

Researchers Use Nanoparticle “Vaccine” to Cure Type 1 Diabetes in Mice

Using an innovative nanotechnology-based “vaccine,” researchers were able to successfully restore normal blood sugar in mice with type 1 diabetes, and also slow the onset of diabetes in mice at risk for the disease. The study, co-funded by JDRF and published today in the online edition of the journal *Immunity*, has several key implications:

- First, it provides important new insights into how to stop the immune attack that causes type 1 diabetes.
- Second, it underscores the potential of “antigen-specific” therapies. Because the nanoparticle vaccine was designed with specific immune system proteins, it effectively blunted the targeted autoimmune response that causes diabetes without compromising the overall immune system – an issue that continues to be a challenge in developing treatments for diabetes.
- And third, it suggests that antigen-specific nanovaccines, because of the effectiveness shown here, might also be developed to treat other autoimmune diseases, such as multiple sclerosis and rheumatoid arthritis. That could make the science more attractive to drug development companies.

Researchers from the University of Calgary in Alberta, led by Dr. Pere Santamaria, were looking to halt the autoimmune response that causes type 1 diabetes, but do so without damaging the immune cells that control and regulate the immune system or that protect against infections. So the team focused on developing a highly targeted antigen-specific immunotherapy – one, they explained, that could address the “internal tug-of-war between aggressive T cells that want to cause the disease and weaker T cells that want to stop it from occurring.”

The researchers produced a unique vaccine comprising nanoparticles, which are thousands of times smaller than the size of a cell. They coated the particles with type 1 diabetes–relevant peptides, or protein fragments, that were bound to certain molecules that play a critical role in immune cell communication (called MHC molecules).

In the mice, the nanoparticle treatment expanded a type of regulatory T cell -- these cells ultimately suppressed the aggressive immune attack that destroys the insulin-producing beta cells of the pancreas. The researchers noted that the expanded cells shut down the immune attack by preventing autoreactive immune cells from being stimulated, either by the peptide contained in the vaccine or by any other diabetes autoantigen presented simultaneously by antigen-presenting cells. With the immune response that causes diabetes blocked, mice with type 1 diabetes regained normal blood sugars. And those that would have contracted the disease didn't.

The study also provides important – and promising – insight into the ability to translate these findings into therapeutics for people: Nanoparticles that were coated with molecules specific to *human* type 1 diabetes were able to restore normal blood sugar levels in a humanized mouse model of diabetes (that is, a mouse that has been genetically altered to biologically simulate type 1 diabetes in people).

According to Teodora Staeva, Ph.D., JDRF Program Director of Immune Therapies, a key finding from the Alberta study is that only the immune cells that specifically focus on aggressively destroying beta cells (or on regulating these aggressive cells) actually responded to the vaccine therapy. That means the treatment did not compromise the rest of the immune system – a key consideration if the treatment is to be safe and effective in an otherwise healthy person with type 1 diabetes. “The potential that nanoparticle vaccine therapy holds in reversing the immune attack without generally suppressing the immune system is significant,” said Staeva. “Dr. Santamaria’s research has provided both insight into pathways for developing new immunotherapies as well as proof-of-concept of a specific therapy that exploits these pathways for preventing and reversing type 1 diabetes.”

The nanoparticle vaccine technology developed by Dr. Santamaria and used in the study has been licensed by Parvus Therapeutics, Inc., a biotechnology company spun out from the University Technology International LP, the technology transfer and commercialization center for the University of Calgary. Parvus is focused on the

development and commercialization of a nanotechnology-based therapeutic platform for the treatment of type 1 diabetes.