

New drug candidate in diabetes research breakthrough

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CSL Limited has developed a new drug candidate that is able to prevent the development of type 2 diabetes and reverse its progression in animal models of the disease.

The drug candidate blocks signalling by a protein known as [Vascular Endothelial Growth Factor](#) B (VEGF-B) and this prevents fat from accumulating in the "wrong" places, such as in muscles and in the heart. As a result, cells within these tissues are once again able to respond to insulin and [blood glucose](#) is restored to normal levels.

This represents an entirely new approach to the treatment of type 2 diabetes and a paper outlining this breakthrough has just been published in the prestigious scientific journal *Nature*.

The research is a joint effort by an international team led by Professor Ulf Eriksson from the Karolinska Institute in Sweden, and involving scientists from CSL's research laboratories in Melbourne, The University of Melbourne and the Ludwig Institute for [Cancer Research](#).

"The results seen in these laboratory studies are very promising for the millions of people around the world who are affected by type 2 diabetes," said Dr Andrew Nash, Senior Vice President of Research at CSL.

"This disease is reaching [epidemic proportions](#) and is a significant public health burden."

"We are very hopeful that the antibody-based drug that we have developed and tested together with Professor Eriksson will ultimately lead to a new treatment option for people with diabetes."

Type 2 diabetes is normally preceded by insulin resistance, which is most often caused by obesity. When this happens, the cells no longer respond sufficiently to insulin, which leads to elevated levels of blood sugar.

Dr Nash said insulin resistance is related to the storage of fat in the "wrong" places, such as the muscles and in the heart, although exactly how this relationship works is not fully understood.

What scientists do know, however, is that the VEGF-B protein affects the transport and storage of fat in [body tissue](#). This was discovered by Professor Ulf Eriksson's research group in a study published in Nature in 2010.

These findings were further developed in this latest study in which VEGF-B signalling was blocked by CSL's [drug candidate](#), known as 2H10, in groups of diabetic mice and rats.

"It's a great feeling to have published these new results," said Professor Ulf Eriksson.

"We discovered VEGF-B back in 1995, and since then the VEGF-B project has been a lengthy sojourn in the wilderness, but now we're making one important discovery after the other."

A total of four related studies are reported in the Nature paper. In one study, mice bred to spontaneously develop diabetes were treated with 2H10. The mice subsequently developed neither [insulin resistance](#), nor diabetes. The research team also crossed this mouse model with one that

lacked the ability to produce VEGF-B, and found that the at-risk offspring were protected from developing diabetes.

In another two studies, the scientists investigated the effects of 2H10 on mice and rats that had developed obesity and type 2 diabetes as a consequence of a fat-rich diet. Again the treatment was able to prevent development and progression of the disease respectively.

"The results generated through this international collaboration represent a major breakthrough and provide for a new way of thinking about the treatment of type 2 diabetes," said obesity and diabetes expert and co-author of the paper, Professor Joe Proietto.

Professor Proietto, who treats many patients with diabetes at Melbourne's Austin Hospital, said there is a "need for new treatment strategies for type 2 [diabetes](#) as existing treatments can cause adverse reactions and their effects can wear off."

On the basis of these latest findings CSL has begun to consider options for progressing the development of 2H10, which includes testing the therapy in people with [type 2 diabetes](#) as well as in those who are-at risk of developing the disease.

More information: 'Targeting VEGF-B as a novel treatment for insulin resistance and type 2 diabetes', Carolina E. Hagberg, Annika Mehlem, Annelie Falkevall, Lars Muhl, Barbara C Fam, Henrik Ortsater, Pierre Scotney, Daniel Nyqvist, Erik Samen, Li Lu, Sharon Stone-Elander, Joseph Proietto, Sofianos Andrikopoulos, Ake Sjöholm, Andrew Nash, Ulf Eriksson. *Nature*, Advanced Online Publication (AOP) 26 September 2012. [doi:10.1038/nature11464](https://doi.org/10.1038/nature11464)

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