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Acuitas Therapeutics Contributes to New Insights into Broadly Neutralizing Antibodies Induced by COVID-19 mRNA Vaccines

Vancouver, B.C. – Acuitas Therapeutics today announced the publication of a new study in *Science Translational Medicine*, titled "Nonstabilized SARS-CoV-2 spike mRNA vaccination induces broadly neutralizing antibodies in nonhuman primates." The research provides critical insight into mRNA vaccine design in which the traditional stabilization of mRNA-encoded SARS-CoV-2 spike protein is not required to elicit broadly neutralizing antibodies (bnAbs). This highlights a new set of considerations for developing next-generation, pan-coronavirus vaccines.

The study – which used Acuitas' proprietary lipid nanoparticle (LNP) technology as the delivery mode for the nucleoside-modified mRNA vaccines – was co-authored by Drs. Ying Tam and Christopher Barbosa from Acuitas Therapeutics, in collaboration with Duke University School of Medicine, the University of North Carolina at Chapel Hill, the University of Pennsylvania, and the National Institutes of Health. It directly explores previous assumptions that diproline substitutions were necessary to stabilize the mRNA-encoded spike protein to enhance the potency of the vaccine and better elicit bnAbs against SARS-CoV-2. However, this new research demonstrates that vaccination with ancestral SARS-CoV-2 spike mRNA lacking these diproline substitutions was equally effective.

Additionally, the research revealed that the mRNA-LNP vaccines induced two distinct groups of bnAbs targeting preserved epitopes on the receptor binding domain (RBD) of the SARS-CoV-2 spike protein:

- **Outer Face Targeting Antibodies:** One group of antibodies targeted the outer face of the RBD. These antibodies were shown to neutralize all tested SARS-CoV-2 variants of concern pseudotyped viruses, including the contemporary Omicron XBB.1.5. This indicates that a key neutralizing epitope remains conserved even in newer variants.
- **Inner Face Targeting Antibodies:** In contrast, another group of vaccine-induced antibodies targeted the RBD's inner face. These antibodies provided protection against multiple sarbecoviruses, a subgenus of coronaviruses that includes SARS-CoV-2 and

bat coronaviruses with the potential for human infection. Crucially, one of these antibodies, DH1338, protected mice challenged with a pre-emergent bat coronavirus, preventing weight loss and lung damage. While effective against sarbecoviruses, inner face targeting antibodies did not neutralize Omicron variants, highlighting the need for diverse antibody responses.

These findings suggest that next-generation pan-coronavirus vaccines incorporating mRNA encoding non-stabilized spike protein will be highly effective at eliciting antibodies that target the inner and outer faces of the spike protein RBD and provide broad neutralizing activity against SARS-CoV-2 variants of concern and sarbecoviruses. Leveraging LNP will be key to rapidly exploring and advancing such next-generation designs that can provide broad protection against current and emerging sarbecoviruses and SARS-CoV-2 variants.

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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