Treating and Preventing Diabetes by Targeting EP3 Receptor

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Technology description

Normally, digested food can be absorbed into the bloodstream in the form of sugars like glucose, which then signals pancreas beta cells to secrete more insulin. This insulin is needed to help the glucose molecules enter cells.

Type 2 diabetes mellitus (T2D) is a disease in which a person has high blood sugar because the body resists the glucose-lowering effects of insulin and beta cells fail to produce enough insulin. More than 18 million Americans have been diagnosed with T2D, at an annual cost of $174 billion. Complications from the disease are the third leading cause of death in the United States.

Treatment has focused on increasing the production of a signal-relaying molecule called cAMP. This molecule in turn boosts insulin secretion by helping beta cells grow and survive. Some agents used to increase cAMP levels target hormonal pathways that activate a necessary adenylate cyclase (AC) enzyme. Unfortunately, many patients do not respond to such treatments. UW–Madison researchers have discovered an additional target for diabetic therapy. The gene, known asPtger3, is over-expressed in diabetics. It encodes a receptor called EP3 that negatively impacts insulin secretion from beta cells. When that activity is suppressed, secretion can be elevated to healthy levels.

Their discovery may be used to develop a new pharmaceutical for boosting insulin secretion from beta cells. To do this, the pharmaceutical would work on two fronts to increase cAMP production. It would include a compound (like sitagliptin) that directly or indirectly activates AC, as well as a compound that blocks EP3 activity. Such an EP3-specific antagonist could be the commercially available agent L-798,106.
The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing a method to increase insulin secretion from beta cells by normalizing the activity of thePtger3gene.

Additional Information

WARF reference number P02201US describes a method to increase glucose-dependent insulin secretion using alphaKG analogs.
http://www.warf.org/technologies/summary/P02201US.cmsx

Kimple et al. 2013. The Prostaglandin E2 Receptor, EP3, is Induced in Diabetic Islets and Negatively Regulates Glucose- and Hormone-Stimulated Insulin Secretion. Diabetes. 62, 1904-1912.
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Application area

Treating and preventing type I and type II diabetes

Advantages

Normalize insulin production to non-diabetic levels
Could prevent onset of diabetes
Since EP3 expression and activity are elevated only in response to diabetes, a drug inhibiting thePtger3gene should be disease-specific.

Institution

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