GLP-1 Combination Therapy for insulin Resistance

Clayton Biotechnologies

Medical Research for Mankind

Since 1933

Insulin resistance (IR), primarily associated with diabetes mellitus type 2, but also diseases such as polycystic ovarian syndrome and nonalcoholic fatty liver disease, is characterized by chronically elevated serum levels of glucose. Although IR may be controlled by diet, there are cases where medical treatment is required. Besides insulin, there are several oral anti-diabetic drugs available. However, they may have contraindications, undesirable side-effects or resistance may develop, so there is a continued need for new therapies for insulin resistance and diabetes mellitus (both types 1 and 2), in particular.

Dr. Montminy and colleagues at the Salk Institute have shown that chronic exposure to high levels of glucose negatively impacts pancreatic cell function. They have identified and dissected the cellular pathways responsible for the impaired pancreatic cell function and beta cell hypertrophy (see Fig. 1). Chronic exposure of beta islet cells to glucose results in attenuated CREB activity. In a step-by-step approach, Dr Montminy and colleagues demonstrated that the attenuated CREB activity is due to reduced protein kinase A (PKA) activity, as a result of increased expression of a protein kinase A inhibitor (PKIB). Increased expression of PKIB is mediated by HIF-1a, which is induced following activation of the mTORC-1 pathway in response to hyperglycemia.

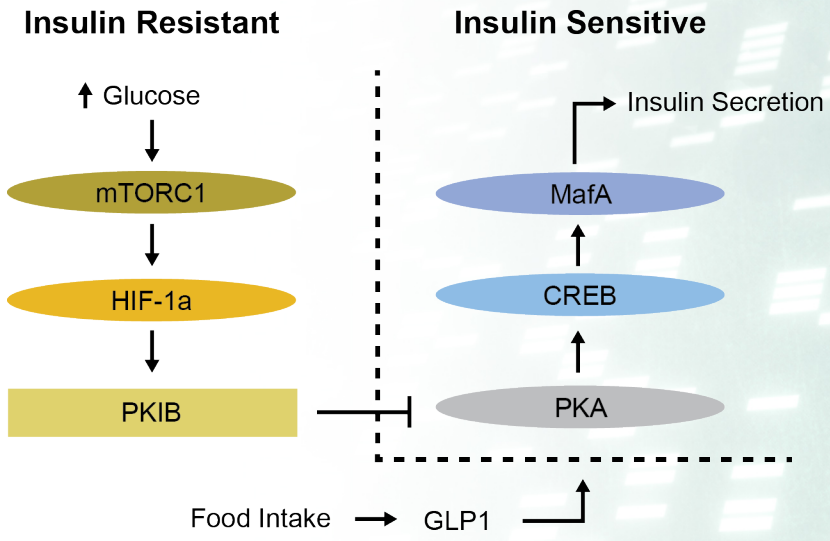

Fig. 1

High levels of glucose induce the mTORC1 pathway and lead to insulin resistance, due to the blockade of the CREB pathway. Dr Montminy and colleagues plan to design inhibitory molecules that will prevent inhibition of the CREB pathway at the level of PKIB (indicated as 1 in the cartoon), thereby improving insulin sensitivity in insulin resistant subjects. These inhibitors may be used in conjunction with GLP-1 agonist therapy, to improve insulin sensitivity.

Blanchet et al., Cell Reports, 2015

Clayton scientist, Dr. Marc Montminy and his team have identified a new strategy to develop therapies for insulin resistance that may be combined with GLP-1 agonists:

- nucleic acid-based inhibitors of the PKI pathway (e.g. inhibitors of PKIB, HIF1, or mTORC1), designed using dsRNA, siRNA, miRNA or shRNA
- small molecule inhibitors of HIF1 or mTOR

We are seeking partners to license our patents and help develop these novel therapeutic strategies.

Clayton Biotechnologies commercializes technologies that are developed and owned by the Clayton Foundation for Research and its supporting entities through research programs at leading research hospitals and institutions in the US and Switzerland.

To date, our research programs have lead to the creation of several successful companies and the launch of 9 products ranging from therapeutic products, medical devices to diagnostics.

Clayton Biotechnologies Inc.
One Riverway, Suite 1520
Houston, TX 77056
+41-76-342-7147
arichardson@claytonbiotech.com

www.claytonbiotech.com