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## FASTING CONDITION AS DIETARY TREATMENT OF DIABETES

### CROSS REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. provisional application Ser. No. 61/841,709 filed Jul. 1, 2013, the disclosure of which is incorporated in its entirety by reference herein.

### STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

The invention was made with Government support under Contract Nos. PO1AG034906 and PO1AG020642. The Government has certain rights to the invention.

### TECHNICAL FIELD

The present invention, in general, relates to compositions and methods for a) regenerating pancreatic cells, 2) treating Type I diabetes, 3) treating Type II diabetes, 4) treating the metabolic syndrome, 5) preventing Type II diabetes and other diseases associated with metabolic syndrome. In particular, the present invention promotes pancreatic regeneration and alleviates multiple common signs, symptoms and risk factors of both diabetes types. In addition to promoting residential pancreatic regeneration, it can also be used to enhance and improve the regenerative functions of transplanted stem cells when it is incorporated with the conventional stem cell therapy.

### BACKGROUND

Human metabolic disorders such as diabetes mellitus Type I, diabetes mellitus Type II, metabolic syndrome, and insulin resistance are serious health conditions affecting over a third of the adult population in the United States. Although effective in delaying morbidity, standard treatments have not generally been able to reverse the associated damage of these disorders.

Chemicals, cytokines/hormones and stem cell or islet transplantation that boost or assist pancreatic regeneration have been used as diabetes therapy in order to augment or replace insulin injections by increasing the number of, or enhancing the function of, endogenous insulin-producing  $\beta$ -cells.

Diabetes mellitus Type 1 and Type 2 diabetes are characterized by progressive beta-cell failure. By far, stem/progenitor cell transplantation is the only therapy available for advanced stages of diabetes in an attempt to restore insulin production and replace insulin injection. However, besides ethical issues, technical and safety challenges in stem cell isolation, maintenance, expansion, donor-recipient matching and transplantation limit the efficacy of these strategies.

Accordingly, there is a need for safe, effective treatment protocols for metabolic disorders such as diabetes that may reverse pancreatic damage and inhibit development of these disorders.

### SUMMARY

In at least one embodiment, the present invention provides a method of alleviating symptoms of or treating pancreatic beta-cell damage in a subject. The method includes a step of identifying a subject having pancreatic beta-cell damage.

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Multiple cycles of a diet protocol are administered to the subject. The diet protocol includes administering of a fasting mimicking diet and a re-feeding diet where the fasting mimicking diet is provided for a first time period and the re-feeding diet is provided for a second time period.

In another embodiment, a method of alleviating symptoms of or treating pancreatic beta-cell damage in a subject is provided. The method includes a step of identifying a subject having pancreatic beta-cell damage and insulin deficiency. The subject's normal caloric intake is determined. Multiple cycles of a diet protocol are administered to the subject. The diet protocol includes administering of a fasting mimicking diet and a re-feeding diet where the fasting mimicking diet is provided for a first time period (e.g., 2 to 6 days) and the re-feeding diet is provided for a second time period (e.g., 2 to 85 days). The fasting mimicking diet provides less than about 50% of the normal caloric intake of the subject with both protein restriction and sugar restriction and the re-feeding provides 60-100 percent of the normal caloric intake of the subject, depending on the need to lose additional weight.

In another embodiment, a method of alleviating a symptom of diabetes is provided. The method includes a step of identifying a subject having diabetes (Type I or II). The subject is provided with multiple cycles of a Fasting Mimicking Diet (FMD) (4-5 days every, 1-12 weeks) to promote a reduction and reversal in symptoms.

In another embodiment, a method of alleviating insulin resistance, insulin deficiency and/or hyperglycemia is provided. The method includes a step of identifying a subject having insulin resistance, insulin deficiency and/or fasting hyperglycemia diabetes. The subject is provided with multiple cycles of a Fasting Mimicking Diet (FMD) (e.g., 4-5 days every 4-12 weeks) to promote a reduction in symptoms.

In another embodiment, a method of alleviating a symptom of metabolic syndrome is provided. The method includes a step of identifying a subject having one or more metabolic syndrome symptoms/risk factors (e.g., high blood pressure, hyperglycemia, excess body fat around the waist, high cholesterol). The subject is provided with multiple cycles of a Fasting Mimicking Diet (FMD) (4-5 days every, 1-12 weeks) to promote a reduction in symptoms.

### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1. Table 1 showing the Calorie overview of the fasting mimicking diet adjusted to human subjects. The fasting mimicking diet (FMD), Prolon, induces a fasting-like response while maximizing nourishment. The consumed calories for each one of the 5 days of the diet are shown, as well as the adjusted kcal per pound and kilogram of body weight. The reduction in calories consumed during the 5 day dietary regimen ( $\Delta$ 5-day) is shown as either 1) based on a 2,000 calorie per day diet, or 2) based on 2,800, 2,400, and 2,000 calorie diets for person's weight  $\geq 200$ , 150-200, and  $\leq 150$  lbs, respectively;

FIG. 2. Table 2 showing the defined macronutrient content for each diet day adjusted to a 180-200 lbs human subject. The macronutrient content for each day of the 5 day FMD regimen is based on an average 180-200 lbs person. Caloric intake on day 1 of the diet is less reduced compared to the following days (2-5) to allow the body to adjust to the low calorie consumption. % of calories contributed by fat, carbohydrate (by sugar in detail) and protein for each day of the Prolon regimen is presented.

FIG. 3. Table 3 showing the defined micronutrient content for each diet day adjusted to a 180-200 lbs human subject in a variation of the invention. The micronutrient content for