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A pharmacological approach to improving pancreatic beta cell growth and function

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β cells in pancreatic islets are responsible for producing insulin, which is essential to regulate blood glucose homeostasis. In type 1 diabetes, pancreatic β cells are destroyed due to an autoimmune attack, whereas in type 2 diabetes, pancreatic β cells may have deficiencies in secreting insulin or insulin-responding tissues can become insulin resistant.

In this month's issue of *JCI Insight*, Morris White and colleagues at Harvard Medical School developed a screen for pharmaceutical compounds that induce pancreatic β cell growth and improve function. Based on preclinical findings indicating that mice with elevated expression of the insulin receptor substrate 2 (*Irs2*) gene are more resistant to developing diabetes, the research team tested over 3,000 compounds for their ability to increase *IRS2* in isolated human pancreatic islets.

The positive hits included 15 tricyclic compounds, several of which have been previously characterized to act as antihistamines or antipsychotics. Further studies focused on trimeprazine, an antihistamine and sedative that has been used clinically outside of the U.S. In multiple mouse models of diabetes and in human islets, trimeprazine improved β cell function and slowed progression of diabetes.

These studies suggest that trimeprazine and related compounds merit further study as diabetes therapeutics.

More information: Alexandra Kuznetsova et al. Trimeprazine

increases IRS2 in human islets and promotes pancreatic β cell growth and function in mice, *JCI Insight* (2016). DOI: 10.1172/jci.insight.80749