Beta Cell Restoration through Fat Mitigation
The BetaFat Study

A Participating Study in the
The Restoring Insulin Secretion (RISE) Consortium

NCT Number: 01763346

Consent Form

Date: April 5, 2018

Study Title: Beta Cell Restoration through Fat Mitigation: The BetaFat Study

Principal Investigator: Thomas A. Buchanan, M.D.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

You have been asked to participate as a subject in a medical experiment. Before you decide whether you want to participate in the experimental procedure, you have a right to the following information:

CALIFORNIA LAW REQUIRES THAT YOU MUST BE INFORMED ABOUT:

1. The nature and purpose of the study.
2. The procedures in the study and any drug or device to be used.
3. Discomforts and risks reasonably to be expected from the study.
4. Benefits reasonably to be expected from the study.
5. Alternative procedures, drugs, or devices that might be helpful and their risks and benefits.
6. Availability of medical treatment should complications occur.
7. The opportunity to ask questions about the study or the procedure.
8. The ability to withdraw from the study at any time and discontinue participation without affecting your future care at this institution.
9. Be given a copy of the signed and dated written consent form for the study.
10. The opportunity to consent freely to the study without the use of coercion.

I have carefully read the information contained above and I understand fully my rights as a potential subject in this study.

Date: _____Time: _____

Signature: _____
(Research Participant)

INFORMED CONSENT
University of Southern California, Keck School of Medicine

Title of Project: Beta Cell Restoration through Fat Mitigation

Principal Investigator: Thomas Buchanan, M.D.

24-hour Telephone Number: (323) 479-4319 (cell)

We invite you to take part in a research study. We are providing you the following information in order to help you make an informed decision whether or not to participate in this study. Please take as much time as you need to read the consent form. You may also decide to discuss it with your family, friends, or your doctor. You may find some of the language difficult to understand. If so, please ask questions. If you decide to participate, you will be asked to sign this form.

This research study is sponsored by Allergan, the company that makes the device (the LAP-BAND) being used in this study, Apollo Endosurgery, the company that supplies the device for this study, and by the National Institutes of Health (NIH). They provide funding to cover the costs of conducting this research study.

WHY IS THIS STUDY BEING DONE

You are invited to participate in a study to evaluate two different approaches for restoring the body's ability to make insulin. Type 2 diabetes and pre-diabetes are caused by a progressive loss of the body's ability to make insulin, the main hormone that controls blood sugar levels. In this study, we will compare two approaches to see which one may result in improving the body's ability to make insulin.

One approach is a medication, metformin, which is commonly used to treat diabetes. Metformin is approved by the Food and Drug Administration (FDA) to treat diabetes. The other approach is a surgery, called gastric banding. Gastric banding is an operation that places a plastic ring around the stomach to help a person to eat less and lose weight. Gastric banding is approved by the FDA to treat obesity in people with diabetes. The use of metformin and gastric banding is not approved by the FDA for people with pre-diabetes and their use in pre-diabetics is experimental. This study will compare the two approaches to see which one is better at stopping or reversing the loss of insulin that causes pre-diabetes to worsen to type 2 diabetes and that causes type 2 diabetes to worsen over time.

You are being asked to participate in this study because you because you are moderately obese (you have a body mass index (BMI) of 30 to 40 kg/m^2) and you have either pre-diabetes (glucose levels above normal, but not yet diagnosed with diabetes) or mild type 2 diabetes. Eighty-eight participants will take part in this study at USC.

WHAT IS INVOLVED IN THE STUDY?

If you decide to take part, this is what will happen:

Screening Visit:

You will come to the Clinical Trials Unit (CTU) or the DORI (Diabetes and Obesity Research Institute) to have a screening visit. The CTU is located in the Keck Hospital of USC, the USC DORI is located in the CSC (Clinical Sciences Building). Both places are on the USC Health Sciences Campus. You must not eat or drink anything except water after 10 pm the night before the visit. The screening visit will include a medical history, physical exam including height, weight and vital signs measured and the following laboratory tests:

- Blood tests to measure your blood cells, body chemistries, fasting glucose level, and liver, kidney and thyroid function
- A urine sample for urinalysis and, if you are a woman of reproductive age, a pregnancy test
- Hemoglobin A1c (a blood tests that reflects your average blood sugar for past three months)
- 2-hour glucose level. You will drink about a cup of a sugary drink that tastes like sweetened soda. Two hours later a blood sample will be collected to test your glucose level. This test will tell us whether you have pre-diabetes or mild diabetes.

The total amount of blood that will be taken for these tests is about 3 tablespoons.

Your labs will be reviewed and your eligibility for the study will be determined. If you are eligible for the study and willing to participate, you will be invited to return to the CTU to have two baseline visits described next. This screening visit will take about 3 hours.

First Baseline Visit:

On this visit you will have the following tests:

Oral Glucose Tolerance Test (OGTT): You must not eat or drink anything except water after 10 pm the night before the visit. The next morning, between 7:00-9:00 am, you will come to the CTU. You will put on a hospital gown. Next, you will lie down in a bed and an intravenous catheter (a small plastic tube) will be placed in a vein in one of your arms. If you are not allergic to lidocaine (numbing medication), we will inject a small amount of that medication under your skin to reduce the pain when the needle is inserted. Approximately 30 minutes later, we will take a blood sample, about 4 tablespoons and five minutes after that you will drink approximately seven ounces (about 1 cup) of a glucose (sugar) drink that tastes like sweetened soda. You will have seven additional blood samples drawn, each about one to two tablespoons, from the intravenous catheter during the three hours after you drink the glucose solution. At the end of the test, we will remove the intravenous catheter from your arm and you will be able to eat lunch.

Blood for DNA: At the beginning of the OGTT, a blood sample will be obtained for DNA. DNA contains your genes, the "blue print" for inherited traits (such as eye color and height). Differences in DNA may determine why some people are predisposed to certain diseases or why they respond differently to treatment than other people. After we complete the study, your DNA may be analyzed to look for genes that contribute to diabetes, obesity and their complications, and responses to study treatment. These analyses would be genetic research. At this time, the

results of genetic research cannot provide meaningful information about your health. The results of genetic research analyses will not be given to you or your personal health care provider.

Diet and Quality of Life Questionnaires: While you are having your OGTT, a member of the research team will help you fill two questionnaires. One will tell us the kinds of food you usually eat, how often you eat those foods, how much you eat. The other will tell us about the quality of life you are experiencing, including bodily pain, physical functioning, limitations due to health problems, general health, vitality, social functioning, limitations due to emotional problems, and general mental health.

This visit will take about 5 hours.

Second Baseline Visit:

Between 3 to 14 days later, you will return for the second baseline visit. You must not eat or drink anything except water after 10:00 pm the night before the visit. Between 7:00-9:00 am the next morning, you will return to the CTU and have the following tests:

Hyperglycemic Clamp: This test will tell us how well your body makes insulin and how that insulin affects your blood sugar. You will put on a hospital gown and lie down in a bed. We will place an intravenous catheter in one of your arms. If you are not allergic to lidocaine (numbing medication), we will inject a small amount of that medication under your skin to reduce the pain when the needle is inserted. We will place a second catheter in a vein in the opposite hand. The hand will be kept warm with a heating pad. Approximately 30 minutes after the catheters are in place, you will have two blood samples drawn, each about a teaspoon, from the hand catheter.

You will then be given an injection of glucose through the arm catheter. This will be followed by an infusion of glucose for approximately 3½ hours. During this time, we will draw small blood samples from the hand vein catheter every 5-10 minutes and adjust the glucose infusion rate. For the first two and a half hours, we will keep your glucose level at about 200 mg/dl. This level is commonly found in people with mild diabetes after they eat. It will help us learn how much insulin your body makes in response to moderately high glucose levels. For the final hour, we will raise your glucose level to about 450 mg/dl and then inject a naturally occurring amino acid, arginine, into the arm vein. The combination of high glucose and arginine will help us determine the maximum amount of insulin your body can make.

At the end of the 3½ hour infusion period, you will be given lunch and we will observe you for one hour to be sure that you do not develop low blood sugar levels. If you do, we will give you orange juice and continue to observe you until your symptoms have gone. Then we will remove your intravenous catheters and send you for a DEXA scan, which is described next.

This visit will take between 5 and 5½ hours.

Abdominal Fat Measurements by MRI

The MRI (Magnetic Resonance Imaging) will measure how much fat is in a specific part of your belly and liver. A machine called an MRI will be used for this measurement. You will be asked to lie on your back inside the machine. The machine has a large magnet inside and will take pictures of the fat near your belly button and liver. The test takes about 30 minutes. It will be done at one of your baseline visits or at a separate visit.

Total Body Fat Measurement by DEXA Scan

The DEXA scan will tell us how much fat you have in your body and where that fat is located. It is important for us to know this information because the amount and location of body fat may change the body's ability to make insulin or use sugar as energy. You will lie on a padded table for approximately 10 minutes. The DEXA machine will administer an X-ray that is like a standard dental X-ray. If you are a woman who can still become pregnant, we will do a pregnancy test on your urine and we will perform the DEXA only if the pregnancy test is negative. It will be done at one of your baseline visits.

Study Group Randomization

At the end of the second baseline visit, you will be "randomized" 1:1 into one of the study groups described below. "Randomized" means that you are placed into a group by chance (like the flip of a coin). Neither you nor the study doctor can choose the treatment you receive. You will have a 50% chance of receiving any one of the two treatments.

Metformin Study Group:

If you are assigned to the Metformin Group, you will be assigned to take the study medication, metformin every day for two years. Metformin will be provided in 1000 mg tablets, scored (notched) so they can easily be broken in half. During the first week, you will be asked to take one half of a tablet each morning, with breakfast. During the second week, you will be asked to take one half of a tablet with breakfast and one half of a tablet with dinner. During the third week, you will take one full tablet with breakfast and one half of a tablet with dinner. During the fourth week and for the rest of the study you will be asked to take one full tablet with breakfast and one full tablet with dinner each day. Your dose might be reduced if you have problems with side effects. This is described below in the section titled "What are the Possible Risks and Discomforts".

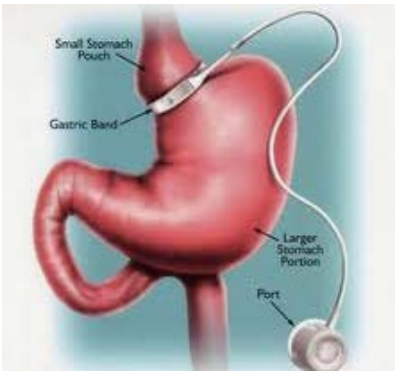
We will provide the metformin to you at each study visit. You will bring any unused pills back to us at each study visit. It is very important that you take only the number of pills that are prescribed to you by the study team. You will continue to take the study drug until you complete all clinic visits or if you end your participation in the study.

LAP-BAND Study Group:

If you are in the Lap-BAND group, you will have a pre-operative evaluation which includes a psychological evaluation, a heart evaluation with an electrocardiogram and a stress test, evaluation by an anesthesiologist, a chest X-ray, and blood tests. In addition, if you are female in the reproductive age, you will have a pregnancy test. You will also meet with a nutritionist for education on dietary restrictions that will apply once the LAP-BAND is in place. If you are a smoker, you will have to stop smoking for two months before the operation. If you are taking blood thinners (for example Coumadin or Plavix) you will have to stop taking them before surgery according to the instructions of your personal medical doctor or cardiologist.

If you qualify for the LAP-BAND on the basis of the pre-operative evaluation, your surgery will be performed by Dr. Namir Katkhouda at Keck Hospital of USC. You will be on a light liquid diet 48 hours before surgery. You must not eat or drink anything after 10 pm the night before the surgery. On the morning of surgery, you will come to the hospital early in the morning. You will be taken to the preoperative area where you will be prepared for surgery. You will be taken to the operating room, where you will have general anesthesia to put you to sleep for the operation.

Surgical Procedure: This operation involves placing a band around the upper part of your stomach. The band contains a balloon that is adjusted to create a small stomach pouch. It is designed to restrict the amount of food you eat. The stomach pouch will fill with a small amount of food, creating a feeling of fullness.



The band will be placed using a laparoscope. Laparoscopic surgery is done using a scope and hollow tube(s) called ports, which are inserted through small cuts in the abdomen. A scope is a thin, lighted instrument with a camera attached. It lets the surgeon see inside the abdomen. The surgeon can pass tools through the ports, or see tools inserted through other ports. Carbon dioxide gas is pumped into the abdomen. This helps the surgeon see inside the abdomen. It also gives him more room to work. The surgeon may not be able to complete the procedure using a scope or robotics. If the surgery is not done with a scope, it may be done through a larger cut. The surgeon will make several cuts in your abdomen. The surgeon will place the gastric band around the upper part of your stomach. The band will be connected to a port that the surgeon will place under your skin on your abdomen. To help you understand where the LAP-BAND will be in your body, we provide two pictures shown above. The one on the left shows how the LAP-BAND fits on the stomach. The structure labeled “Gastric Band” is the ring that is placed around the stomach. The structure labeled “Port” is the port that is placed under the skin. It is connected to the LAP-BAND by a long tube which allows fluid to move from the port to the gastric band. The picture on the right shows the stomach is in the body with a LAP-BAND and port in place.

When the procedure is complete, the cuts will be closed. A dressing will be applied. The surgeon may stop the procedure if he discovers severe liver disease or for any other safety reasons.

A doctor from the research team will adjust the band after you have recovered from surgery. This is done by filling the balloon inside the band with a salt water solution. The doctor will insert a needle through your skin to inject salt water that will inflate the band around your stomach. The initial inflation will be done approximately four to six weeks after your operation. At each of the follow-up visits described in the next section, a member of the study team will ask you questions about how hungry you are and how easily you get full when you eat. Based on your answers, fluid will be added to or taken out of your band.

If at any time during the study you decide you no longer want to have the band in place, it can be removed. Removal would require an operation almost identical to the operation for placing the band.

Follow-up Visits: You will be asked to return for follow-up visits at approximately15 days and 45 days and then 2, 4, 6, 8, 10, 15, 18 and 21 months after your surgery (if you are in the gastric banding group) or 2, 4, 6, 8, 10, 15, 18 and 21 months after the first day of metformin (if you are in the metformin group). You must not eat or drink anything except water after 10:00 pm the night before each visit. Between 7:00-9:00 am the next morning, you will come to the CTU where you will have a short medical history and a physical exam to record your weight and to look for signs and symptoms related to the lap band or metformin. You will also have blood tests done at the, 6-, 12-, and 18-month visits to evaluate your response to your treatment. At the six-month visit you will be asked to complete the same diet and quality of life questionnaires that you completed at the baseline visit. In general, these visits will take 1½ to two hours each. A hemoglobin A1C blood test will be done at the 4, 6, 10, 12, 18 and month visit. The results of this test reflect your average blood sugar levels over the prior three months. If the result indicates that your blood sugars are high enough to need additional treatment (that is, greater than 8.0%) on two successive visits, you will complete your participation in the study. We will perform your end-of-study tests and refer you for care of your diabetes.

Some of these follow-up visits will be done at the USC DORI (Diabetes and Obesity Research Institute) and they might be also done at your home if convenient for you.

Mid-study and End of the Study Visits

Mid Study Visit: After 12 months on your assigned study treatment, you will have two visits like the ones you had at baseline. The first visit will be for an OGTT and MRI and the second visit will be for a hyperglycemic clamp. You will also have MRI and DEXA scans at the time of these visits. These are called mid-study visits. The OGTT, DEXA, hyperglycemic clamp and MRI at the mid-study visit will be performed just like the same tests at your baseline visit

End of Study Visit: At the end of the two years on your study treatment, you will again have two visits. One will be for an OGTT, the other will be for a hyperglycemic clamp. You will also have MRI and DEXA scans at the time of these visits. These are called end-of-study visits. The OGTT, DEXA, hyperglycemic clamp and MRI at the end-of-study visit will be performed just like the same tests at your baseline visit.

Post-Study Care: After you complete your participation in the study, you will return to your regular health care provider for ongoing medical care. If you are assigned to metformin, we will stop the metformin at the time of your final study visits. If you are assigned to LAP-BAND, the band will remain in place and you will need to be followed by a provider who is experienced in management of patients with LAP-BAND in place. We can offer referral to such a physician if you need one.

WHAT ABOUT PREGNANCY?

You cannot participate in this study if you are pregnant or planning to become pregnant because some of the study procedures might hurt an unborn baby. We ask that you use effective contraception throughout the study. We will discuss contraceptive options that you can use, but those must be prescribed by your personal medical doctor. If you think you might be pregnant now or at any time during the study, tell us immediately and we will do a pregnancy test to find out for sure. If you are a woman who could become pregnant, you will have a urine pregnancy test done prior to your DEXA scan. You will have the DEXA scan only if the pregnancy test is negative.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Possible risks and discomforts you could experience during this study include:

LAP-BAND

Placement of the LAP-BAND is major surgery and the LAP-BAND is intended for very long-term use. The risks associated with surgery to place the LAB-BAND are:

- Death, which has occurred in fewer than 1/1000 patients
- Damage to the liver, spleen, intestine and other organs near the stomach has occurred in fewer than 5/1000 patients
- Risk of general anesthesia, which are death and damage to heart or lungs with pre-existing risk factors such as heart disease, smoking or emphysema
- Bleeding or infection, which occur in fewer than 1/1000 patients
- Blood clots, which are rare

Following surgery, some pain and discomfort at the site of the surgical incisions may be experienced. You will be able to eat only small amounts of food after surgery. Most of the information on long-term complications of the LAB-BAND is from people with severe obesity (BMI more than 40 kg/m2, who will not be included in this study). The following additional complications were reported in such severely obese people who received the LAP-BAND:

- 51% had nausea and vomiting
- 34% had reflux of stomach acid and/or food into the esophagus and throat
- 27% had stomach pain
- 24% had the band slip out of position
- 14% had blockage of the stomach
- 9% had constipation
- 9% had difficulty swallowing
- 9% had pain at the site of the fluid port under the skin
- 8% had weakness
- 8% had problems with healing of the surgical incision
- 8% had some degree of hair loss
- 7% had an infection
- 7% had diarrhea
- 6% had fever

- 5% had pain in the chest
- 5% had chronic pain at the incision site
- 2% had dilation (enlargement) of the esophagus
- 2% had gallstones
- 2% had leakage from the fluid port used to inflate the LAP-BAND
- 1% had erosion of the LAP-BAND into the stomach
- 1% had dehydration
- 1% had a hernia develop between the stomach and esophagus
- 1% had a blood clot
- Fewer than 1% had bleeding from the stomach
- Fewer than 1% had stomach ulcers or erosions or perforation

Many of these complications can be treated medically. However, approximately 9% of severely obese patients required a new operation to correct serious problems such as band slippage, dilation (enlargement) of the stomach, obstruction of the stomach, and poor location of the band.

There is less information on complication rates in people who are not as obese as the patients listed above. For example, in people with BMI between 30-40 kg/m2 (the range that will be included in this study), complication rates in the first year after surgery were:

- 29% had vomiting
- 22% had trouble swallowing
- 19% had pain
- 15% had reflux of food from the stomach to the esophagus
- 5% had stomach pain or pain at the site of the port used to fill the LAP-BAND
- 5% had nausea
- 5% had indigestion
- 3% had constipation
- 2% had shoulder pain
- 2% had malfunction of the LAP-BAND

Approximately 5% of patients with BMI 30-40 kg/m^2 required a new operation to correct serious problems such as band slippage, dilation of the stomach, obstruction of the stomach, and poor location of the band

Your operation will be performed at USC by Dr. Katkhouda and his experienced surgical team. They have done more than 200 gastric banding operations. No patients have died during the surgery or had stomach erosions or stomach perforations. The rate of slippage, leak or malfunction requiring a second operation is less than 5%. If you do require another operation, it will be done as described above for your initial operation. Infection of the port occurred rarely. Blood clots have occurred very rarely and damage to the liver or surrounding organs are also rare. The rate of hernia at the site of incision has been less than 0.5%.

Metformin

There are three main risks associated with taking metformin:

Stomach problems: The most common risks are stomach problems like nausea, bloating and diarrhea. In general, these occur in 15-25% of people when starting metformin. The frequency will be minimized by having you take metformin with meals and by having you take the medication in slowly increasing doses during the first four weeks of the study. If you develop stomach problems when taking the full dose of metformin, you will have the option of reducing the dose. If you still have symptoms on the lowest possible dose (one pill per day) you may decide to stop taking the medication.

Lactic acidosis: The second and most serious risk is development of a condition called lactic acidosis. This very rare condition results from the buildup of lactic acid in the blood which can cause tiredness and weakness. Lactic acidosis only occurs in about one person in every 1 out of every 33,000 people who take metformin. Usually it occurs in people who have kidney problems or congestive heart failure. We will examine you at baseline and during the study to be sure you don't have kidney problems or heart failure. If you do, we may stop your metformin.

Low Vitamin B12: The third risk associated with metformin is a small lowering of vitamin B12 levels in the body. In other studies, this has happened in about7% of people who took metformin. Those people did not develop any signs or symptoms from low B12 levels. We will measure your blood count every year to be sure you are not developing an important lowering of you B12 level.

Oral glucose tolerance test (OGTT)

Placement of Intravenous Catheter: There will be some pain during the placement of the intravenous needle and catheter. Some bruising and soreness at the site for 1-2 days after the test will probably occur. If you are allergic to lidocaine, please notify the research team and we will instead attempt to numb your skin with ethyl chloride, a cold spray. It is less effective than lidocaine, but does not cause a lidocaine allergy. There is a small (less than 1 in 1000) chance of infection at the site where the catheter is placed.

Sweetened Sugar Drink: Some people experience nausea or upset stomach immediately after drinking the sweetened sugar drink. If you become nauseous and do not wish to complete the test, we will stop the procedure.

Blood Collection: The risks of the blood draw include pain, bruising, and rarely infection.

Hyperglycemic Clamp

Placement of Intravenous Catheters: The risks of the intravenous catheter are the same as for the OGTT. A flushing sensation, which lasts for less than a minute, may be experienced when we first inject the glucose. There is a risk of low blood sugar in the hour after the glucose infusion is stopped. You will be fed right after we stop the glucose and we will observe you for an hour for any symptoms of low blood sugar. If they occur, we will give you orange juice and observe. Muscle cramps have been reported rarely (fewer than 1 per 300 clamps). If they occur and do not resolve, we may have to stop the clamp and ask you to return to repeat it at a later date.

Blood Collection: The risks of the blood draw include pain, bruising, and rarely infection. The Hyperglycemic Clamp will be done at a different time if your blood count is too low.

DEXA Scan

The DEXA scan will expose you to a very small amount of radiation, much less than most routine X-ray procedures. Exposure to radiation can increase the risk of getting cancer. The amount of radiation to which you will be exposed during a DEXA scan is so small that the precise risk is unknown.

MRI

There are no known risks associated with the magnetic field exposure during the MRI scans. Since the machine is shaped like a large tube and there is limited space inside the tube, some people may feel nervous and uncomfortable in this enclosed area or when they hear the loud tapping noise the machine makes. To help minimize this, you will be given earplugs to block the noise or headphones to listen to music. If for some reason you are unable to do this test at the time of your visit, you may be rescheduled and will still be able to participate.

Diet and Quality of Life Questionnaires

Some of the questions included in the diet and quality of life questionnaires may make you feel uneasy or embarrassed. You can choose not to answer such questions.

Genetic Research

There have been concerns about the possibility of discrimination based on genetic analysis. Despite these concerns, this has not been a problem to date. Federal and State laws provide some protection against employment or health insurance discrimination based on genetic findings. These protections do not extend to life insurance, disability insurance, or long-term care insurance. We will use our best efforts to keep the genetic findings in this study as confidential as possible.

WILL YOUR INFORMATION BE KEPT PRIVATE?

Officials of the Food and Drug Administration (FDA) and officials of the study sponsor, the National Institutes of Health (NIH), Allergan Corporation, and Apollo Endosurgery may look at your research records and medical records related to the study. The University of Southern California's Institutional Review Board (IRB) may review your records. The IRB is a research review board that is made up of professionals and community members who review and monitor research studies to protect the rights and welfare of research participants. Other people who provide medical care or who handle billing and payment at USC may review your research records and medical records, if necessary to conduct the research. All personal information from this study will be stored in password-protected computerized databases. All paper forms will be stored in secured file cabinets. Only personnel directly associated with this study are intended to have access to this information. Your personal information will not be provided to anyone outside this study. We may publish the information from this study in journals and we may present it at meetings. If we do, we will not use your name or any unique personal identifying information.

We have obtained a Certificate of Confidentiality from the National Institutes of Health to help protect your privacy. This certificate means that the researchers cannot be forced to tell people who are not connected with the study, including the court system, about your participation in this study.

There are some exceptions to the privacy protection offered by the Certificate of Confidentiality.

- If you ask us to give someone your information, we will. The Certificate of Confidentiality does not prevent you or a member of your family from voluntarily giving out information about you or your participation in this study.
- If the study staff learns of possible abuse, neglect, or a risk of harm to yourself or others, we are required to tell the proper authorities.
- If government agencies need to perform audits or evaluate a study that is funded by the Federal Government, including evaluations performed by the Federal Food and Drug Administration (FDA), we are required to share information about the study.

This Certificate of Confidentiality does not mean the government approves of this research. If you enter the study after the Certificate of Confidentiality has expired, the researcher will tell you this and can no longer rely on the Certificate to protect your confidentiality.

A description of this clinical trial will be available on http://www.Clinical Trials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS STUDY?

You may not receive any benefit from participating in this study. If you are assigned to the Lap-Band, you may lose weight which could improve your general health and lower your blood sugar levels. If you are assigned to metformin, your blood sugar may be lowered to a safer level. Your participation in this study may help diabetic patients in the future.

WHAT OTHER OPTIONS ARE THERE?

An alternative would be not to take part in this study and continue with your current care. Metformin is an approved treatment for Type 2 diabetes. The LAPBAND is approved for obesity (BMI>30 kg/m2) in people with diabetes. Other treatments include lifestyle changes and medications other than metformin to lower your blood sugar levels.

ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

As reimbursement for your time and any out of pocket expenses that result from your participation in the study, you will receive the following payments at the end of each visit:

Screening Visit:	$50
OGTT+MRI Visit:	$75
Clamp+DEXA Visit:	$125
Follow Up Visits:	$ 25/visit

You will still be compensated for each visit that you attend even if you do not complete all of the study procedures.

If you receive more than $600 per year for taking part in one or more research studies, including this study, you may be required to pay taxes on that money. This does not include any payments you receive to pay you back for expenses like parking fees. You may receive an Internal Revenue Service (IRS) Form 1099 if you receive more than $600 in one year for taking part in one or more research studies.

WHAT ARE THE COSTS?

All research tests and procedures provided to you for this study are being paid for by the sponsor. Neither you and/or your health plan/insurance company will be charged for the cost of any research tests or procedures that are being done for this study. If you require any routine tests or procedures to treat your illness that are not related to this study (meaning you would normally receive them if you were not participating in this study), you and/or your health plan/insurance company will be billed for the costs of the routine tests and procedures in the same way as if you were not in a study. You will also be responsible for any co-payments and deductibles that are standard for your health plan/insurance coverage. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. If you have any questions about which tests or procedures will be billed to you and/or your health plan/insurance company, ask the study doctor.

WHAT HAPPENS IF YOU GET INJURED OR NEED EMERGENCY CARE?

You are participating in this study under the supervision of Dr. Thomas Buchanan, and his co-investigators, Drs. Elizabeth Beale and Namur Katkhouda. Some or all of the study procedures will be performed on the USC Clinical Trials Unit (CTU) or by staff of the CTU. If you get hurt or sick from participating in the study, you will be offered treatment for the injury. Who will pay for the treatment depends on how and where it occurs. If the injury is from the procedures performed or directed by Dr. Buchanan or a member(s) of his research team, you will be offered medical treatment. You and/or your health plan/insurance company/government must pay for the treatment. If you get hurt from a procedure performed by one of the CTU staff that was not part of the BetaFat research team, the CTU will review your case and decide payment.

WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the study, we may learn new things about the risks or benefits of being in the study. If we do, we will share this information with you. You might change your mind about being in the study based on this information.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT, AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?

Your participation in this study is voluntary. Your decision whether or not to take part will not affect your current or future care at this institution. You are not waiving any legal claims or rights. If you do decide to take part in this study, you are free to change your mind and stop being in the study at any time. If you are removed from the study, you will be referred to your care provider for follow-up.

CAN YOU BE REMOVED FROM THE STUDY?

You may be removed from this study without your consent for any of the following reasons: you do not follow the instructions of the research team, the study doctor decides to remove you from the study, or the study is closed for any reason. If you are removed from the study, you will be referred to your primary care provider for follow-up.

WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

You may contact any one of the following individuals with questions, concerns, or complaints about the research or your participation in this study:

Thomas Buchanan, M.D. ..... 323-479-4319 Cell
Elizabeth Beale M.D……626-232-5348 Cell, 213-287-0123 Pager
Namir Katkhouda M.D. 323-442-5709
Enrique Trigo 323-313-2741

If you feel that taking part in this study has hurt you, please contact Thomas Buchanan, MD at the work number listed above or at the 24 hour number (323) 479-4319. If you have questions, concerns, or complaints about the research and are unable to contact the research team, , contact the Institutional Review Board (IRB) Office at 323-223-2340 between the hours of 8:00 AM and 4:00 PM. (Fax: 323-224-8389 or email at irb@usc.edu).

If you have any questions about your rights as a research participant or want to talk to someone independent of the research team, you may contact the Institutional Review Board Office at the numbers above or write to the Institutional Review Board at the LAC+USC Medical Center, General Hospital, Suite 4700, 1200 North State Street, Los Angeles, CA 90033. You will get a copy of this consent form.

Future Analysis of Your Blood Samples:
Please mark yes or no for **each** question below about how your blood samples may be used for research outside this study.

a) My blood samples may be kept for use in future research on diabetes and related diseases

Yes _____ No _____ Initials _____

b) My blood samples may be kept for use in any future medical research.

Yes _____ No _____ Initials _____

c) I agree to have my blood samples shared with other researchers.

Yes _____ No _____ Initials _____

d) We would like you to agree to have your research data and a part of your blood, urine and DNA samples stored in the Central Repository of the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) at the National Institutes of Health (NIH). The Central Repository collects, stores, and distributes biological samples and associated data from people with many kinds of disorders and from healthy people. If you agree to provide your data and samples, the Repository would make them available for future research about diabetes, obesity and related disorders after the BetaFat Study is over. Your data and samples could be valuable research material that could help researchers develop new diagnostic tests, treatments, and preventive measures.

If you agree to place you data and samples in the Repository, the Repository will take measures to protect your privacy, although it cannot absolutely guarantee confidentiality. Before researchers in the BetaFat Study send your samples to the Repository, we would give each sample a code number and remove your name or other personal identifying information such as address, social security number, or date of birth. Therefore, the Repository would not be able to give out this personal information to any scientists who receive your samples. However, the Repository would have and could share some information, such as your age, sex, diagnosis, race, and outcomes of the BetaFat Study.

You will not receive any direct benefit or payment for allowing your data and samples to be placed in the Central Repository. Neither you nor your physician will get the eventual results of studies that might be performed using your samples. It is possible that data resulting from use of your samples may be used in a research publication. In that event, your name or other identifying information will not be included. There is a small chance that some research may yield results that may indirectly have a negative impact on insurability, employability, and/or family relationships of some individuals or groups of people. If research conducted using your samples in the Central Repository leads to findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits from this may be paid back to the researchers and the organizations doing this study, but you will not receive any financial benefits.

Your decision whether or not to allow your data and samples to be placed in the Central Repository is voluntary and will not affect your other participation in the BetaFat Study. If you choose not to participate there will be no penalty or loss of benefits to which you are otherwise entitled. If you agree to have your data and samples stored in the Repository, you can change your mind up until the end of the BetaFat Study. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the BetaFat Study ends, you will not be able to withdraw your sample because the Repository will not know which one is yours. The sample will stay in the Repository indefinitely.

I agree to have my data and parts of my blood, urine and DNA samples stored in the Central Repository of the NIDDK at NIH.

Yes _____ No _____ Initials _____

The results of our research testing will not be provided to you or to your health care provider because no one knows how to apply these results to your medical care.

AGREEMENT:

I have read (or someone has read to me) the information provided above. I have been given a chance to ask questions. All my questions have been answered. By signing this form, I am agreeing to take part in this study.

Name of Research Participant	Signature	Date Signed

I have personally explained the research to the research participant and answered all questions. I believe that he/she understands the information described in this informed consent and freely consents to participate.

Name of Investigator/Person Obtaining Informed Consent	Signature	Date Signed

A witness is required when: (1) the participant cannot see, read, write, or physically sign the consent form, or (2) the Short Form method is used to obtain consent. If no witness is needed, leave this signature line blank.

Name of Witness	Signature	Date Signed