Tech Session 3: Immuno Delivery

Dylan Hendy

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Advanced Delivery Science

Ace-DEX Microparticles for Broadly Active Influenza Vaccination

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Ainslie Lab @ UNC

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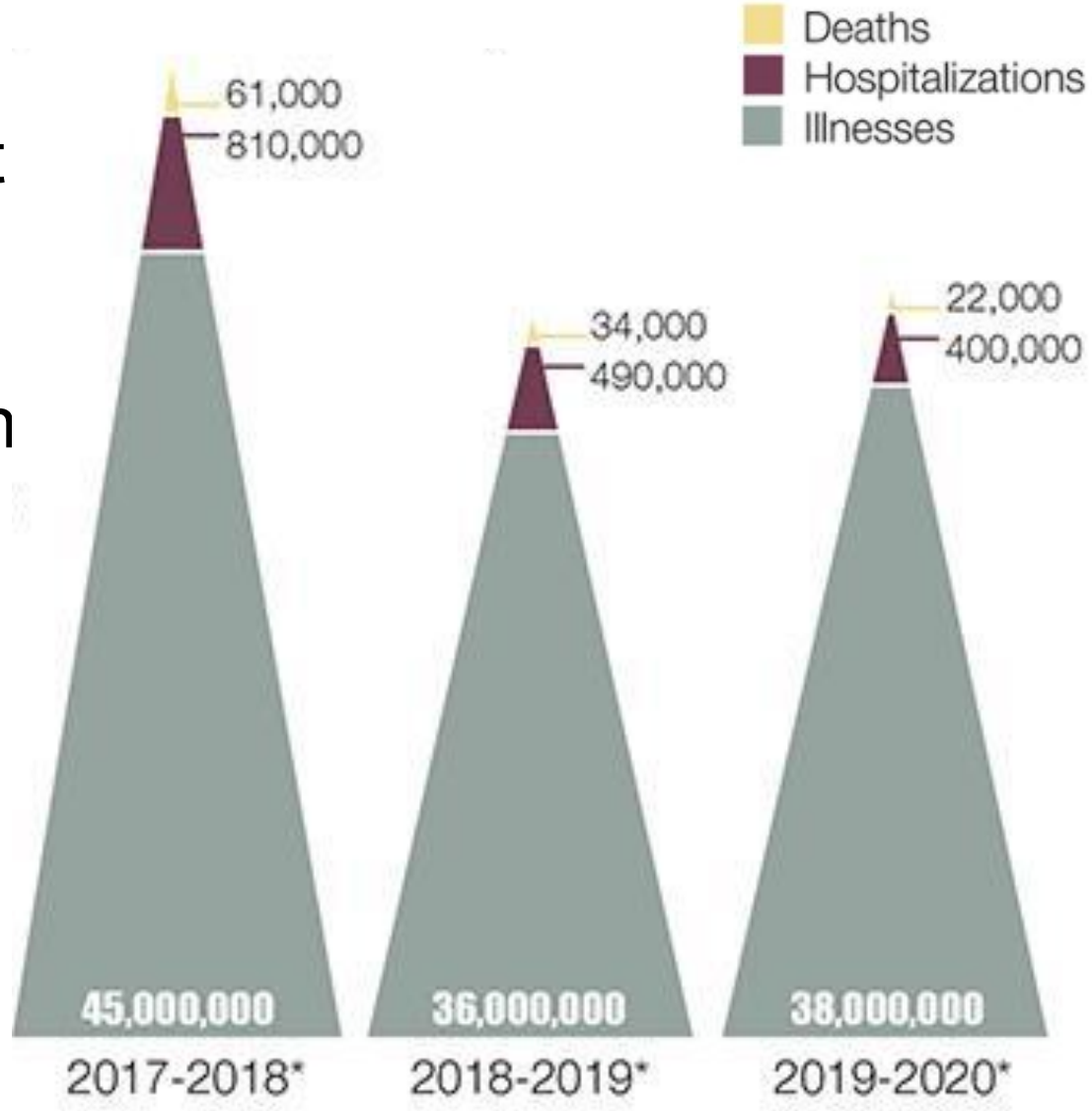
Influenza Affects Millions Worldwide

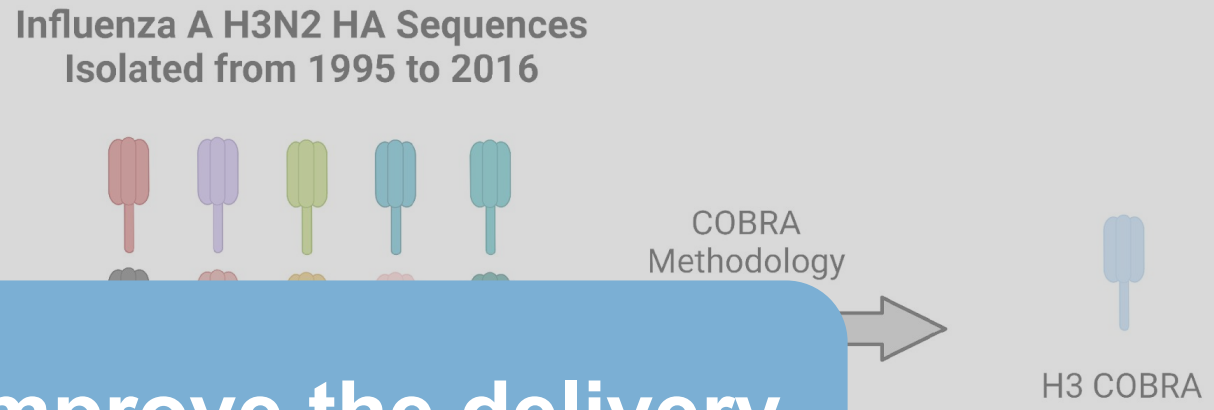
- Seasonal influenza is estimated to cost the U.S. an average of **$11.2 billion each season**
- **H1, H3,** and **H5** are of greatest concern for pandemic potential
- Current vaccination strategies are inadequate
  - Antigenic Drift
  - Humoral Biased Immune Response



WHO and CDC Websites

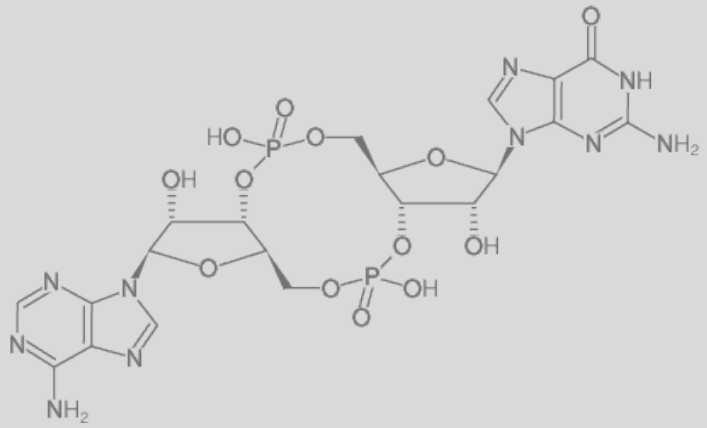
Computationally Optimized Broadly Reactive Antigen (COBRA)

- Methodology for creating broadly reactive HA antigens from the Ross group at UGA
- Vaccination wit
  broadly respon
  antibodies
- Poorly immunc



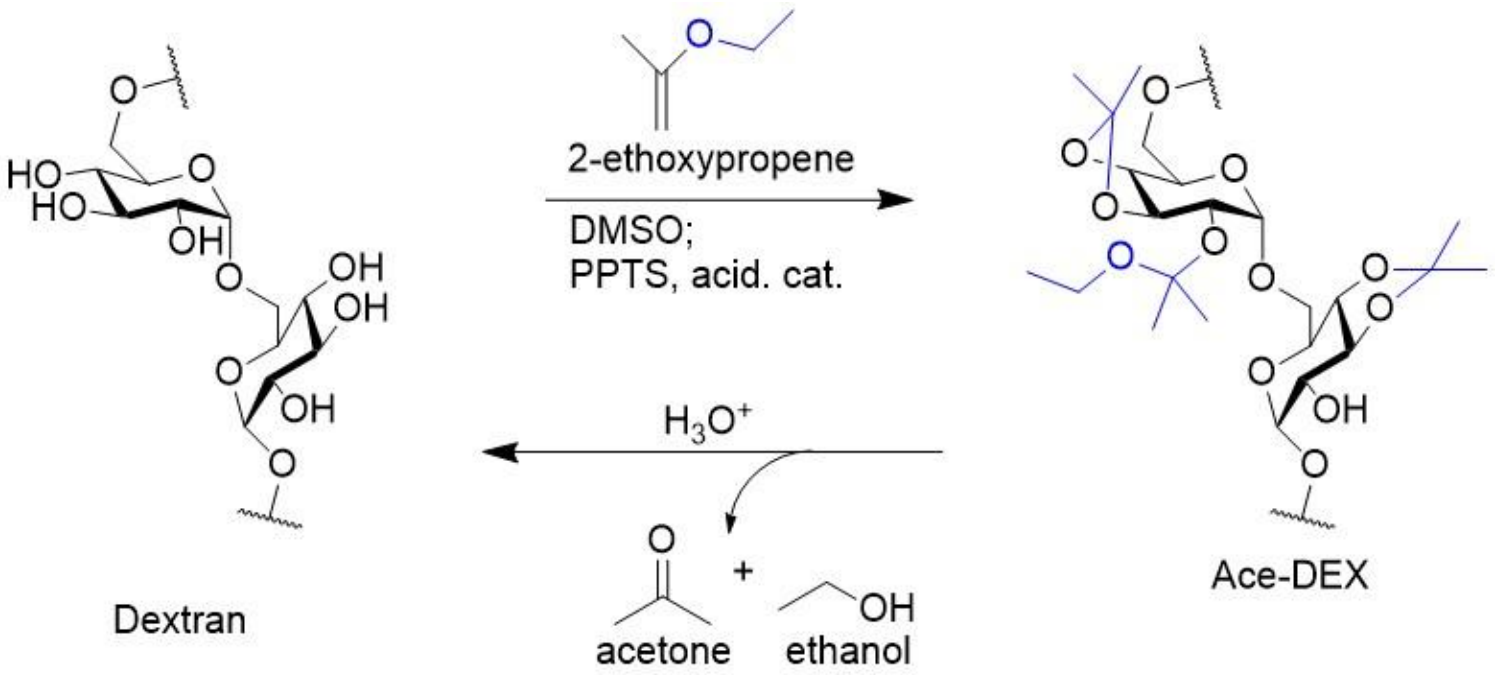
How can we improve the delivery of these vaccine components?

cGAMP:
- STING agonist
- Promotes a balanced humoral and cell mediated response



Giles and Ross., *Vaccine* 2011

Acetalated Dextran is an Acid-sensitive Polymer Used For Vaccine and Drug Delivery



Advantages of Ace-DEX Microparticles:

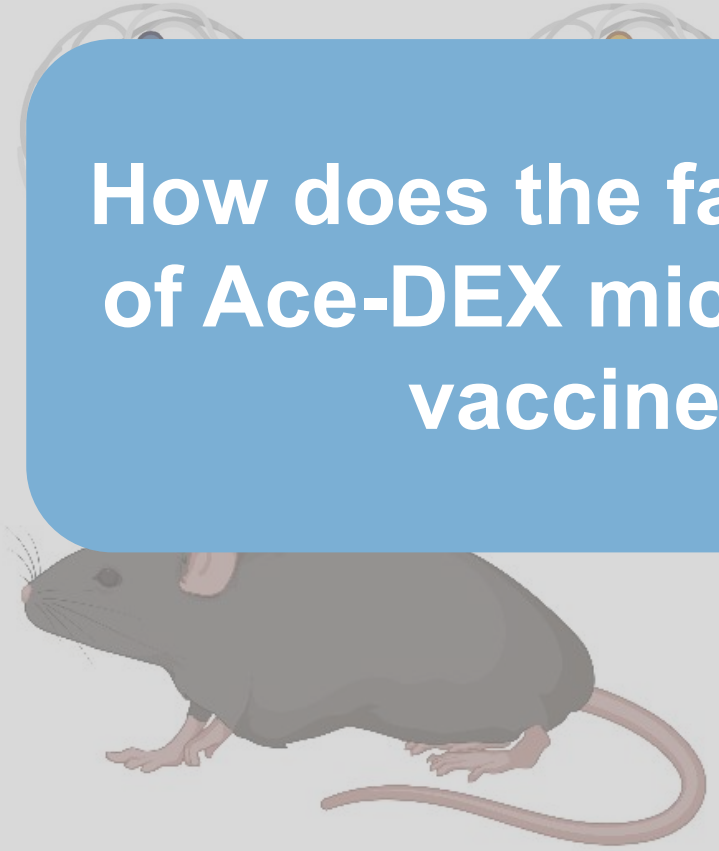
- Passive targeting to phagocytes
- Sustained release of antigen
- Acid sensitivity
- Increased efficiency of presentation of protein antigen to CD8+ and CD4+ T cells

Kauffman et al. *ACS Appl Mater Interfaces 2012*
Broaders et al. *PNAS* 2009

cGAMP Adjuvanted COBRA Ace-DEX Microparticles

● = COBRA

● = cGAMP



How does the fabrication method of Ace-DEX microparticles effect vaccine efficacy?

OBRA
ctivity from

Ace-DEX

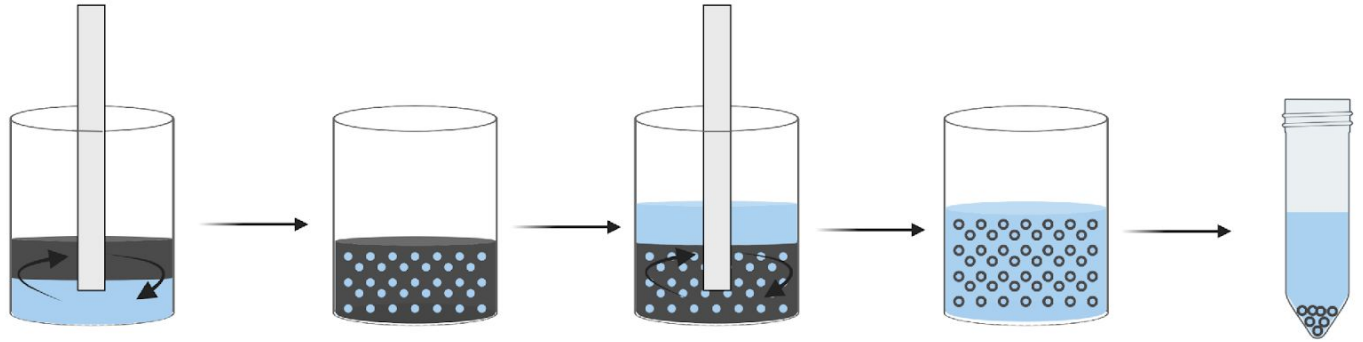
elivery

Chen et al. *JCR* 2018

Fabrication of Vaccine MPs

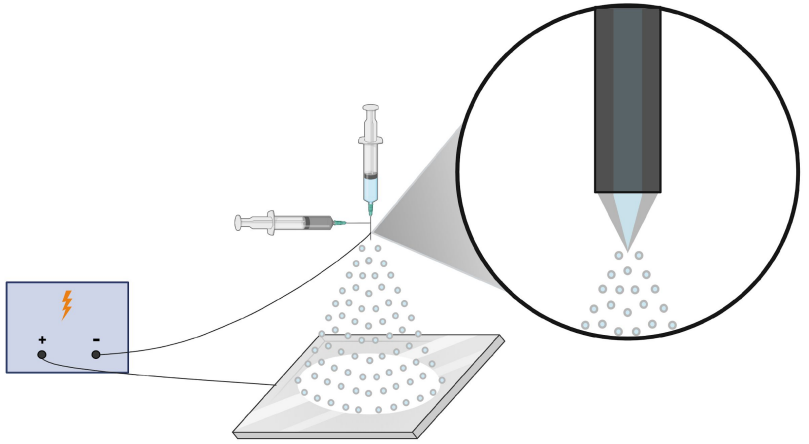
Double Emulsion:

- Allows for the encapsulation of water-soluble cargo
- This process could be harmful to protein antigens



Electrospray:

- Allows for the encapsulation of water-soluble cargo
- Highly scalable
- Less harsh on proteins than other fabrication techniques

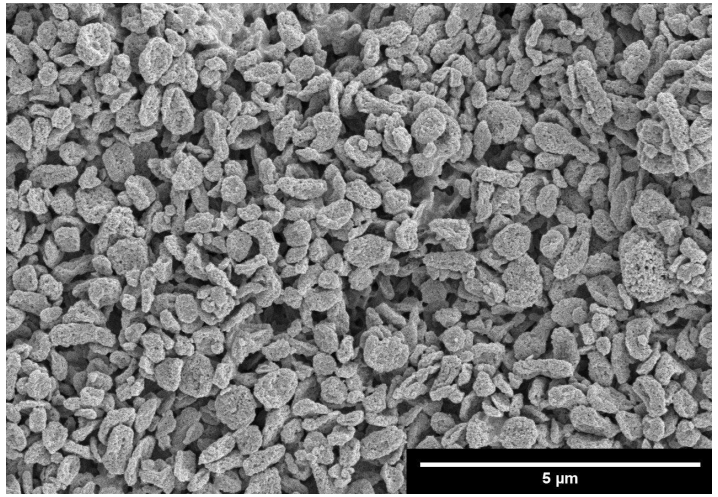


Gallovic et al. *Adv Healthc Mater* 2016

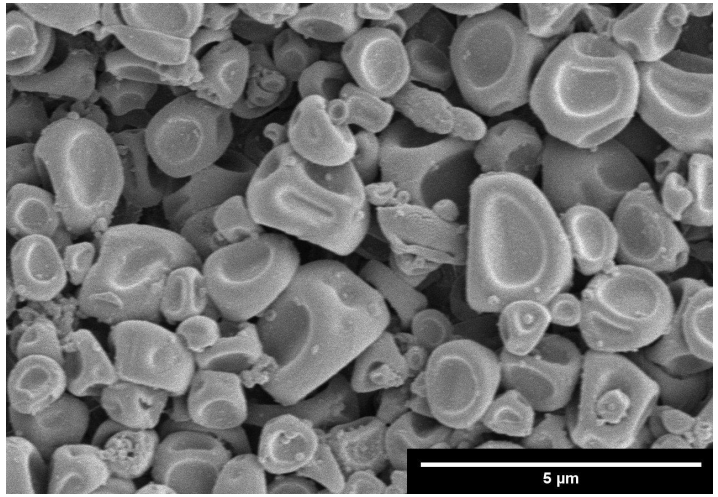
cGAMP MPs (1% loading)

H3 COBRA MPs (0.765% loading)

Electrospray

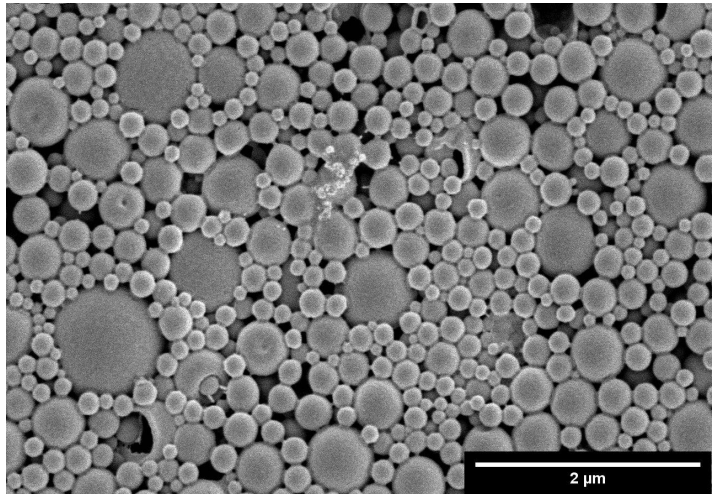


EE = 108% ± 1%

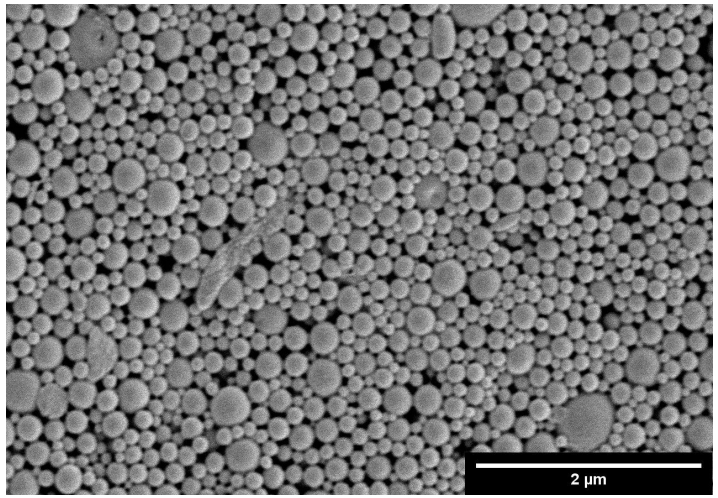


EE = 92% ± 2%

Homogenization



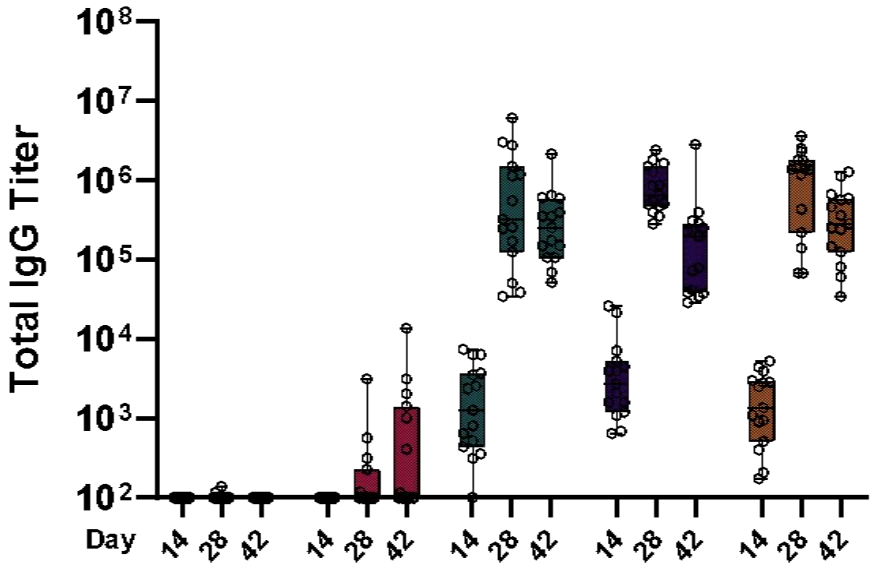
EE = 61% ± 7%

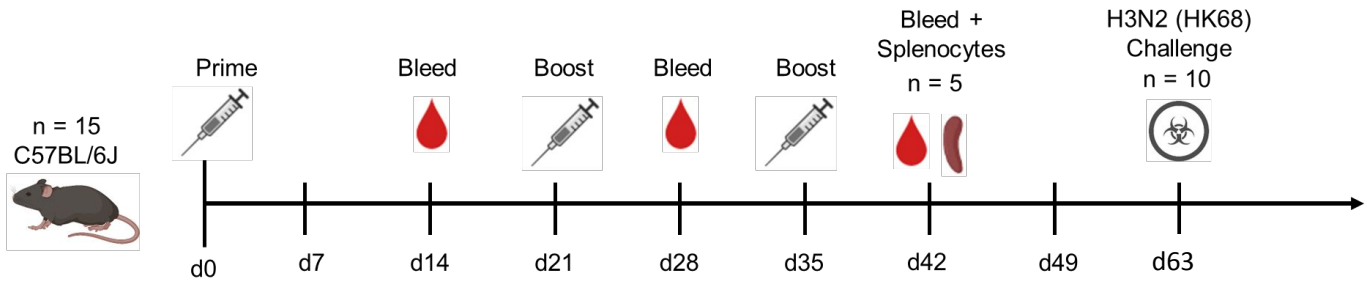


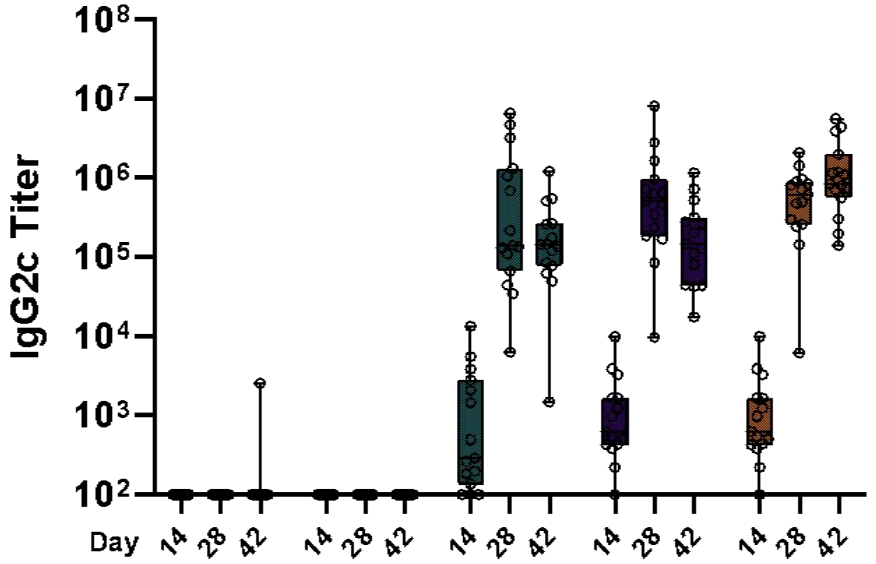
EE = 100% ± 7%

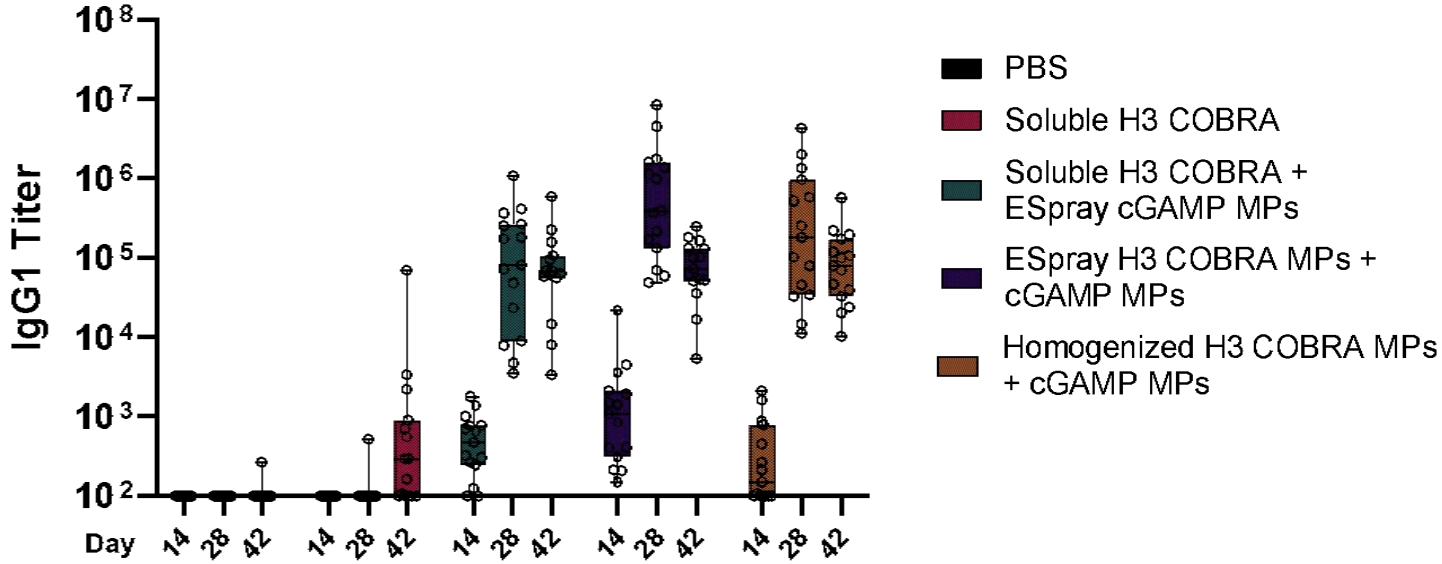
EE = Encapsulation Efficiency

Vaccination Produced a Strong Humoral Response

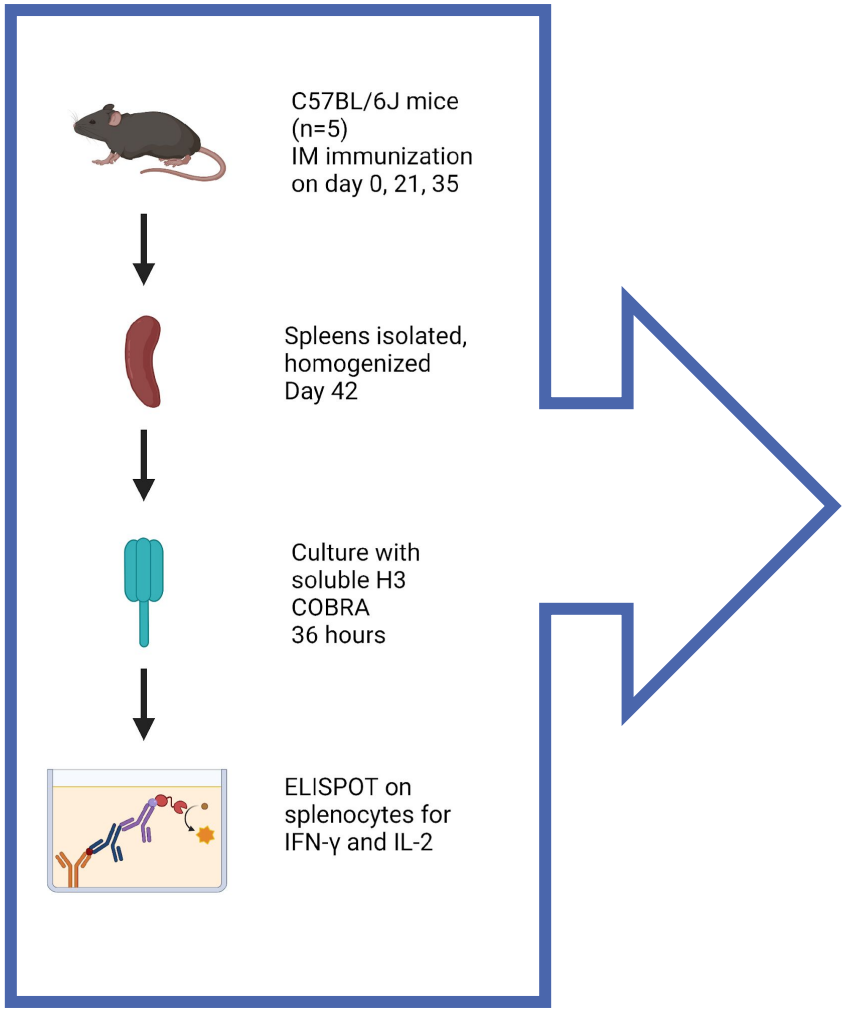


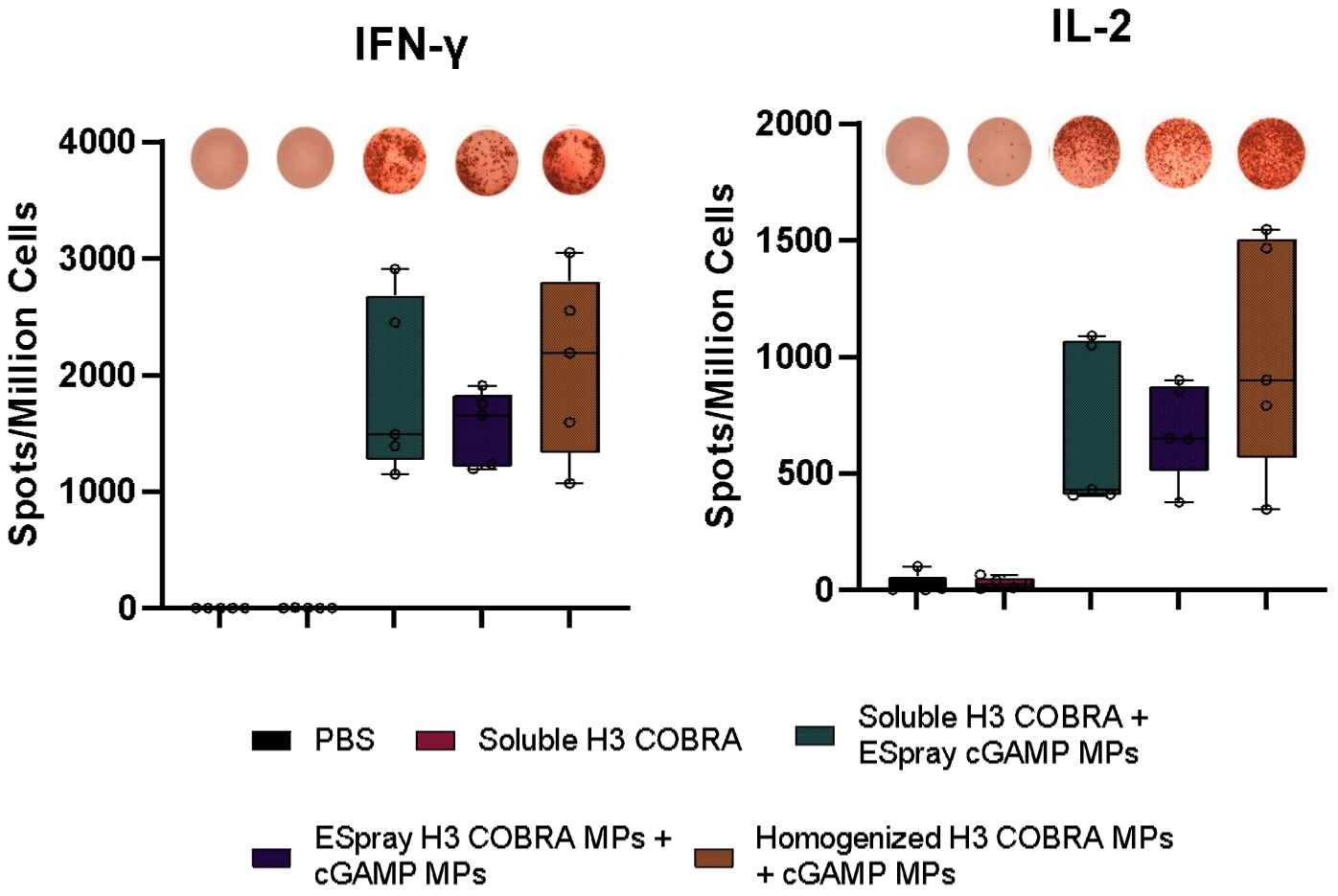






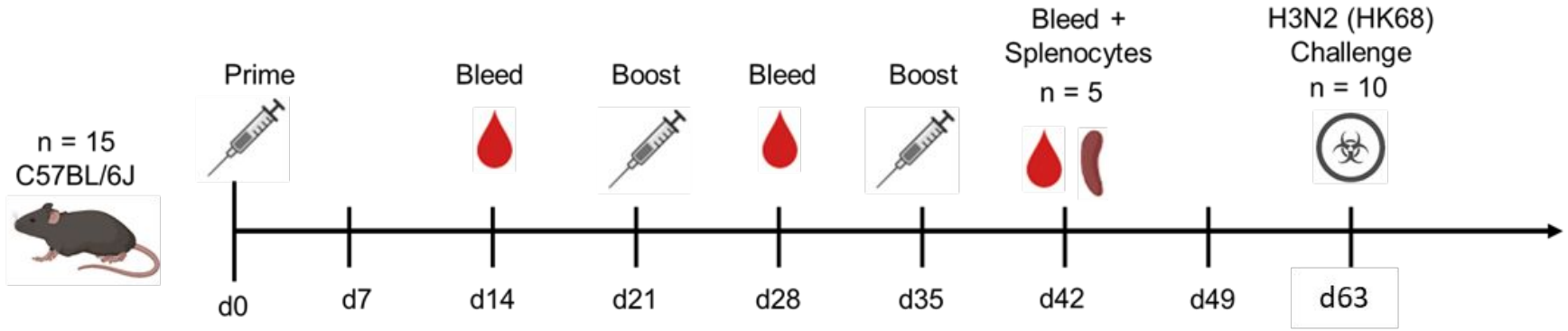
Vaccination Produced a Strong Cellular Response

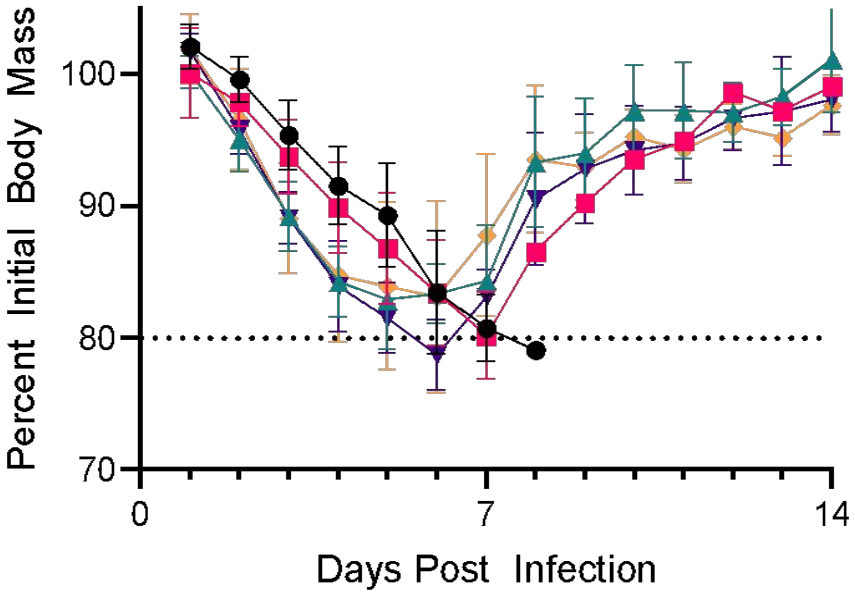


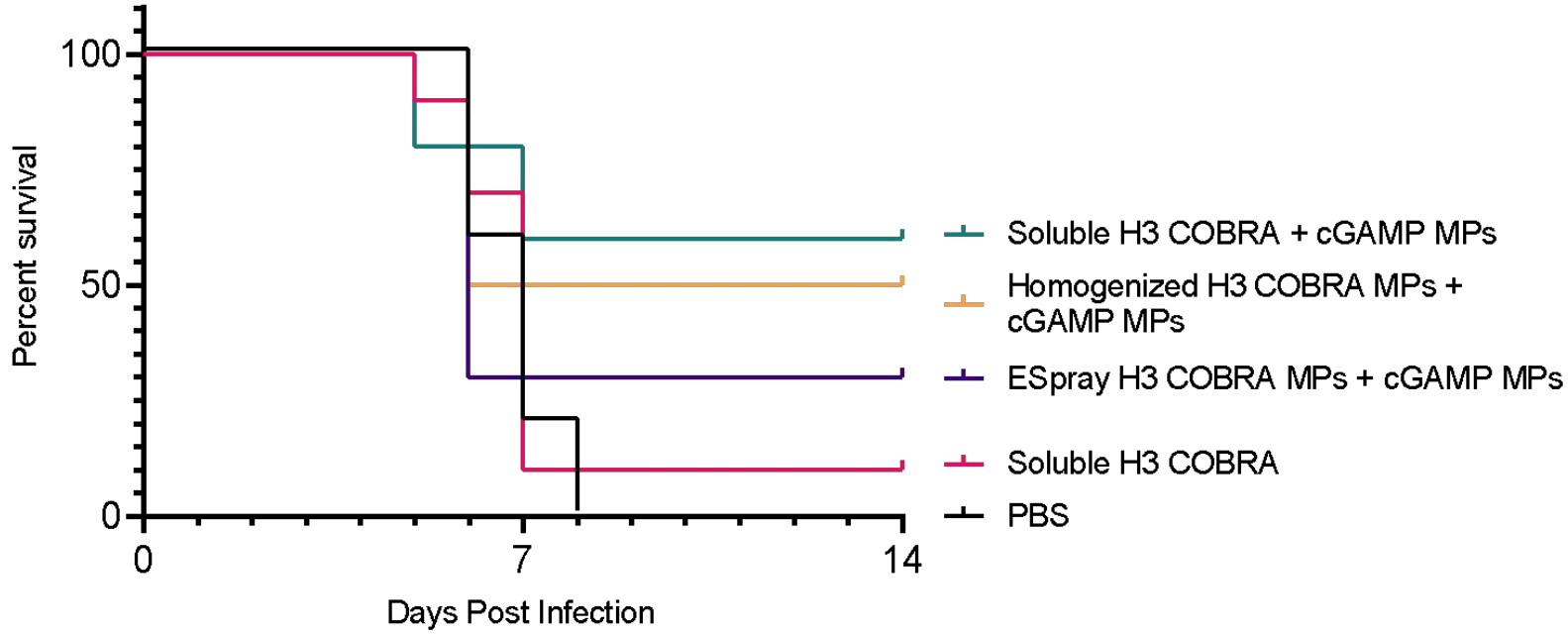


Similar trends were observed with soluble cytokines using an ELISA

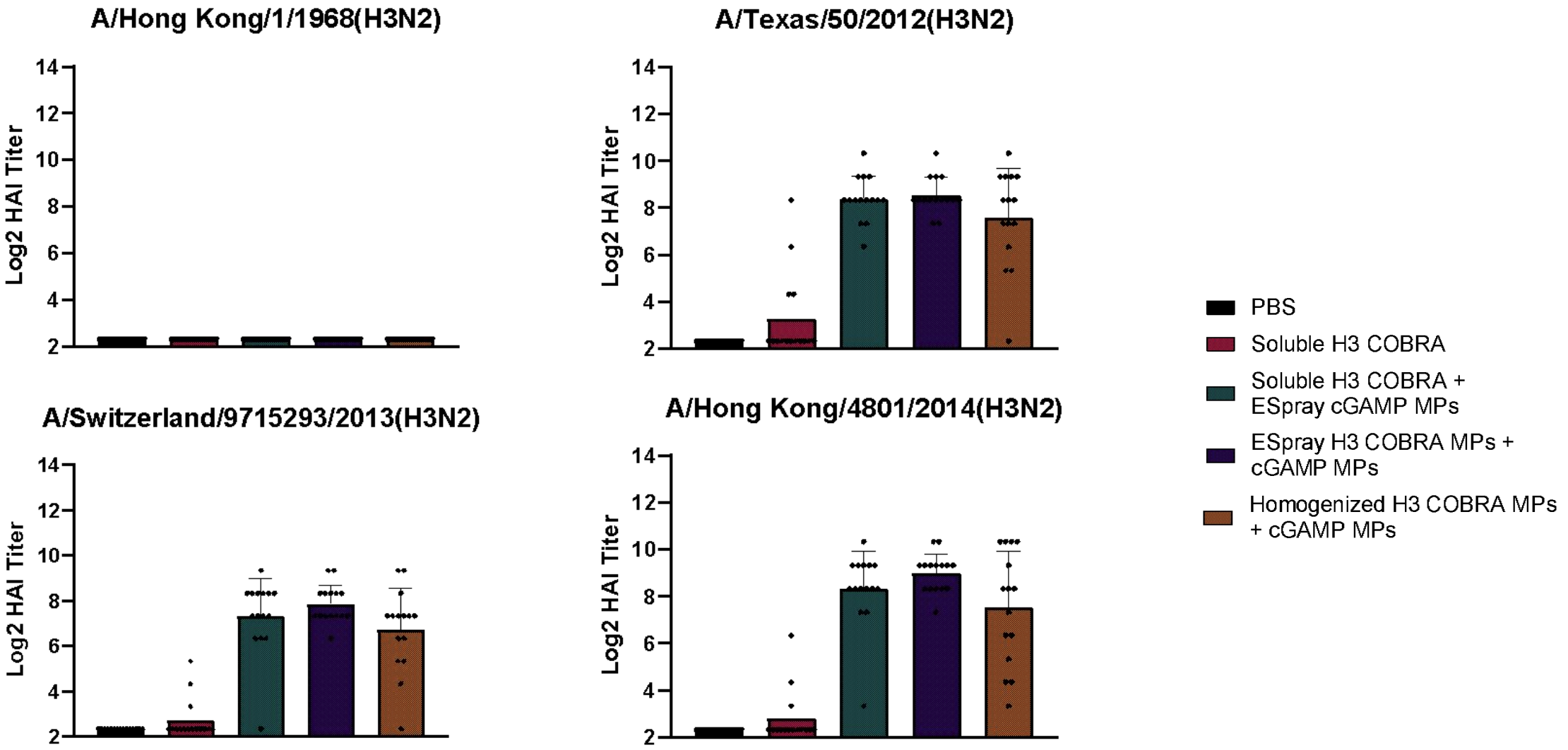
Vaccination Produced Protection Against Influenza Challenge





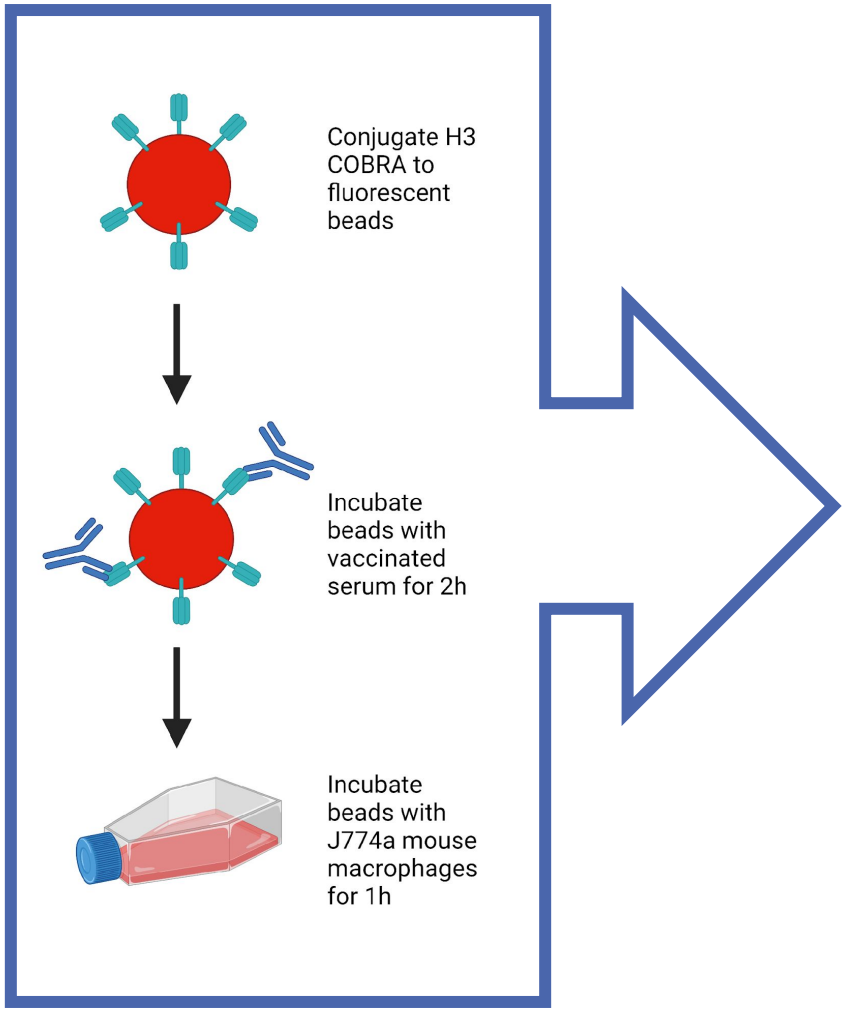


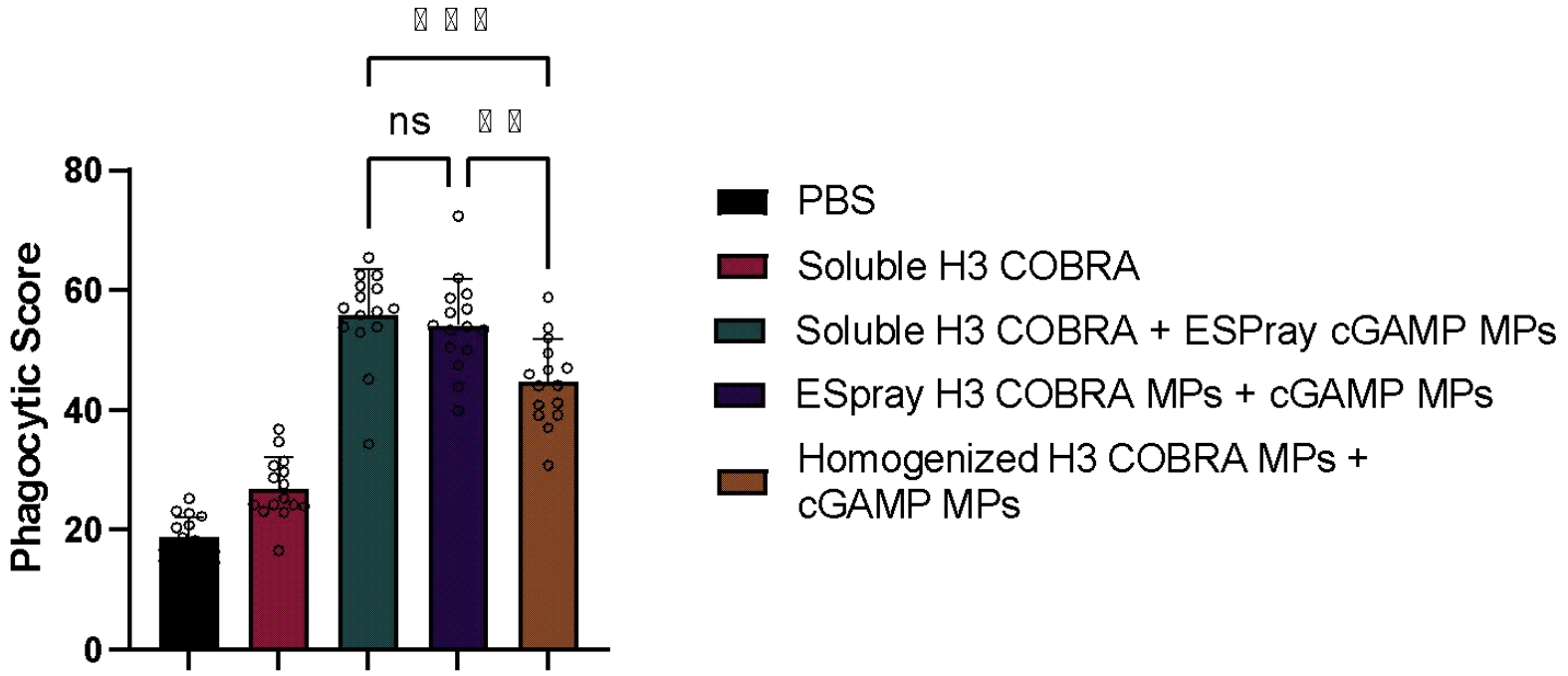
Vaccination with Ace-DEX MPs Elicited High HAI Titers



Serum from Day 42 HAI = hemagglutination inhibition

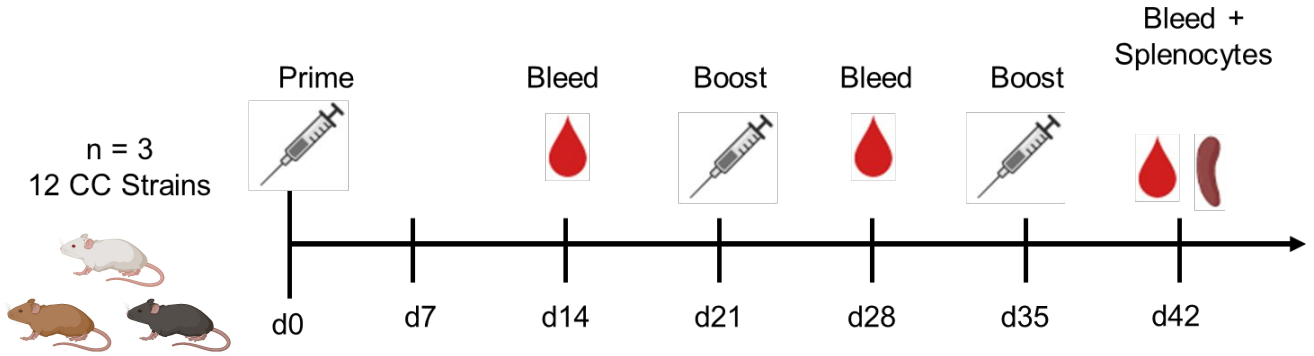
Vaccination with Ace-DEX MPs Elicited Antibodies with Antibody Dependent Cellular Phagocytosis Activity

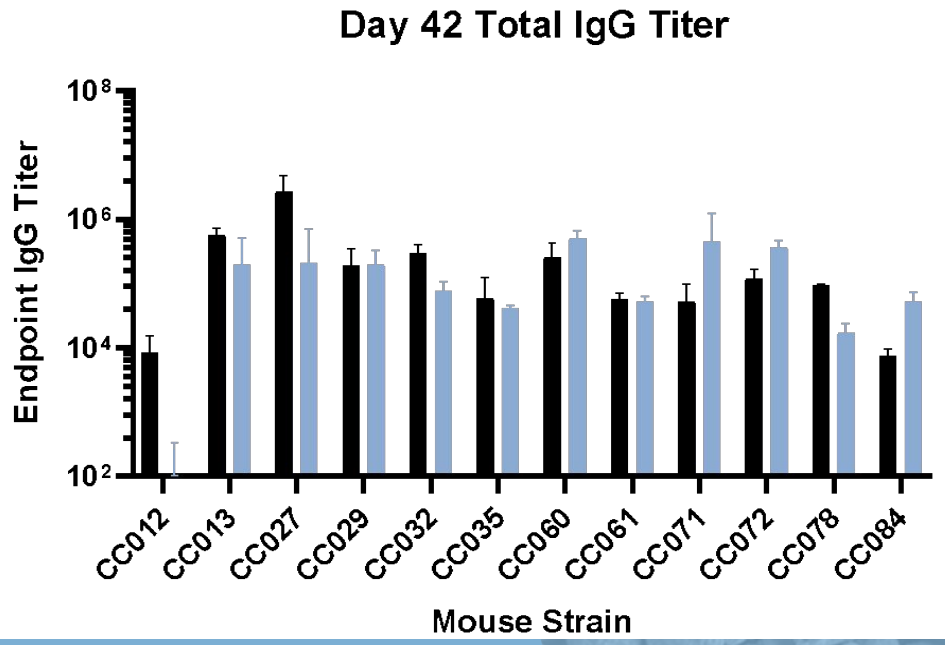


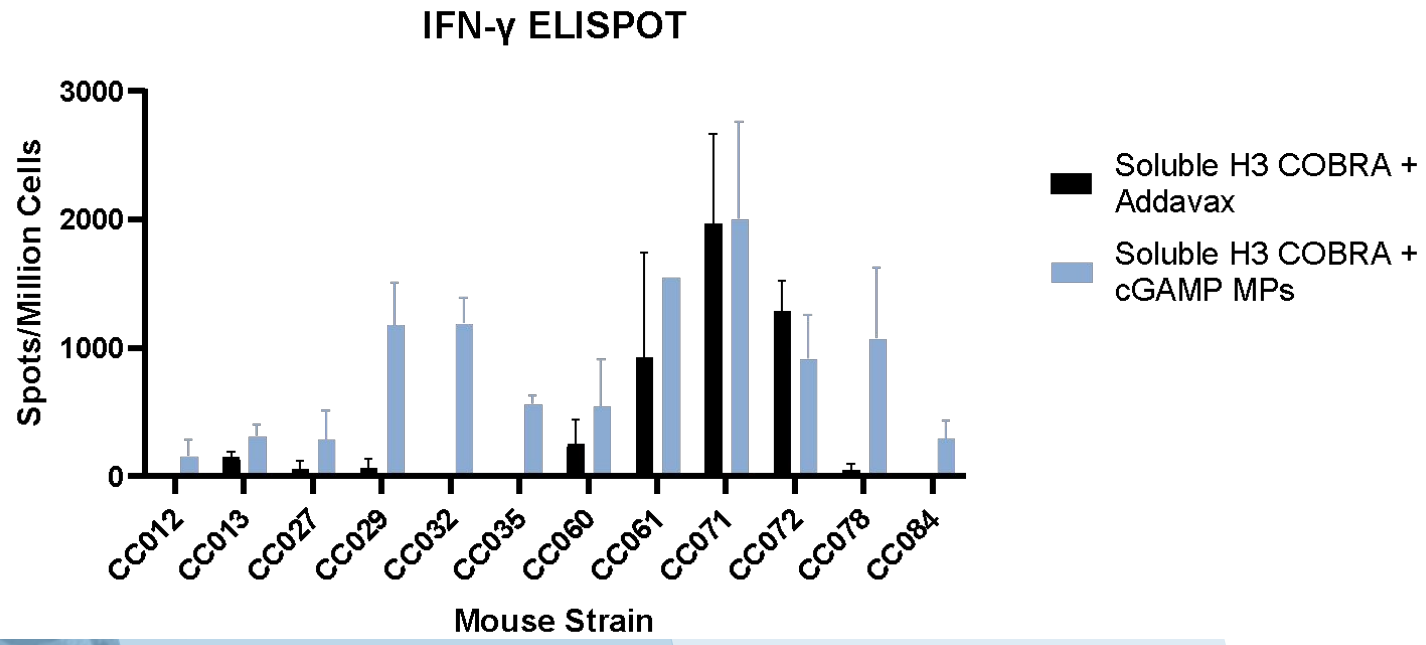


Future work will include the investigation of ADCC and ADCD

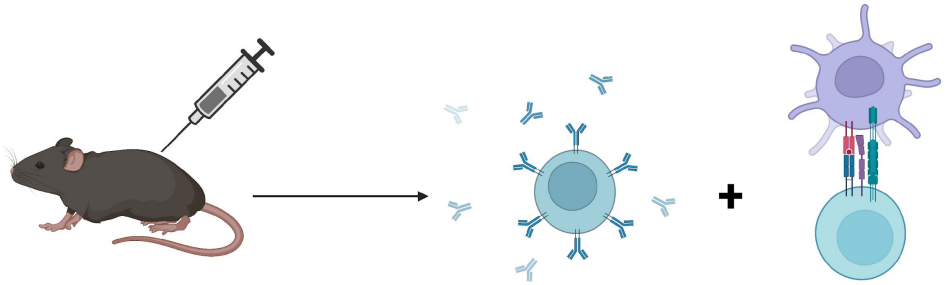
cGAMP MPs Provided Strong Cellular Response in Cross Collaborative (CC) Mice







Conclusions



Vaccination produced high cellular and humoral responses as well as broad neutralization

Future Directions

Evaluate the long-term storage of COBRA and cGAMP microparticles

Compare the efficacy of encapsulated COBRA to surface conjugated COBRA microparticles

Acknowledgements

Lab Members

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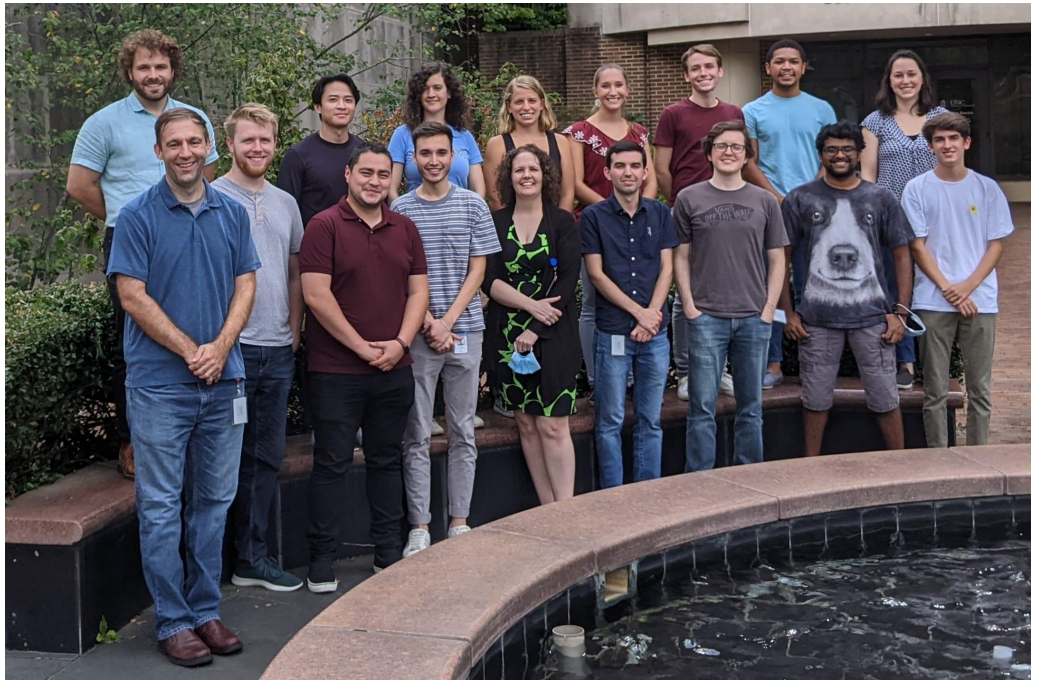

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bio RENDER

CIVICs Collaborative Influenza Vaccine Innovation Centers

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