A Lymph Node Targeted Protein Subunit Vaccine Induces Robust Cellular and Humoral Immunity to SARS-CoV-2 in Non-human Primates

Lochana M. Seenappa[1], Aniela Jakubowski[1], Martin P. Steinbuck[1], Erica Palmer[1], Crystal Carter[2], Jane Fontenot[2], Francois Villinger[2], Lisa K. McNeil[1], and Peter C. DeMuth[1]

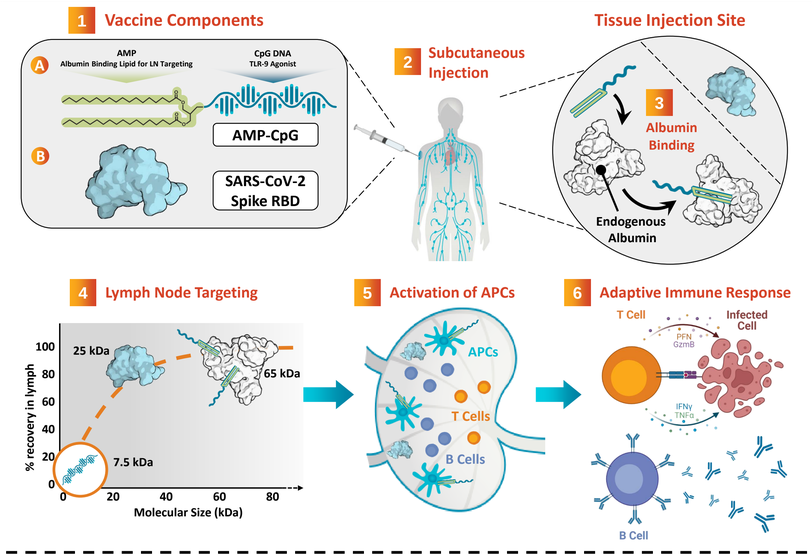
[1]Elicio Therapeutics, Inc., 451 D Street, Suite 501, Boston, MA 02210
[2]New Iberia Research Center, University of Louisiana at Lafayette, New Iberia, LA 70560

Overview

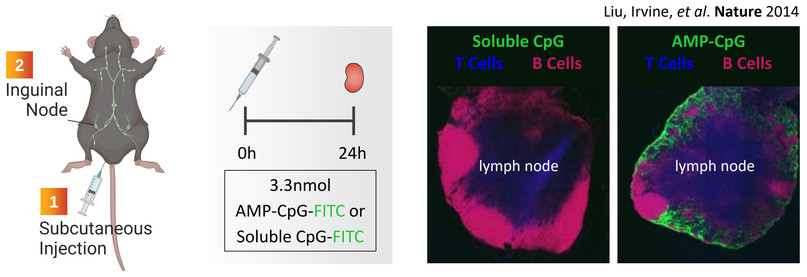
The pandemic of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in worldwide public healthcare challenges as well as social and economic consequences. Despite the success of currently authorized vaccines, the profound effects of quickly emerging variants of the virus continue to drive ongoing pandemic waves of infection. Development of safe and effective SAR-CoV-2 vaccine candidates capable of generating potent cross-reactive T cell immunity alongside cross-reactive antibody responses will be required to resolve these on-going challenges.

ELI-005 is a novel vaccine composed of Spike receptor-binding domain (**RBD**) protein admixed with Amphiphile (**AMP-CpG**), a diacyl lipid-modified CpG DNA adjuvant. AMP-CpG is known to "hitchhike" on albumin present at tissue injection sites to accumulate in lymph node resident antigen-presenting cells. In mice, ELI-005 induces long-lived and highly potent T cell responses in peripheral blood, lungs, and spleen with frequencies of circulating cytokine producing CD8⁺ T cells rising to >60%, greatly outperforming soluble CpG comparators. Cross-reactive serum IgG responses specific to several variants of concern (VOC) are observed up to 32 weeks after immunization in mice. To further evaluate the potential of adjuvant lymph node targeting, ELI-005 with AMP-CpG was investigated in non-human primate for safety and immunogenicity.

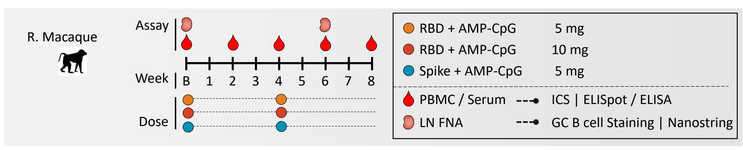
Our Platform: AMP Targets its Cargo Directly to the Lymph Nodes



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



Methods



IFNγ ELISpot: 200,000 PBMCs were added to IFNγ ELISpot plates for overnight stimulation with WH-01, Beta and Delta peptides. The spots were developed using Monkey IFNγ ELISpotPLUS kits.

Intracellular Cytokine Staining (ICS): PBMCs supplemented with co-stimulation were stimulated for 8h with WH-01, Beta and Delta peptides and stained for IFNγ producing T cells the next day.

Germinal Center B cell Staining: Lymph Node cells were incubated with biotinylated RBD complexed with Streptavidin-APC and stained for RBD⁺ Germinal Center B cells (CD20⁺ Bcl6⁺ Ki67⁺).

ELISA: Antibody titers in sera against RBD were determined using HRP-goat anti-human IgG at an absorbance cutoff of 0.5 OD.

RBD Neutralizing Antibody Assay: SARS-CoV-2 pseudovirus neutralization assay was performed by Genecopoeia (Nie, J. *et al*. **Nature Protocols** 2020).

LN Nanostring: Lymph nodes were assessed using the nCounter NHP Immunology Panel of 770 macaque immune response gene by NanoString Technologies.

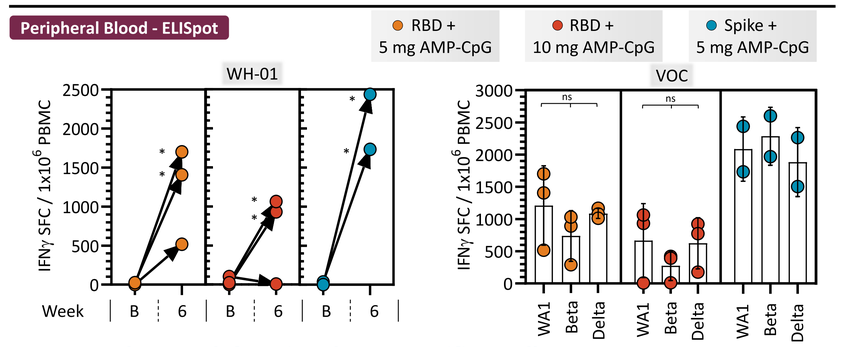
More Information on ELI-005 and the AMP-platform

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

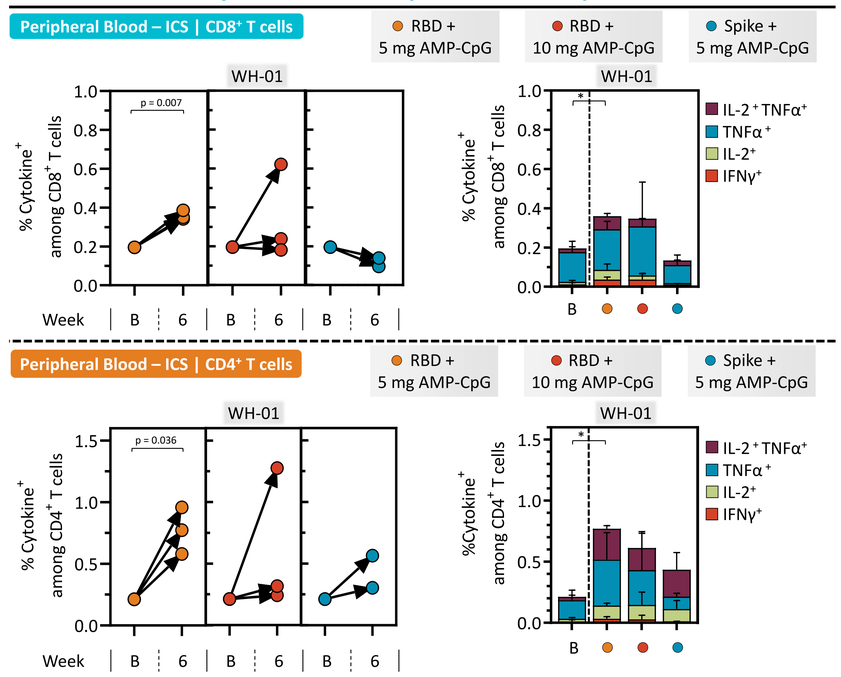
Poster 2047
AMP-CpG Activates the Lymphatic Innate Immune System

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

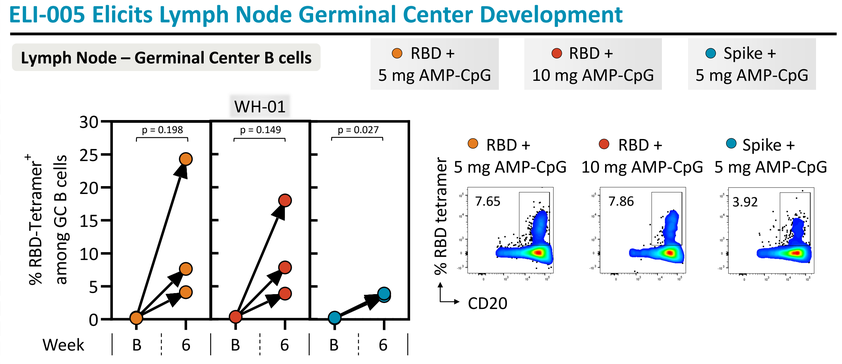
ELI-005 Induces Robust T cell Responses to Multiple Variants of SARS-CoV-2



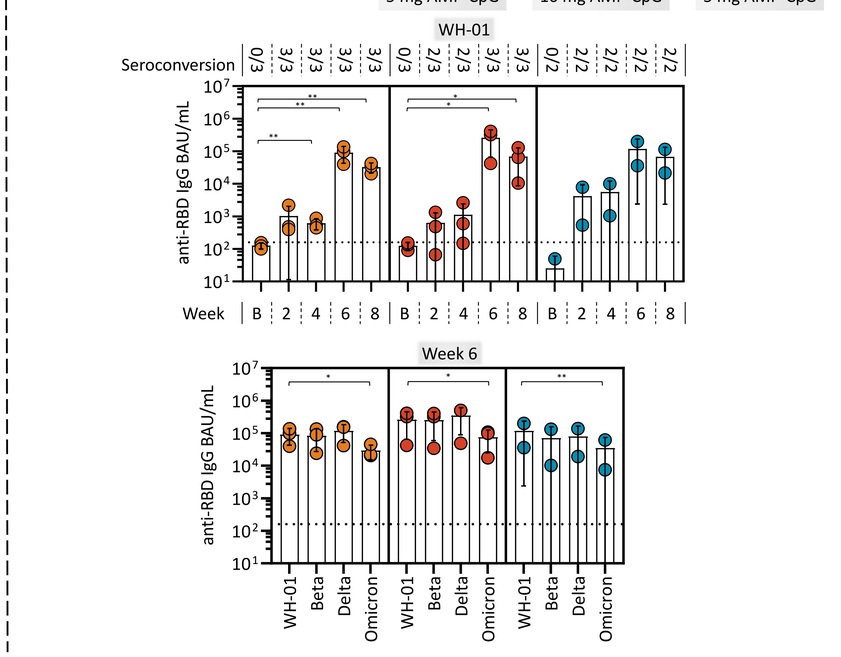
ELI-005 Induces Polyfunctional RBD-specific T cell Responses



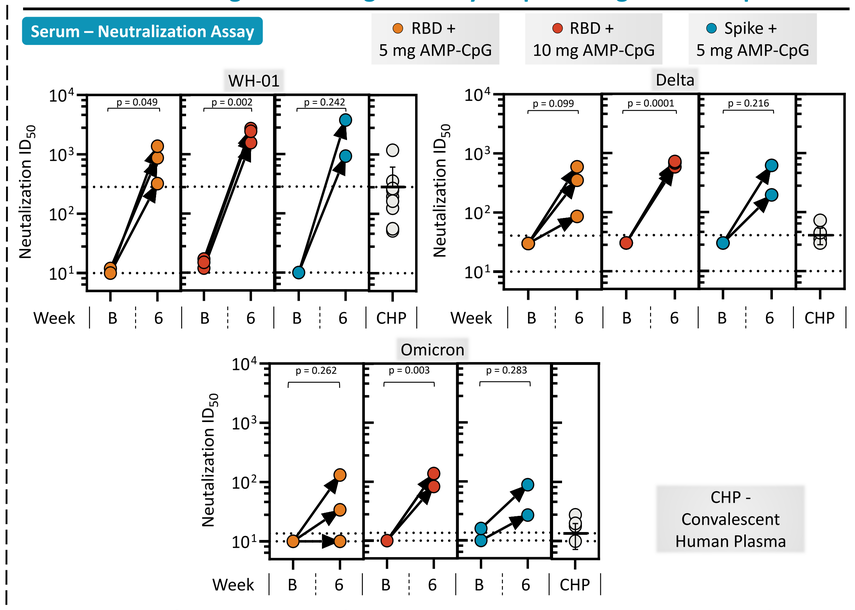
ELI-005 Elicits Lymph Node Germinal Center Development



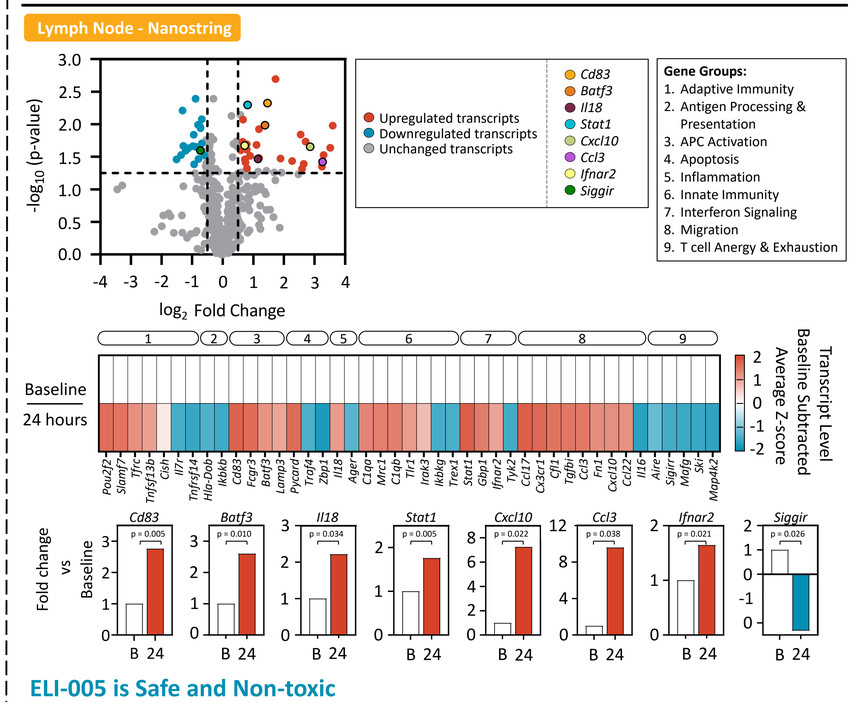
ELI-005 Stimulates Rapid and Potent Humoral Responses to Multiple VOC



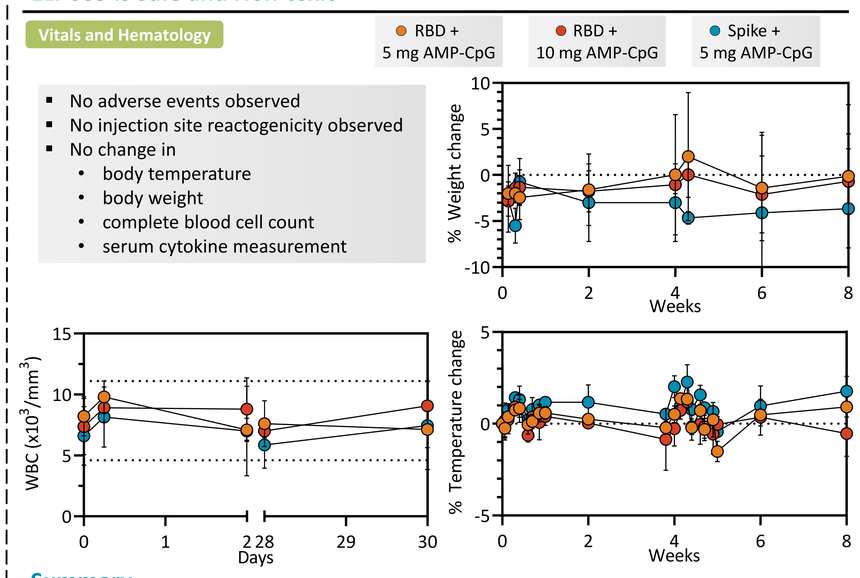
ELI-005 Elicits Strong Neutralizing Antibody Responses against Multiple VOCs



ELI-005 Stimulates Dynamic Changes in Immune Gene Transcript Levels



ELI-005 is Safe and Non-toxic



Summary

1. ELI-005 induced polyfunctional CD8⁺ and CD4⁺ T cells in peripheral blood of NHPs
   - 0.8% of CD4⁺ and 0.45% of CD8⁺ T cells produce IL-2, TNFα, IFNγ or combinations
2. ELI-005 rapidly induced potent antibody responses along with strong neutralizing antibody responses against multiple VOCs
   - Peak responses IgG at week 6 elevated up to 5,000-fold relative to baseline
   - Antibody responses exceed the ability of convalescent human plasma to neutralize VOC
3. ELI-005 vaccination safe and non-toxic.