Versatility of the CoPoP platform for antigen discovery and tuberculosis vaccine testing

Andres Obregon-Henao[1], Yang Jiao[2], Kristina Tran[1], Wen Ling Hsu[2], Brennen Troyer[1], Marcela Henao-Tamayo[1], Jonathan F. Lovell[2]

1 Colorado State University, Fort Collins, CO, 80523
2 University at Buffalo, Buffalo, NY, 14260

Background

-Tuberculosis (TB) continues to plague humankind.

-century-old BCG only licensed vaccine, yet limited protection against pulmonary TB.

-Recently, subunit proteins as prime vaccines or BCG boost: protection!

-Herein, Cobalt Porphyrin Phospholipid (CoPoP) liposome platform developed by Lovell: -antigen discovery and TB vaccine testing

-his-tagged proteins and/or synthetic peptides

-single, fusion or multiplexed antigens for plug-n-test

Methods

1. Antigen selection (+ his-tag)

-Lit search

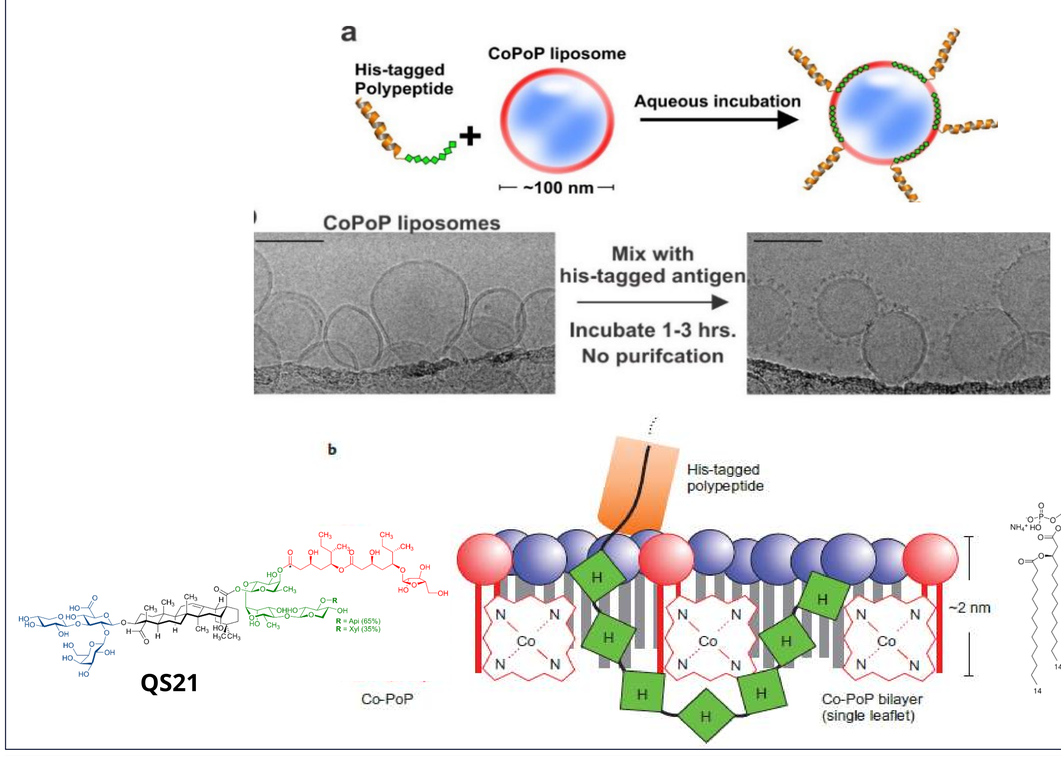
-Commercially available

-Bioinformatics:
-NetMHCII
-optimization by structural biology

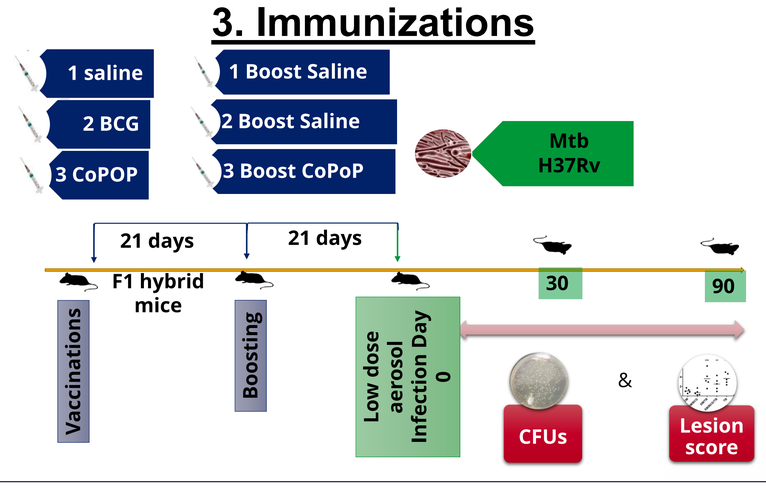
-Synthetic

-Recombinant (in house)

2. CoPoP platform



3. Immunizations



Results

1. Peptides

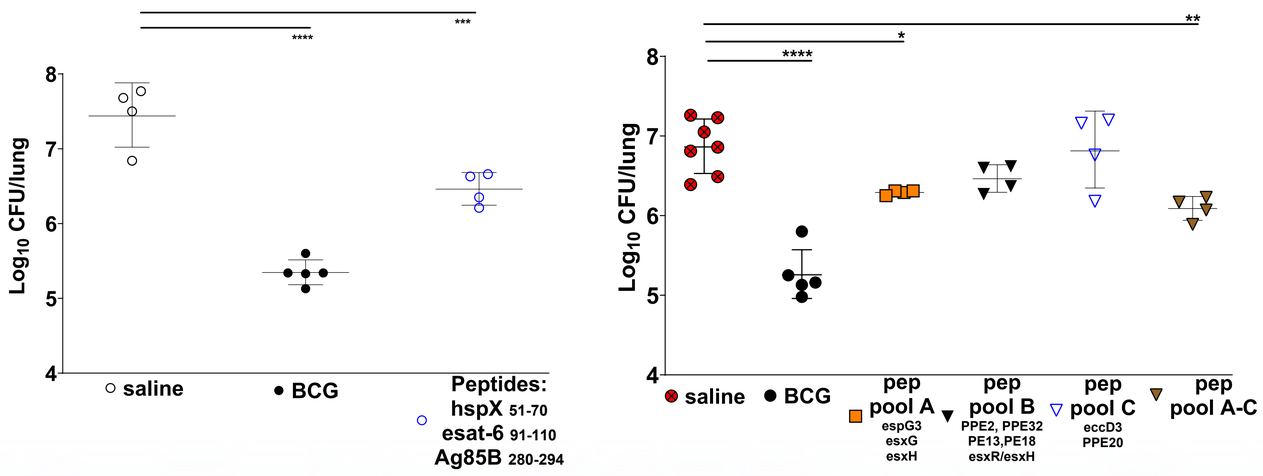


Figure 1. Antigen screening using His-tagged peptides and CoPoP platform.

2. Proteins: single or fusion

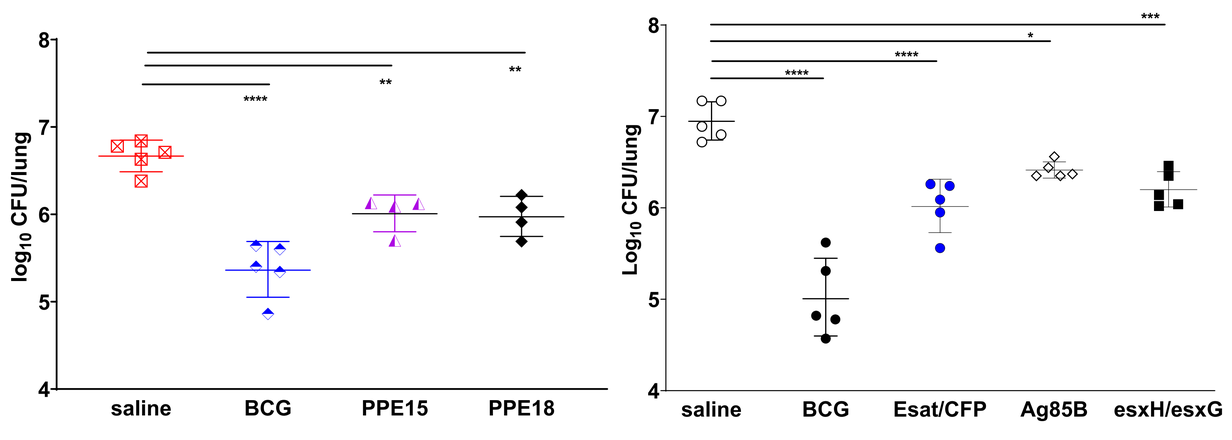


Figure 2. Single or fused antigens + CoPoP inducing protection at day 30.

-Proteins inducing protection

-cfp10	-esxG	-cfp10/esat6 fusion
-esat6	-PPE18	-TB10.4/esxG fusion
-TB10.4	-PPE15	-Ag85B

3. Protein Multiplexing

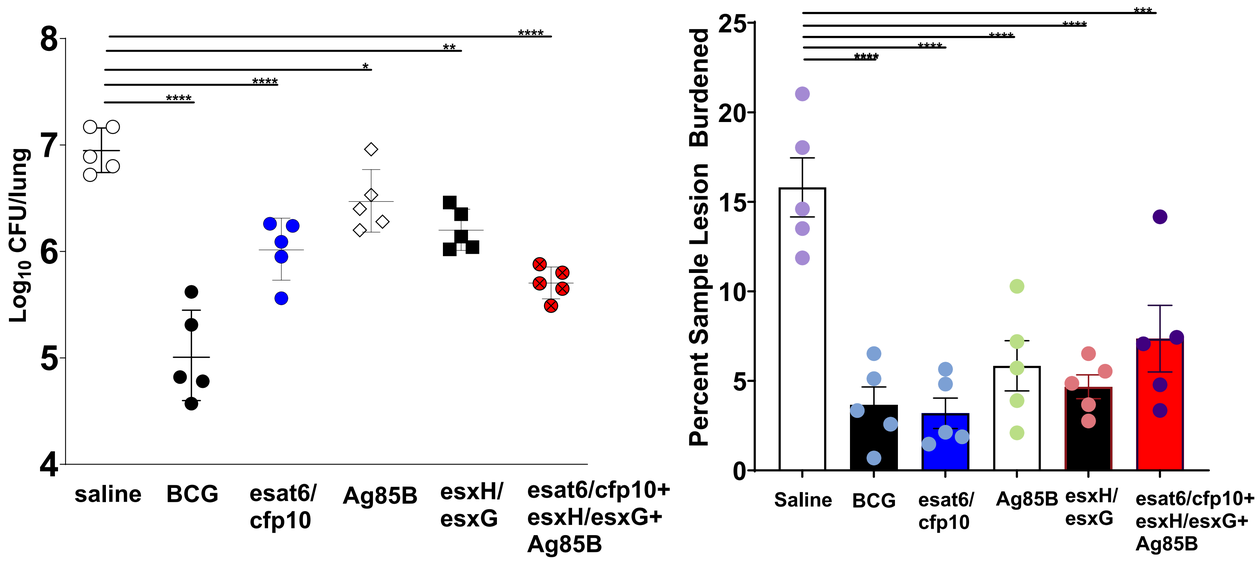


Figure 2. Single or multiplexed antigens + CoPoP inducing protection at day 30 as determined by lung CFUs (left panel) and histopathological analysis (right panel).

-Proteins NOT inducing protection

-MPT64	-TrxC	-GlcB	-hspX	-PepA
-MPT63	-lprA	-lpqH	-lprG	-lppZ
-MPT70	-GroEL2	-EspK	-BfrB	-PE_PGRS3
-GroES	-katG	-HbhA	-Zmp1	-FtsQ

>50 antigens (peptides/recombinant proteins)screened in 2 years.

-Several antigens induced 1-month protection (lower CFUs and pathology)

-Ongoing studies: multiplexing, long-term protection, BCG boost and additional antigen screening.

Discussion/Conclusion

CoPoP: versatile vaccine platform for TB antigen discovery/testing

Versatility

-ease to manufacture/store

-compatibility: -single/fusion/multiplexed antigens

-synthetic peptides from difficult to express Mtb proteins

-plug-n-test: -against different clinical isolates

-human genetic HLA variability

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Andres Obregon-Henao
aobregon@colostate.edu

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