

Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

The Genetics of Mitochondrial Diseases

H-11469- GENETICS OF MITOCHONDRIAL DISEASES

Background

Mitochondria are structures present in almost all cells of the body and provide energy for the cell, along with other important functions. Inherited mitochondrial diseases are a group of disorders that are estimated to occur in 1/5,000 individuals, and can affect both children and adults. All forms of inheritance can be seen, including unaffected parents having affected children (called recessive inheritance), affected parents having affected children (called dominant inheritance) or where the disease is only passed on through females (mitochondrial inheritance). Clinically, there are lots of ways mitochondrial diseases can occur ranging from brain disease to weak heart muscle or skeletal muscle, blockage of the intestines, kidney disease or liver failure. The wide variety of features reflects the fact that mitochondria are present in almost all cell types of the body, and certain tissues that require oxygen more than other tissues, such as brain and heart, are particularly prone to mitochondrial disease. Despite the essential nature of mitochondria, little is known about the genetic basis of these diseases. This reflects that fact that over a thousand individual proteins are required for normal mitochondrial function, and hence many different genes are potential disease causing genes. To date, only a handful of genes are recognized to cause mitochondrial diseases, however there are undoubtedly many more to be discovered. We are interested in determining the molecular basis of mitochondrial disease in patients seen in the Kleberg genetics clinic and cardiovascular genetics at Texas Children's Hospital or within the hospitalized patients. In addition, patient samples such as blood, skin cells, or muscle and liver biopsies are sent to the Mitochondrial Diagnostic Laboratory at Baylor College of Medicine for diagnostic testing. We will use blood, skin, muscle, liver, or other tissue samples that have been obtained for the purpose of standard patient care or clinical diagnostic testing to carry out genetic, biochemical and functional studies and DNA sequencing to determine the genetic changes present in these patients.

Purpose

The long term goal of this study is to identify genes contributing to human mitochondrial diseases. This protocol will establish a bank of tissue and/or cell lines from skin cells or other available tissues in order to make DNA samples or carry out biochemical tests from patients, parents, and related family members affected with mitochondrial diseases. These samples will be used in biochemical studies, genetic mapping and DNA mutation studies that may ultimately uncover the molecular origin of these genetic defects. Identification of disease causing gene mutations and understanding the basic mechanisms of disease may contribute to the development of preventive and/or treatment strategies aimed at reducing the degree of illness of mitochondrial diseases. This study is expected to last up to 10 years and involve up to 500 subjects.

Procedures

You will be one of approximately subjects to be asked to participate in this trial. The research will be conducted at the following location(s): Baylor College of Medicine.

We are interested in determining the molecular basis of human mitochondrial diseases. Mitochondria generated energy for the cells of the body. Since there are hundreds of possible genes that could cause abnormal mitochondrial function it has been difficult to identify these genes. This study will use genetic and biochemical techniques to identify changes (mutations) in known disease-causing genes

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and to identify new genes that cause mitochondrial disease by studying families that have multiple affected individuals or by sequencing suspected genes. This is done by obtaining blood and/or tissue samples from affected individuals and possibly their unaffected relatives and making either a single source of DNA from a blood sample or a permanent source of DNA in the form of a cell line derived from a skin sample. The tissues available for standard clinical testing will be used for biochemical tests to help identify the possible molecular defects. The sources of samples include affected individuals evaluated by the Genetics physicians associated with this protocol or samples referred to the Mitochondrial Diagnostic Laboratory at Baylor College of Medicine for standard diagnostic testing. Tissue samples will be used to better define the mitochondrial abnormality and DNA will be used to try localize the gene by following different chromosomal regions within a family and looking for the consistent inheritance of particular regions that would point to the location of the genetic abnormality. While it is difficult to make an accurate prediction at this point, given the large number of possible disease-causing genes we expect that it may require enrolling up to 500 subjects over the course of 10 years.

You can see and get a copy of your research related health information. Your research doctor may be able to provide you with part of your information while the study is in progress and the rest of your information at the end of the study.

Potential Risks and Discomforts

In many cases, tissues such as muscle or liver may already be available because they have previously been obtained for other tests as part of standard patient care. If these tissue specimens are not available, a blood sample or skin biopsy may be recommended for additional studies to help in the diagnosis of mitochondrial disease. There is risk of discomfort involved in obtaining a teaspoon of blood or a small (3 mm) skin sample. This may be associated with bruising at the site where the sample was obtained and there is a slight possibility of a local infection from a skin biopsy, although sterile procedures are employed and thus unlikely but readily treatable. In addition, because parents may want to be tested for any genetic changes found in the patient, there is a chance of uncovering unwanted information about whether the parents are in fact the biological parents. Families may also not want to know what genetic changes are present in the family. This will be discussed before samples are obtained and any of this information may or may not be provided depending on the family's wishes. In addition, patient confidentiality will be maintained by coding the patients' samples using a number code, with this information available to only the investigator. Any relevant medical information is maintained in a secure location. No information obtained in the course of this study is released without the family's approval.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study.

Potential Benefits

You will receive no direct benefit from your participation in this study. However, your participation may help the investigators better understand how mitochondria work and an improvement in the diagnosis of genetic mitochondrial disorders..

Alternatives

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The only alternative to this study is non-participation.

Subject Costs and Payments

You will not be asked to pay any costs related to this research.

You will not be paid for taking part in this study.

This institution does not plan to pay royalties to you if a commercial product is developed from blood or tissue obtained from you during this study.

Research Related Injury

Research personnel will try to reduce, control, and treat any complications from this research. If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care.

Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to be a part of the study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

The investigator or sponsor may decide to stop you from taking part in this study at any time. You could be removed from the study for reasons related only to you (for example, if you move to another city, if you do not take your study medication, or if you have a serious reaction to your study medication) or because the entire study is stopped. The sponsor may stop the study at any time.

There may be unknown risks/discomforts involved. Study staff will update you in a timely way on any new information that may affect your health, welfare, or decision to stay in this study.

If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care. You will not be paid for the injury.

Your Health Information

We may be collecting health information that could be linked to you (protected health information). This protected health information might have your name, address, social security number or something else that identifies you attached to it. Federal law wants us to get your permission to use your protected health information for this study. Your signature on this form means that you give us permission to use your protected health information for this research study.

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If you decide to take part in the study, your protected health information will not be given out except as allowed by law or as described in this form. Everyone working with your protected health information will work to keep this information private. The results of the data from the study may be published. However, you will not be identified by name.

People who give medical care and ensure quality from the institutions where the research is being done, the sponsor(s) listed in the sections above, representatives of the sponsor, and regulatory agencies such as the U.S. Department of Health and Human Services will be allowed to look at sections of your medical and research records related to this study. Because of the need for the investigator and study staff to release information to these parties, complete privacy cannot be guaranteed.

The people listed above will be able to access your information for as long as they need to, even after the study is completed.

If you decide to stop taking part in the study or if you are removed from the study, you may decide that you no longer allow protected health information that identifies you to be used in this research study. Contact the study staff to tell them of this decision, and they will give you an address so that you can inform the investigator in writing. The investigator will honor your decision unless not being able to use your identifiable health information would affect the safety or quality of the research study.

The investigator, WILLIAM JAMES CRAIGEN, and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: WILLIAM JAMES CRAIGEN at 713-798-8305.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970.

HIPAA Compliant

CONSENT FORM
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Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Parent Date

Legally Authorized Representative
Parent or Guardian Date

Legally Authorized Representative
Parent or Guardian Date

Legally Authorized Representative - Parent Date

Legally Authorized Representative - Adult Date

Investigator or Designee Obtaining Consent Date

Witness (if applicable) Date

Translator (if applicable) Date