Determination of Beta-Cell Responsiveness to the Incretin Hormones GLP-1 and GIP in Cystic Fibrosis (Aim 1)

Sponsor: Cooperative study between CHOP and Upenn, The study is being conducted with general research funds from National Institute for Diabetes, Digestive & Kidney Diseases at the National Institute of Health

Brief Description:

- The purpose of this research study is to examine and understand the various mechanisms that contribute to Cystic Fibrosis Related Diabetes (CFRD) and gain a better understanding of potential means to treat it.
- **Type 1 and Type 2 diabetes**-result when either the body does not make enough insulin or the body does not respond correctly to this insulin.
- **Insulin**-a hormone which is made by cells in the pancreas and helps carry glucose (sugar) from the food we eat to the cells of the body for energy.
- In recent years, diabetes has emerged as one of the most significant co-diseases that many cystic fibrosis (CF) patients develop. While CFRD has many features similar to both Type 1 and Type 2 diabetes, it is very different; therefore, treatment and care of CFRD should not be the same.
- Participation in this study will include 3-4 study visits (between 4-6 hours), depending on the individual subject, to the Clinical Translational Research Center (CTRC) at the Hospital of The University of Pennsylvania (UPenn).
- Study visits will be completed over approximately 1 month
- Potential to be compensated up to $550 (on a Visa gift card) for study participation

Eligibility:

Currently recruiting patients:

- With cystic fibrosis
- Who have been diagnosed with pancreatic insufficiency (take enzymes with meals)
- Who are ≥18 years of age

Key Exclusion Criteria:

- If you are a woman who is pregnant or plans to become pregnant within the next year
- Have had acute pancreatitis within the past year
- Have had a prior lung or liver transplant
- Have been diagnosed with severe CF liver disease (defined by portal hypertension)
- Have been diagnosed with fundoplication-related dumping syndrome

Contact Information:

Jack N. Eiel
Clinical Research Coordinator
Phone: (215) 746-2081
Email: jack.eiel@uphs.upenn.edu

Study Procedures

Oral Glucose Tolerance Test* (Visit 1):

- We will test your body's response to glucose by taking some of your blood from a blood drawing intravenous (IV) catheter.
- You will then be given a large dose of sugar to drink.
- We will then take blood samples at 60 and 120 minutes after drinking the sugar drink.
- A total of 6 mL (or less than one tablespoon) of blood will be drawn for this test.
- This test is recommended annually for most patients with Cystic Fibrosis in order to screen for CFRD
- If you qualify to participate, you can continue with the study procedures.

*If an oral glucose tolerance test was completed within 6 months prior to study procedures, this visit is not required

Mixed Meal Tolerance Test (Visit 2):

- This test will look at your body's response to food.
- Prior to this visit, you will work with the study team to decide on a breakfast that is appealing to you but is comprised of a specific combination of calories, protein and carbohydrates.
- After you eat, you will have blood drawn from your IV multiple times over a 4 hour period.
- The total amount of blood for this test is about 4½ tablespoons.
- Compensation for this part of the study is $150.

Glucose Potentiated Arginine (GPA) test with incretin infusion (Visits 3 & 4):

- 1 GPA at baseline and another at 1 month
- Arginine- a naturally occurring amino acid in your body. In this study it is given in your IV to make the cells in your pancreas secrete the hormone insulin.
- The GPA test will measure the insulin and other glucose controlling hormones which will assist in measuring pancreas cell function.
- Infusion of an incretin hormone one visit and placebo during the other: You will be randomized to receive one of two incretin hormones, GLP-1 or GIP.
- Incretin Hormones- are produced by the cells in your small intestine and help to make your body more sensitive to glucose.
- You will receive your assigned incretin hormone during one time at visit 2 or 3, and a placebo infusion at the other visit. (These 2 visits will occur 1 –4 weeks apart)
- After baseline blood levels are drawn, the study team will follow a schedule of administering arginine, glucose, and checking your blood levels over approximately an hour.
- You will be allowed to eat lunch and your blood sugar will continue to be monitored over at least the next hour.
- You may be discharged once we confirm that your blood sugar level has normalized.
- The study team will monitor you closely during this testing, checking your blood glucose levels approximately every 5 minutes.
- The total amount of blood drawn for this test is approximately 9 tablespoons.
- Compensation for this part of the study is $150 for each GPA

Continuous Glucose Monitoring System (CGMS)(optional)(Visit 3):

- CGMS is a way to measure blood sugar continuously for 3 days.
- You will be taught how to use CGMS during a GPA visit.
- CGMS requires the placement of a thin tube under the surface of the skin.
- After you complete 72 hours of CGMS at home, you will send the equipment back to CHOP with an envelope that we will provide.
- Compensation for this part of the study is $100.

What are the possible risks associated with the study?

- **Blood sample collections and IV catheter:** The process for collecting blood samples requires a needle to be inserted into a vein. Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection.

- **Hypoglycemia/Fasting:** Most people do not have medical problems associated with fasting; however, some people have medical conditions that limit their ability to tolerate a fast. If your doctor has told you not to fast, we ask that you not participate in this study.

- **GPA test:** There is the possibility of experiencing a burning or stinging sensation as a result of the glucose infusion. Administration of arginine may briefly cause a metallic taste in your mouth. Rarely, arginine may also cause nausea, vomiting, headache, flushing, numbness, allergy or rash, and irritation of the vein.

- **GLP-1 and GIP infusion:** There is a possibility that you may experience nausea or low blood sugar as a result of the incretin infusion. If present, the nausea will likely be very mild. Rarely, either GLP-1 or GIP could cause an allergic reaction, for which you will be monitored closely.