DGIM Project Summary

(1 page preferred, 2 pages maximum)

Name of Project: Role of Growth Hormone Antagonism in Modulating Insulin Sensitivity with Insulin Resistance but Without Diabetes

Investigator(s). (Include phone numbers and email address, indicate PI and primary contact)
Ethan Weiss – PI. ethan.weiss@ucsf.edu
Ada Lee – Study clinician – primary contact. ada.lee@ucsf.edu
Sarah Nordstrom – Study coordinator. Sarah.nordstrom@ucsf.edu.
Morrie Schambelan- Co PI. morrie@sfghcrc@ucsf.edu
Elizabeth Murphy – Other investigator. emurphy@medsfgh.ucsf.edu.
Kathy Mulligan – Co PI. Kathleen.mulligan@ucsf.edu.

Research question(s):
Does antagonism of the human growth hormone receptor improve peripheral and hepatic insulin sensitivity in patients with insulin resistance but not diabetes?
Does antagonism of the human growth hormone receptor change basal lipolysis in patients with insulin resistance but not diabetes?

Brief Background/Significance:
Clinical and animal data suggest that growth hormone (GH) can cause insulin resistance. People born with genetic mutations in the GH receptor (GHR) are extremely insulin sensitive and are protected from diabetes. Mice engineered without GHR are similarly protected. Pegvisomant (PEGV) was developed to treat acromegaly that specifically blocks GHR. In patients with acromegaly, there is a dramatic improvement in insulin sensitivity in patients taking PEGV. We are hoping to evaluate insulin sensitivity in patients without acromegaly who have documented insulin resistance.

Inclusion/exclusion criteria (list)
Inclusion criteria: Men and women age 18-80, women must not be pregnant, BMI between 18.5-35, insulin resistance as calculated by HOMA-IR >2.77, normal liver function, able and willing to administer daily subcutaneous injections of pegvisomant, on a stable diet and exercise regimen for at least 4 weeks prior to the study and willing to maintain this throughout the duration of the study, stable weight for at least 3 months prior to the start of the study.

Exclusion criteria: Diabetes (type 1 or type 2), unstable hypertension, pregnant or breastfeeding within the last 6 months, history of major gastrointestinal surgery, evidence of kidney disease (serum creatinine >1.7 in men and 1.5 in women), fasting glucose >126, A1c >6.5%, fasting triglycerides > 300, or history of pancreatitis or liver, biliary or intestinal disease.

Method of contact/recruitment (be specific)
We would like to recruit from the GIM clinics. Potential subjects will be screened over the telephone and if eligible will participate in a screening visit at the GCRC at SFGH.
Benefits/burden for participants (clearly identify potential for harm)
Patients who participate in our study may have temporary improvement in insulin sensitivity and decreased circulating free fatty acids. Pegvisomant is a very safe drug that has been approved for use in patients with acromegaly. Participants may experience local injection discomfort from administering pegvisomant. As there are two inpatient hospitalizations, those will a significant time commitment from the study participants.

Any benefits or burden to DGIM practitioners?
None forseen

Timeline for recruitment (projected start and stop dates)
Ideally we would like to recruit as soon as possible. We would like to start the inpatient hospitalization in January 2014. Our projected stop date is July/August 2014.

Funding source
Pfizer

Potential for DGIM collaborators? (We encourage DGIM resident and fellow involvement in particular)
Possibly.

Do you agree to notify us when recruitment is completed?
Yes

Date form completed: 12/12/13