

Plasmodium falciparum CSP Technology
Development
Vaccine to Interrupt Malaria Transmission

FMVCC

17 March 2011

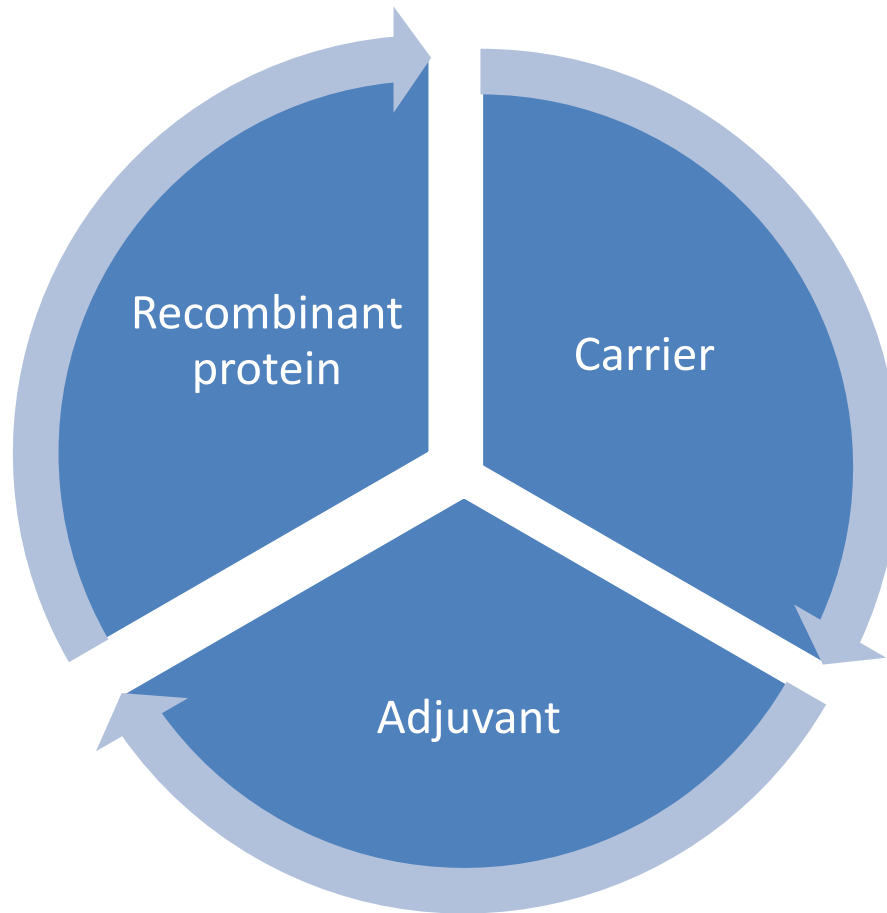
Laboratory of Malaria Immunology and
Vaccinology

LMIV Mission

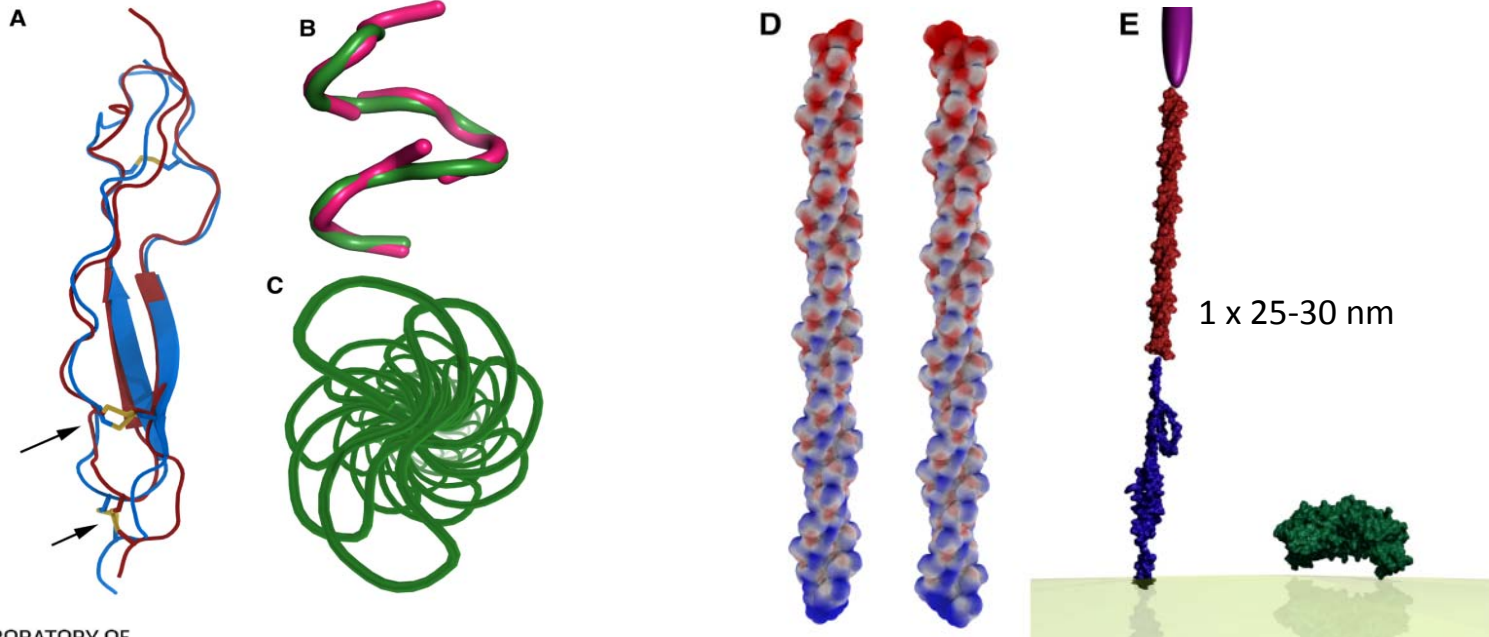
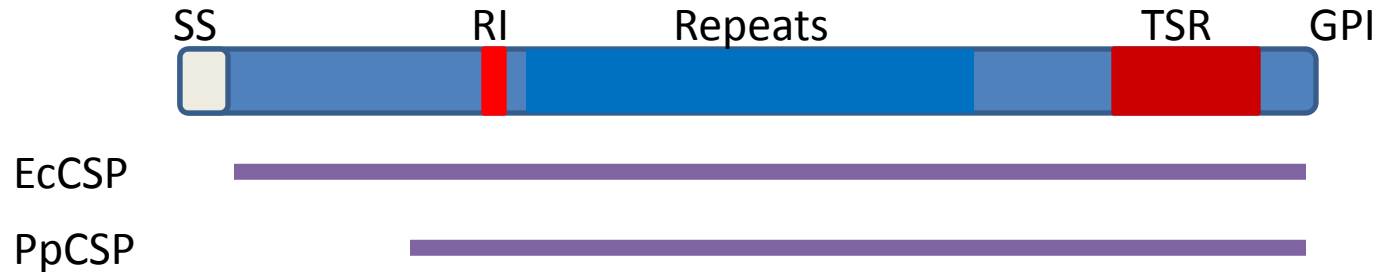
Technology Development:

- Vaccines that Interrupt Transmission
 - Transmission blocking vaccines
 - Preerythrocytic vaccines
- Vaccines that Prevent Disease
 - Pregnancy malaria
 - Severe childhood malaria

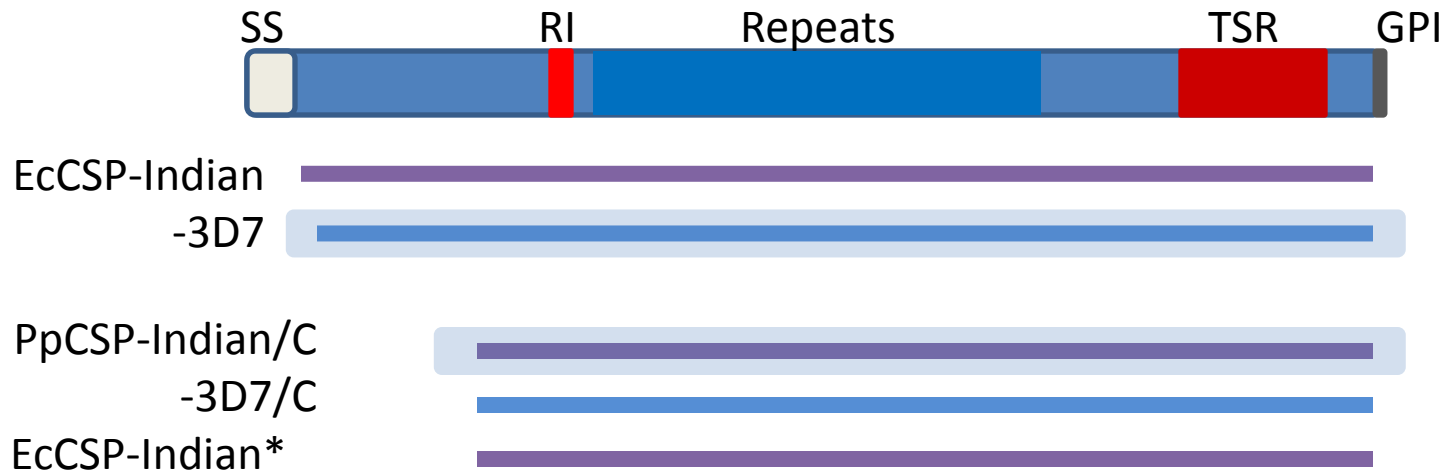
Technology Development



Computational structure of CSP

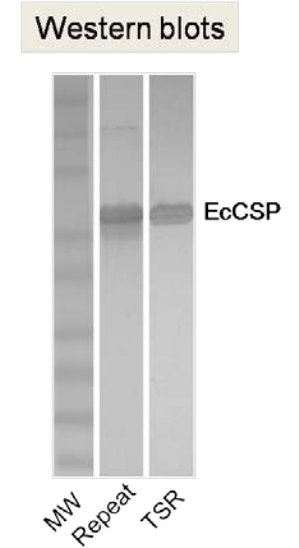
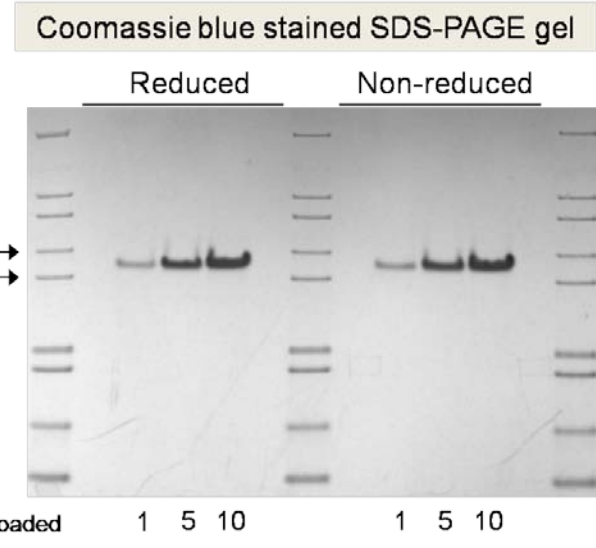
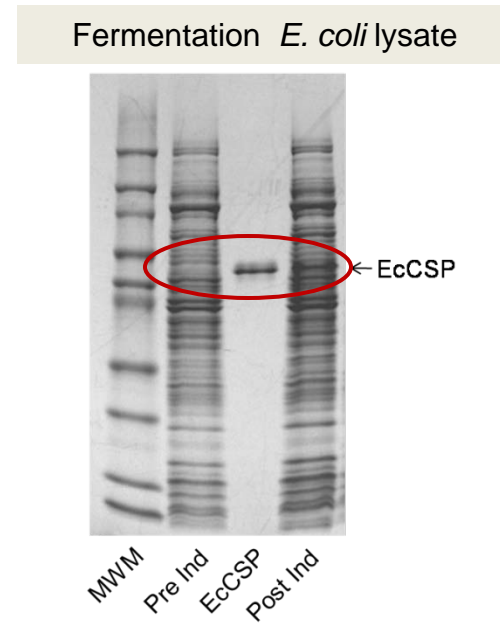
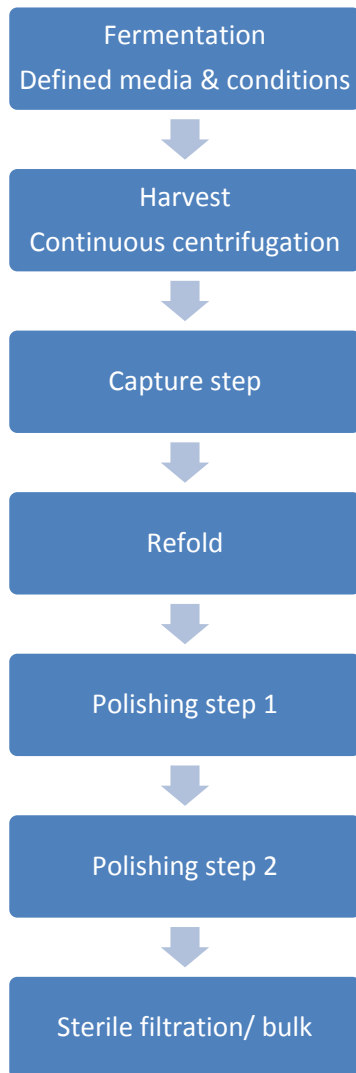


Recombinant CS protein production



*His₆ tagged

Process overview of EcCSP-3D7 production



Production of EcCSP-3D7

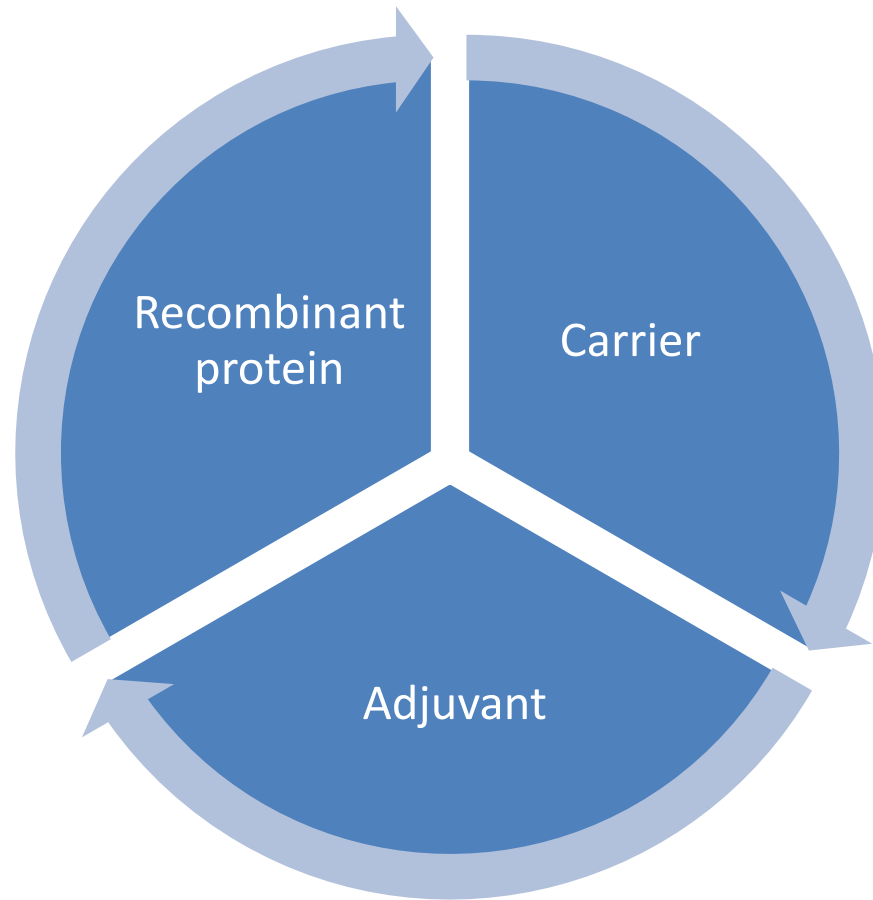
Development parameters

- Yield and scalability
- Biochemical and biophysical properties
- Host cell protein level
- Endotoxin

Acceptance criteria achieved

- ✓
- ✓
- ✓
- ✓

Technology Development

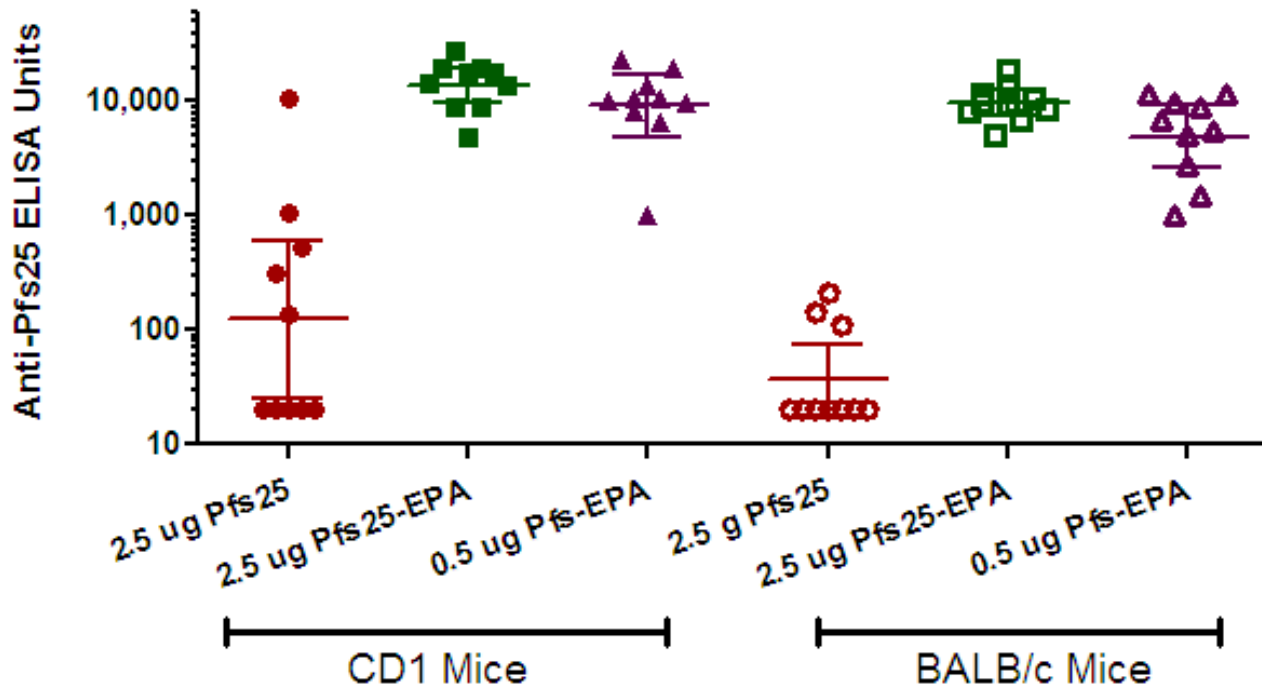


EPA and other carriers

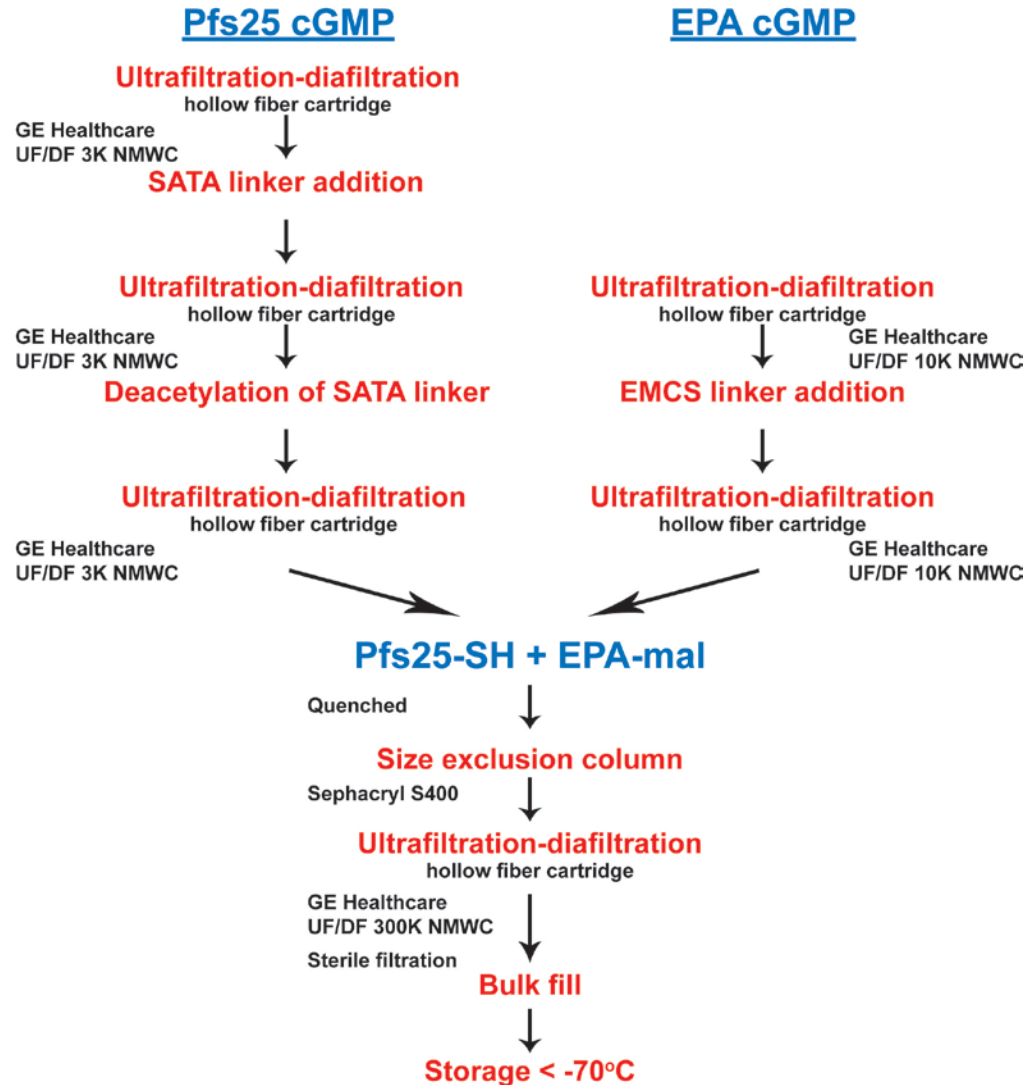
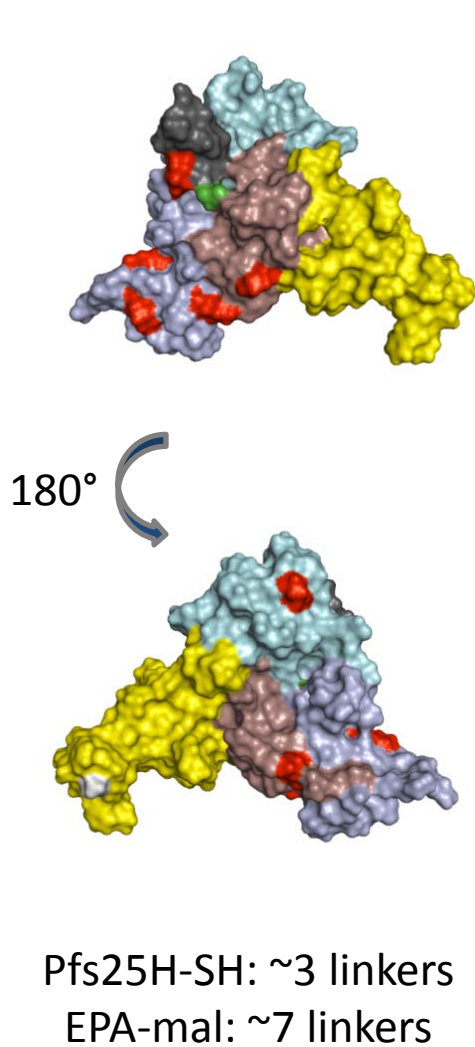
- EPA
 - IP owned by NIH
 - Production process knowledge available
 - Carrier of a polysaccharide of *Salmonella typhi* vaccine Vi-EPA
 - Safety data in children
 - Lin et al, NELM 2001, n=5991, age 2-5 yrs
 - Canh et al, I&I, 2004, n=241, age 2-5 yrs
- CRM197
 - External source
- Qbeta
 - LMIV research grade product, collaboration with Bryce Chackerian, University of New Mexico

Pfs25-EPA/Alhydrogel in Mice

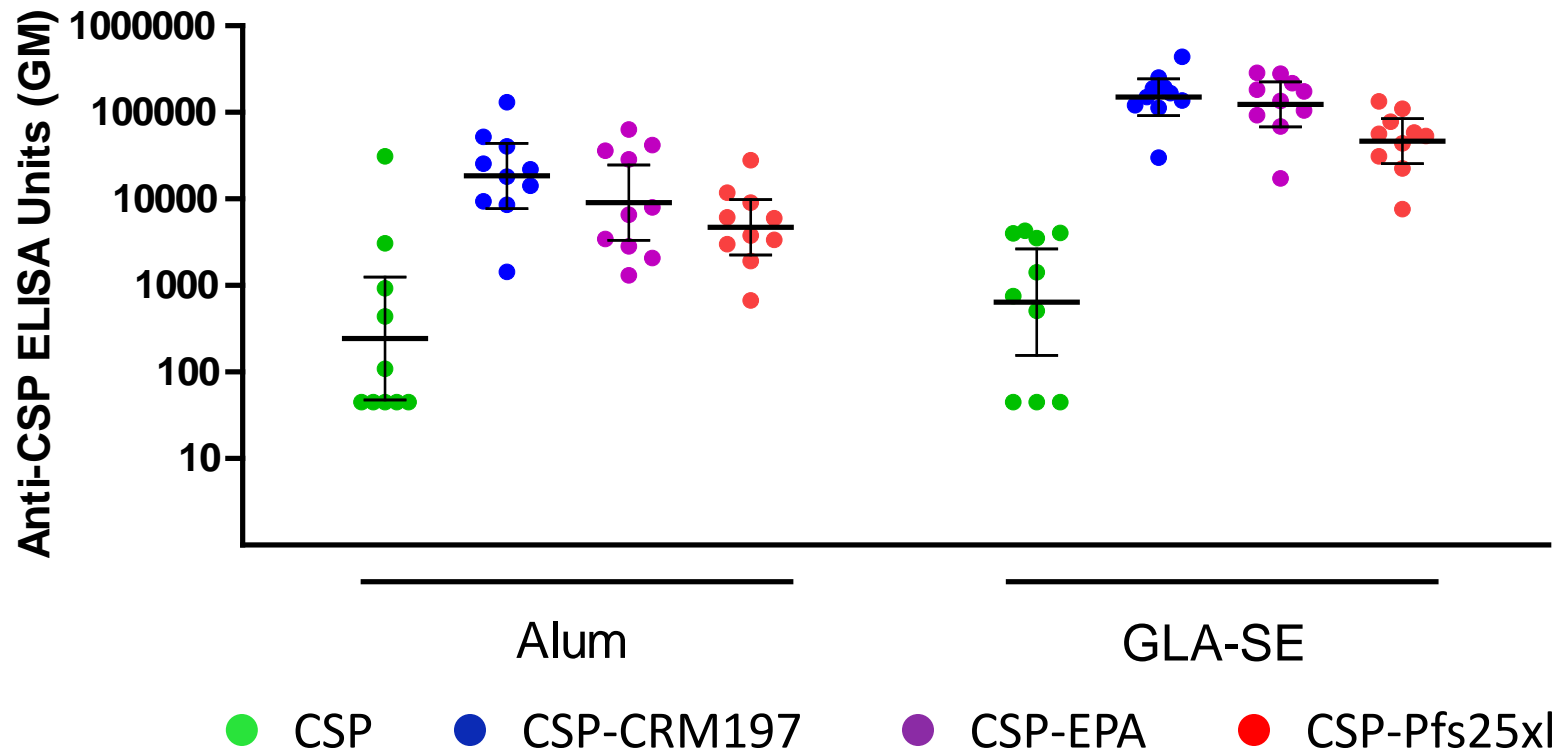
- Administered IM D0 and D28
- Anti-Pfs25 titers on D42
- TBA demonstrated in immune sera



Pfs25H-EPA pilot-scale process overview



Effect of carrier on immunogenicity of CSP



- CD-1 mice immunized IM with 0.5 μ g of CSP on Day 0 and 28
- ELISA units determined on day 42

Immunogenicity of conjugates

- Conjugation of CSP increases immunogenicity
- Cross-linked conjugates appear as potent as radial conjugates; no need for unpaired cysteine (data not shown)
- Potency trends depend on carrier and adjuvant, although no superiority observed with EPA or CRM197

Production of EcCSP-3D7 conjugate vaccine

Development parameters

- Yield and scalability
- Biochemical and biophysical properties
- Host cell protein level
- Endotoxin
- Assessment of conjugation/conjugate
- Assessment of adjuvant

Acceptance criteria achieved

✓

✓

✓

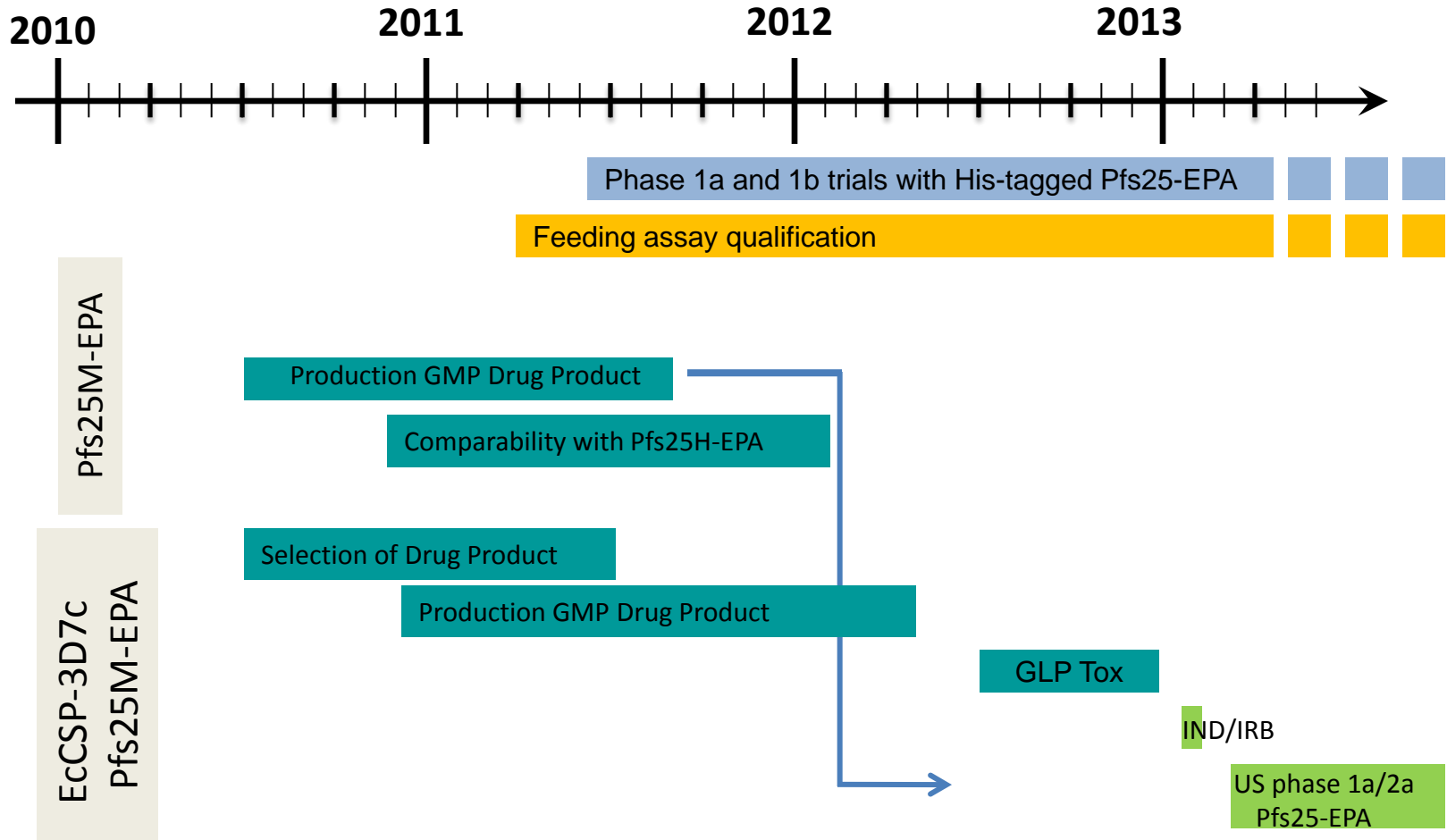
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Ongoing

Ongoing

Vaccine to Interrupt Malaria Transmission

Pfs25-EPA & EcCSP-3D7c



Acknowledgements

- Vaccine Core Units