

Research leads to promising combination therapy for type 1 diabetes

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A promising therapeutic candidate for type 1 diabetes combines anti-IL-21 antibody with the diabetes drug liraglutide. Credit: La Jolla Institute for Immunology

Translational research led by scientists at La Jolla Institute for Immunology (LJI) has resulted in a promising combination therapeutic candidate for adults with recent-onset type 1 diabetes.

The [combination therapy](#) was recently tested in a randomized, double-blind, placebo-controlled, phase 2 trial run and funded by

pharmaceutical company Novo Nordisk. The results, published recently in *The Lancet Diabetes and Endocrinology*, point to a potential way to treat the autoimmune disease without leaving the body vulnerable to infectious disease.

The therapeutic candidate combines anti-IL-21 antibody with the [diabetes](#) drug liraglutide. This two-pronged approach is based on research findings from the lab of LJI Professor Matthias von Herrath, M.D., who also serves as vice president and senior medical officer, Global Chief Medical Office, at Novo Nordisk.

"This is the first large trial for a combination [therapy](#), and the data suggest it has value for patients," says von Herrath. "The groundwork for choosing a combination therapy was laid through preclinical work at La Jolla Institute."

Type 1 diabetes is an autoimmune disease that occurs when the body's own T cells mistakenly target insulin-producing [beta cells](#) in the pancreas. When beta cells die, the body loses its ability to regulate glucose levels, which can eventually lead to severe organ damage and death.

One challenge in treating type 1 diabetes is that therapies targeting "system-wide" T cell responses also run the risk of hindering the immune system's ability to fight real threats, such as viruses and bacteria.

The von Herrath Laboratory at LJI is focused on uncovering the molecular triggers of type 1 diabetes. Their work has pointed to ways to modulate parts of the immune system without suppressing overall immune system function.

In 2012, the von Herrath Laboratory published a study in *Immunity*

showing the importance of the interleukin (IL)-21 receptor in allowing harmful T cells into the pancreas. Follow-up studies showed that an anti-IL-21 antibody could interrupt that signal and potentially shield the pancreas from attack.

Importantly, because the anti-IL-21 antibody appears to only affect a group of T [cells](#), von Herrath and his colleagues believed the antibody might help treat type 1 diabetes without dampening the overall immune system.

In 2017, Novo Nordisk published a pre-[clinical study](#) in the Journal of Autoimmunity showing the effects of a combination therapy that consisted of anti-IL-21 monoclonal antibody combined with the FDA-approved type 2 diabetes drug liraglutide. Liraglutide has been shown to protect beta cell function. The study, which included von Herrath as a co-author, showed that this combination could reverse type 1 diabetes in a mouse model.

For the new study, von Herrath and his collaborators tested the combination therapy in a randomized, parallel-group, placebo-controlled, double-dummy, double-blind, phase 2 trial. Compared with the placebo group, patients who received the 54-week course of treatment had higher levels of endogenous insulin secretion. No safety concerns were identified.

The researchers followed up with study participants for 26 weeks after the treatment ended and found that the effects diminished during that time. They also found no lasting adverse changes to the immune system. The researchers note that the combination therapy will need to be assessed for long-term safety and efficacy in a phase 3 clinical trial.

Going forward, von Herrath and his laboratory at LJI are focused on translating their findings on both type 1 diabetes and type 2 diabetes

from the laboratory to the clinic.

More information: Matthias von Herrath et al, Anti-interleukin-21 antibody and liraglutide for the preservation of β -cell function in adults with recent-onset type 1 diabetes: a randomized, double-blind, placebo-controlled, phase 2 trial, *The Lancet Diabetes & Endocrinology* (2021). DOI: [10.1016/S2213-8587\(21\)00019-X](https://doi.org/10.1016/S2213-8587(21)00019-X)

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