

DIABETES

Betatrophin—inducing β -cell expansion to treat diabetes mellitus?

Betatrophin, a newly identified hormone, increases the production and expansion of insulin-secreting β cells in mice, research from Harvard University suggests.

When insulin resistance develops, pancreatic β cells undergo an expansion in mass and proliferation to compensate for increasing insulin needs. To date, the mechanisms regulating β -cell replication are unclear.

Yi *et al.* developed a mouse model of insulin resistance using the insulin receptor antagonist S961. Subcutaneous injections of the S961 peptide into mice led to dose-dependent, instant β -cell proliferation and hyperglycaemia.

Microarray analysis revealed that a highly conserved mammalian gene, betatrophin, was upregulated fourfold in liver and threefold in white adipose tissue cells in response to the acute peripheral insulin resistance induced by S961. Yi and co-workers show that betatrophin

encodes a secreted protein that can be detected in human plasma. Intravenous injection of betatrophin-expressing constructs into mice resulted in a 17-fold higher β -cell proliferation rate compared with control vectors, and ultimately led to increased islet size and insulin content, with improvements in glucose tolerance, in betatrophin-injected animals.

The mechanisms of action of betatrophin are still unknown, and the next step is to test the effects of recombinant betatrophin protein on β -cell mass. The authors conclude that the identification of betatrophin and its control of β -cell proliferation opens a new door to possible diabetes therapy.

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