September 4th, 2025

Acuitas Therapeutics and Collaborators Demonstrate Strong Protection Against *P. vivax* Malaria with mRNA-LNP Vaccine

Vancouver, B.C. – Acuitas Therapeutics recently announced the publication of a new study in *Molecular Therapy - Nucleic Acids*, titled "mRNA-LNP vaccine encoding the *Plasmodium vivax* circumsporozoite protein is highly immunogenic and confers protection in mice."

Co-authored by Dr. Ying Tam, Chief Scientific Officer from Acuitas Therapeutics, in collaboration with the University of Pennsylvania, Kanazawa University, University of South Florida, and the Walter Reed Army Institute of Research, the study demonstrates that a nucleoside-modified mRNA-lipid nanoparticle (LNP) vaccine expressing the *Plasmodium vivax* (*P. vivax*) circumsporozoite protein (PvCSP) can generate strong antibody and T cell responses and provide high levels of protection in a preclinical mouse model of malaria.

P. vivax is the leading cause of malaria across the Asia-Pacific and South America and features dormant liver stages that cause frequent relapses, creating major challenges for control and prevention. With malaria responsible for 249 million cases and 608,000 deaths in 2022 (World Malaria Report 2023), and few safe or effective vaccines available, new approaches are urgently needed.

In the study, researchers tested two distinct PvCSP mRNA-LNP constructs. The construct, which included both a native signal peptide (SP+) and a glycosylphosphatidylinositol anchor (GPI+), drove strong cell-surface expression and significantly higher antibody responses compared to the construct lacking the GPI anchor, despite lower protein expression *in vitro*. Both vaccines elicited T cell responses in the spleen and liver. Additional key findings of the research include:

- Vaccination schedule strongly influenced protection, with protection rates rising in dosing regimens that contained a longer interval between the second and third dose. Protection rates were: 70% when dosed at the 0-, 1-, and 2-month mark; 80% when dosed at the 0-, 1-, and 4-month mark; and 90% when dosed at the 0-, 1-, and 6-month mark.
- Intradermal (ID) and intramuscular (IM) routes produced strong, dose-dependent antibody responses, with ID outperforming IM at lower doses (10 ug). Intravenous (IV) delivery yielded negligible responses.
- Antibody titres against the PvCSP repeat region correlated with protection, while antibody responses against the AGDR tetramer (a common target epitope for malaria vaccines) were modest and not protective. Similarly, the IgG2a/IgG1 ratio was not associated with protection, but the IgG avidity to the repeat region was correlated with protection.

The results highlight how both vaccine design, administration route and the timing of doses play a decisive role in achieving effective immunity, with delayed mRNA-LNP doses offering the strongest protection. This proof-of-concept establishes mRNA-LNP technology as a compelling tool for addressing *P. vivax* malaria and informs strategies that could accelerate global malaria prevention.

Click here to read the full publication.

About Acuitas Therapeutics

Acuitas Therapeutics, Inc. is a Vancouver-based company focused on developing and optimizing lipid nanoparticle (LNP) delivery systems for nucleic acid-based therapeutics. They collaborate with pharmaceutical and biotech companies, academic researchers, and global health organizations to advance a broad range of medicines for a variety of diseases.

Acuitas' clinically validated LNP technology has had a profound global impact — most notably enabling the Pfizer-BioNTech COVID-19 vaccine, **COMIRNATY®**, which has protected billions of people in more than 180 countries. The technology also enables **ONPATTRO®** by Alnylam Pharmaceuticals, the first FDA-approved RNAi therapeutic for treating the rare and fatal disease transthyretin amyloidosis. More recently, Acuitas' LNP technology has delivered other groundbreaking firsts: the **first in-human proof of concept** for genome base editing and the **first personalized CRISPR therapy.**

Today, they are advancing next-generation LNP to support a variety of therapeutic modalities. This includes targeted LNP for extrahepatic and *in vivo* CAR-T cell therapies, epigenetic medicines to modulate gene expression without altering DNA, multivalent vaccines for infectious diseases — such as malaria, HIV/AIDS, and tuberculosis — as well as oncology vaccines, including personalized cancer vaccines.

For more information, visit www.acuitastx.com.

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