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Acuitas Therapeutics and Researchers at the University of Pennsylvania Demonstrate Enhanced T Cell Immunity with IL-12 mRNA-LNP Adjuvant

Vancouver, B.C. – Acuitas Therapeutics today announced the publication of a new study in Science Immunology, titled "An *IL12* mRNA-LNP adjuvant enhances mRNA vaccine-induced CD8 T cell responses." The study demonstrates that incorporating an mRNA-encoded interleukin-12 (IL-12) lipid nanoparticle (LNP) adjuvant into mRNA vaccines can substantially enhance CD8+ T cell responses. IL-12 has previously been shown to increase immunity against infectious parasites, bacteria and viruses as well as cancer.

Co-authored by Dr. Ying Tam, Chief Scientific Officer at Acuitas, in collaboration with researchers from the University of Pennsylvania, the study found that while endogenous IL-12 is not required for CD8+ T cell responses to mRNA vaccines, the deliberate inclusion of an IL-12 mRNA-LNP adjuvant led to much stronger T-cell-mediated immunity, offering a strategy to tailor the magnitude of immune responses to vaccinations.

In a preclinical model, immunization with a model tumour antigen in the presence of the IL-12 mRNA-LNP adjuvant resulted in a more than fourfold expansion of antigen-specific circulating CD8+ T cells. Furthermore, inclusion of the IL-12 mRNA-LNP adjuvant with SARS-CoV-2 and influenza mRNA-LNP vaccines increased the number of IFN-γ+ and TNF-α+ producing effector CD8+ T cells by two- to threefold. Finally, using a cytotoxicity assay, IL-12 mRNA-LNP nearly doubled the ability of the CD8+ effector T cells to specifically kill target cells – with 66% of target cells eliminated, compared to 30% with standard mRNA vaccination alone.

Beyond systemic effects, the IL-12 mRNA-LNP markedly enhanced the generation of tissue-resident memory T cells (TRM), which are essential for long-term protection at tissue barriers such as the lung, skin, and gut. In the lung, TRM populations increased by approximately two- to fourfold, with similarly robust gains in the skin and gut.

The enhanced T cell immunity translated to improved disease outcomes in animal studies including in the *Listeria monocytogenes*-OVA model of infection. In this disease mouse model, mice receiving the IL-12 adjuvant showed a ~100-fold reduction in bacterial burden. Similarly in a B16F0-OVA melanoma cancer model, the inclusion of the IL-12 mRNA-LNP adjuvant delayed

tumour growth and improved survival. Importantly, these immune benefits were achieved without detectable signs of liver toxicity.

These findings reveal a strategy for optimizing mRNA vaccine performance by pairing antigen delivery with cytokine-driven immune modulation. The ability to expand and sustain effector and memory T cell populations may help address key challenges in vaccine design – particularly for cancers and infectious diseases in which robust and durable T cell responses are needed.

Click here to read the full publication.

About Acuitas Therapeutics

Acuitas Therapeutics is a global leader in lipid nanoparticle (LNP) technology and partners with pharmaceutical and biotechnology companies, as well as non-governmental organizations and academic institutions, to advance nucleic acid therapeutics into clinical development and commercialization. Acuitas' clinically validated LNP technology has enabled COMIRNATY® (Pfizer-BioNTech), the first approved mRNA vaccine, which has been deployed globally, and ONPATTRO® (Alnylam), the first approved RNAi therapeutic. Acuitas has also enabled k-abe, the first LNP enabled personalized CRISPR gene editing therapy, in addition to the first in-human genome base editing trial.

Current efforts focus on enhancing LNP to advance novel gene therapies, in addition to the identification of potent new lipids to enable partners to develop vaccines for infectious diseases, multivalent vaccines, and novel therapeutic vaccines against cancer, including personalized cancer vaccines.

For more information, visit www.acuitastx.com.

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