A lymph node targeted CpG, TLR9 agonist induces potent activation of lymphatic innate immune responses resulting in robust cellular and humoral immunity to SARS-CoV-2

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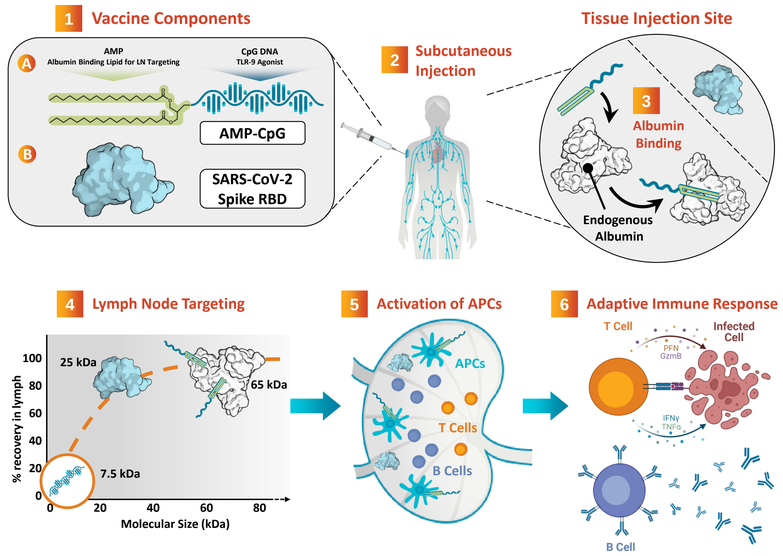
Overview

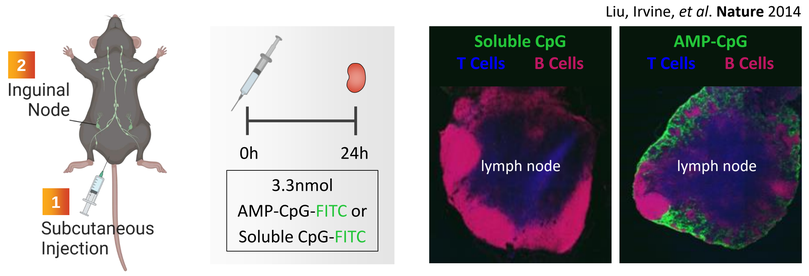
The evolving pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused worldwide waves of infection with significant morbidity and mortality, despite widespread use of effective vaccines. Ongoing emergence of mutations in SARS-CoV-2 providing partial escape from neutralizing antibodies, along with declining antibody titers within months of vaccination or natural infection, emphasize the need for more broadly protective COVID-19 vaccines. Thus, development of vaccine candidates capable of inducing more potent and durable cross-reactive T cells and antibody responses, may provide improved patient outcomes.

ELI-005 is a lymph node targeted vaccine based on the amphiphile (AMP) platform, comprised of the diacyl lipid-conjugated TLR9-agonist CpG7909 (**AMP-CpG**), admixed with SARS-CoV-2 Spike receptor binding domain (**RBD**) protein. Upon injection, AMP modification of CpG promotes its binding to endogenous albumin, which naturally drains into lymph nodes and accumulates in antigen-presenting cells (**APCs**). Subsequent robust APC stimulation results in strong lymphatic T and B cell activation.

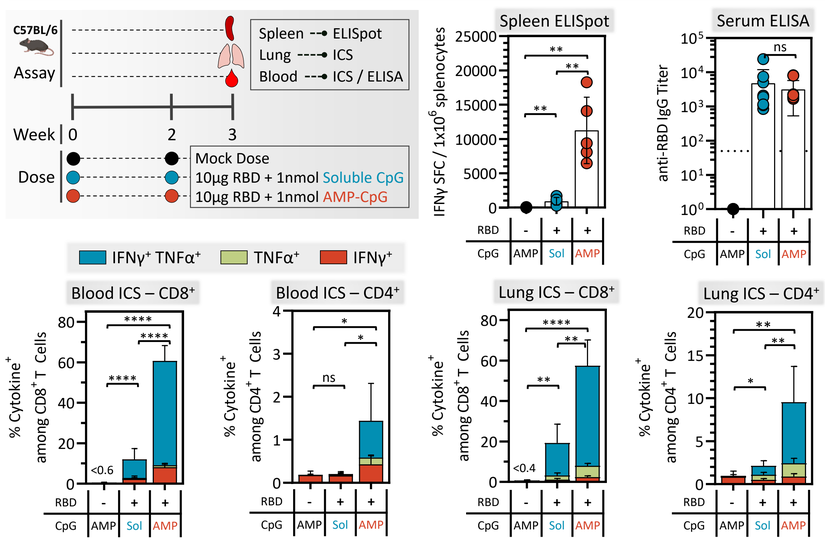
Here, we describe the effects of AMP-CpG on lymph node innate immune responses underlying the potent immunogenicity of ELI-005.

Our Platform: AMP Targets its Cargo Directly to the Lymph Nodes

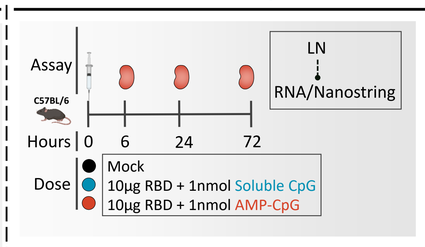


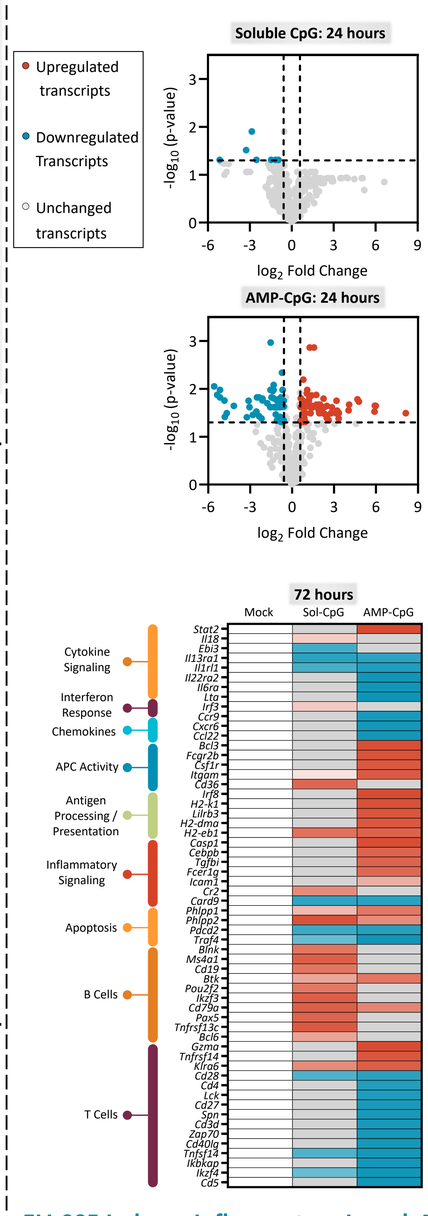


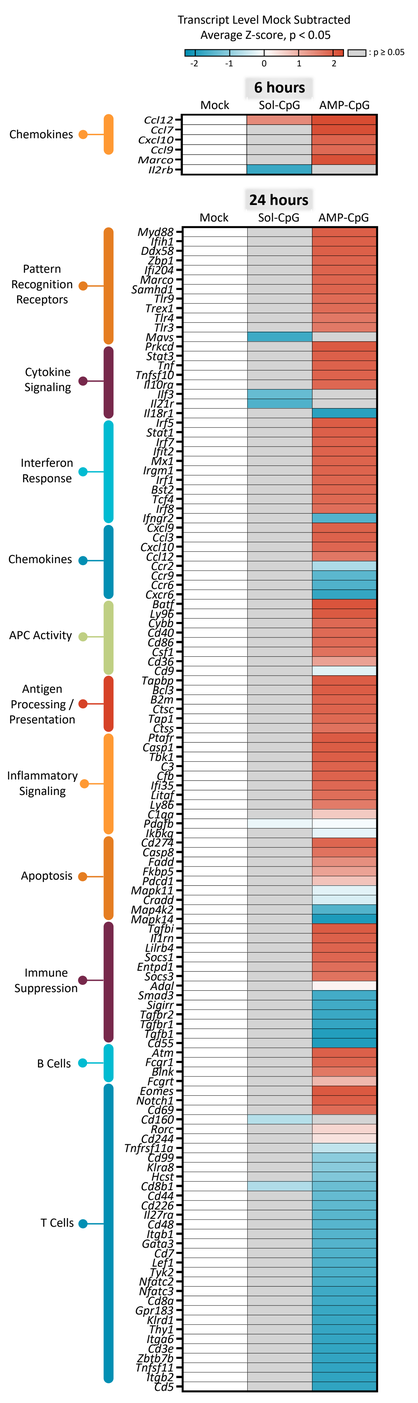
ELI-005 Induces Potent Immune Responses upon Prime-Boost Vaccination



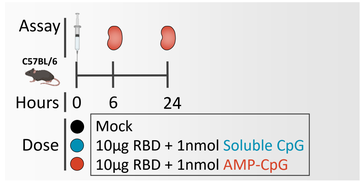
ELI-005 Induces Transcriptional Profile of Innate Cell Recruitment and Activation

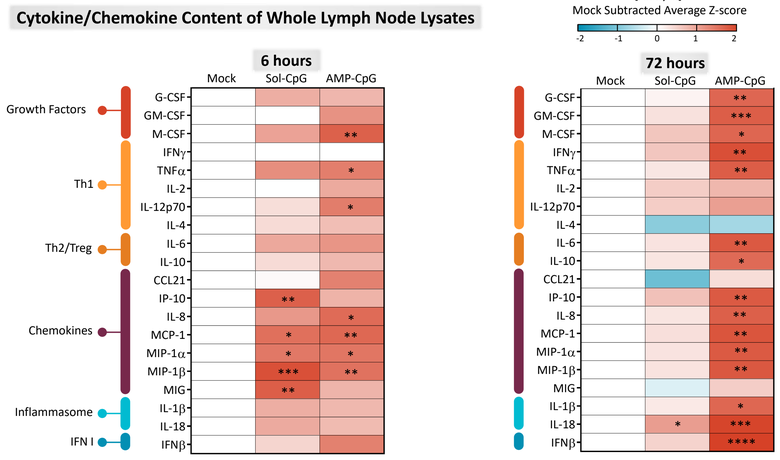




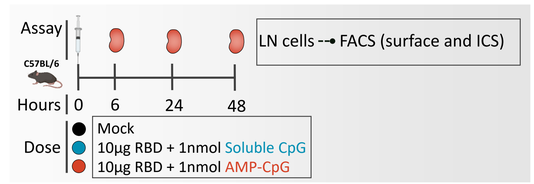


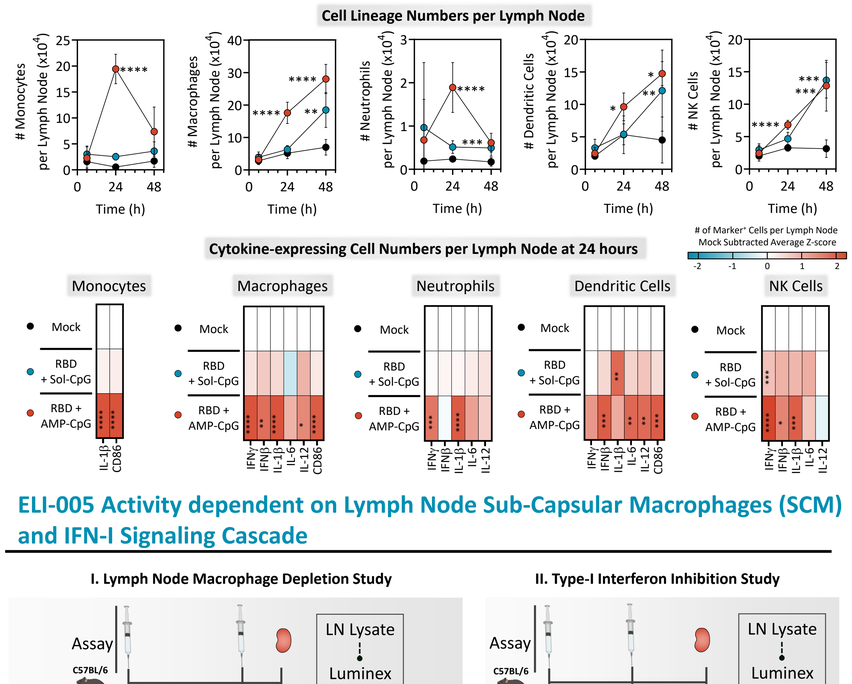
ELI-005 Induces Inflammatory Lymph Node Proteomic Milieu



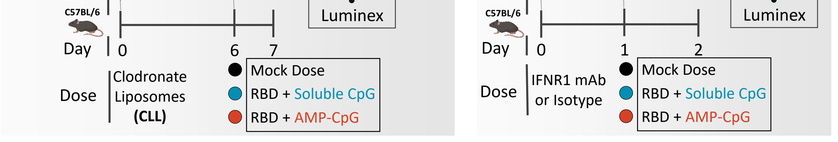


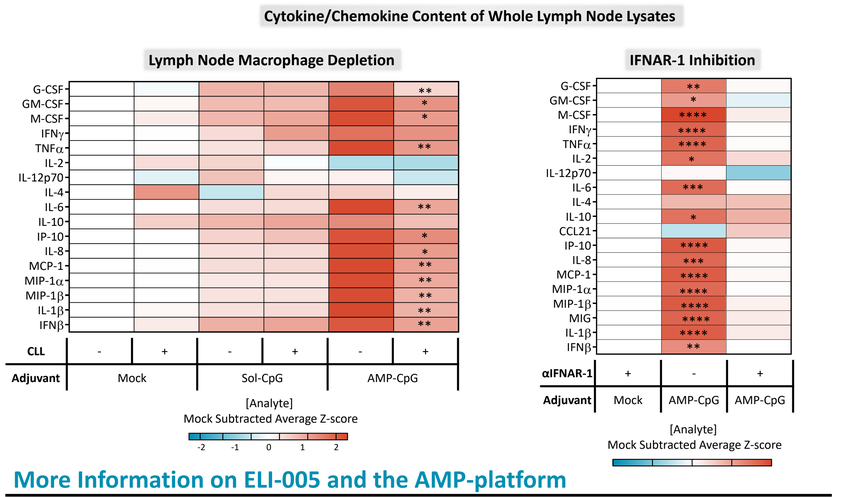
ELI-005 Potently Activates Lymph Node Cellular Innate Responses





ELI-005 Activity dependent on Lymph Node Sub-Capsular Macrophages (SCM) and IFN-I Signaling Cascade





More Information on ELI-005 and the AMP-platform

Poster 2034
ELI-005 Generates Strong Immune Responses with Long-Term Memory

Poster 2026
ELI-005 Induces Robust Immune Responses in Non-Human Primates

Poster 2005
AMP-CpG Induces Immune Responses to Epstein Barr Virus

Summary

1) AMP-CpG Enhances Lymph Node Immune Activation

- **Transcriptional reprogramming:** immune cell recruitment, co-stimulation, antigen processing and presentation and anti-viral functionality.
- **Inflammatory proteomic milieu**
- **Increased numbers of innate immune cell lineages:** monocytes, macrophages, dendritic cells, NK cells and neutrophils
- **Strong innate immune cell activation:** cytokine production and co-stimulatory CD86

2) AMP-CpG Activity is Dependent on IFNAR Signaling and Macrophage Activity

- Induction of lymph node inflammatory proteomic milieu is impaired upon macrophage depletion or IFNAR blockade

3) Robust Lymph Node Immune Activation Promotes Potent T and B Cell Immunity Against SARS-CoV-2