# 'Nanovaccine' reverses type 1 diabetes in mice

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A new study, published online April 8 by Cell Press in the journal *Immunity*, describes a unique therapeutic "nanovaccine" that successfully reverses diabetes in a mouse model of the disease. In addition to providing new insight into diabetes, the research also reveals an aspect of the pathogenesis of the autoimmune response that may provide a therapeutic strategy for multiple autoimmune disorders.

Type 1 diabetes (T1D) is a chronic autoimmune disease that results from destruction of insulin-producing pancreatic cells by certain white blood cells, called T cells. "Unfortunately, eliminating the rather extensive repertoire of harmful T cells that attack the pancreas cannot currently be done without also eliminating T cells that protect us from infections and cancer," explains Dr. Pere Santamaria, from the Julia McFarlane Diabetes Research Centre at the University of Calgary in Alberta.

Dr. Santamaria and colleagues wanted to find a way to counteract the harmful autoimmune response without compromising general immunity. They discovered that our bodies have a built-in mechanism that tries to stop the progression of autoimmune diseases like T1D. "Essentially, there is an 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," says Dr. Santamaria.

The researchers also developed a unique and inventive nanotechnology-based "vaccine" that selectively boosted the weak white blood T cells, enabling them to effectively counter the damage caused by their

overactive T cell relatives. The vaccine consisted of nanoparticles (NPs, spheres thousands of times smaller than a single cell of the body) "coated" with individual T1D-relevant protein fragments bound to self MHC molecules (pMHC). MHC molecules are used by another type of white blood cell, called an "antigen presenting cell" to "present" antigen to T cells as part of all immune responses.

Using a mouse model of T1D, the researchers discovered that their nanovaccine blunted T1D progression in prediabetic mice and restored normal blood sugar in diabetic mice. Further, NPs displaying human diabetes-relevant complexes restored normal blood sugar levels in a humanized model of diabetes. The authors pointed out that only the disease-generated white blood cells responded to the pMHC-NP therapy, so the treatment would be inconsequential in healthy individuals because it would not have nonspecific effects on the immune system.

"If the paradigm on which this nanovaccine is based holds true in other chronic autoimmune diseases, such as multiple sclerosis, rheumatoid arthritis, and others, pMHC-nanovaccines might find general applicability in autoimmunity," suggests Dr. Santamaria. "In principle, the pMHC nanovaccines could be engineered with any disease-relevant pMHC complex as long as it is involved in the diseases process."

**More information:** Tsai et al.: “Reversal of Autoimmunity by Boosting Memory-like Autoregulatory T Cells.” Publishing in Immunity 32, Vol, 4, April 23, 2010. www.immunity.com/

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