



Potential to prevent loss of insulin in Type 2 diabetes

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There are two completely different diseases known as diabetes. Type 1 is an autoimmune condition that often starts in childhood or adolescence. Type 2 is a metabolic disorder sometimes associated with lifestyle. In both cases, the insulin-secreting beta cells in the pancreas die, albeit at different rates.

Until now, it was thought that the processes leading to beta cell death were similar in both diseases. Scientists at the Garvan Institute of Medical Research in Sydney have now shown that the causes of cell death are quite different.

In April 2007, Garvan's Associate Professor Trevor Biden and Dr Ross Laybutt published a landmark paper establishing the existence of ER (Endoplasmic Reticulum) stress in people with Type 2 diabetes. The ER is the part of a cell where simple strings of amino acids are structured into three-dimensional proteins which then go on to perform specific tasks in the body. Insulin is one such protein. When the correct re-structuring of proteins is disrupted, beta cells suffer ER stress, and eventually die.

The new study, undertaken by PhD student Mia Akerfeldt, expands our knowledge about ER stress in Type 2 diabetes, while ruling out its importance in Type 1 diabetes. The paper is now online in the international journal *Diabetes*.

Mia is hopeful that the findings will translate quickly into treatments. "Garvan was first to show that ER stress was present in people with Type 2 diabetes, and that reducing it could slow down beta cell death," she said. "We've not only shown the same thing again, we've identified a potentially useful therapeutic agent."

Project leader Ross Laybutt echoes Mia's optimism. "One interesting aspect of the new study is that we used a "chemical chaperone", an agent that helps the secretory protein, in this case insulin, to form properly. This compound relieved cell death and ER stress in laboratory experiments."

"The compound, known as PBA, is already FDA approved for use in another clinical application. That suggests it could be fast tracked for use in humans to prevent or delay beta cell dysfunction."

"A study conducted in the United States demonstrated that this compound cures diabetes in animals. The next step would be to conduct clinical trials on people."

ABOUT GARVAN

The Garvan Institute of Medical Research was founded in 1963. Initially a research department of St Vincent's Hospital in Sydney, it is now one of Australia's largest medical research institutions with approximately 400 scientists, students and support staff. Garvan's main research programs are: Cancer, Diabetes & Obesity, Immunology and Inflammation, Bone, and Neuroscience. The Garvan's mission is to

make significant contributions to medical science that will change the directions of science and medicine and have major impacts on human health. The outcome of Garvan's discoveries is the development of better methods of diagnosis, treatment, and ultimately, prevention of disease.

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