Participant Information Statement and Consent Form

HREC Project Number:	64193
Title of Project:	Leukodystrophy and White Matter Disorders Research Program
Principal Researchers:	Professor Richard Leventer, Head, Neuroscience Research Group and Dr. Cas Simons, Head, Translational Bioinformatics Research Group, Murdoch Childrens Research Institute.
Version Number:	5 **Version Date:** 1/03/2021

Thank you for taking the time to read this **Information Statement and Consent Form**. We would like to invite you to take part in a research project that is explained in this form.

This form is 10 pages long. Please make sure you have all the pages.

What is an Information Statement and Consent Form?
An Information and Consent Form tells you about the research project. It explains what the research project involves. This information is to help you decide whether or not you would like to take part in the research. Please read it carefully.

Before you decide if you want to take part or not, you can ask us any questions you have about the project. You may want to talk about the project with your family, friends or health care worker.

Taking part in the research project is up to you
It is your choice whether or not you take part in the research project. You do not have to agree if you do not want to. If you decide you do not want to take part, it will not affect your treatment and care.

Signing the form
If you want to take part in the research, please sign the consent form at the end of this document. By signing the form you are telling us that you:

- understand what you have read
- had a chance to ask questions and received satisfactory answers
- consent to taking part in the project.

We will give you a copy of this form to keep.

1. What is the research project about?

We are inviting your child to take part in a project about white matter disorders. The white matter in your brain, also known as myelin, makes up the insulation around the nerve wires in the brain and spinal cord. This protective covering acts much like the coating around electrical wire in that it is responsible for the rapid transmission of signals to and from the brain to nerve cells throughout the body. Without white matter, communication between the brain and nervous system becomes disrupted or non-existent. This can cause problems with movement, speaking, vision, hearing and mental and physical development.

The aim of this project is to look closely at your child's genes and compare them to you and closely related family members to try to find a diagnosis for the white matter condition in your family. As part of this project we want to collect information about your child from their medical records to store on our registry. This is to help us further our understanding of these conditions and to involve Australian patients in future research projects when available

Our bodies are made up of different types of cells. Inside these cells you find genes. Genes are passed down in families from parents to children. You get half your genes from your mother and half from your father. A gene is like a small microchip. It contains all the information that makes us what we are, including our eye colour and blood type.

There are about 23,000 genes that make up a human being and genes are arranged along a chemical substance called DNA. Sometimes a gene contains a "spelling mistake" that upsets the gene's coded message. This mistake is also called a "variant" or a "mutation". These types of variants can change the way the gene works and cause different diseases.

Many health conditions or diseases are caused by a change in one or more genes. These conditions are usually present at birth or may sometimes appear later in life. Rare genetic conditions may occasionally occur in more than one person in a family, or can occur for the first time in the person with the condition.

Until recently, doctors and scientists were only able to test one gene at a time. Advances in technology now allow us to test many of our genes at once (genomic testing). For some rare genetic diseases, we already know the gene variant that causes the condition. For others, the exact variant that causes the condition is not known. If we cannot find the gene variant that explains the white matter condition in your family, we will look for new variants and new genes to try to find a diagnosis.

2. Who is running the project?

The project will recruit families Australia-wide and is based at the Murdoch Childrens Research Institute (MCRI) and The Royal Childrens Hospital (RCH) in Melbourne.

The project is funded by the Medical Research Futures Fund (MRFF).

3. Why am I being asked to take part?

We are asking you to take part in this project because you have a confirmed or suspected white matter disorder.

4. What do I need to do in this research project?

You will need to do different things depending on whether or not you have a diagnosis.

If you **have a diagnosis** you do not need to do anything. We will collect medical information about you for the registry. A registry is a collection of information about individuals, usually focused around a specific condition. For this project, we are collecting information about Australians who have a white matter disorder.

If you **do not have a diagnosis,** we will collect medical information about you for the registry. We will also ask to collect a blood and/or saliva sample for genomic testing. We will talk to you before we take any samples. If there is already a sample stored, with your permission, we will use that sample. Sometimes it is helpful to use other types of samples like urine or a skin biopsy. Collecting and testing different samples increases the chance that we will be able to find a genetic variant that causes the white matter disorder in your family. You do not have to agree to these samples being collected in order to participate in the study. We may also need to collect a sample from related family members

		Will you complete these tasks?	
Part of study	**What does this part involve?**	**If you have a diagnosis**	**If you do not have a diagnosis**
Collection of medical records for registry	We will collect demographic and medical information about you for the registry. This includes your • name • date of birth • family history • medical and developmental history We will collect this information from your medical records and/or treating team. In some instances, we may ask you to provide this information.	✓	✓
Blood sample	We may ask to collect a blood sample if you do not have a genetic diagnosis. We may collect a small blood sample of up to 10mL (2 teaspoons). We can collect this in person at the hospital or you can have it collected at your local collection centre.	✘	✓
Saliva sample	We may ask to collect a saliva sample as well, or instead of, a blood sample if you do not have a genetic diagnosis. This can be done by the use of a simple saliva collection swab. We can collect this in person or we can post the kit to your home address.	✘	
Skin biopsy	We may ask to collect a skin biopsy if you do not have a genetic diagnosis. This is optional. The skin sample involves taking a small piece of skin about the size of a grain of rice. It usually takes about 5 minutes. Normally, a cream is applied 30 minutes before taking the sample. The biopsy site usually bleeds immediately after the procedure, but this stops once light pressure is applied. The area will be closed by a type of sticky plaster stitch and covered with a bandaid if required. Skin samples are done using a sterile technique by a qualified nurse or doctor, who will explain the procedure to you in detail and seek your consent before proceeding. If you are having a general anaesthetic for another purpose, it may be possible to collect the skin biopsy during that procedure.	✘	Optional

Urine sample	We may ask to collect a urine sample if you do not have a genetic diagnosis. This is optional. We can collect this in person at the hospital.	✘	Optional

Previous genetic or genomic testing
If your child has had genetic or genomic testing in the past, but the genetic variant that caused their condition was not found, we may ask you to consent for us to re-analyse that existing genetic data.

Sample storage and use:
Samples will be kept indefinitely unless otherwise requested. When your child turns 18 years of age we will not contact them to ask them to re-consent to this research. We ask that you pass on information about their samples stored for this study when they are an appropriate age. We will store samples at The Royal Children's Hospital, the Murdoch Children's Research Institute or the Victorian Clinical Genetics Services. We will use these samples to try to find and understand the cause of the white matter disorder in your family.

Data and sample sharing:
It may be that we will need to share the samples collected with research colleagues in Australia or overseas to be able to do specialised genetic or other tests, such as cellular function studies. We therefore ask your permission to send DNA and/or cells to other research collaborators if needed. **Any samples that we send overseas are not protected by Australian laws and regulations.** All of these samples will be uniquely coded to protect your child's privacy. Information such as your child's detailed medical history, name and date of birth, will not be shared, but the collaborators will be given information about the type of condition present in you, your child or family member.

We may send your child's health information and/or DNA sample for inclusion on an international, 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 this information. The information will not have any personal, identifying details attached to it. It will be sent with an ID number that is used only by the research team here at the MCRI. Researchers approved to access information in the database will agree not to attempt to identify you. The information generated from testing will be made available to our research team, and we will add this information to our research data we have already collected about your family as part of this project.

After we have received information about your child's test results, the international database will make your child's genetic and health information available to approved clinicians to access so it can be used to 'match' genetic changes and clinical features that are the same or similar as your family with their families to help with identifying the genetic cause of another family's condition.

It could also be used by other researchers to answer research questions, such as to understand what causes certain diseases, development of new scientific methods, or to study where different groups of people may have come from.

Information will be stored on these databases for an unlimited period of time.

By working with other research groups, we increase the chance of finding the cause of the rare disease in your family.

There are **no out-of-pocket costs** associated with participating in this research project. You and your child will not be paid for your participation.

Optional consents

a. **Establishment of a permenant cell line**

In this project, we may establish a permanent cell line from your tissue samples. A cell line is formed when we take cells from the blood, skin or other tissues and grow them in the laboratory. This allows the creation of a continuous supply of cells for research purposes and reduces the need to collect further samples.

b. Clinical photographs

We may ask to take clinical photographs of your child for inclusion in this research and in scientific journal articles written about the results of this study. Images may be used in medical journals and electronic publications be seen by health professionals, scientists and researchers. Identifying information will not be published. You can say no to this if you want to.

c. Future research

We would like you to consider letting us use clinical data and samples that we collected as part of this research project for use in future ethically-approved research studies related to white matter disorders. We do not plan to contact you or your child to use the data and samples in future research. You can say no to this if you want to.

We would also like you to consider letting us to send you information about new research projects that may be suitable for your child. The information we send will give you the full details about the project. It is your choice whether your child takes part in these projects. You can say no to them if you want to.

5. Can I stop taking part in the project?

You can withdraw from the project at any time. You just need to tell us so. You do not need to tell us why.

If you leave the research project, we will use the information we have collected about you.

If you request it, all collected data will be destroyed unless already sent overseas in a de-identified form. However, we cannot withdraw the data if analysis has commenced or is completed. Your decision will not affect any treatment or care you or your relatives receive at The Royal Children's Hospital or any other health service.

6. What are the possible benefits for my child and other people in the future?

We cannot guarantee that you will get any benefits from this project.

However, for undiagnosed people, we may find the exact genetic cause of the white matter disorder affecting your family. This may help with management of the condition. Your family may benefit from this information as it might be possible for your doctor to give you more accurate information about the chance of having further children with the gene variant, or if other members of your family might develop the condition.

This research may benefit others in the future, as the aim of this study is to improve the welfare of patients and families affected by white matter conditions. Participation in the registry will also provide the opportunity for Australian families be involved in future international research projects when available.

7. What are the possible risks, side-effects, discomforts and/or inconveniences?

Blood test

There are no major risks associated with a blood test. However, you may feel some discomfort during the test. You may feel a sting when the needle is put in their arm. We can use a cream to numb the skin before we take blood.

You may get some bruising, swelling or bleeding where the needle enters the skin. Some people can feel a little light-headed when blood is taken.

Skin Biopsy

A skin biopsy is generally a simple and safe procedure using a local anaesthetic. There may be some bleeding and/or bruising where the skin is taken and some may experience minor discomfort. The procedure will leave a small scar – about 5mm. It is unlikely to happy but in some cases your wound might get infected. If you are having another procedure under anaesthetic, we may ask if we can collect a skin biopsy. This will minimise the discomfort for you.

Genetic testing – issues for you

A genetic test has a number of potential results. These include an informative result that explains your rare genetic condition, a negative or uninformative result where no genetic explanation is found, or an uncertain result that we do not understand at this point in time. Sometimes, samples from parents or other close relatives (usually siblings), may help us understand uncertain results.

We are only searching for genes that are related to white matter disorders However, it is possible that we may find genes responsible for other genetic conditions. Overall, the chance of this is low. However, if we find that you have a genetic condition for which we have specific treatment recommendations, we will contact you to discuss the findings. These results might also be important for the medical care of others in the family, such as siblings or parents. We will also refer you, and your family if appropriate, to a genetic counsellor. With your permission, we will share these results with your doctors

Genetic testing – issues for your family

The genetic tests may tell us something about you or your wider family. This could affect you and your family emotionally and interfere with your relationships. For example, by chance, we may discover that parents and children or siblings may not be biologically related. While the identification of non-paternity is extremely unlikely, if this is identified, we will not disclose this to you or any family members. This is in keeping with standard clinical genetics practice.

Some people in your family might want to know about your results. They may want to know whether the results have implications for them. You get to decide whether you want to tell them about the test results.

Genetic testing – issues to think about

If you decide to go ahead with your genetic test, this may have implications for you in the future. For example, you may need to reveal these test results to third parties such as insurance companies, employers, and financial or educational institutions.

Some people find it stressful to get information about their genetic make-up and possible future health issues. Your participation in this project could raise personal issues for you. If this happens we can refer you to an independent genetic counsellor. This will be free of charge. We are also available to discuss any concerns you may have.

We will keep your test results private but we cannot guarantee complete confidentiality. Some genetic variants are very rare, and we aim to publish results from this study in scientific journal articles. Therefore, it may be possible to identify you from the test results or the name of the gene.

If the testing shows important information about your relatives, contact with your relatives about the testing is encouraged. You may wish to do this yourself or you may ask your doctor to assist you in this if you choose.

8. What will be done to make sure my information is confidential?

We will collect and use personal and health information about you for research purposes. We can disclose the information only with your permission, except as required by law.

All study data will be stored in a secure, controlled-access database at the MCRI that meets international security standards and Australian laboratory accreditation requirements. Information about your participation in this research project may also be recorded in your health records.

Samples will be stored securely in the Royal Children's Hospital, Victorian Clinical Genetics Services and Murdoch Children's Research Institute laboratories unless being sent to external collaborators. DNA sequence data will be stored on secure servers at the Murdoch Children's Research Institute.

The following people may access information collected as part of this research project:

- The research team involved in this project.
- The RCH Human Research Ethics Committee.

To advance science, medicine and public health, we may also need to share your re-identifiable data with other ethically approved research projects, biobanks, or medical journals. If we need to do this, we will make sure your data is anonymous before we share it. This means we will remove personal information such as your name, date of birth, and anything else that could identify you. We will only share their general health data.

We will put security measures in place to protect your data if and when we give it to other people. An agreement regarding the use of the samples will be in place before we send anything. A record of the use and sharing of samples will be maintained by the research team. You can request for your data and/or samples to be disposed of however it may not be if information is sent overseas.

Despite our best efforts, there is a small chance that you could be re-identified. In the unlikely event that this happens, someone from the research team will contact you. If, at any point, you think that you may have been re-identified, please let us know.

You have the right to access and correct the information we collect and store about you. This is in line with relevant Australian and/or Victorian privacy and other relevant laws. Please contact us if you would like to access this information.

We may send your sample to another laboratory for genetic testing or analysis, this may be a laboratory in Australia, or possibly overseas. If we do this, your samples will be labelled with their code number only. It will not be possible for the testing laboratory to identify you. It is important to note that any samples sent overseas are not protected by Australian laws and regulations.

At the end of the research project, we may present the results at conferences. We may also publish the results in medical journals. We will do this in a way that protects your privacy.

9. Will we be informed of the results when the research project is finished?

Your individual results will be given to you during a scheduled appointment with your treating specialist doctor, a clinical geneticist or a genetic counsellor. These results will not be shared with any other family member without your permission. Results will be entered into your medical record and shared with their doctors, with your permission.

At the end of the project we will send you a summary of the overall research results. This will be for the whole group and will not identify you. Your results will not be shared with any other family members without your permission.

10. Who should I contact for more information?

If you would like more information about the project or if you need to speak to a member of the research team in an emergency please contact:

Name	Eloise Uebergang
Position	Clinical Research Coordinator
Telephone	+613 8341 6382
Email	leukonet@mcri.edu.au

You can contact the Director of Research Ethics & Governance at The Royal Children's Hospital Melbourne if you:

- have any concerns or complaints about the project
- are worried about your rights as a research participant
- would like to speak to someone independent of the project.

The Director can be contacted by telephone on (03) 9345 5044.

Participant consent form

HREC Project Number: 64193

Project title: Leukodystrophy Research Program

Version Number: 5 **Version Date:** 01/03/2021

- I have read this information statement and I understand its contents.
- I understand what I have to do to be involved in this project.
- I understand the risks I could face because of my involvement in this project.
- I voluntarily consent to take part in this research project.
- I have had an opportunity to ask questions about the project and I am satisfied with the answers I have received.
- I understand that this project has been approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee. I understand that the project and any updates will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
- I understand I will receive a copy of this Information Statement and Consent Form.

By signing this form, I consent to:

- My DNA samples being analysed for this research if having genetic testing.
- Sharing my genetic data, relevant medical information, DNA and cellular material with relevant research collaborators working on ethically approved research in this field.
- Sharing my de-identified genomic data with approved national and international databases.

Optional consent

☐ I do	☐ I do not	Consent to the establishment of a permanent cell line from my blood cells, tissue or skin biopsy to allow future genetic and functional testing
☐ I do	☐ I do not	Consent to have clinical photographs taken for the purposes of this research, and for inclusion of these photograph in scientific/medical journal articles.
☐ I do	☐ I do not	Consent to the storage and future use of my clinical data, blood/DNA/tissue sample in future ethically approved research related to white matter disorder.
☐ I do	☐ I do not	Consent to be contacted about future research projects related to white matter disorders.

Participant Name _____ Signature _____ Date _____

Declaration by researcher: I have explained the project to the parent/guardian who has signed above. I believe that they understand the purpose, extent and possible risks of their involvement in this project.

Research Team Member Name	Research Team Member Signature	Date

Additional Family Consent

I consent to:

- Genetic testing on my sample for the purposes of clarifying results of the genomic testing that is being performed on my child's/relative's DNA sample.
- The sharing requirements of my data and samples as part of this research project (stated above).

A separate report may not be issued for family members who have given a sample for the purpose of understanding the result of the person recruited to this study.

Relative 1

Relationship to the participant _____

Name	Date of Birth
Signature	Date of Signature

Relative 2

Relationship to the participant _____

Name	Date of Birth
Signature	Date of Signature

Relative 3

Relationship to the participant _____

Name	Date of Birth
Signature	Date of Signature

Note: All parties signing the consent form must date their own signature.