A Lymph-node Targeted Protein Subunit Vaccine Induces Potent and Cross-reactive Cellular and Humoral Immunity to COVID-19 in Mice and Non-Human Primates

Vaccines Summit Boston 2022

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Chief Scientific Officer

Boston, Massachusetts

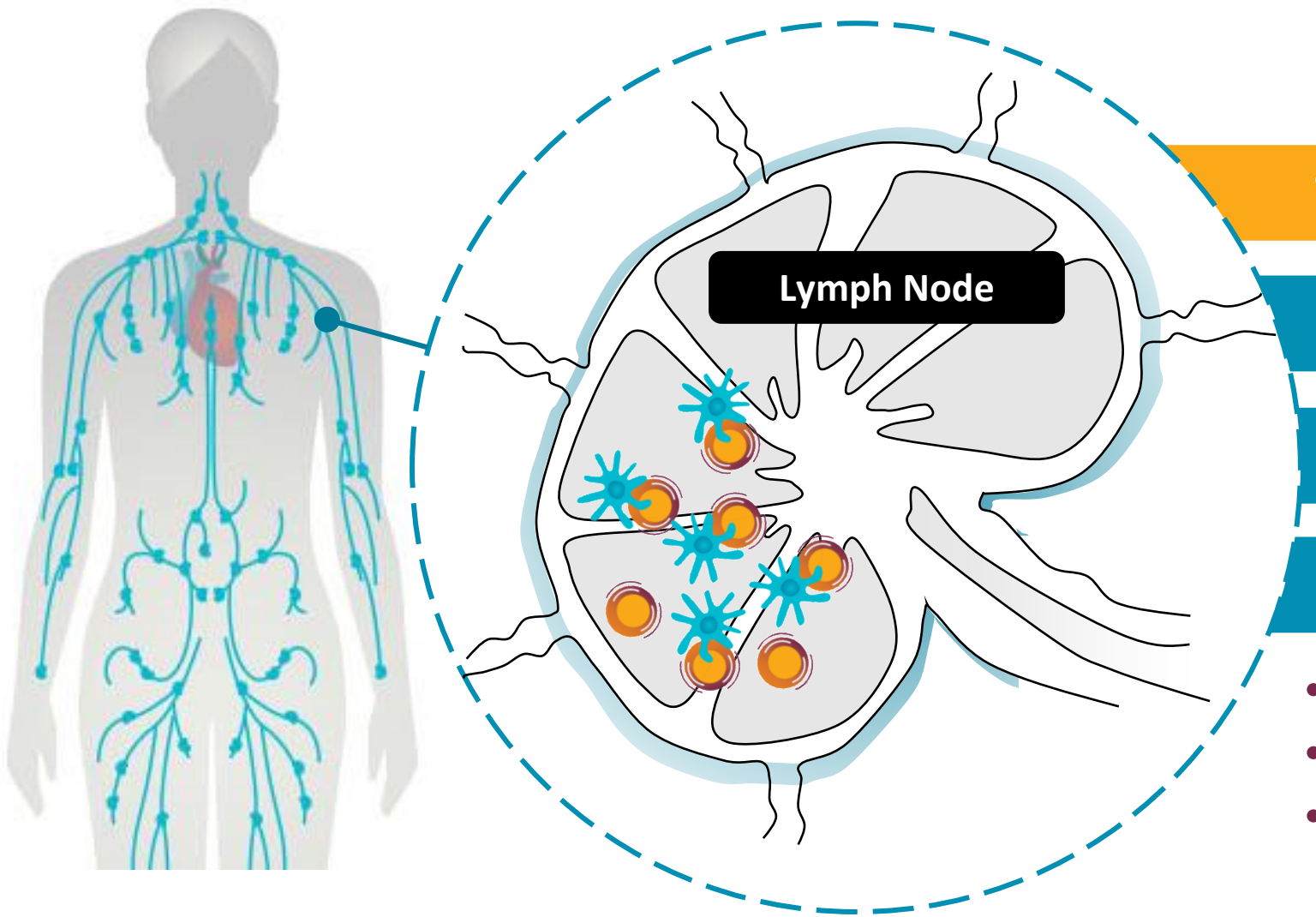
Lymph Node Targeting with the AMP Platform

ELI-005: A Lymph Node Targeted Vaccine Against SC-2

- T Cell Responses in Blood, Lung, Spleen
- Antibody Responses
- Dose Sparing
- Responses in Aged Animals
- Cross-reactive Responses to VOC

- T Cell Responses
- Antibody Responses: IgG and nAb
- Germinal Center B Cells
- Variant-specific Responses

Lymph Nodes are Where the Immune Response is Orchestrated



The Immune "School House"

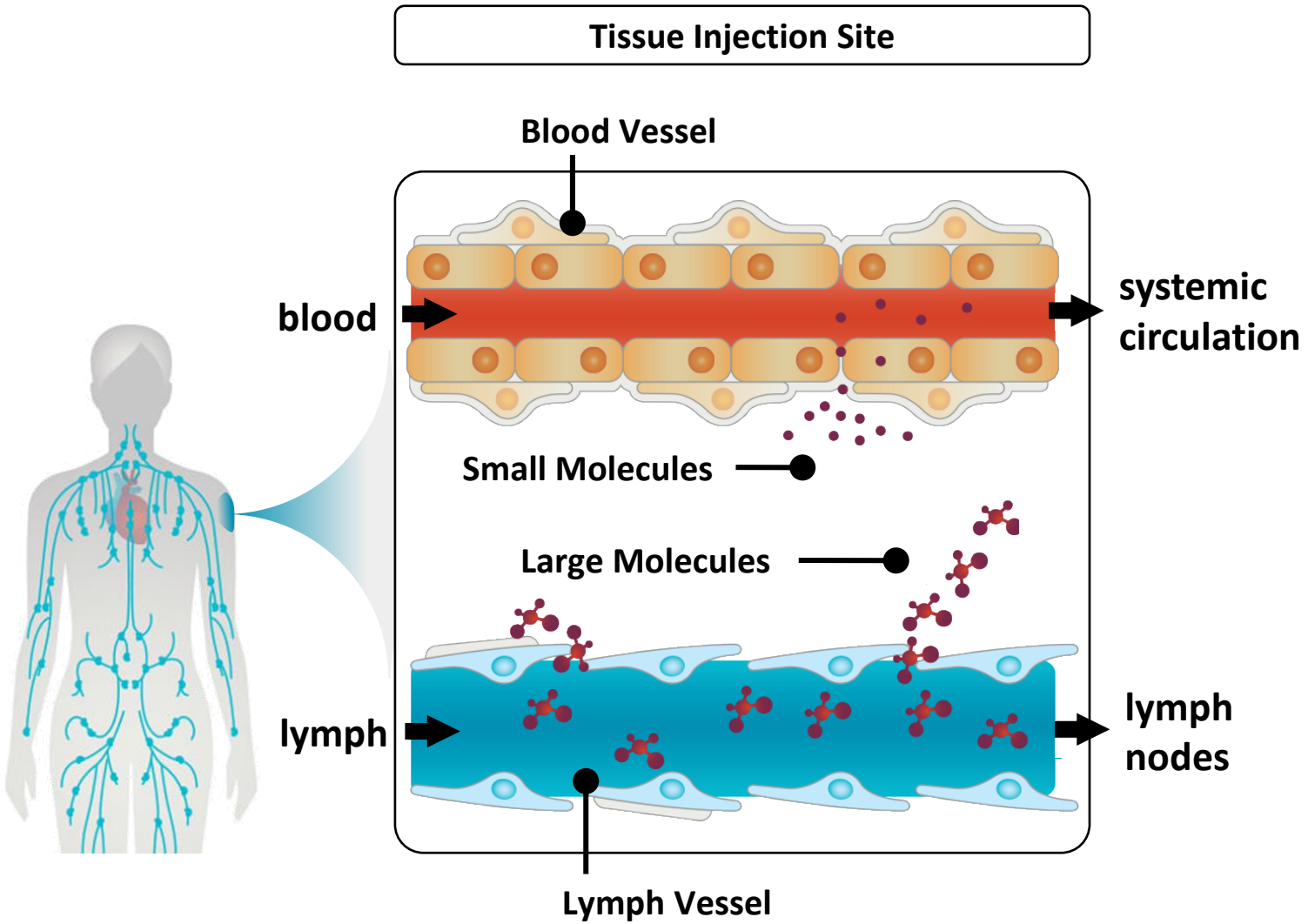
Numerous Immune Cells

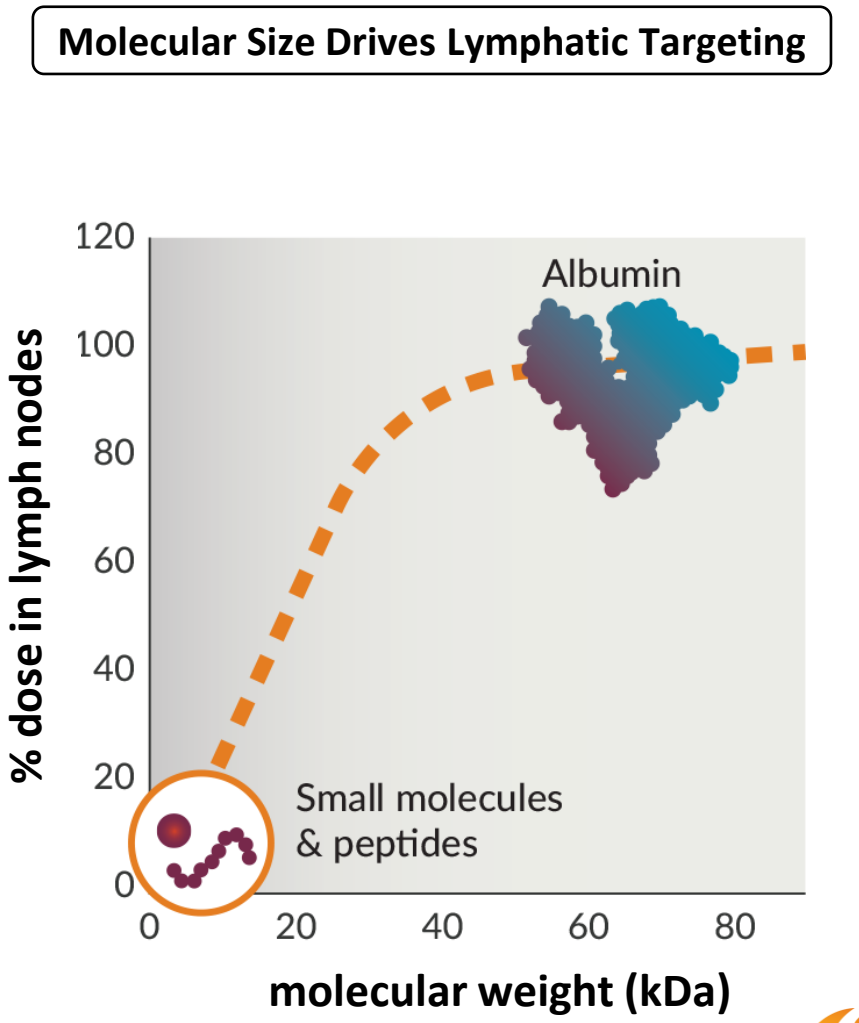
Response Coordination

APC : T and B Cell Interaction

- **Expansion**
- **Persistence**
- **Effector Function**

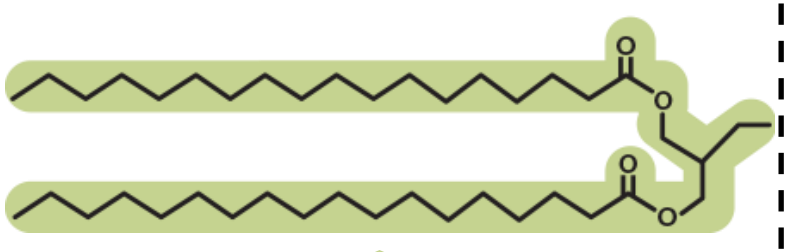
Albumin is the Ideal Carrier to Transport Immuno-therapies and Vaccines into Lymph Nodes





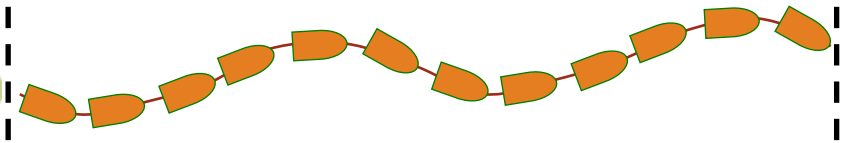
Amphiphile (AMP) Platform Enables Lymph Node Delivery of Validated Therapeutics with Modular Application

AMP: A Modular Conjugation Approach for Delivery of Immune Therapeutics to the Lymph Nodes



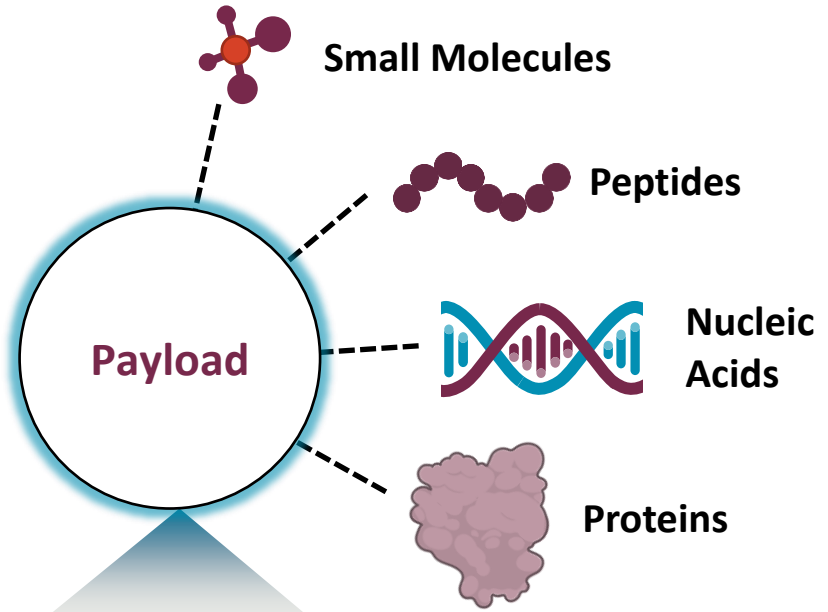
Albumin-binding Lipid

- ✓ *Lymph Node Targeting*
- ✓ *Lymph Node Retention*



Polymeric Linker

- ✓ *Improve Solubility*
- ✓ *Control Payload Release*

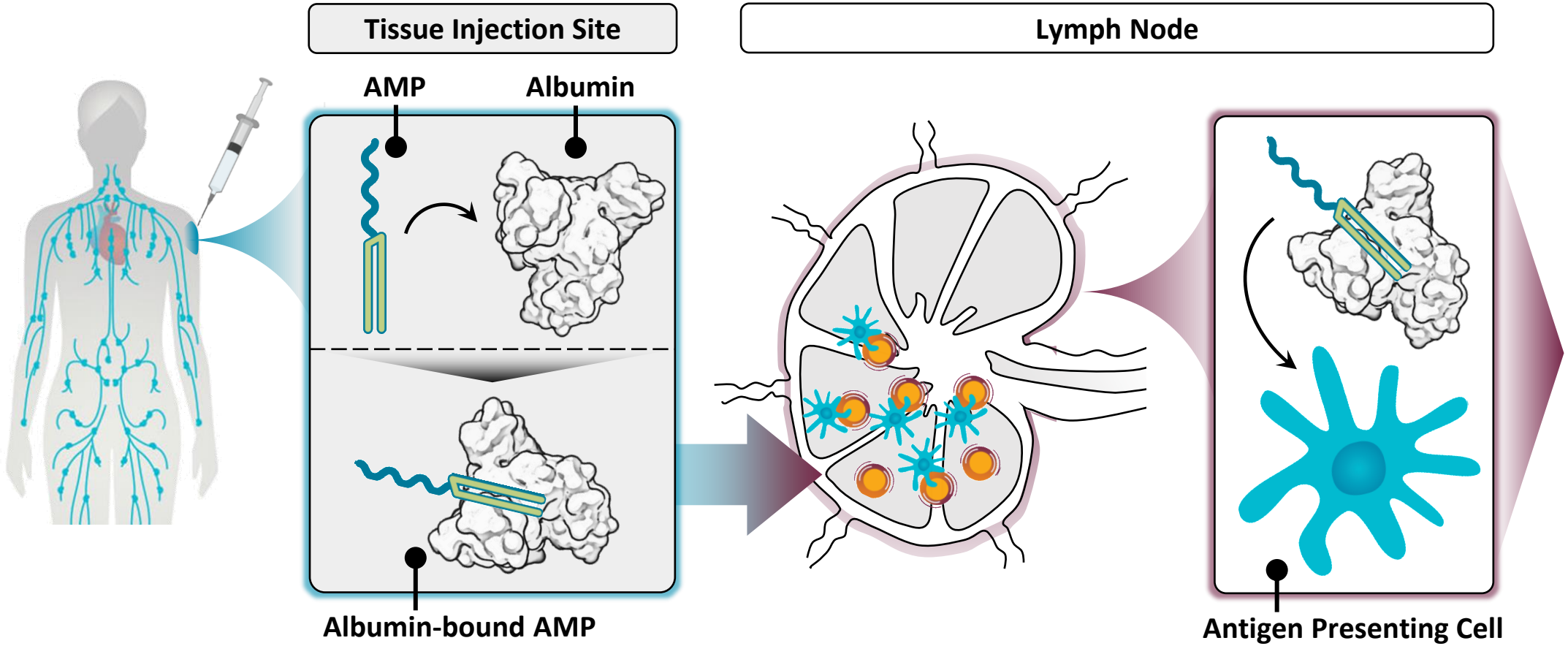


Payload

- ✓ *Antigens*
- ✓ *Adjuvants*

Targeting the Lymph Nodes with AMP to Orchestrate Immunity

1. Subcutaneous Injection
2. Albumin Binding
3. Lymph Node Targeting
4. Delivery to Immune Cells
5. Immune Activation



- APC Activation
- Cytokines
- T Cell Priming
- Ab Generation

Designing a Lymph Node Targeting CpG DNA

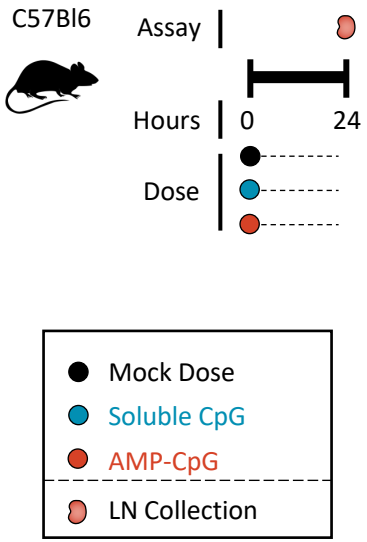
AMP Modification: Albumin Binding Lipid for Lymph Node Targeting

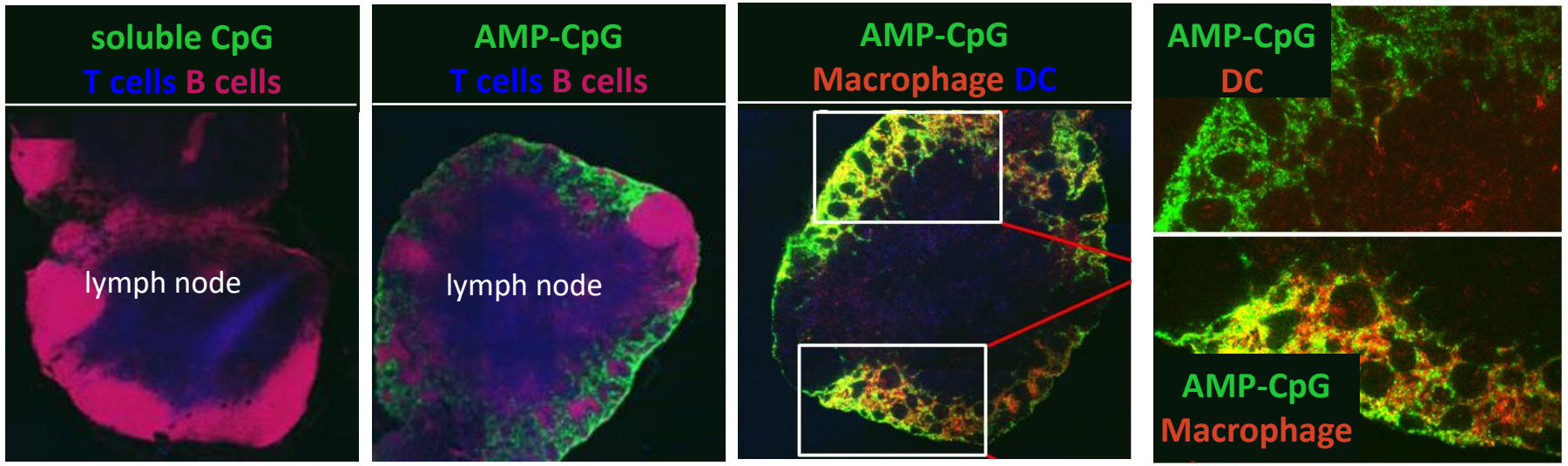
CpG DNA: TLR-9 Agonist

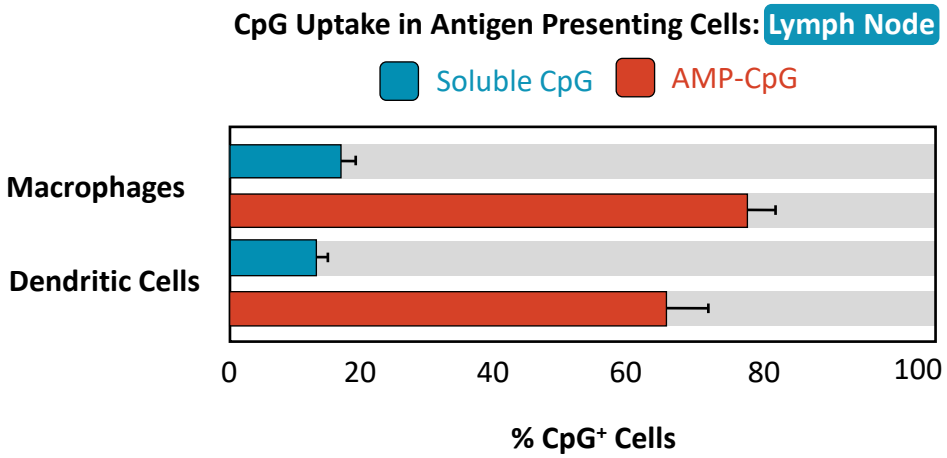
- Potent TLR-9 immuno-activator
- AMP modification gives >10-fold improved lymph node targeting

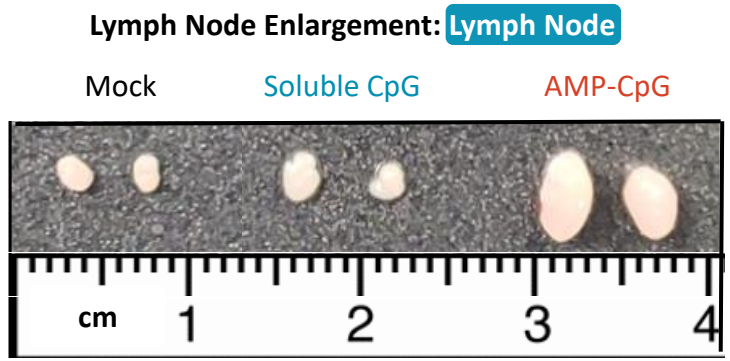
AMP-CpG Targets the Lymph Nodes for Efficient Uptake into Resident APCs

Experimental Schema:





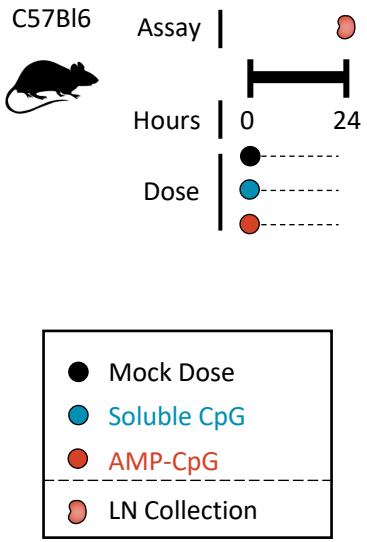




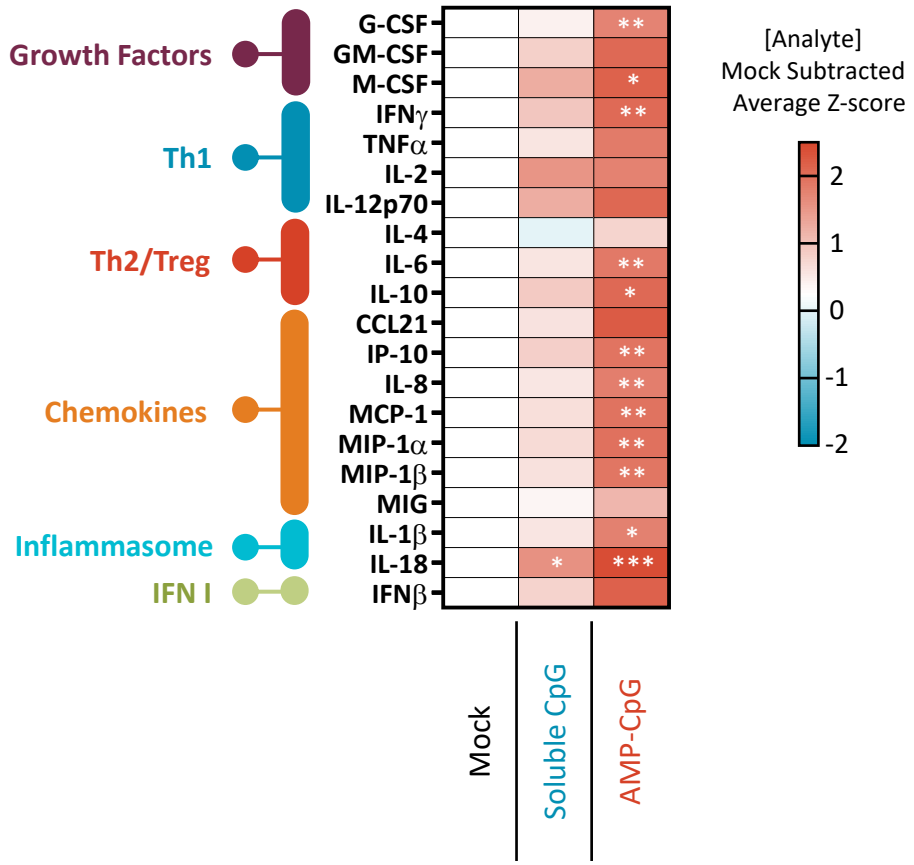
Liu, Irvine, et al. **Nature** 2014

AMP-CpG Induces Coordinated Inflammation, Innate Immune Cell Activation in Draining Lymph Nodes

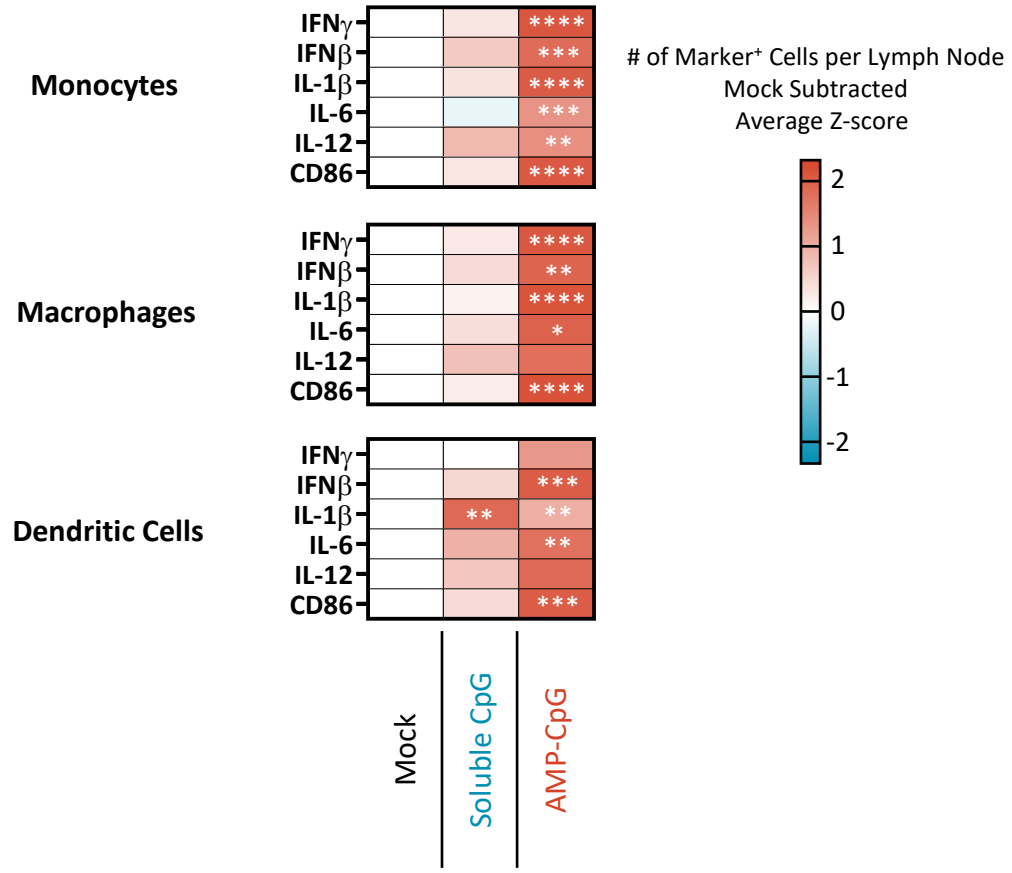
Experimental Schema:



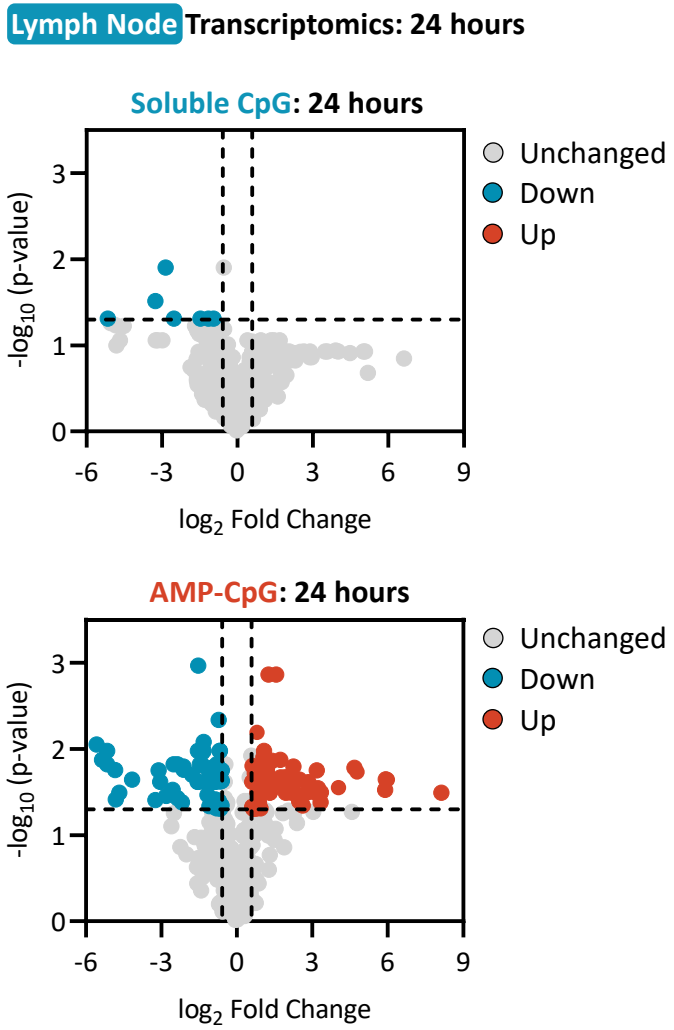
Lymph Node Proteomics: 24 hours

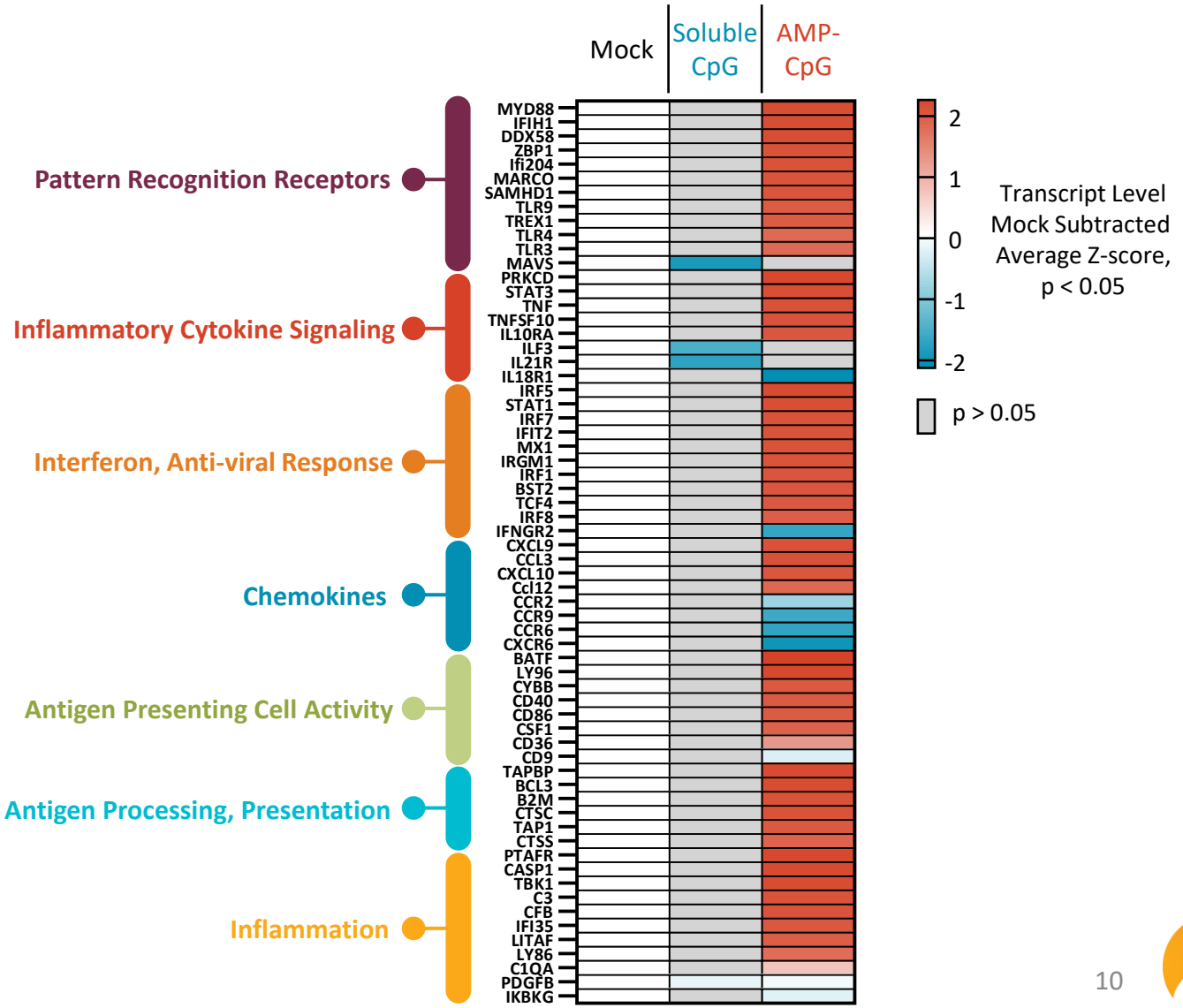


Lymph Node Innate Cell Recruitment and Activation: 24 hours



AMP-CpG Induces Potent Transcriptional Reprogramming of the Lymph Node Immune Response

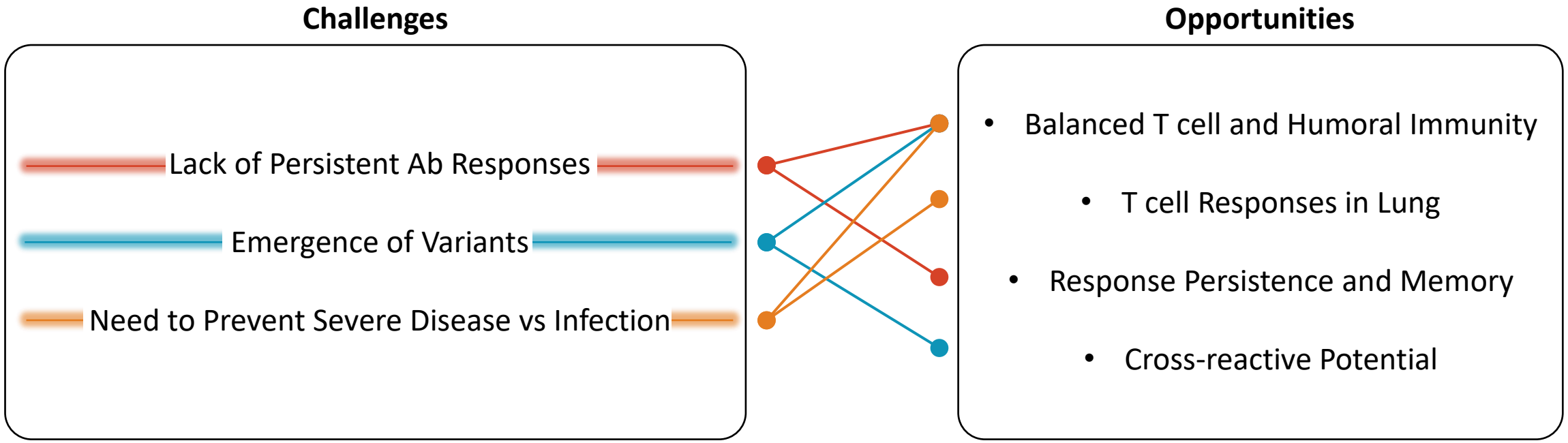




The AMP Platform Efficiently Targets the Lymph Nodes

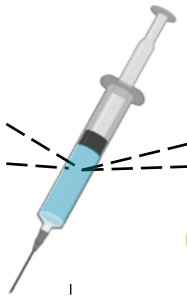
- Enhanced Lymph Node Delivery and Retention
  - Increased Uptake into APCs
    - Potent APC Activation
- Inflammatory Transcriptional Programming
  - Robust Cytokine/Chemokine Milieu

How can Lymph Node Targeting Improve TLR-9 Adjuvant Activity to Generate Potent T and B Cell Responses Against Infectious Disease?

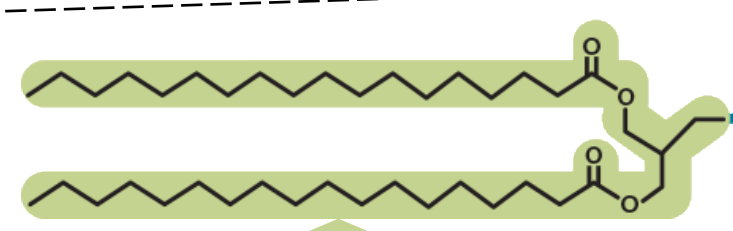


ELI-005: Designing a Lymph Node Targeted Protein Subunit Vaccine for SARS-CoV-2

(1) SARS-CoV-2 Spike RBD Protein Antigen



(2) AMP-CpG Adjuvant



AMP Modification: Albumin Binding Lipid for Lymph Node Targeting

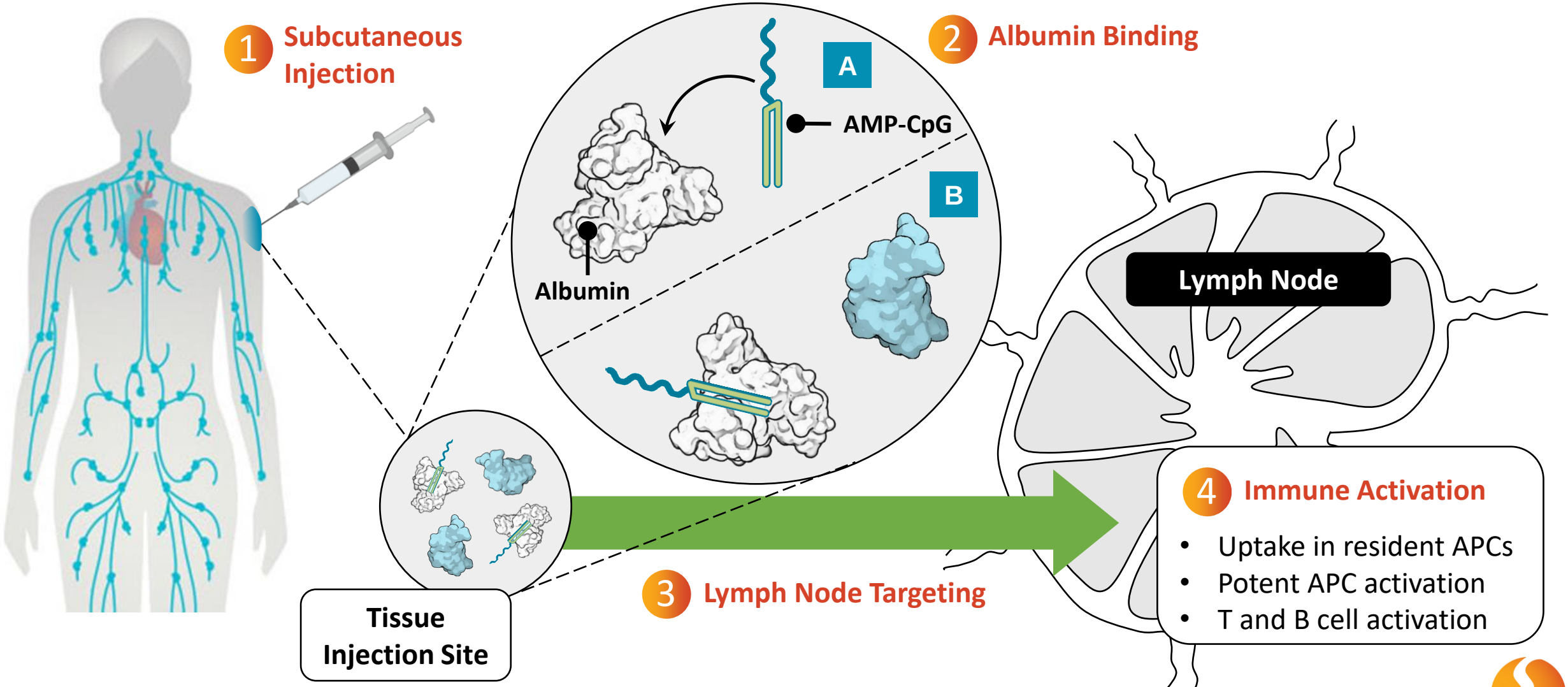
CpG DNA: TLR-9 Agonist

- Target of nAb responses
- Known CD4 and CD8 T cell target
- MW~34 kDa predicts suitable lymph node targeting

- Potent TLR-9 immuno-activator
- AMP modification gives >10-fold improved lymph node targeting
- CpG has proven safety and activity in humans

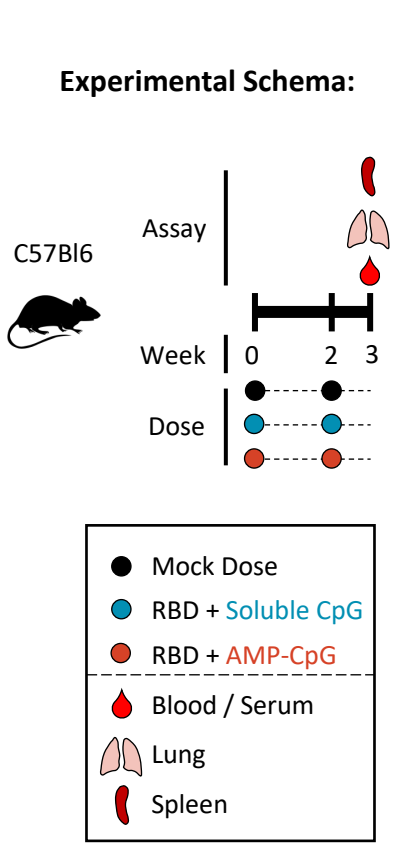
Steinbuck, et al. **Science Advances**. 2021.

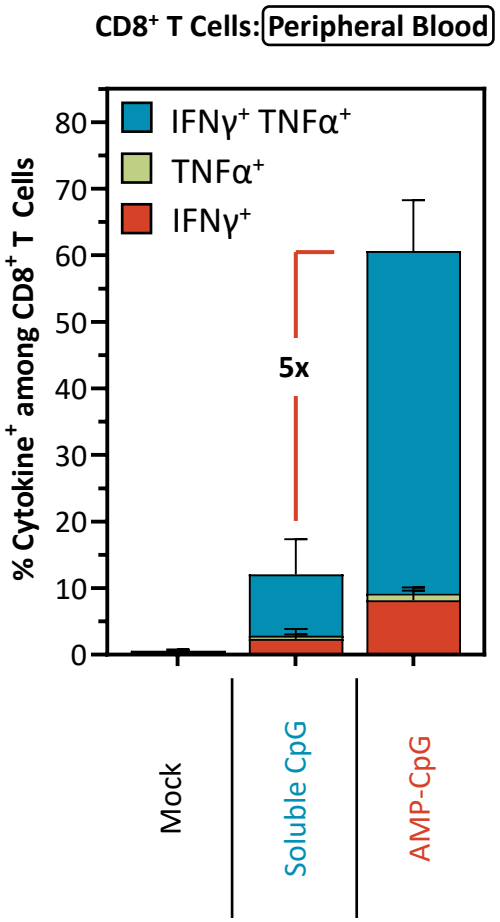
ELI-005: Designing a Lymph Node Targeted Protein Subunit Vaccine for SARS-CoV-2

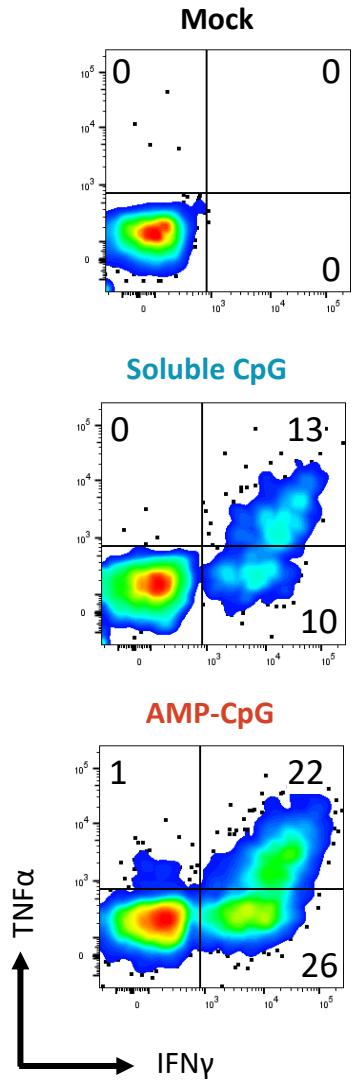


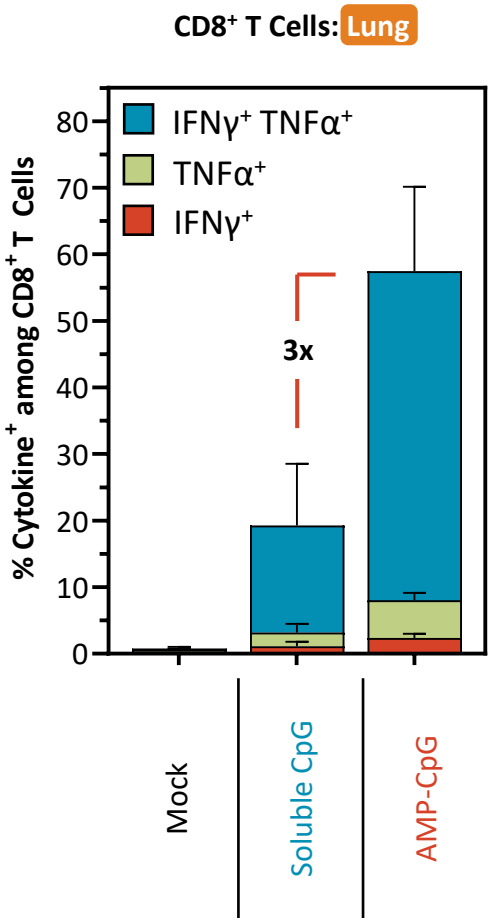
Steinbuck, et al. **Science Advances**. 2021.

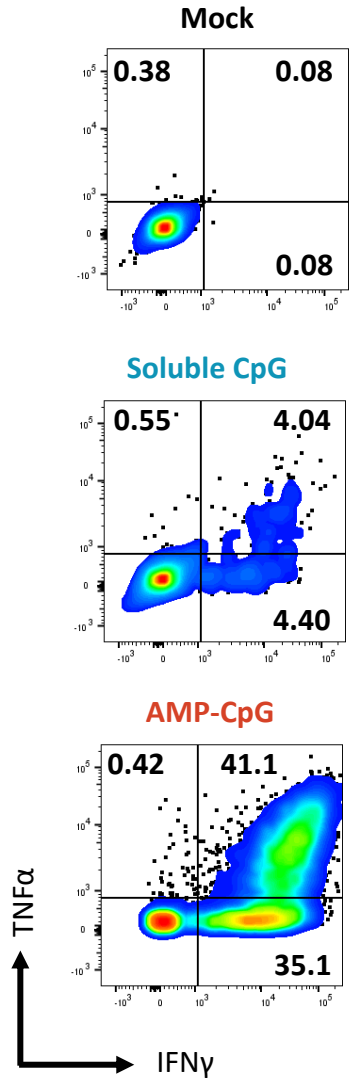
AMP-CpG Vaccination Induces Potent Polyfunctional CD8 T Cell Responses Targeting SARS CoV-2





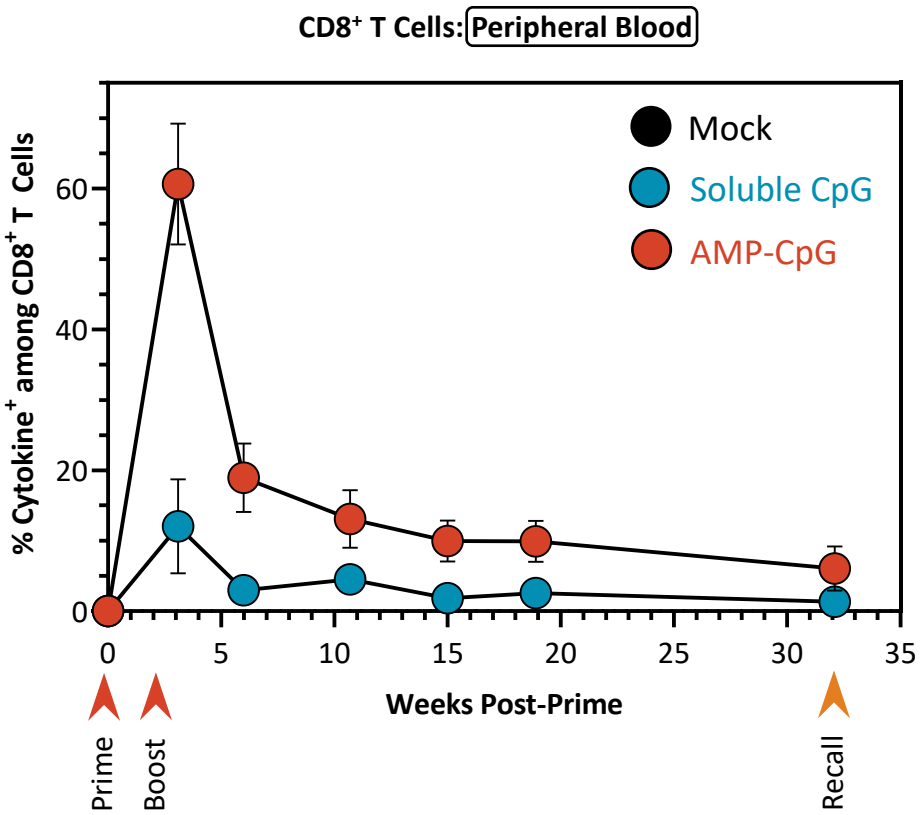




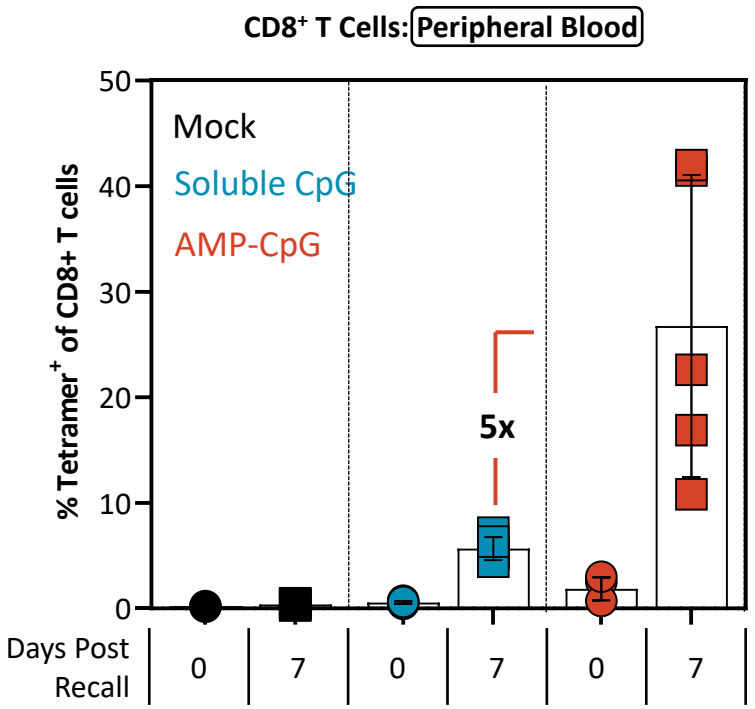


Steinbuck, et al. **Science Advances**. 2021.

AMP-CpG Vaccination Induced T cell Responses Persist for Months After Dosing, Expand upon Recall

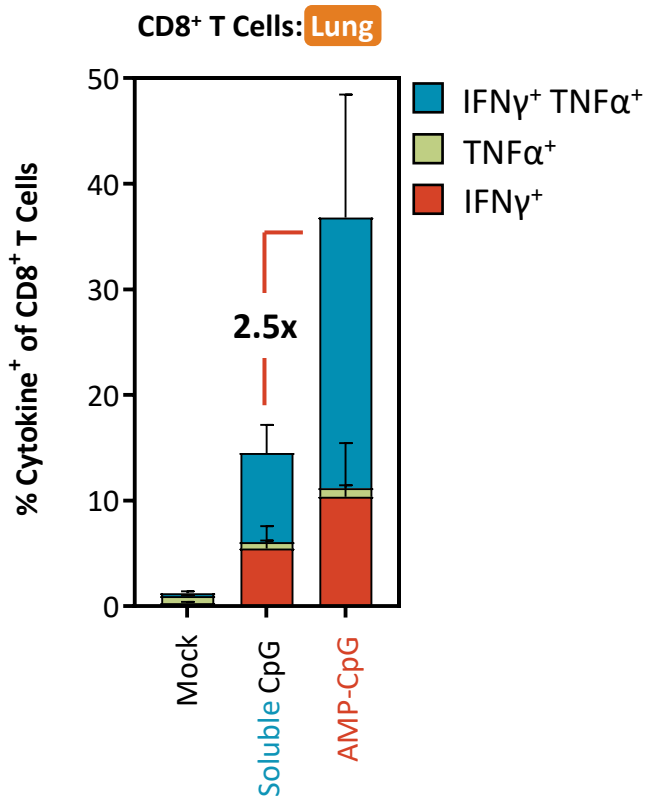


Recall Responses



sc RBD Recall on Week 32

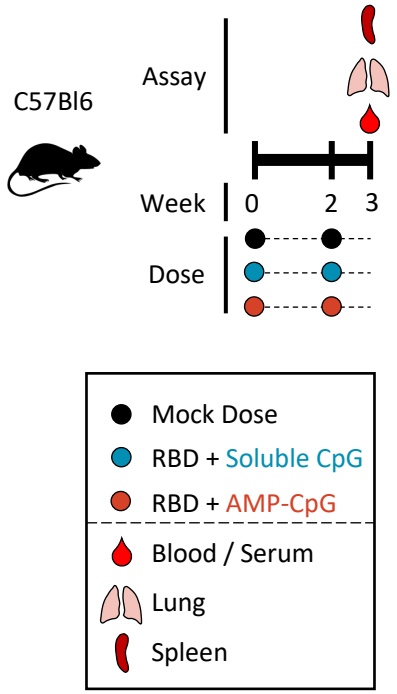
VNFNFNGL
H2K(b) Tetramer

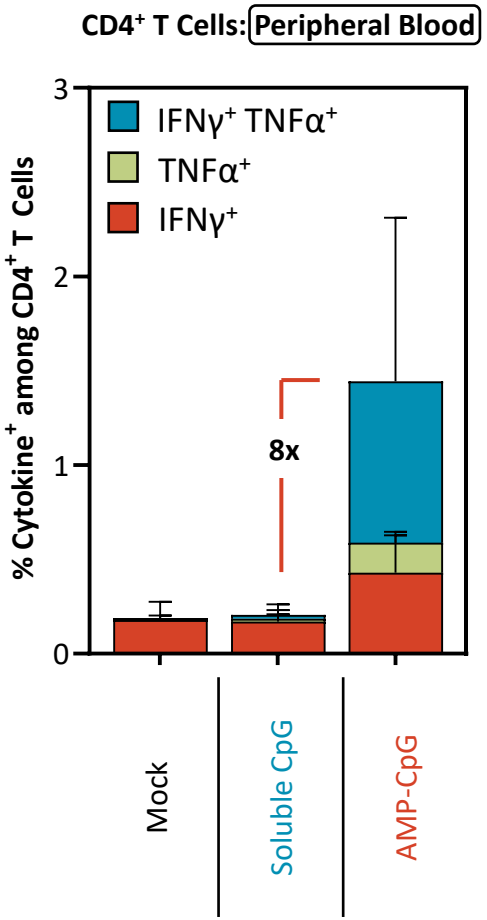


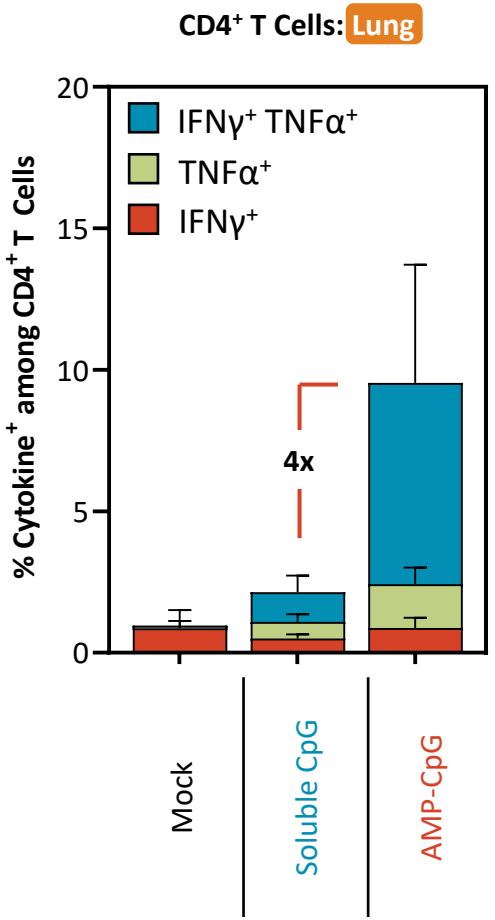
Day 7 Post sc RBD Recall

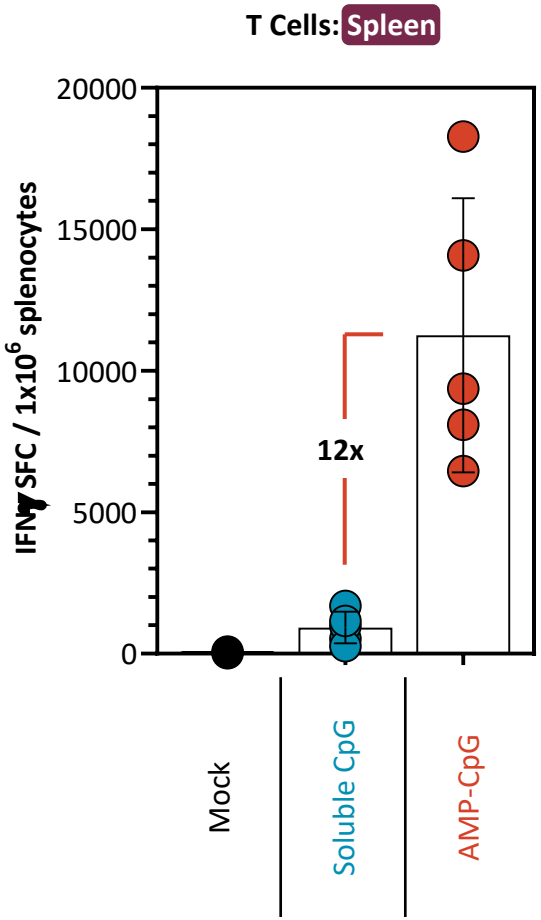
AMP-CpG Vaccination Induces Polyfunctional CD4 T Cell Responses, Potent Splenic T Cells Targeting SARS CoV-2

Experimental Schema:



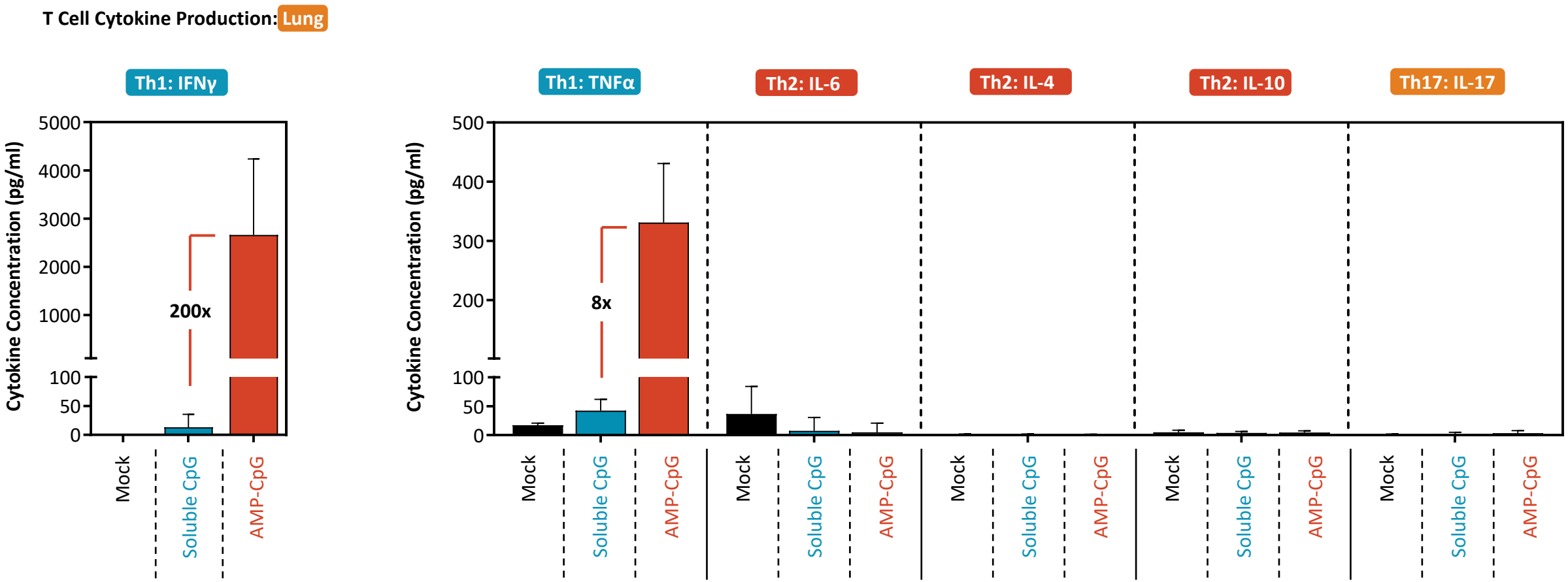






Steinbuck, et al. **Science Advances**. 2021.

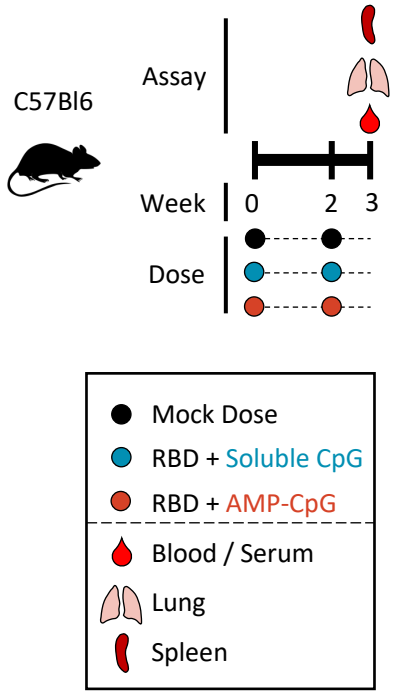
AMP-CpG Vaccine-Induced Lung Resident T Cells Potently Produce Multiple Th1 Cytokines, no Th2/Th17 Cytokines



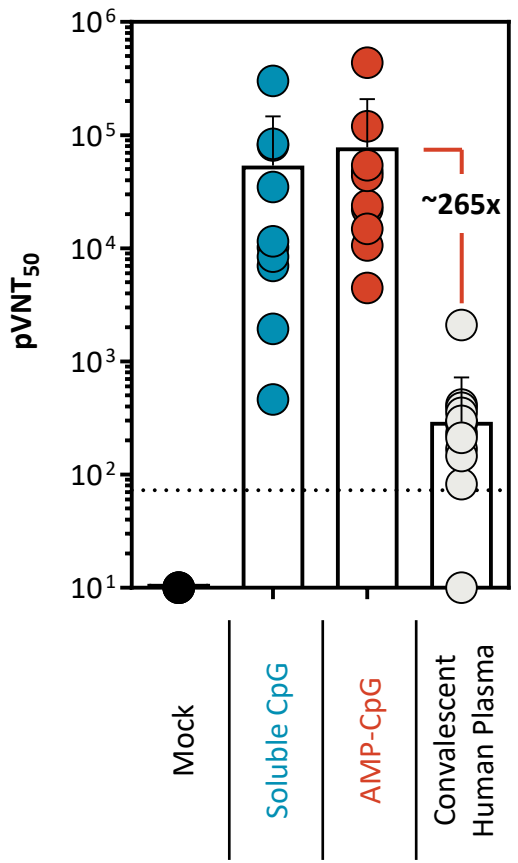
Steinbuck, et al. **Science Advances**. 2021.

AMP-CpG Vaccination Induces Potent Neutralizing Antibodies with Optimal Th1 Dominant Isotype Profile

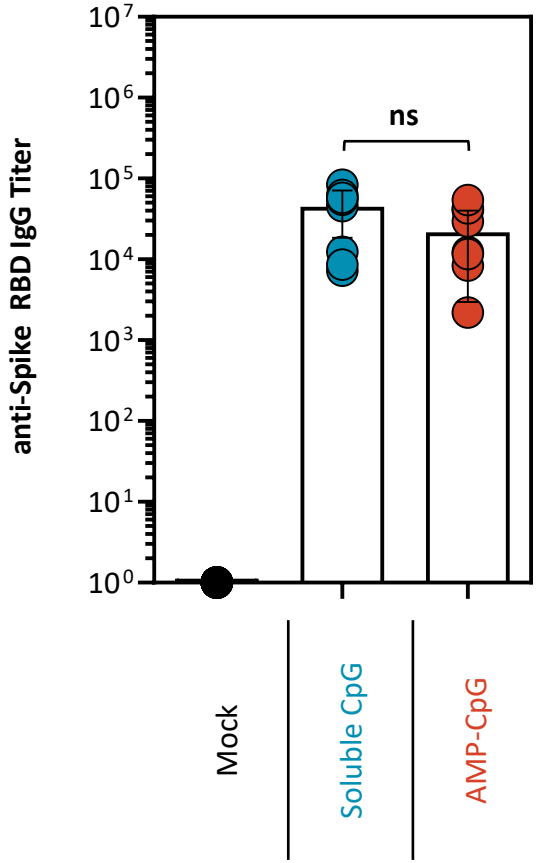
Experimental Schema:



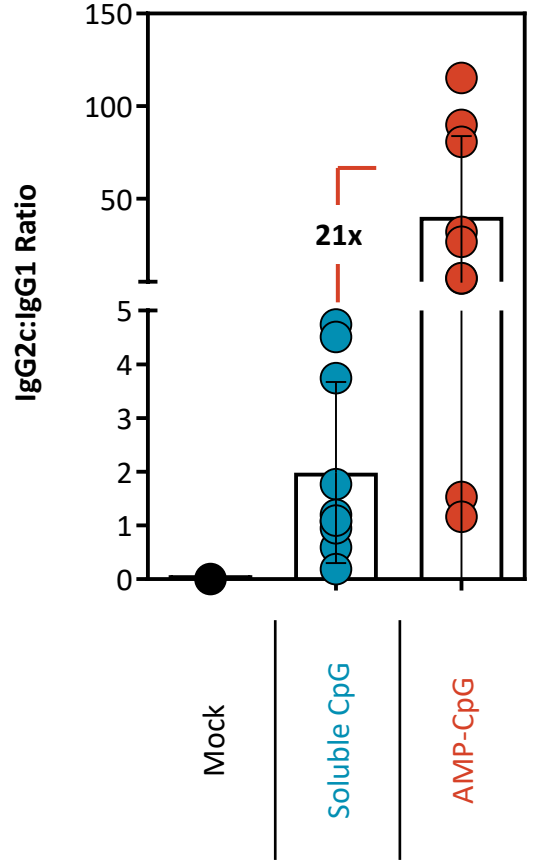
Neutralizing Activity: Serum



IgG Titer: Serum



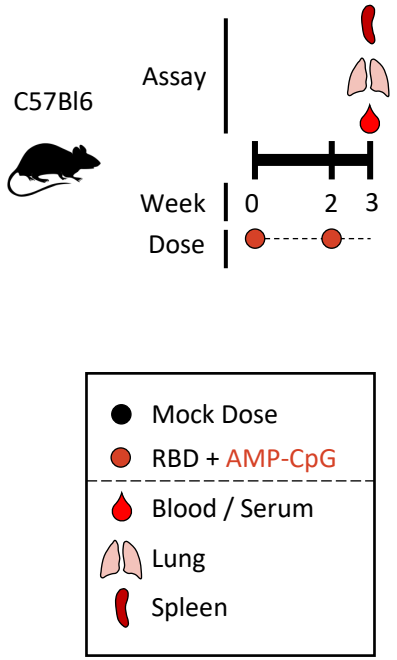
Ig Isotype: Serum

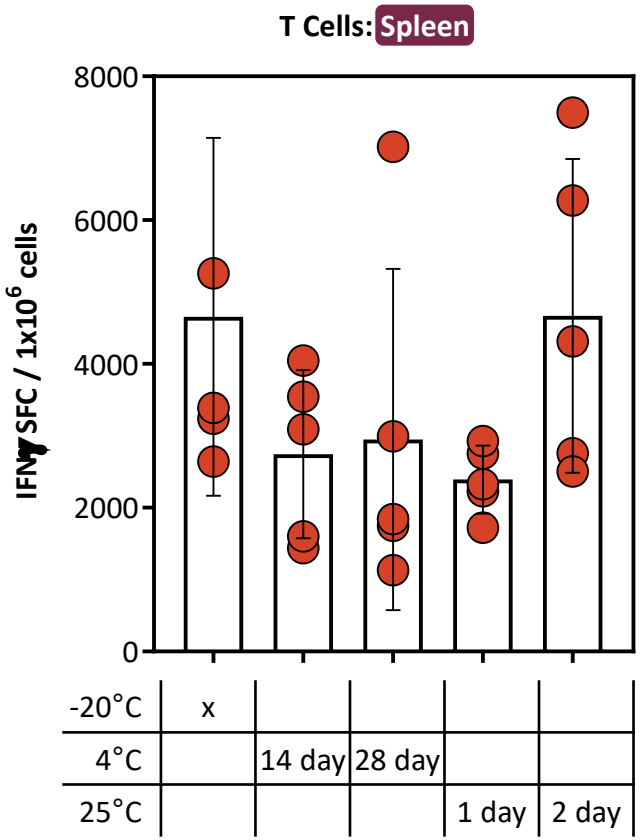


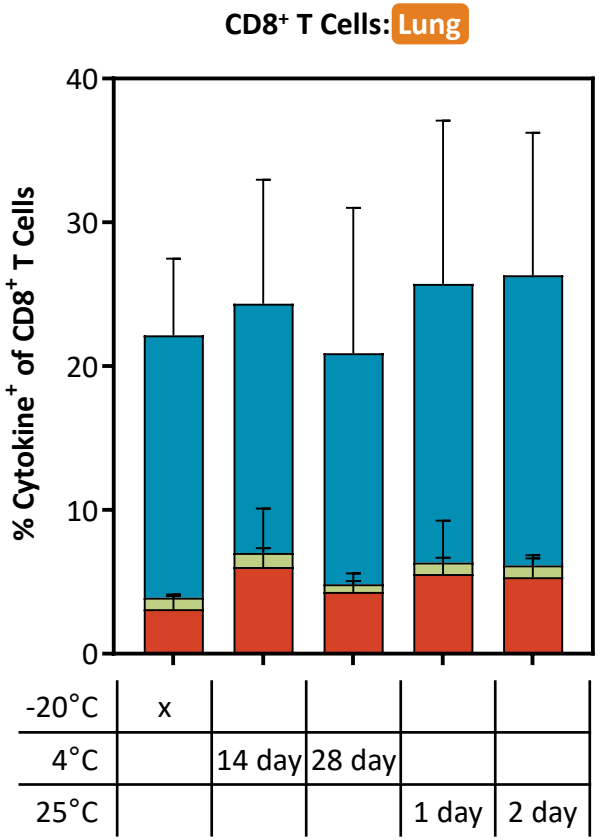
Steinbuck, et al. **Science Advances**. 2021.

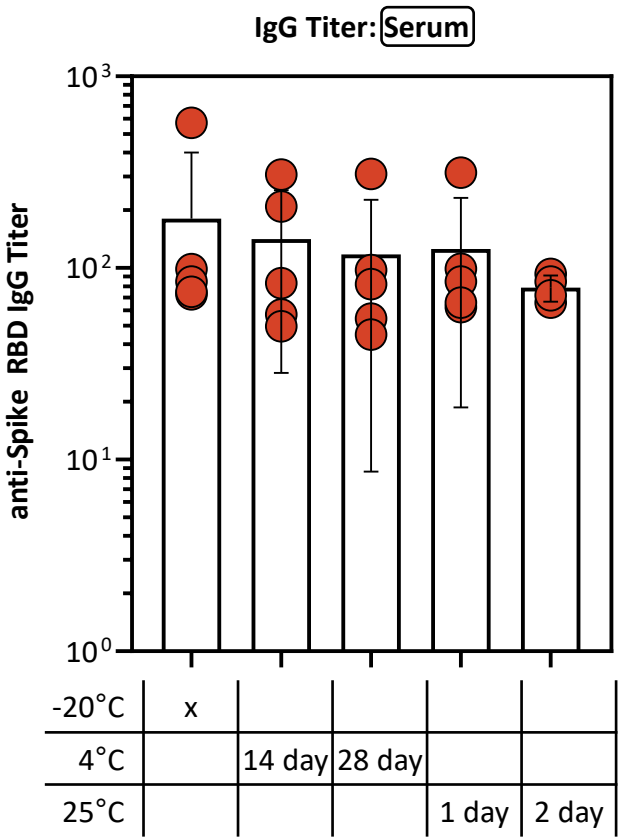
Storage at Refrigerated or Ambient Temperature Does Not Impair Immunogenicity

Experimental Schema:









ELI-005: A Lymph Node Targeted Vaccine Against SC-2

- T Cell Responses in Blood, Lung, Spleen
- Antibody Responses
- Dose Sparing
- Responses in Aged Animals
- Cross-reactive Responses to VOC

SCIENCE ADVANCES | RESEARCH ARTICLE

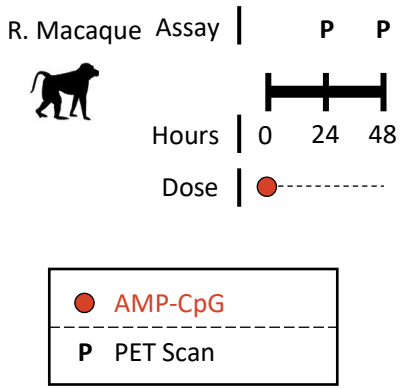
CORONAVIRUS

A lymph node–targeted Amphiphile vaccine induces potent cellular and humoral immunity to SARS-CoV-2

Martin P. Steinbuck, Lochana M. Seenappa, Aniela Jakubowski, Lisa K. McNeil, Christopher M. Haqq*, Peter C. DeMuth

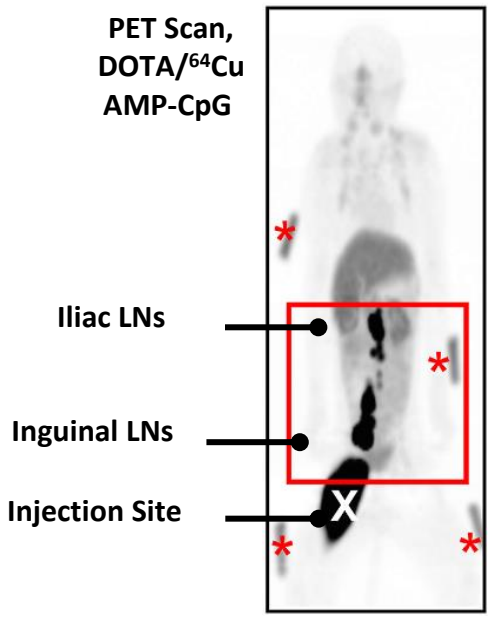
AMP-CpG Accumulates in NHP Lymph Nodes and Induces Potent T cell Responses

Experimental Schema:



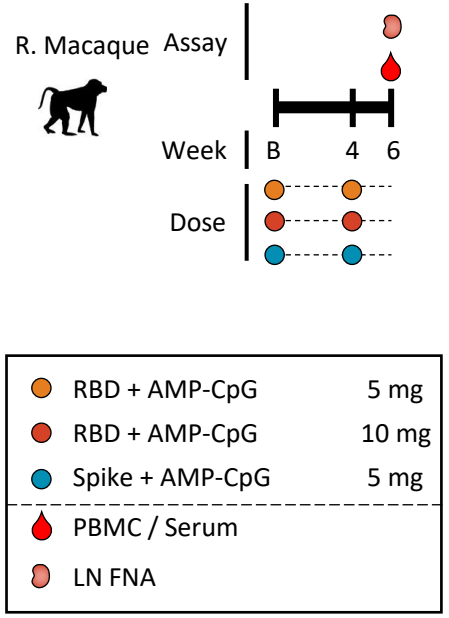
Lymph Node

PET Scan, DOTA/^{64}Cu AMP-CpG

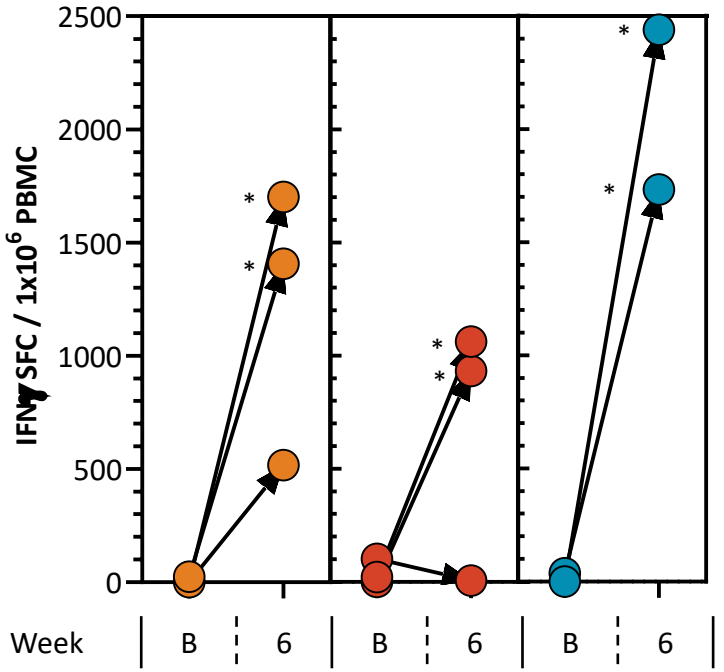


Lymph Nodes	% Dose 48h
Inguinal	~12%
Iliac	~30%

Experimental Schema:



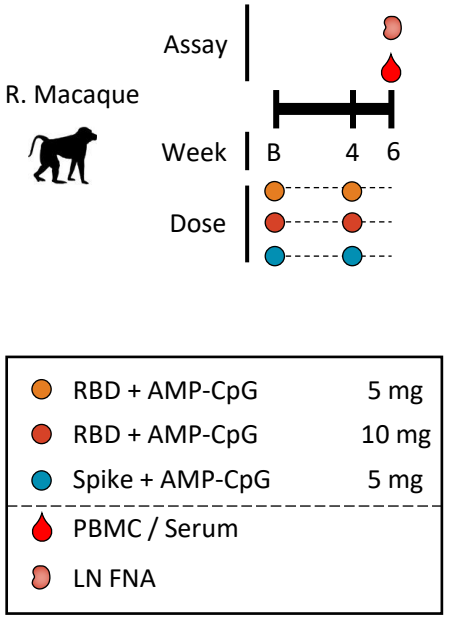
T Cells: Peripheral Blood



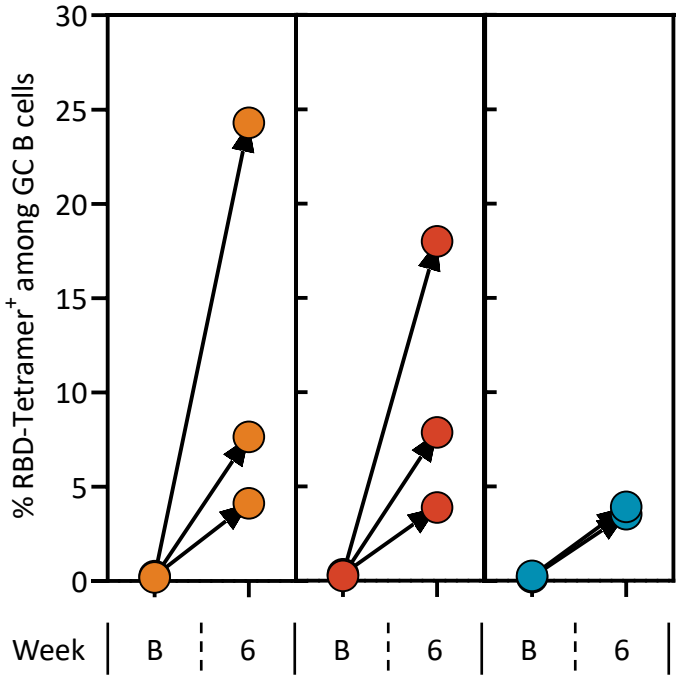
Martin, Irvine, et al. **Biomaterials** 2021

AMP-CpG Promotes Expansion of RBD-specific Germinal Center B Cells in NHP Lymph Nodes

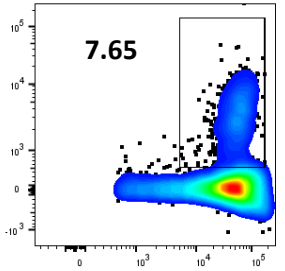
Experimental Schema:



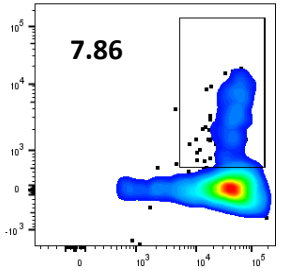
Germinal Center B Cells: Lymph Node



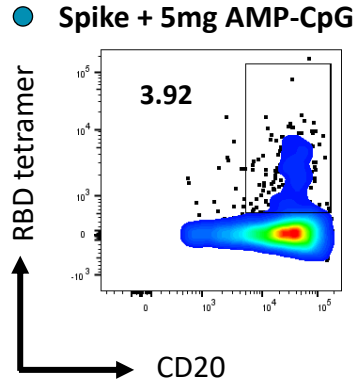
RBD + 5mg AMP-CpG



RBD + 10mg AMP-CpG

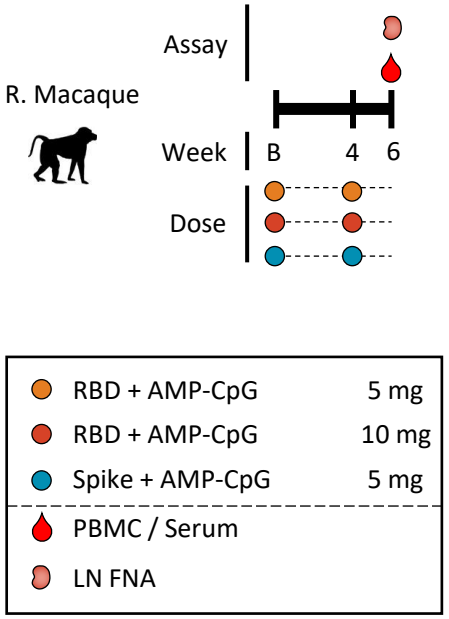


Spike + 5mg AMP-CpG

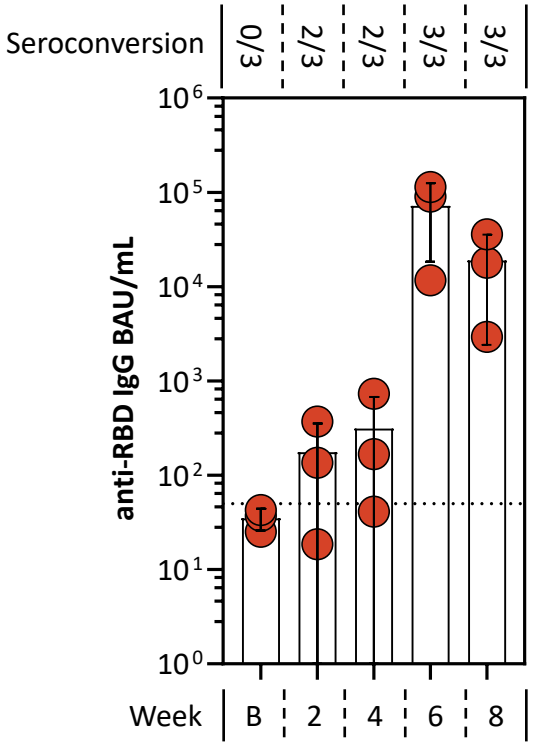


AMP-CpG Induces Potent Cross-reactive Neutralizing Antibody Responses

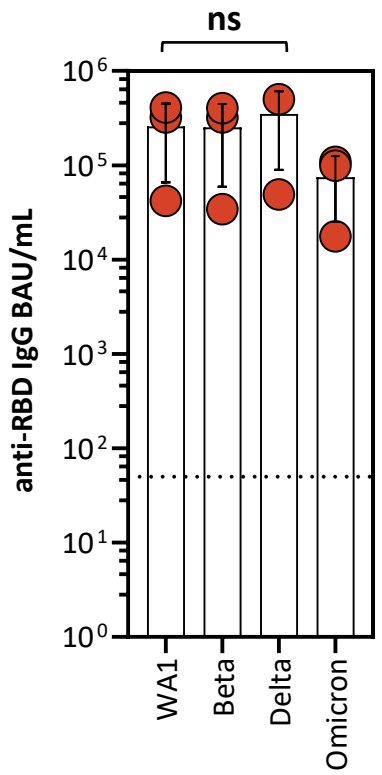
Experimental Schema:



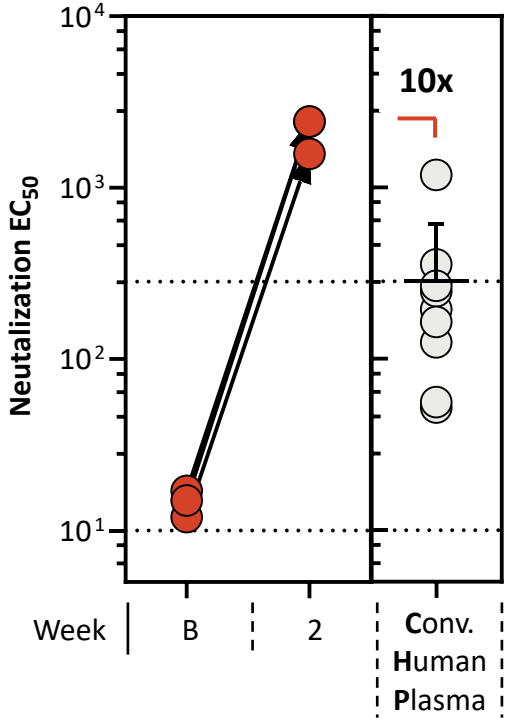
WA1 IgG Titer: Serum



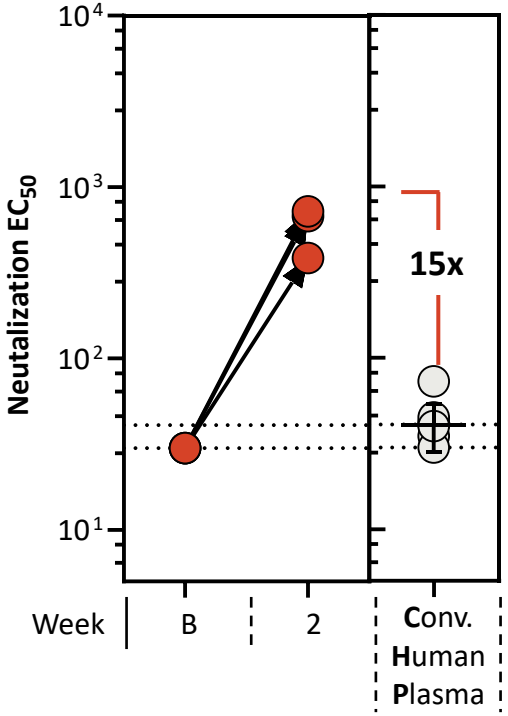
IgG Titer: Serum



Neutralization: Serum WA1



Neutralization: Serum Delta

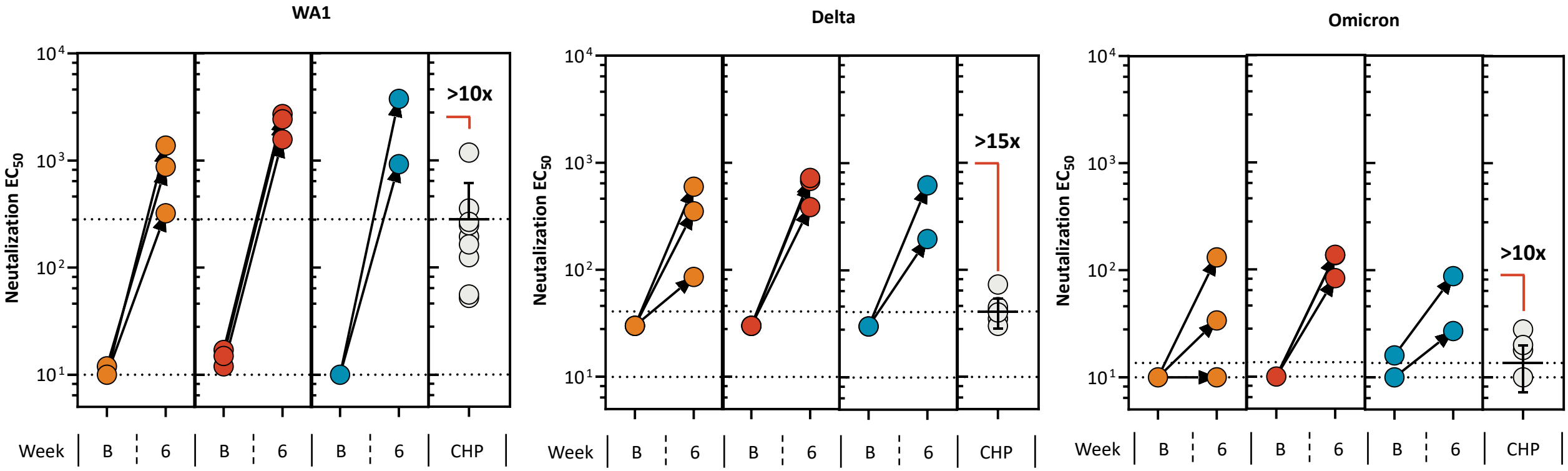


AMP-CpG-Induced Antibody Responses Effectively Neutralize Multiple Viral Variants

Neutralization: Serum

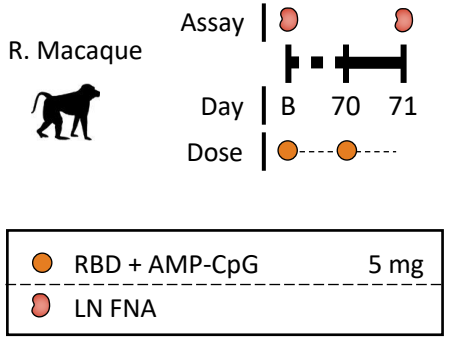
R. Macaque

RBD + AMP-CpG	5 mg
RBD + AMP-CpG	10 mg
Spike + AMP-CpG	5 mg

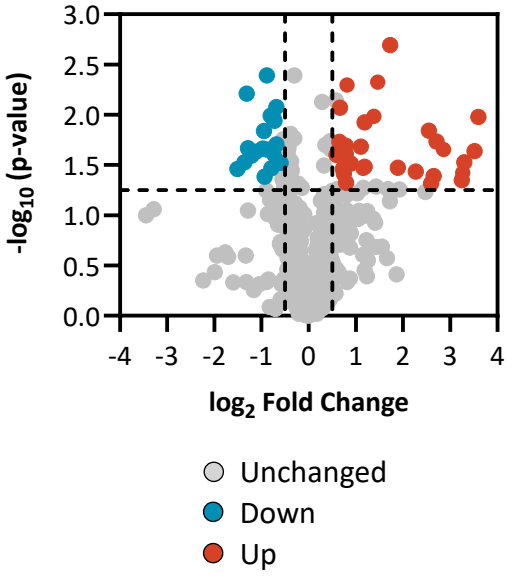


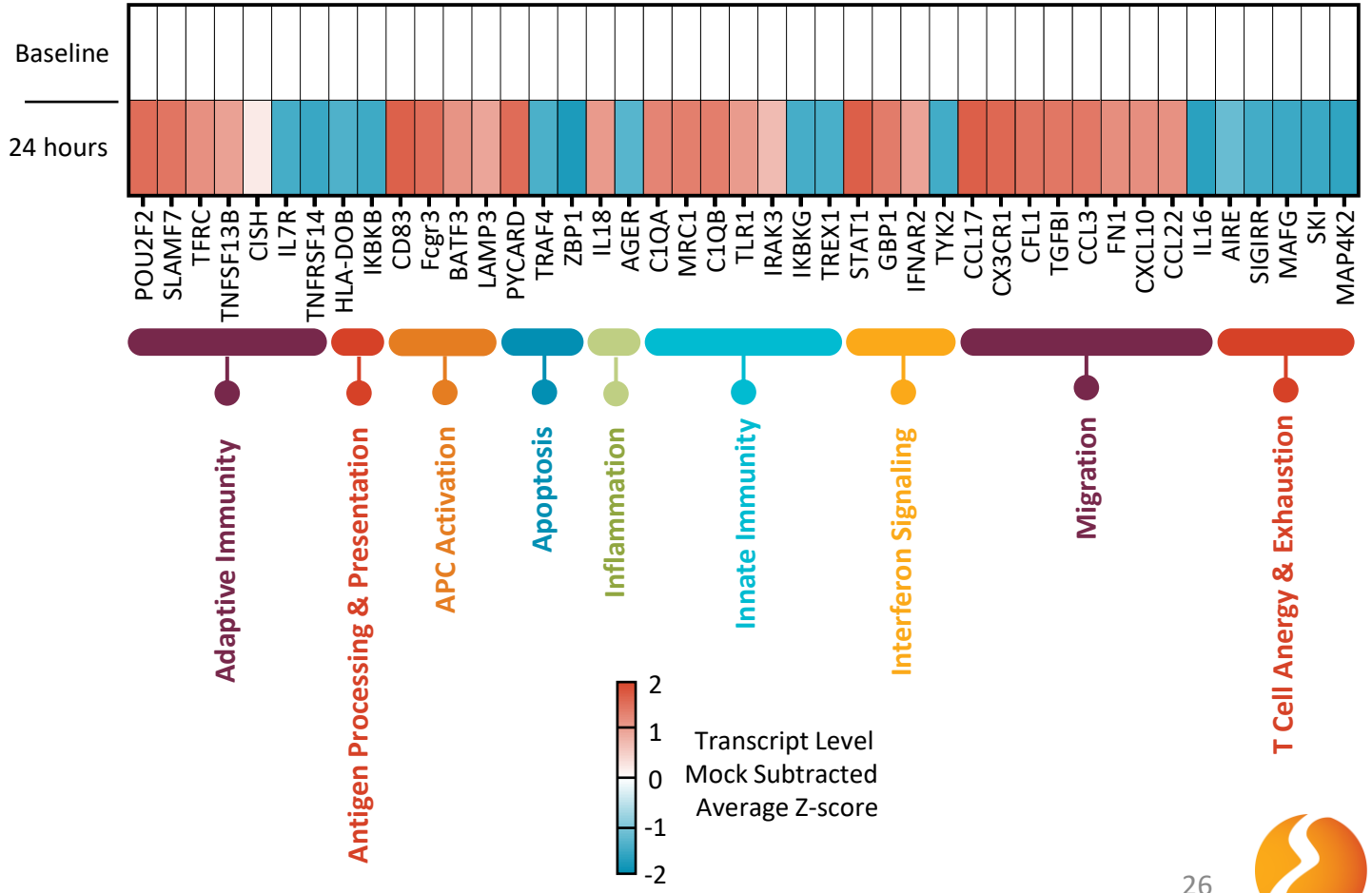
AMP-CpG Induces Transcriptional Reprogramming of the Lymph Node Immune Response in NHPs

Experimental Schema:



Lymph Node Transcriptomics: 24 hours





ELI-005: A Lymph Node Targeted Vaccine Against SC-2

- Potent T Cell Responses
- High Titer Antibody Responses: IgG and nAb
- Germinal Center B Cell Expansion
- VOC Neutralizing Antibody Responses

The AMP Platform Efficiently Targets the Lymph Nodes

- Enhanced Lymph Node Delivery and Retention
- Potent APC Activation
- Inflammatory Transcriptional Programming
- Robust Cytokine/Chemokine Milieu

ELI-005: A Lymph Node Targeted Vaccine Against COVID-19

- Potent T Cell Responses in Blood, Lung, Spleen
- Neutralizing Th1-biased Antibody Responses
- Dose Sparing
- Responses in Aged Animals
- Cross-reactive Responses to VOC

- Lymph Node Accumulation
- Potent T Cell Responses
- Cross-reactive Neutralizing Antibody Responses

Steinbuck, et al. **Science Advances**. 2021
Martin, Irvine, et al. **Biomaterials** 2021

elicio THERAPEUTICS

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CORONAVIRUS

A lymph node–targeted Amphiphile vaccine induces potent cellular and humoral immunity to SARS-CoV-2

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