

## Researchers extend innovative research towards a cure for type I diabetes

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Associate Professor Shane Grey, of Sydney's Garvan Institute of Medical Research, together with collaborators from the Westmead Millennium Institute for Medical Research and the Children's Hospital at Westmead, have been awarded \$3.3 million to extend their innovative research towards a cure for type I diabetes. The grant was awarded by the Type 1 Diabetes Clinical Research Network (T1DCRN), an innovative clinical research program led by the Juvenile Diabetes Research Foundation (JDRF Australia) and supported by the Australian Research Council.

The researchers aim to make significant improvements in the outcome of islet transplantation therapy (see below), making it a clinically realistic and attractive therapeutic option for more individuals with type 1 diabetes, including children.

Their approach focuses on calming the immune response of patients to islet transplantation. The strategy may make it possible for treated individuals to live drug-free in the long term.

In type 1 diabetes, the body destroys the cells within the pancreas that produce insulin. Without insulin to mastermind the uptake of sugar from the blood, glucose levels can rapidly become damagingly high or plummet to life-threatening lows.

Islet transplantation therapy - in which insulin-producing structures called islets, derived from donor pancreas, are transplanted into the recipient's liver - can cure individuals of diabetes by restoring glucose-responsive insulin production. However, recipients must take powerful immunosuppressive drugs for the rest of their lives to avoid the introduced islets coming under attack from their own immune system.

A/Prof Grey says, "Islet transplantation therapy has had a big impact on the lives of [people with type 1 diabetes](#) who also experience a dangerous condition called hypoglycemic unawareness. But the need to use immunosuppressive drugs stops us from being able to give this promising therapy to more people with type 1 diabetes, including children."

A/Prof Grey's team has discovered that the transplanted islet cells provoke and encourage the immune attack that they are subjected to. Members of his research group, particularly PhD graduate Nathan Zammit, have pioneered research into how factors intrinsic to islets affect whether they transplant successfully.

This work led to the development of the idea of the 'death-defying islet' - an islet for transplantation that could be protected from immune attack by modulating the molecular signals it emits.

In research funded by the grant, A/Prof Grey will determine whether engineering islets to produce more of the anti-inflammatory protein A20 can improve the function of islets after transplantation, decrease the need for immunosuppressive therapies and improve overall success rates.

"We know from Nathan Zammit's extensive PhD studies on A20 that this protein has remarkable properties in pancreatic islets," A/Prof Grey explains. "Nathan showed that it 'calms' the islets by inhibiting key inflammatory pathways within the islet cells - and he showed that it has a strong positive effect on the function of transplanted islets.

"More than that, we have observed that A20 also promotes immune tolerance to the introduced islets. The challenge now is to explore whether this protein can exert these powerful effects in the clinic, leading to improved immune tolerance to islet transplantation."

A/Prof Grey can't wait to get started. He says, "This is a fantastic opportunity to make a real difference to people with type 1 diabetes and completely do away with the need for immunosuppression. And if we are successful one could imagine this new approach could be extended to other types of transplants and possibly used for the treatment of autoimmune conditions."

A/Prof Grey is part of a large team headed by Professor Phil O'Connell (Westmead Millennium Institute for Medical Research). The team's grant is one of five awarded on 9 September by T1DCRN, with a total value of \$14 million.

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Source:

Garvan Institute of Medical Research

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