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A step towards a type 1 diabetes vaccine by using nanotherapy

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For the first time, liposomes that imitate cells in the process of natural death have been used to treat diabetes. Researchers at Germans Trias Research Institute (at UAB-Campus of International Excellence Sphere) generated liposomes in collaboration with professionals from the ICN2. The journal *PLOS ONE* publishes the work. The next steps are to confirm the efficacy in vivo with cells from patients and to carry out clinical trials to prevent the disease and to cure it.

Two years ago, the Immunology of Diabetes Research Group at the Germans Trias Research Institute (at Universitat Autònoma de Barcelona - Campus of International Excellence Sphere) reported a new experimental immunotherapy that prevented the onset of type 1 diabetes in mice predisposed to the disease. This work led to more studies with the support of the Spanish government, Catalan government and private patrons. The article published today in *PLOS ONE* describes a new step towards the creation of a vaccine, which in the medium-term could be capable of preventing and even curing the disease in humans.

Initially, the researchers avoided the destruction of the insulin-producing pancreatic cells (beta cells) in the body by modifying the individual's immune cells, known as dendritic cells. This important step requires the extraction of the subjects' dendritic cells for their subsequent manipulation and re-injection. The process is complex and costly. In a new study with mice, researchers have achieved the same effect with a much simpler process. Nanoparticles called liposomes are created in the laboratory; when they are introduced into the body they arrest the

destruction of the beta cells and avoid diabetes development. This technique could be a much better candidate for a human vaccine. The invention is commercially protected and an international patent is pending.

Droplets of fat and water which can be produced on a large scale

Liposomes have been used in several medical treatments. They are not cells, but droplets with an external fat membrane, similar to cell membranes. They can be made using a very specialized process, but one that is easy and safe and also easy to scale up.

The key: beta cells in process of natural death

The diameter of the liposomes created for this collaborative work measure from half to one micron. They were specifically generated to imitate beta cells of the pancreas that are in the process of programmed cell death (apoptosis). As the researchers showed during the previous studies, this is the way to prevent the body from destroying the beta cells and to allow it to develop immunological tolerance. The Catalan researchers are the first group in the world to use liposomes that imitate naturally dying cells to fight against diabetes. The Universities of Barcelona and Lleida also contributed to this work.

Next steps

After showing that liposomes prevent the onset of type 1 diabetes in mice, the next steps are to test it in human cells in vitro, to start clinical trials on human candidates for preventive vaccination and to cure the disease by combining the vaccine with regenerative therapies. The Germans Trias Institute plans to carry out these steps with patients at the

hospital and to optimize the product by dosage and guideline studies. Researchers plan to optimize the product for personalization. To achieve these objectives, more competitive funding will be necessary from public agencies. The group is also studying collaborations and investment opportunities from the pharmaceutical industry. Private funding continues to be important and the Germans Trias Institute is studying the possibility of organizing a local campaign.

Growing incidence and complex consequences

Type 1 diabetes is an illness in which the body does not recognize the beta cells of the pancreas as its own and destroys them. The organ produces less and less insulin, the hormone that allows us to process the sugar we eat. Patients must prick their fingers several times a day to check blood sugar levels and inject themselves with insulin in the stomach or other parts of the body. This constant control is not always easy, and having too much or too little insulin can have severe consequences. The most serious is that in the long term, hyperglycemia provokes retinal damage that can lead to blindness, renal insufficiency, destruction of nerve fibers or what is called "diabetics foot" in which ulcers form, leading eventually to the need to amputate.

The causes of the disease are unknown, although there are both genetic and environmental factors involved. About 0.3% of the population is affected and the incidence is increasing by 3-4% a year. It usually appears in children and young adults and it is incurable. This immunotherapy presents a possible solution for type 1 diabetes.

More information: "Use of Autoantigen-Loaded Phosphatidylserine-Liposomes to Arrest Autoimmunity in Type 1 Diabetes." *PLOS ONE.* DOI: 10.1371/journal.pone.0127057