University of California, San Diego
Consent to Act as a Research Subject

Generating human neuronal models of childhood neurological disorders

Who is conducting the study, why you have been asked to participate, how you were selected, and what is the approximate number of participants in the study?
Joseph G. Gleeson, MD, Professor of Pediatrics and Neurology, and his collaborators are conducting a research study to find out more about the causes that may have caused the brain disease in you or your family. We will be enrolling approximately 50 patients with genetic disease and 50 healthy sibling or parent volunteers in this study every year. Children affected with the disorder and their healthy siblings will follow the same procedure in this study. The study will be done in one visit of no more than 1 hour in length. Most of the time will be spent in a discussion of the study as described in this consent form, and in describing the method to obtain the skin sample.

You have been asked to participate because:
1. You have a childhood neurological disorder.
2. You are a healthy family member of a child with a neurological disorder.
3. Your child has a childhood neurological disorder.

Why is this study being done?
This project is sponsored by Howard Hughes Medical Institute and you are being asked to provide skin cells from one of your extremities for the purpose of generating human pluripotent stem cells. Human pluripotent stem cells are unique cells that have the potential to become many kinds of cells in the body. For example, they can be turned into muscle cells, blood cells, or even brain cells, called "neurons". The specific type of cell that a stem cell can become is dependent on the way in which they are grown in the laboratory. In the laboratory these stem cells will be used to generate human brain cells (neurons) that have the same genetic makeup as you do. For this reason, they can tell us more about the cause of the genetic disease in your family. None of the skin cells that you provide will be used to produce a cloned human person. We hope to create a "laboratory model" using some of your cells in a dish, which can help to inform us as to why you or your family member developed his/her specific disease. Since we do not yet fully understand the genetic causes of the disease in your family, by studying your cells, it can help us create better laboratory models, which can be used to test new medications and therapies.

There is no guarantee that stem cells will be successfully created from your skin sample. If you are curious and you wish to know later whether any of your skin cells produced stem cells, you may contact Dr. Gleeson at 858-246-0547 or email at contact@gleesonlab.org.

Providing your skin cells for this research project is completely voluntary. You have the right to agree or refuse to provide your skin cells for this project. The quality of your current or future medical care and your ongoing participation in Dr. Gleeson's other studies or any other research

studies will not change in any way whether you agree or refuse to provide any cells for this research project.

By signing this consent, you authorize the use and storage of your sample and its derivatives by Dr. Gleeson, his associates and collaborators, who may keep your sample indefinitely. You may also revoke your authorization to share your genetic material with other researchers to be used in future research at any time. You may revoke this authorization by submitting a statement in writing to Dr. Gleeson (UCSD 9500 Gilman Drive, La Jolla, CA). However, if the sample is shared with other collaborators, it may be impossible to locate all of the samples.

What will happen to you in this study and which procedures are standard of care and which are experimental?

If you agree to be in this study, the following will happen to you:
Skin biopsy (to be performed by Dr. Gleeson or trained appointee) is a standard clinical procedure used routinely for diagnosis.
a. The area of skin will be cleaned with disinfectant.
b. A numbing solution of 1% xylocaine will be injected just under the skin.
c. A small sterile punch will be used to collect a circle of skin, similar to how a cookie cutter works. This sample will be about the size of a drop of water. The loose piece of skin will be placed into a tube.
d. The wound will be sewn with a suture, or may be just closed with antibiotic ointment and a Band-aid. You may shower or bathe the following day.
e. In the unlikely event that there is any pain following the procedure, acetaminophen (600 mg) may be used up to three times per day.
f. You will be told to watch for signs of redness or swelling. If these occur, please call Dr. Gleeson at 858-246-0547 or your referring doctor.
g. Infection is rare but it will be treated with antibiotics.
h. A follow-up appointment will be made for 1 week later to remove the Band-aid and to check for healing.

The skin sample will be coded so that no identifying information will be stored with it. The skin sample will be transferred to Dr. Gleeson's laboratory for culture, where special factors will be used to reprogram the cell into another cell type.

One possible research use of the stored stem cells might involve changing some of the genes in the sample, to correct the genetic defect in the cells. Another possible research use might involve studying the DNA of the sample or injecting the cells into laboratory animals to watch how they behave. In addition, some of the cells may be used in research related to human transplantation, in an attempt to cure the disease. These are just three examples of what might happen to the stored cells. But there are other future possible research uses that we simply cannot know about now, because the field of stem cells is just at its beginning. You agree to possibility of sending these cells to other laboratories and institutions with which Dr. Gleeson collaborates. If they are sent to collaborators, they will be "deidentified"; that is, labeled only with an identification code, not with a name. You also agree that you do not control who may be

a recipient of transplanted cells if this option ever becomes possible. If medically appropriate, and if cells are available, they will be made available to you for transplantation if you so desire.

How much time will each study procedure take, what is your total time commitment, and how long will the study last?
The skin biopsy procedure will take approximately 15 minutes.

It is likely that the retrieved stem cells, which will be genetically matched to you, will be stored for many years. These stored stem cells may also be used by researchers at other institutions and for other research purposes. However, Dr. Gleeson will be responsible for deciding how your cells will be used. The specimens collected from you and the DNA that they contain may also be used in additional research to be conducted by the University of California or other researchers at collaborating institutions. These specimens, DNA and other derivatives may have significant therapeutic or commercial value.

Even though this genetic material might have some commercial or therapeutic value, you will not receive any compensation. By signing this consent form, you understand that commercial development and scientific patents of discoveries made through the use of these cells will not lead to your compensation. You consent to such uses.

What risks are associated with this study?
Risks or discomforts from skin biopsy
Participation in this study may involve some physical risks or discomforts, which include:
a. There is a slight risk that an individual might be allergic to the anesthetic. To minimize this possibility, you will be asked if there has been any reaction to anesthetics, and if so, they will not be enrolled in this study.
b. A pinprick needle will be felt during injection of the numbing medicine. There is risk of infection if the area is not kept clean.
c. A small scar will develop at the site of the biopsy, about the size of the biopsy, but it may grow over time.
d. There may be psychological risks. Some people who provide cells for research might experience anxiety or regret, especially when considering that the cells will be reprogrammed to stem cells.
e. Providing skin cells may involve some risk to your privacy. Efforts to protect you are discussed below.
f. Because this is an investigational study, there may be some unknown risks that are not foreseen. You will be informed of any significant new findings.

What are the alternatives to participating in this study?
The alternative is to not donate the skin specimens.

What benefits can be reasonably expected?
You will be providing your skin cells solely for the advancement of knowledge of childhood neurological diseases and stem cell research. There will be no direct benefit to you from these procedures. Dr. Gleeson may learn more about the disease in your family, and possibly design new therapies. This knowledge may help you or others with the disease in the future.

Can you choose to not participate or withdraw from the study without penalty or loss of benefits?
Participation in research is entirely voluntary. You may refuse to participate or withdraw at any time without penalty or loss of benefits to which you are entitled. If you decide that you no longer wish to continue in this study, you will be requested to contact the research team at contact@gleesonlab.org or 858-246-0547 and indicate that you would like your skin cells and/or their derivative cells to be discarded. Please note that this may be possible only if your skin cells or their derivative cells have not been widely distributed to other researchers.

You will be told if any important new information is found during the course of this study that may affect your wanting to continue.

Can you be withdrawn from the study without your consent?
You may be withdrawn from the study if you do not follow the instructions given you by the study personnel.

Will you be compensated for participating in this study?
You will not be compensated for participating in this study.

Are there any costs associated with participating in this study?
There will be no cost to you for participating in this study.

What if you are injured as a direct result of being in this study?
If you are injured as a direct result of participation in this research, the University of California will provide any medical care you need to treat those injuries. The University will not provide any other form of compensation to you if you are injured. You may call the Human Research Protections Program Office at (858) 246-HRPP (858-246-4777) for more information about this, to inquire about your rights as a research subject or to report research-related problems.

What about your confidentiality?
All of the information we collect during the course of this study will be kept locked and secured and it will be released to no one unless you ask us to do so. All samples will be stored in Dr. Gleeson's laboratory and labeled with a code, not with your name or any other identifying information. The result of any experiments will also be kept linked only to the identification code instead of names. The key that links your code with your name will be stored in a password-protected file that is available only to Gleeson Lab members. Despite these careful measures, it remains possible that a breach in protocol or a theft in the lab could result in loss of your confidentiality.

No information will be entered into your medical record. The PI and staff of Gleeson laboratory will have an access to your records as long as you are involved in our research study. However, if you wish to withdraw from our study your information will be destroyed. Research records may be reviewed by the UCSD Institutional Review Board or Howard Hughes Medical Institute.

If as a result of participation in this study we obtain information that may significantly affect your health or well-being, we will attempt to inform you of the existence of this information, if you are interested in receiving it. Please indicate your preference here:

Are you willing to be contacted about study results that may affect your health or well-being?

_____Yes _____No Initials_____

However, it may not be possible in all circumstances to report this information. Participation in this study does not mean that you have had comprehensive genetic testing or that genetic information will be provided to you.

Local and state agencies as well as project sponsors may review the research project records to ensure that your rights as a skin cell donor are being adequately protected.

Any report that the researchers publish will not include any information that will make it possible for readers to identify you as a donor.

You have received a copy of this consent document and the Experimental Subject's Bill of Rights to keep for yourself.
Federal and State laws generally make it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways: a) Health insurance companies and group health plans may not request your genetic information that we get from this research. b) Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. c) Employers with 5 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that these laws **do not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Who can you call if you have questions?
Joseph Gleeson, MD and/or _____ has explained this study to you and answered your questions. If you have other questions or research-related problems, you may reach Dr. Gleeson at 858-246-0547.

You may call the Human Research Protections Program Office at (858) 246-4777 to inquire about your rights as a research subject or to report research-related problems.

Signature Block for Adults Able to Provide Consent

Participant

I have received a copy of this consent document and a copy of the "Experimental Participant's Bill of Rights" to keep. I agree to participate in the research described in this form.

Printed Name of Participant

Signature of Participant Date

Person Obtaining Consent

I document that:

- *I (or another member of the research team) have fully explained this research to the participant.*
- *I have personally evaluated the participant's understanding of the research and obtained their voluntary agreement.*

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent Date

Witness (if applicable)

I document that the information in this form (and any other written information) was accurately explained to the participant. The participant appears to have understood and freely given consent to join the research.

Printed Name of Witness

Signature of Witness Date

Signature Block for Adults Unable to Provide Consent

Participant

I have received a copy of this consent document and a copy of the "Experimental Participant's Bill of Rights" to keep. I give my permission for the named person below to participate in the research described in this form.

Printed Name of Participant

Printed Name of Legally Authorized Representative

Signature of Legally Authorized Representative Date

Person Obtaining Consent

I document that:

- *I (or another member of the research team) have fully explained this research to the legally authorized representative of the participant.*
- *I have personally evaluated the legally authorized representative's understanding of the research and obtained their voluntary agreement.*
- *I have personally evaluated the participant's understanding of the research and, if capable of providing their assent, obtained their assent to participate in the research as indicated below.*

Assent	❑ Obtained ❑ Not obtained because the capability of the subject is so limited that the subject cannot reasonably be consulted.

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent Date

Witness (if applicable)

I document that the information in this form (and any other written information) was accurately explained to the legally authorized representative. The legally authorized representative appears to have understood and freely given consent for the participant to join the research.

Printed Name of Witness
Signature of Witness Date

Experimental Participant's Bill of Rights

Every individual asked to participate in a research study has the right to be:

1. Informed about the nature and purpose of the study.

2. Provided an explanation of the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. Given a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. Informed about any benefits that would reasonably be expected from the participation in the study, if applicable.

5. Informed about of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. Told of the types of medical treatment, if any, available if complications should arise.

7. Provided an opportunity to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. Informed that individuals can refuse to participate in the research study. Participation is voluntary. Research participants may refuse to answer any question or discontinue their involvement at any time without penalty or loss of benefits to which they might otherwise be entitled. Their decision will not affect their right to receive the care they would receive if they were not in the experiment.

9. Provided a copy of the signed and dated written consent form and a copy of this form.

10. Given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study contact the researchers listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research participant, please contact:

- UC San Diego Office of IRB Administration at irb@ucsd.edu or 858-246-4777