

Information Sheet: Parent of Case (v2)

TITLE: Genetic Characterization of Neurodevelopmental Disorders in South African Populations (NeuroDEV South Africa)

REFERENCE NUMBER: 810/2016
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You and your child are invited to take part in a research study. Please take some time to read the information here. Please ask questions about any part of this project that you do not understand. It is very important that you feel you understand what this research is about and how you could be involved. Also, being in the study is voluntary. You are free to choose not to join. If you say no, this will not affect you in any way.

This study has been approved by the University of Cape Town Human Research Ethics Committee (HREC ref 801/2016) and the Harvard School of Public Health, in the United States of America. The study will be carried out according to the highest ethical standards.

What is the study about?

This study looks at development in childhood. The study will try to find out about genes that may be related to why some children develop differently than others. We will be asking over 5,000 people to take part in this study. The reason is to better understand the cause of delays in development and other social and thought problems.

Background

Our body is made up of many tiny parts called cells. These cells contain DNA, which tell the cells how to grow and work. We get our DNA from our parents. Nobody else in the world has the same DNA as you, unless you are a twin. Difference in DNA can be why some people are tall and others are short. Some illnesses are caused by problems with DNA. The study of DNA is called genetics. DNA can be found in blood and in saliva.

A cell line is a culture made from cells of the same type. Under the right conditions, these cells can make copies of themselves. So without having to draw blood again, researchers can keep studying the cells in your blood for many years. This makes cell lines very useful. A stem cell is a special type of cell. Stem cells can form many different types of cells in the body. Stem cells are made of the same DNA as all other cells in your body. A stem cell made from your blood is called an induced pluripotent stem cell (iPS cell).

Do I have to take part?

It is your choice to be in this study. This study does not have anything to do with the care you or your child receives at this hospital or school. If you do not want to answer some questions or if you do not want some tests to be done, you can tell us. If you would like to stop at any time, you can. You can say "Yes" and join the study; or you can also say "No", you don't want to join.

What does being in this study include?

What your child will do

If you choose to join your child in this study, we will ask you some questions about your child to

assess your child's behavior, reasoning, and movements. We will also examine your child's body and look at your child's medical records to find out about his or her health. The whole process could take up to 3 hours. We would be happy to provide the names of the tests and explain these tests to you before we start.

A nurse will ask your child to give some blood. Your child will give up to two teaspoons (10 ml) of blood. If you agree, we may also ask for your child to give us some saliva in a small plastic tube. If we collect saliva, we will ask for less than half a teaspoon (2 ml or less) of saliva. DNA is in blood and saliva, which we call a 'sample'.

The sample will be sent for DNA processing in the United States of America. We will analyse your child's DNA using chemicals and computers. Then we will compare your child's DNA to the DNA of other children in the study to look for differences. No one testing your child's DNA will know your child's name.

You also have the choice of contributing your child's sample for cell line and stem cell research. Stem cells are important because they can become all types of cells in the body, such as muscle cells, brain cells or heart cells. Stem cells also can make copies of themselves, and for this reason a stem cell line growing in a lab could exist for a very long time, even longer than your child's lifetime.

With your permission, we will also photograph your child's face, hands and feet. The photographs are to help doctors and other health experts recognize children with or without delays. Your child does not have to be photographed to be in the study. If you agree to have your child photographed, the photos will be used for clinical, educational and research purposes. You can also choose to allow public use of the photo to help improve diagnosis of children with difficulties like your child.

What you will do

You are also invited to enroll yourself in addition to your child. If you accept, you will give about three teaspoons (14,5 ml) of blood, which contains your DNA. In addition, we will ask you to do a puzzle that looks at how you reason. . In the same way as for your child, your blood will be sent for DNA processing in the United States of America. Then we will compare your DNA to your child's DNA to look for differences. No one analyzing your or your child's DNA will know your names. If you agree to be part of the cell line research, we may make cell lines from your blood, and we may try to make stem cells.

Storage and sharing of your information and samples

With your permission, your and your child's blood sample and health information will be sent to and stored in the United States of America. Some of the sample may also be stored here in South Africa. Your child's donated DNA can last a very long time. The samples will be stored and may be used for other tests in the future. Access to your child's DNA will continue to be guarded into the future by a set of strict controls to make sure that it is only used to study questions that are important to science.

Creating a cell 'bank' or library

The samples will be stored at the National Institutes of Mental Health Repository and Genomics Resource (NIMH-RGR). This is a 'bank' or library for biological samples funded by the department of health in the United States government. Some of the samples will also be stored in South Africa at the Department of Human Genetics in the University of Cape Town. That way, your and your child's samples can be shared with other researchers at universities, hospitals, government agencies and companies around the world. One place your DNA will be shared with is the Broad Institute, a non-profit American research institute with skilled scientists who know how to analyze DNA.

If you agree to be part of the cell line research, the cells and your health information will be stored in the

cell library and distributed for a long time, possibly forever. None of the researchers who study your cells or health information will know your name.

The samples and information will be available to scientists all around the world, to study any research question. Examples include research to understand the cause of diseases (for example heart disease, cancer, or psychiatric disorders). Other examples include research to develop new methods, to study human behaviors, or to find out where different groups of people come from.

If you agree to participate in the cell line and stem cell research, your samples could be of even greater use. Researchers around the world may use your cells to study the biology of stem cells, certain illnesses, and whether it is possible to transplant stem cells (or things made by those cells) to treat diseases. Common examples of what might happen to the stem cells include:

- Testing the cells' DNA
- Using cells to test drugs to treat disease
- Changing some of the genetic code within the cells
- Transplanting the cells (or things made by those cells) to humans or animals
- Sharing cells widely for research, training or to make commercial medical products

Because these samples can last forever, scientists may come up with new ways of working with them in the future. Right now, we do not know what the future uses may be.

Creating a photo library

If you allow us to photograph your child, we will ask you to choose one or both of the following options:

- The photos can be shared on a mobile application that will improve technology for diagnosing children with delays in development in the future. One example of a mobile application that uses photos to help diagnose genetic conditions is Face2Gene. If a photo is shared this way, a computer breaks it up into thousands of bits of information and compares it other photos. When the photo is broken up in this way, it cannot be used to identify your child.
- The photos can also be shared on a public website called the NIH Atlas of Human Malformations in Diverse Populations. The NIH Atlas is an online photo library that can be used by doctors to help diagnose children now. The website is made for doctors and health professionals, but anyone can see it.

If you agree to one or both of these uses of your child's photos, they will be shared together with some pieces of health information (eg age, ethnicity & diagnosis).

Putting information in public databases

Some of the genetic and health information from this study will be freely available in public databases that anyone can use. Examples of these databases are ClinVar and the Genome Aggregation Database (GnomAD). These public open-access databases may include information about your DNA, as well as your ethnic group and sex. This public information will not be labeled with your name or other information that could easily identify you.

Your and your child's DNA and health information will also be put in one or more controlled-access database. This means that only researchers who apply for and get permission to use the information for a specific research project will be able to access it. Your and your child's DNA and health information will not be labelled with your names or other information that could be used to identify you.

Securing information on a group of computers

Your and your child's DNA and health information will not be labeled with your names or other information that could be used to identify you. To ensure safety, the information will be stored and

analyzed in the Cloud. "The Cloud" refers to a group of computers in a data center that is accessible through the Internet. The Cloud is managed by a company or other institution that is not part of the research team. The study information will be stored on a secure Cloud server to prevent unwanted access. The company or other institution that will process and store your data is located in the United States. It may also come to be located in other countries where the laws may not protect your privacy to the same level as in your country. However, all reasonable steps will be taken to protect your privacy.

What if I change my mind?

If you join the study, you can change your mind later and decide that you don't want to be part of it anymore, and you do not want your child's blood or saliva to be used. Please let us know and we will destroy the sample. If your or your child's sample has already been tested at the time you change your mind, your results and other data may have already been shared with other investigators. In that case, we will not be able to destroy this data. However, the code that links your child's name to their information and samples can be destroyed. Whether or not you decide to join the study, the way we look after you and your child in the clinic or at school will be the same. It is your choice whether to be in the study or not.

Benefits and Risks

Benefits

For most people, there are no direct benefits to being in this study. However, in some cases we may find something in your child's DNA that helps explain what caused his or her condition. If we find something, we would have to double check it. That would mean inviting you back to give more blood and say if you still want to get the results. In most cases, we will not find results to return. Not finding a result does not mean there is no genetic cause, but only that we do not yet know what the genetic cause(s) might be.

One reason somebody might want to share their DNA without direct benefit is that it may help scientists to learn more about the human body, and better understand problems of child development. We hope this will help make better treatments in the future.

Risks

The risks of taking blood include pain, as with a pin prick, a bruise at the point where the blood is taken, and redness and swelling of the vein. There is also a rare risk of infection, if the area is not kept clean, and a rare risk of fainting.

When answering questions about yourself or your child, you may experience distress or discomfort. You do not have to answer questions if they make you uncomfortable. You may also ask to take a break at any time.

If you agree to have your child photographed and to share the photo publically, it is possible that somebody somewhere - perhaps, somebody who looked after your child in hospital, or a friend or relative - may identify your child..

There are some risks related to the use of your or your child's information and samples. It is possible that someone could break into the system that stores information about you and your child. All the computers with study results are protected by several strong passwords, so this is very unlikely. It is also possible that your child could be identified through the photographs, which will be stored on the Cloud. Security of the Cloud is high, so breaking into the Cloud is very unlikely. There may be other

privacy risks that we do not know.

If someone has another DNA sample from you or your child, which has not been protected, it is possible that you could be identified from your sample. This would happen if the two samples were matched, and one of them was linked to your name. The risk of this happening is very small but may grow in the future as genetic processing is more widely used.

As certain conditions and traits run in families and are inherited. You may learn something about your health that relates to the health of your relatives. Although your DNA is unique to you, you share some similarities with your children, parents, brothers, sisters, and other blood relatives. Therefore, finding out about your results could mean you learn something that relates to the health of your family members and might cause you or your family distress

Since some genetic information can help predict future health problems for you and your relatives, this information might be of interest to health care providers, insurance companies and others. However, South African law and policy provides some protections against discrimination on the basis of an individual's "state of health" (eg. the South African Medical Schemes Act No. 131 of 1998).

Privacy

The information we get from you and your child will not be shared with your health insurance. Nobody outside the study will be able to know which results belong to you or your child. The researchers will not tell anyone else that either of you are in the study.

Reimbursement

You will be reimbursed for your time, travel costs and the inconvenience of taking part in this study. Once you have been interviewed and you and your child have given your blood, and possibly saliva, the study staff will reimburse you. You will be reimbursed 250 Rand. As a thank you, we will also give your child a goodie bag, which may include a small toy, snacks and a polaroid photo of your family.

The control over the samples you and your child donate will be held by the University of Cape Town and The Broad Institute. Your and your child's samples will not be sold, but investigators may make products based on studying these and other samples, images or information. If this happens, you will not be able to share in any profits. This is not likely to happen for many years, if at all.

Future Contact

Individual results from this research project will not be given back to you or put into your or your child's medical records, but we may learn something from this study that we would like to follow up on in the future. We may also want to contact you in the future to see if you or your child would be interested in enrolling in another study. Please indicate on the consent form if you are willing to be contacted in the future. You have the right to withdraw your consent for future contact at any point in the future.

When your child turns 18, he/she has the right to decide whether to be in research and the right to withdraw from this study. We will not get back in touch when your child turns 18, unless you or your child seeks to do so. However, if your child reaches the age of 18 during the course of the study, we will contact you and your child, and offer your child consent. If your child does not have the capacity to consent, we will offer you to re-consent. If we cannot reach you, or your child, or you or your child chooses not to consent, we will break all links to their identity.

Questions:

If you have any questions about this study please ask the research nurse. You can also contact **the Project Manager** emma.eastman@uct.ac.za and **the Primary Investigator** Kirsty.donald@uct.ac.za;

081 810 2614 to have your questions answered. If you wish to withdraw your consent later you may also contact the project manager. For questions about your rights as a research participant, please contact a representative of the **University of Cape Town Human Research Ethics Committee on 021 406 6338**. This can include questions about your participation, complaints or concerns about the study, including if you feel pressure to enroll.

You will be given a copy of this information sheet and signature page for your records. Please keep a copy of these documents in case you want to read them again.

Consent Form: Parent of Case (Child participating)

I, _____, the parent of

_____ agree to allow my child to take part in this study, which will use his/her DNA to try to learn about developmental delays and other social and thought problems.

- I give permission to be interviewed and for my answers to be recorded.
- I give permission for a sample of my child's blood and saliva to be taken.
- I give permission for my child's DNA to be stored at the Human Genetics Lab at the University of Cape Town, at the National Institute of Mental Health Repository and Genomics Resource in the United States, and at the Broad Institute in the United States.
- I agree to my child's DNA being made available on both open and controlled access databases.
- I understand that:
 - a. My child's identity will be protected.
 - b. I will be compensated 250 Rand for the time and inconvenience of being part of the study.

Additionally, I am choosing to give permission for the following.

1. Do we have your permission to create cell lines and stem cells from the blood we draw?
 - Yes
 - No
2. Do we have your permission to photograph your child?
 - Yes, and the photo can be publicly shared outside the study (for example with the NIH Atlas of Human Malformation in Diverse Populations)
 - Yes, but the photo can only be shared outside of the study with health care providers or researchers for clinical, educational or research purposes (for example with the Face2Gene application)
 - No
3. If we find something in your child's DNA that could have caused his or her condition, would you like us to contact you to follow up and confirm the finding?
 - Yes
 - No
4. Do we have your permission to contact you in the future to follow-up on this study or for future studies?
 - Yes
 - No

Address: _____

Telephone/Cell: _____

Email/Other: _____

5. If you agree to be contacted again, and we cannot find you, may we try to reach you through a friend or relative?

- Yes
- No

Contact information of a relative/friend (1):

Name: _____

Relationship: _____

Telephone/Cell: _____ Email/Other: _____

Contact information of a relative/friend (2):

Name: _____

Relationship: _____

Telephone/Cell: _____ Email/Other: _____

I have read, or have been read, the accompanying information sheet in my own language. I understand this consent form and the information sheet. Any questions I had have been answered. I understand that I may withdraw my consent from any, or all, aspects of this study without any impact on my medical care, and without any repercussions.

Signed in _____ (place) on _____ (day) of _____ (month) _____ (year)

Signature _____

Witness 1 Name _____ Signature _____

Consent Form: Parent of Case (Parent participating)

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_____ agree to take part in this study, which will use my DNA to try to learn about developmental delays and other social and thought problems.

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 - Yes
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2. Do we have your permission to contact you in the future to follow-up on this study or for future studies?
 - Yes
 - No

Address: _____

Telephone/Cell: _____

Email/Other: _____

3. If you agree to be contacted again, and if we cannot find you, may we try to reach you through a friend or relative?
 - Yes
 - No

Contact information of a relative/friend (1):

Name: _____

Relationship: _____

Telephone/Cell: _____ Email/Other: _____

Contact information of a relative/friend (2):

Name: _____

Relationship: _____

Telephone/Cell: _____ Email/Other: _____

I have read, or have been read, the accompanying information sheet in my own language. I understand this consent form and the information sheet. Any questions I had have been answered. I understand that I may withdraw my consent from any, or all, aspects of this study without any impact on my medical care, and without any repercussions.

Signed in _____ (place) on _____ (day) of _____ (month) _____ (year)

Signature _____

Witness 1 Name _____ Signature _____