, 400 ng CoPoP, 160 ng MPLA/QS21



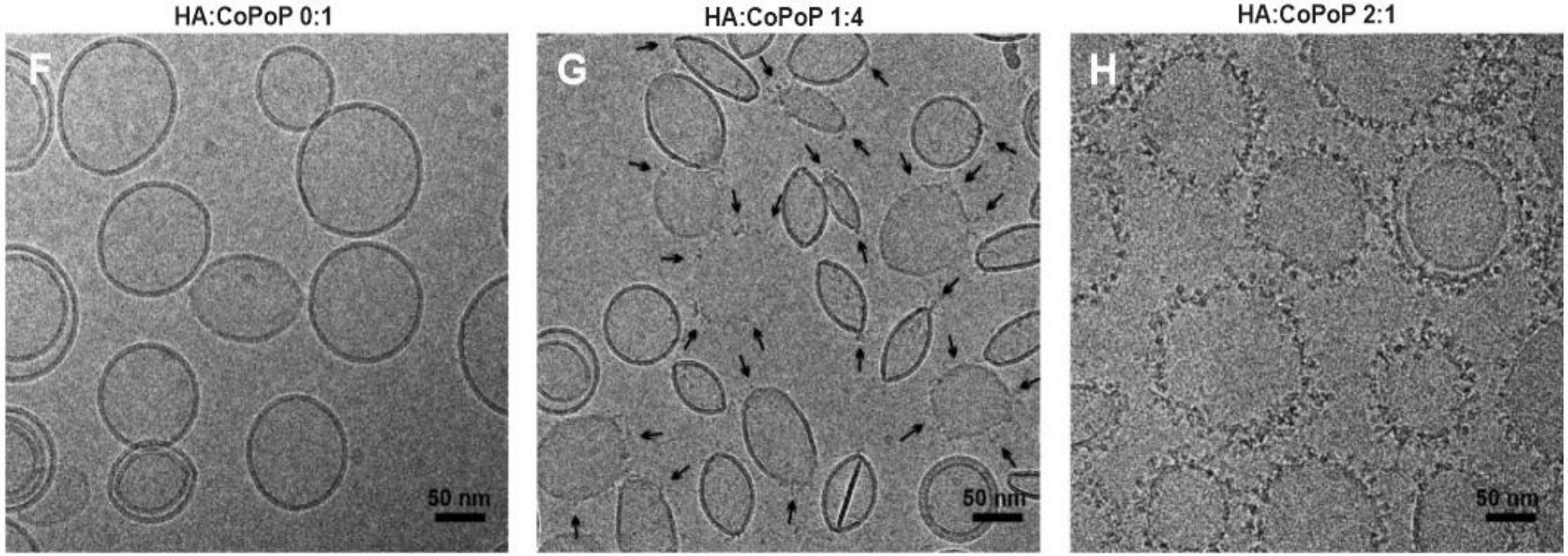
Phase 2 human clinical trial interim results

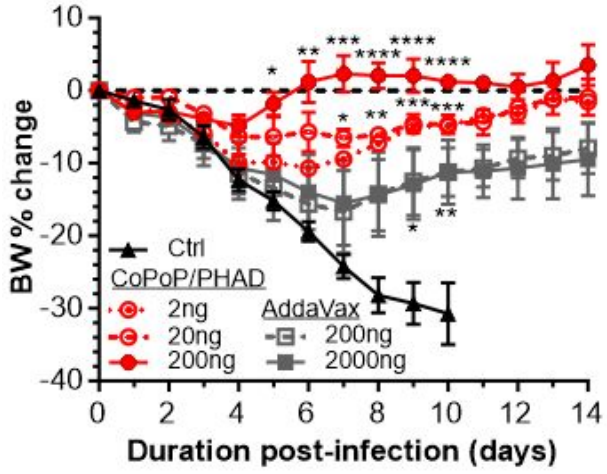
- S. Korea, 5 sites, randomized placebo-controlled with 230 participants
- High dose: 20 ug antigen, 20 ug MPLA (Shingrix: 50 µg Ag, 50 µg MPLA and 50 µg QS21)
- Low-grade injection site tenderness and pain were observed in most participant
- No increased AE during booster. No anti-his-antibodies detected

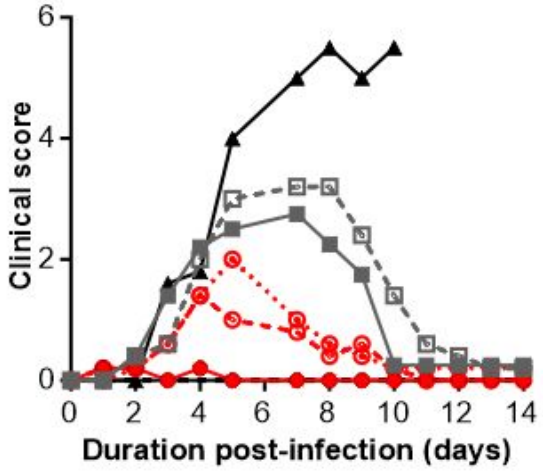


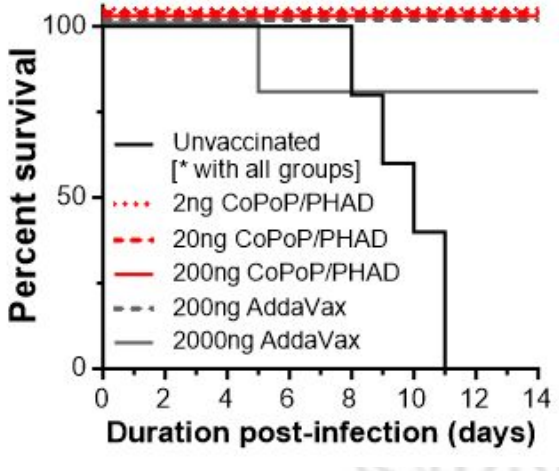


Decorating large proteins on liposome surfaces





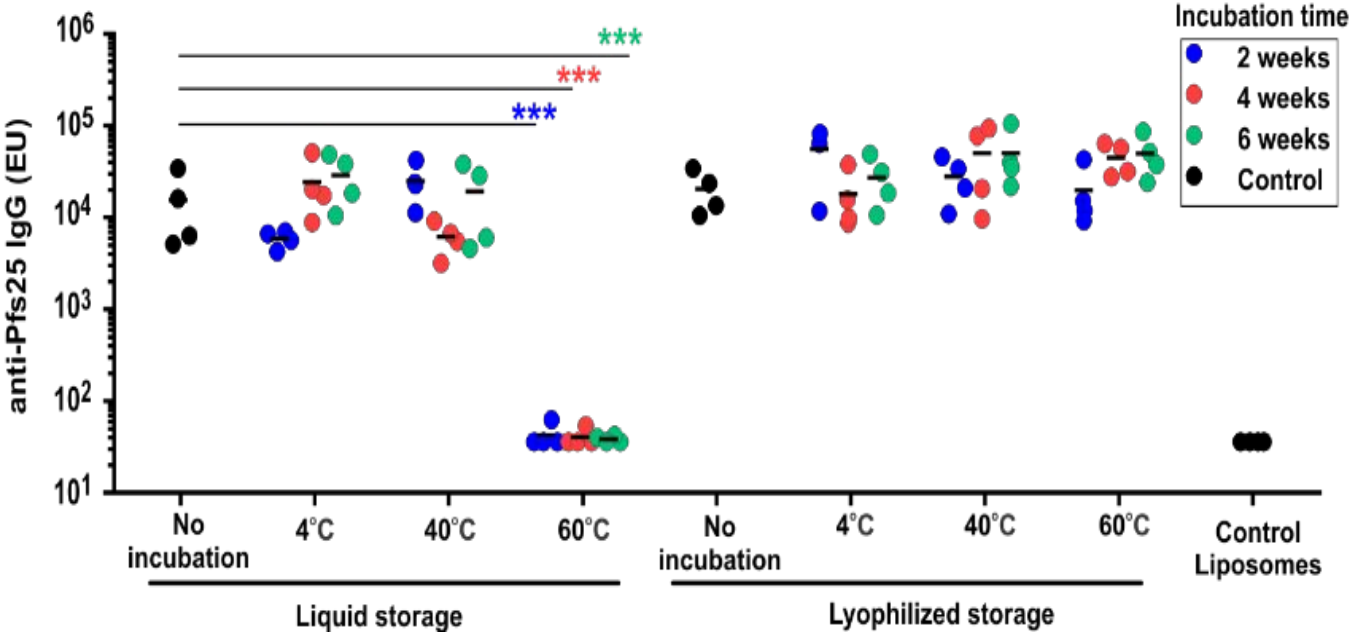


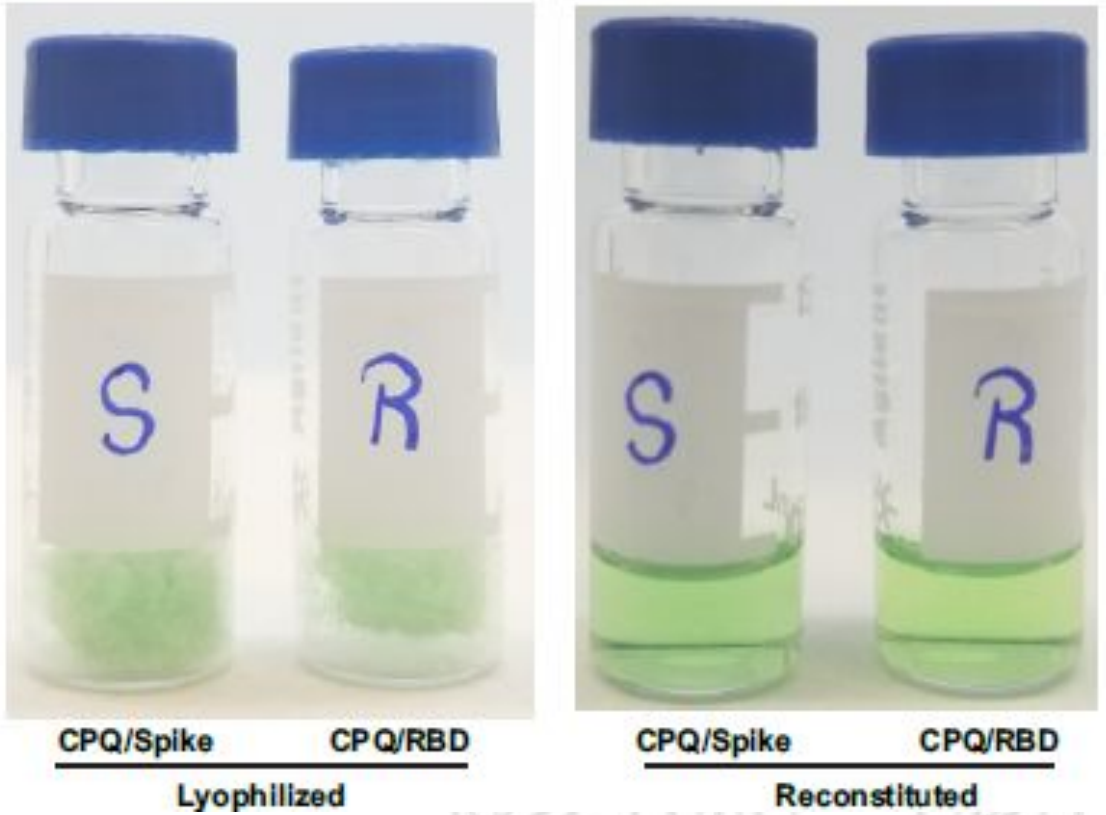


Sia et al., PNAS 2021

Potential for Lyophilization

- Use of sucrose or trehalose enables reconstitution or CoPoP/antigen particles without aggregation
- Enhanced thermostability observed for lyophilized formulation

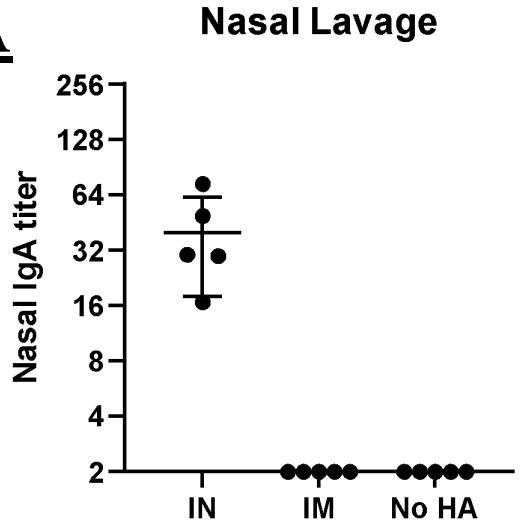


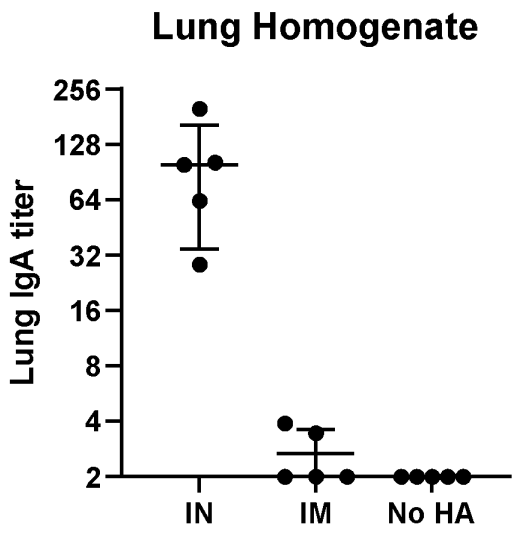


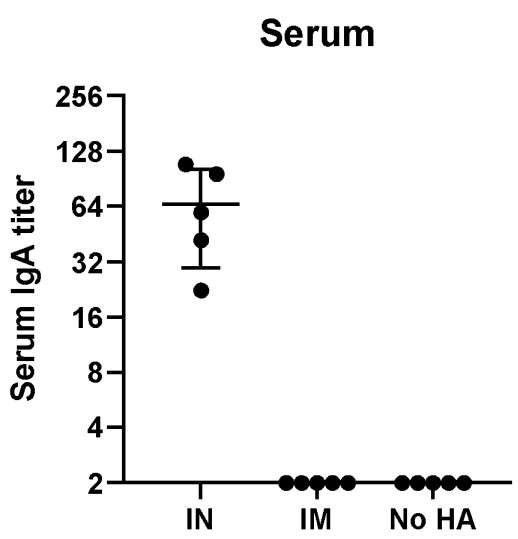
Mabrouk *et al.*, Int. J. Pharm (2020), Science Advances (2021)

Potential for Intranasal delivery

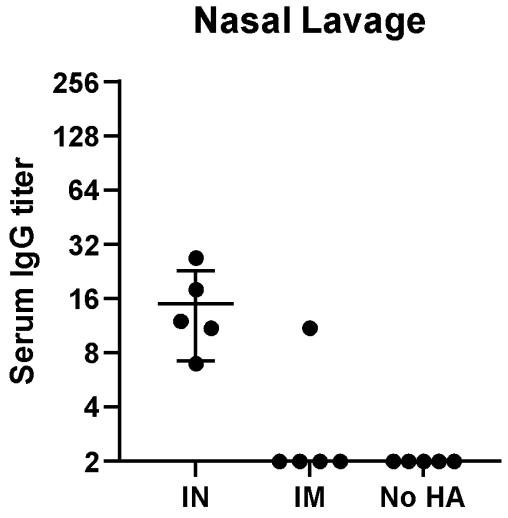
HA-specific IgA

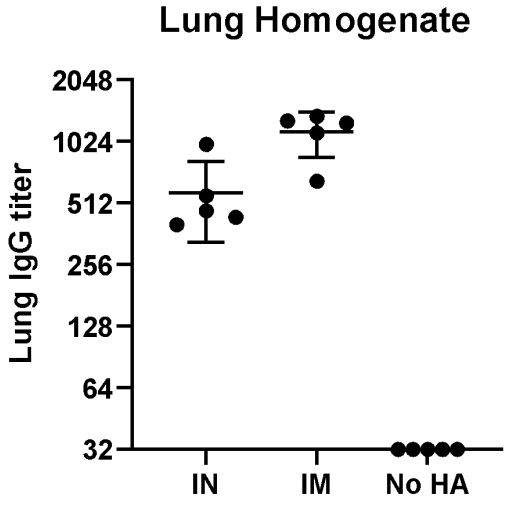


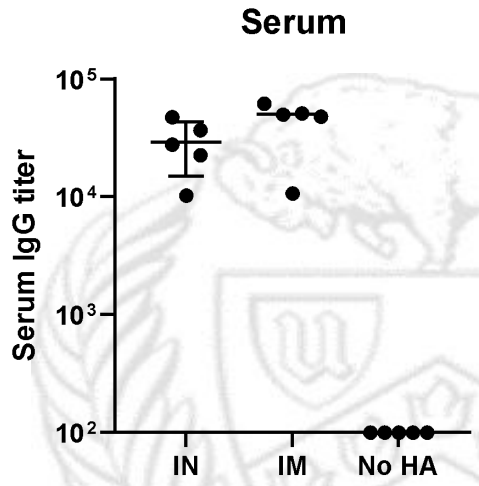




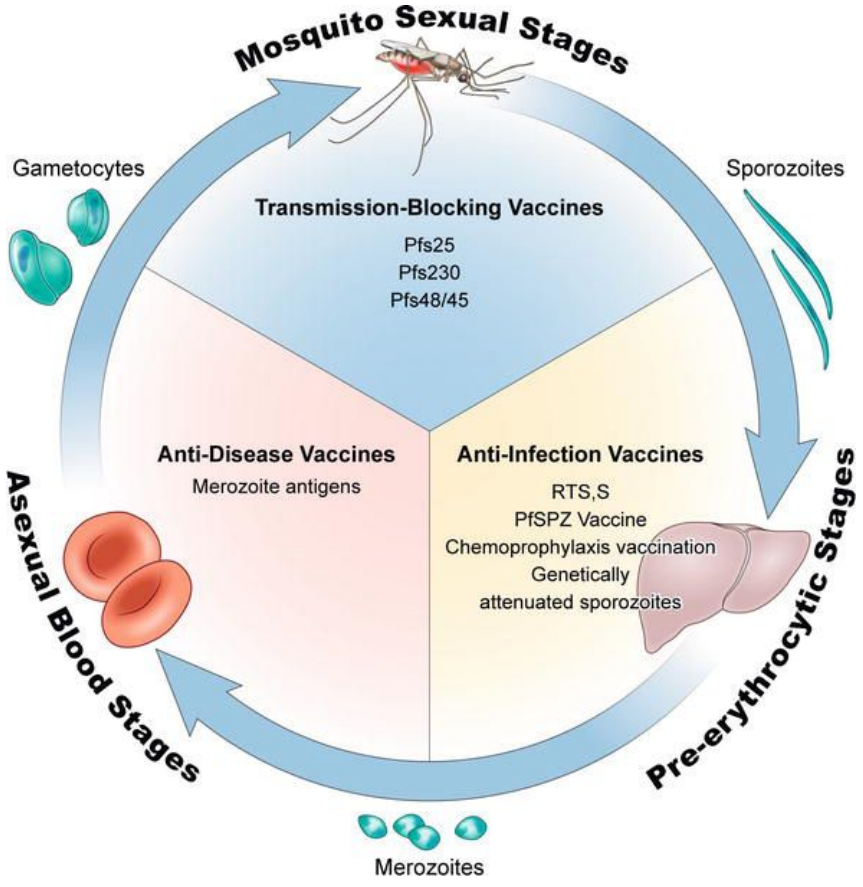
HA-specific IgG



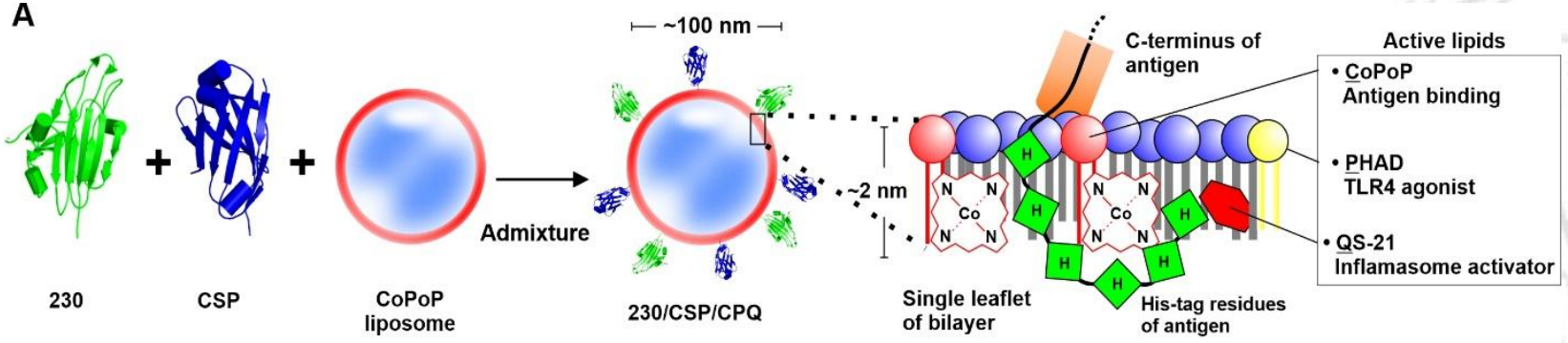




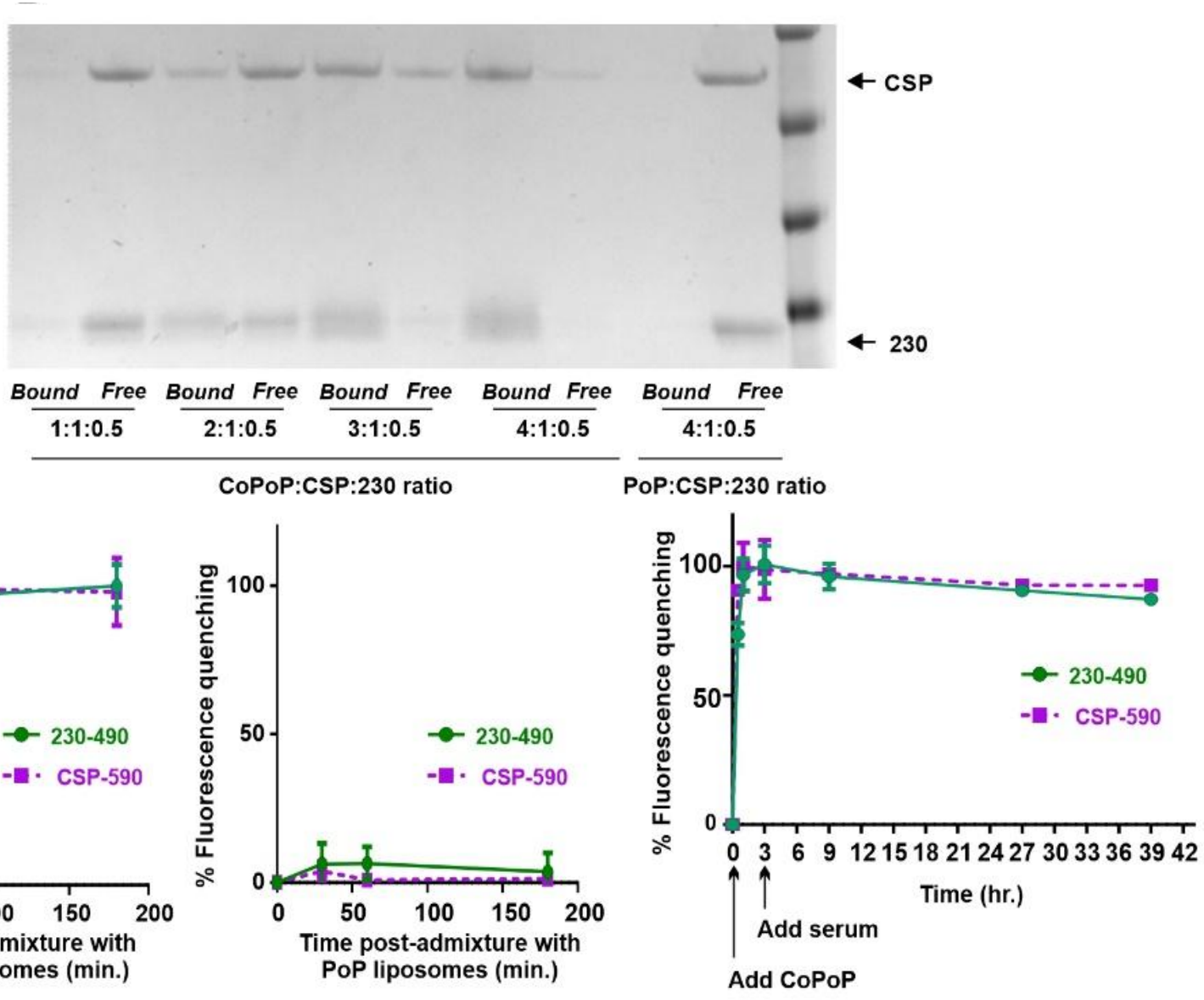
Targeting multiple stages of the P. falciparum cycle



Collaborators:
PATH-MVI
Ehime
NIAID



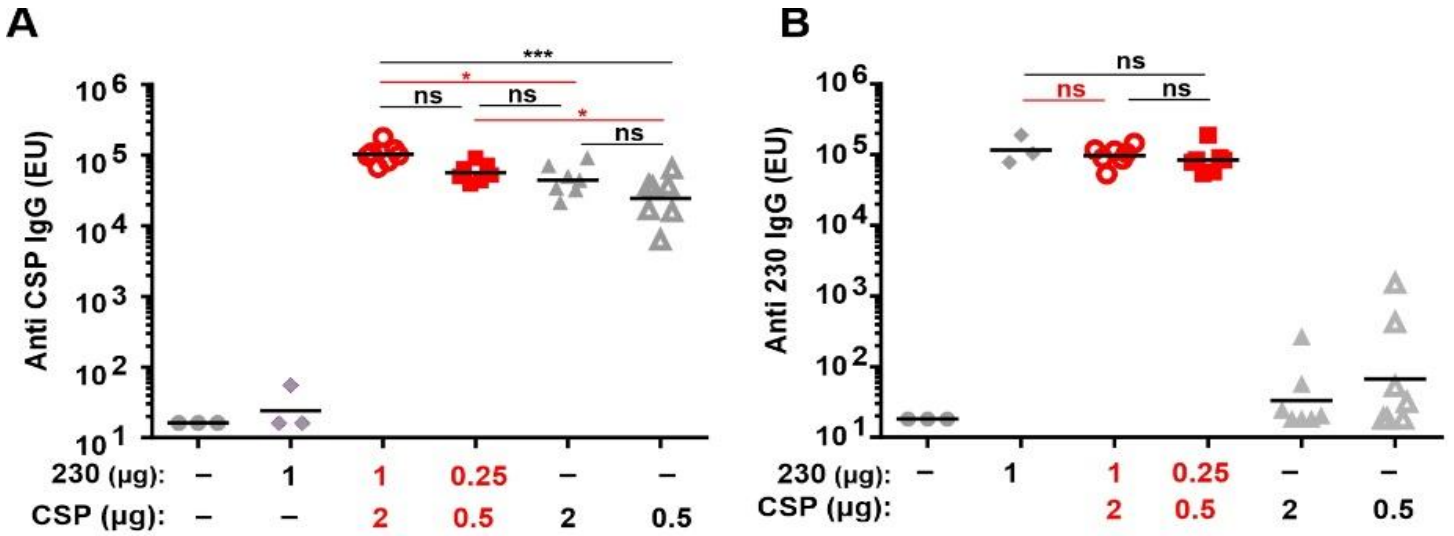
Assessing antigen binding to liposome



Huang et al., Communications Biology, in press

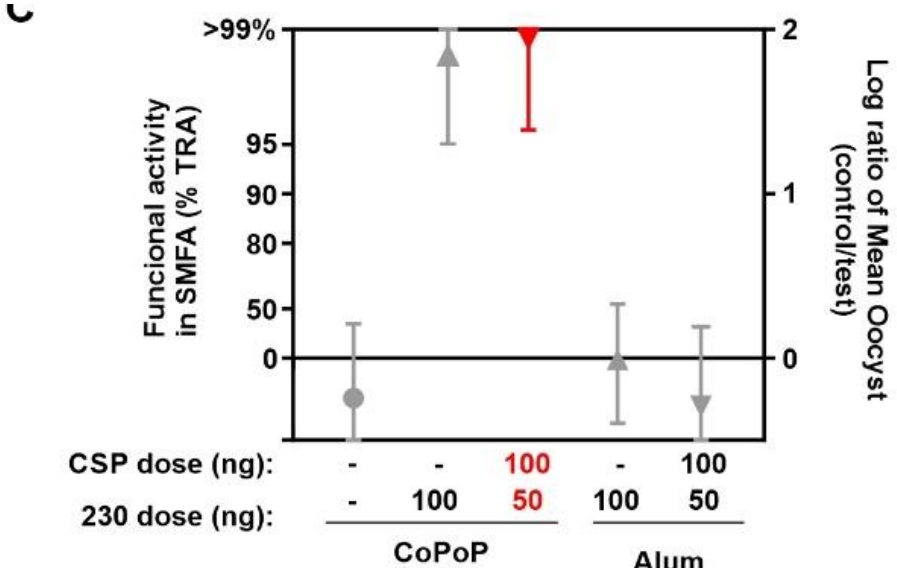
Induction of functional immunity

Antibody induction:

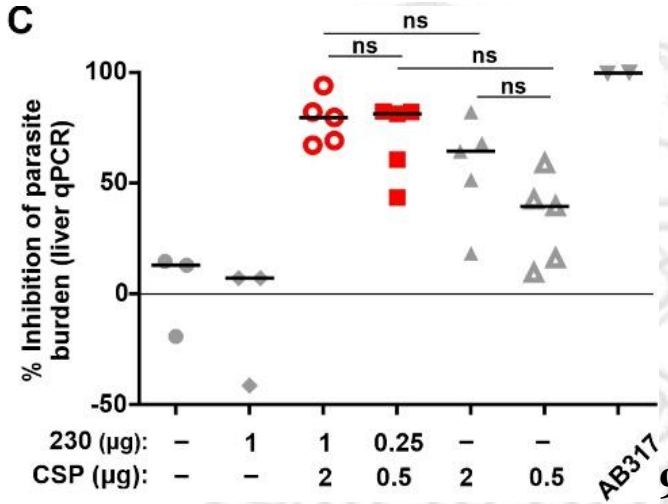


Functional activity:

Transmission blocking

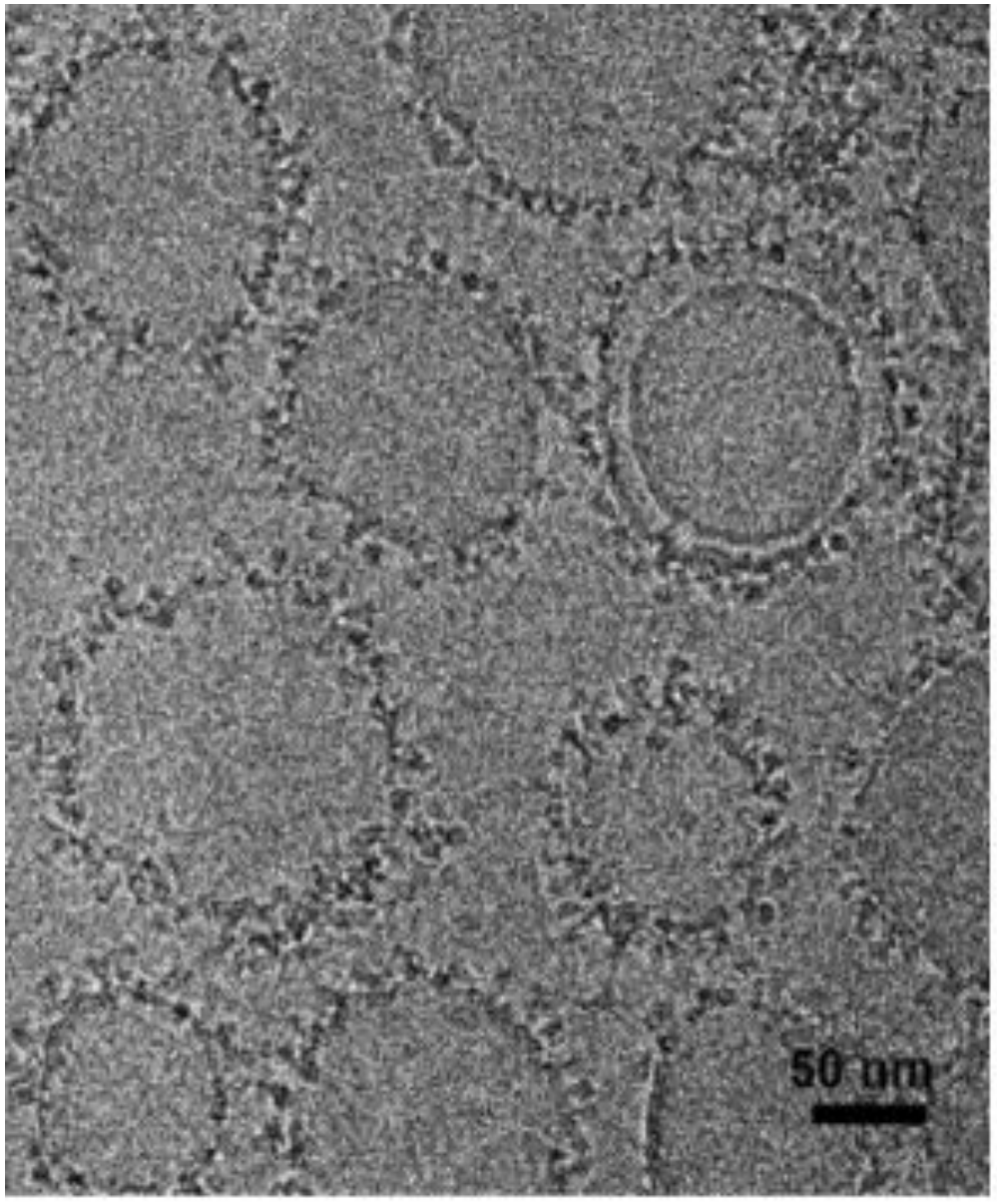


Infection blocking



Summary

- We are advancing a next generation vaccine adjuvant system
  - Simple, rapid, biostable conversion of soluble antigens into highly immunogenic particles
- EuCorVac-19 demonstrates clinical feasibility
- Potent, durable IgG responses
- Seek to establish more collaborations



Thank you!!!!