Austin HEALTH

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Participant Information Sheet/Consent Form

Genetic Study – *Parent/Guardian consenting on behalf of participant*
Genetic Basis of Epilepsy

Austin Health

Title	Genetic Basis of Epilepsy
Coordinating Principal Investigator	Professor Ingrid Scheffer
Principal Investigator(s)	Prof Sam Berkovic and A/Prof Piero Perruca
Location	Austin Health

1 Introduction

Your child has been invited to take part in this research project. This is because they, or someone in their family, has experienced seizures, or a related condition such as a speech and language problem, cognitive, psychiatric or behavioural problem, intellectual disability or a structural abnormality of the brain. This research project aims to gain a better understanding of the genetic relationships between different types of epilepsy and these related conditions and improve understanding of the mechanisms that cause epilepsy.

This Parent/Guardian Information and Consent Form tells you about the research project. It explains the procedures involved. Knowing what is involved will help you decide if you want your child to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether to take part, you might want to talk about it with a relative, friend or healthcare worker.

Participation in this research is voluntary. If you don't wish your child to take part, they don't have to. They will receive the best possible care whether you take part or not.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- understand what you have read;
- consent to your child taking part in the research project;
- consent to your child participating in the research processes that are described;
- consent to the use of your child's personal and health information as described.

The consent form can be signed and returned in several ways and any one of these is fine:

a. Sign the consent form by hand and return directly to the researcher, or send via post.
b. Sign the consent form by hand and photograph or scan it to send via email.
c. Sign the consent form online (or with an electronic signature) and send via email.

You will be given a copy of this Parent/Guardian Information and Consent Form to keep.

2 What is the purpose of this research project?

Epilepsy affects at least 5% of the population at some time in their lives. We know that some types of epilepsy are inherited or have a genetic cause, some types may be the result of an illness or injury, while in some people it is not clear what has caused the seizures. Our previous studies have identified specific genes causing epilepsy. However inheritance of epilepsy often involves many genes.

In many families there is only one person with epilepsy, while in others, a number of people may have seizures. By studying individuals with no family history of epilepsy and also families where more than one person has experienced seizures, we hope to gain a better understanding of the genetic relationships between different types of epilepsy and improve understanding of the mechanisms that cause seizures. This may eventually help with new treatments, better genetic counselling and better diagnostic tests. Studying twins is also a very important part of epilepsy

research, because they can help us understand the role of genetic and other factors in the development of epilepsy.

In some individuals or families, structural abnormalities of the brain (where parts of the brain have not formed normally), speech and language disorders or cognitive, psychiatric and behavioural problems may occur with or without seizures. In these families it is thought that there may be a connection between epilepsy and these disorders. We now know of some families where the main finding is a structural abnormality of the brain, or a speech and language difficulty, or a cognitive, psychiatric or behavioural problem, rather than seizures. We will also study these families as part of this project to further explore how these disorders are related.

So far, several thousand people with epilepsy or a related disorder and their family members have participated in this project. We hope that many more will participate over the coming years as each individual adds more to our understanding of epilepsy.

This research has been initiated by Professor Ingrid Scheffer & Professor Sam Berkovic and has been funded by research grants.

3. What does participation in this research project involve?

If you agree to your child participating in this research project we will contact you and arrange to interview you and your child (if appropriate) either in person or via a phone call or video call. We are interested in checking the details of any seizure or seizure-like events experienced. Birth history, a history of any head injury and other neurological disorders is also taken as this may be relevant. The interview usually takes between 20 minutes and 1 hour in total. We would also like to know the results of any genetic testing your child may have had. With your permission the researchers will access your child's medical records to obtain relevant information.

Blood samples of up to 2 tablespoons (40ml, less for young children) will be requested with the aim of looking for genes that cause epilepsy. For twins who are the same sex, some of the blood will be used to test whether or not they are identical. This sample is separate from any routine blood tests requested by your child's doctor and it can be collected at a time and location convenient for you. It can be collected when your child visits the hospital for a clinic appointment or we can arrange for it to be taken at a local pathology collection centre. In some cases, repeat samples may be requested for additional tests.

If it is not possible to collect a blood sample from your child, we may request a sample of saliva instead. This is collected by spitting into a tube that we will provide. There are some tests that can only be performed from a blood sample so a saliva sample is not suitable in all situations. In rare cases a scraping of cheek cells may be used, particularly in infants where collecting saliva or blood may be difficult.

You do not have to agree to a blood or saliva sample being collected. Some people will still be able to participate in other parts of the research, such as completing an interview, however in other cases (for example if your child is the only person in your family who has had seizures) this may mean that they are unable to participate in the study.

You and your child will not be paid to participate in the research project and you do not stand to gain financially from participation even if useful scientific discoveries are made.

Family studies

We may ask to involve your extended family as part of this research. If so, we will ask you to speak with your relatives about the study first. When we contact your relatives, we will discuss the study in detail, then send them a copy of this information sheet and our consent forms for them to consider. You and your immediate family can still participate in the study, even if your extended family does not wish to. If you are not happy to contact your relatives, we may contact them directly with your permission.

Twin studies

If your child is a twin, we would like to interview you about both twins to obtain a developmental and birth history and a family tree. In addition we would like to see both twins to conduct a neurological examination, EEG and blood test. We will also take a photograph which will be used

to compare the twin's features. Photographs will not be published under any circumstances without your written permission.

Possible additional tests

In rare instances, we may ask your child to have additional tests done to help us fully understand the seizures or related disorder in your family. If any of these tests are required, they will be explained to you in detail at the time and you can decide whether you agree to have them done. Any tests your child has for research will be paid for from our research grants. Additional time will be necessary depending on which tests are involved, generally less than two hours.

In some rare cases we may ask for more than one blood sample; 1 collected before, and up to 6 samples collected after, a seizure. These samples will help us understand if we can detect brain derived cell free DNA in the blood after a seizure.

We may ask your child to have an EEG (electroencephalogram - a brain wave reading), and a neurological examination. The neurological examination will include checking reflexes and strength and a screening examination of the eyes.

Some participants may be asked to have a Magnetic Resonance Imaging scan (MRI), where pictures of the brain are taken, or an EEG-fMRI. This is where an EEG is recorded whilst having an MRI.

If your child or another family member has experienced difficulty with their speech, language, cognition or behaviour, we may ask your child to have a targeted assessment of these functions. This may involve an assessment of their understanding of language, their spoken language, a hearing screen or neuropsychological testing. This involves completing some written and verbal tasks so that different aspects of your child's learning, thinking and behaviour can be assessed, as well as some questions about psychological history, and an online questionnaire. We may ask to record your child doing some of the tasks on a video.

In some cases, the underlying problem causing the seizures may also affect how messages are passed along nerves in other parts of your child's body (for example to their arms and legs). We may ask your child to have specialised neurophysiology tests of the nerve function to their arms and legs, or an ECG (electrocardiogram – a heart trace). Some people with epilepsy may also experience difficulties with sleep, which may be due to changes in their breathing or heart rate. To help understand this further we may ask to measure the oxygen level in your child's blood while they sleep. This is done by wearing a small plastic clip on their finger for one or two nights in your home. We may also ask your child to wear a wrist, ankle or waist band for several days that monitors physical activity. We may also ask you to collect hourly saliva samples in the hours leading up to sleep to assess levels of a sleep hormone called melatonin. All of this gives us further information regarding quality and quantity of sleep. Once completed we would appreciate if you return the clip and/or activity band to us.

Some participants may be asked to complete a questionnaire asking questions about quality of life and other disorders associated with epilepsy. This questionnaire will take approximately 30 minutes.

4. What will happen to my child's test samples?

Your child's blood, saliva or cheek cell sample, labelled with their name, date of birth and diagnosis will be sent to our laboratory and the DNA (genetic material) extracted. The DNA sample will be stored in a coded form with the key to the code kept on a password-protected database only accessible to members of the research team. In some cases, the serum or plasma from the blood sample may also be used to look for specific biomarkers and be used in other biochemical tests that might help us understand the cause of their seizures. Saliva samples collected before sleep will be labelled with a code and sent to a commercial laboratory for testing of the sleep hormone, melatonin.

In specific cases we may ask if you are happy for us to use some of your child's blood sample to grow a culture of cells. This will enable us to do more tests than we can with a single blood sample. We may use some of your child's blood sample to make "induced pluripotent stem cells" (iPS cells). iPS cells are a new technology that allows us to produce specific cell types, such as brain

cells, in a laboratory dish. This allows us to study your child's genetic variation in cells relevant to epilepsy. We will tell you if we would like to grow some cells from your child's blood sample and what we would like to use the cells for, and this will only be done with your consent.

Your child's sample will be stored by:
Professor Sam Berkovic & Prof Ingrid Scheffer

Department of Medicine, University of Melbourne
Austin Health, Heidelberg VIC 3084
Telephone: (03) 9035 7330
Fax: (03) 9035 7307

As this is an ongoing research study, we would like to store your child's DNA sample for the duration of the study so we can test it when new genes for epilepsy are identified. However, if this project ceases, your child's DNA sample will be destroyed. Also, you can request that your child's DNA sample be destroyed at any time by contacting us.

Your child's DNA sample will be used to investigate changes in genes that may be causing their seizures or related disorder. This may involve looking for changes in specific genes, or it may involve looking at a large number of genes and comparing the information in their genes with other people in the family or other people with similar types of epilepsy.

We work closely with other research groups within Australia or internationally who are also trying to identify genes that cause seizures or related disorders, or who are trying to understand how the genetic changes cause seizures. This means we may send some of your child's DNA sample to another research group. We would routinely send your child's name with the DNA sample to ensure sample identification so that we can tell you if there are any important results. We may also send details about the type of seizures they have had and other relevant medical history or test results to assist interpretation of further testing. All collaborators are strictly bound by confidentiality requirements.

In recent years, large databases of genetic sequences have been set up to help researchers. For some of our collaborating projects, the funding bodies (such as the National Institutes of Health in the US) prefer that de-identified genetic data obtained be shared with other researchers to bring greater benefits to society. In some cases, de-identified genetic information from your child's DNA sample may be made available to researchers working separately from us at other hospitals or universities for use in research investigating the genetic causes of epilepsy and related conditions. There is unlikely to be any direct benefit to you or your child from this. Your child's age, gender and brief information about their seizures may be included with the genetic data, but no identifying information will be included. However, your child's genetic information is unique to them alone and therefore there is some risk of lack of confidentiality. For example, people not involved with our study who have information about your child's DNA (e.g. researchers from another study they have taken part in) could potentially identify them by comparing their genetic data to the information we make available. We believe this is unlikely to happen, but you do not have to agree to your child's de-identified genetic information being released to researchers who are working independently from us, and you have the option to indicate this specifically on the consent form.

Your child's DNA will not be used for any purpose other than for the study of genes thought to be relevant to epilepsy and related conditions and to determine the zygosity of same sex twins (whether the twins came from the same or different eggs) and their sample will not be released for other uses, except as described above, without your specific written consent.

Rarely, genetic analyses on families reveal unexpected results, such as the discovery that a person thought to be a parent is not the true biological parent. This information would not be revealed to you or your family.

If you would like to discuss any personal issues or require independent genetic counselling before deciding whether to participate in this study, or as a result of your child's participation in this study, this can be arranged by speaking to one of the research staff. The independent counselling would be free of charge and is provided by specially trained staff from the Genetic Health Services Victoria or the equivalent service interstate.

5. What are the possible benefits?

We cannot guarantee or promise that you or your child will receive any benefits from this research, however possible benefits may include identifying the genetic cause of your child's seizures which could assist in their diagnosis and treatment, or help understand the risk of future generations developing seizures or related disorders. In most cases this will not change the treatment your child receives from their doctor, so it is possible that there will be no clear benefit to your child from their participation in this research. Genetic results may take many years, and in some cases, we may never find meaningful results.

6. What are the possible risks?

Possible risks, side effects and discomforts include:

- Having a blood sample taken may cause some discomfort or bruising. Sometimes, the blood vessel may swell, or blood may clot in the blood vessel, or the spot from which blood is taken could become inflamed. Rarely, there could be a minor infection or bleeding. If this happens, it can be easily treated.
- Magnetic Resonance Imaging (MRI) is a computerised scan that provides a 3-dimensional picture of the inside of the body using a strong magnetic field. A MRI scan is performed like a CT scan. It is performed in a large, tunnel-shaped machine but it does **not** use X-rays. The MRI uses radio frequency waves, like those in an AM/FM radio, and a powerful magnet. The space inside the MRI scanner is quite confined and consists of a long, open cylinder that may produce feelings of claustrophobia or unease from being in a confined space. The MRI scanner is noisy while it is operating so your child will wear earplugs or earphones to minimise the noise, the examiners talk with your child via an intercom throughout the procedure in case they require anything. These scans are painless and your child is required to remain still during the procedure. **Your child must not have any metal objects on or in their body, for example, brain aneurysm clips or a pacemaker to be able to have a MRI scan.**
- Some people may find it distressing to receive information about their genetic make-up and future health, or the risk of having a child with seizures or a related condition in the future.
- There is the potential that genetic information given to families could affect their ability to obtain life and health insurance or employment opportunities.

There may be additional risks that the researchers do not expect or do not know about.

7. Can my child have other treatments during this research project?

Your child's participation in this research project will not affect any treatments or medications recommended to them by their doctor.

8. Does my child have to take part in this research project?

Participation in any research project is voluntary. If you do not wish your child to take part, they don't have to. If you decide to allow your child to take part and later change your mind, you are free to withdraw them from the project at any stage. Your decision whether they take part or do not take part, or to take part and then withdraw, will not affect your child's routine treatment.

9. What if I withdraw my child from this research project?

If you decide to withdraw your child, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to inform you if there are any health risks or special requirements linked to withdrawing.

If you decide to leave the project, the researchers would like to keep the personal and health information about your child and the samples that were collected. This is to help them make sure the results of the research can be measured properly. If you do not want them to do this, you must tell them when you notify a member of the research team that you would like to leave the project.

10. Could this research project be stopped unexpectedly?

We expect this research project will continue for many years. However it may be stopped unexpectedly or some aspects of the project may be stopped if we are unable to obtain ongoing research funding.

11. How will I be informed of the results of this research project?

If we find a change in your child's DNA that is thought to cause seizures, we will write to you to let you know we have some results, then you have the option to contact us for further information. If you choose to receive your child's results, we will explain what the results mean and give you the opportunity to ask any questions you may have. It is important to remember that we may not always know what the results mean. If you would like to discuss the results further with someone separate from the study, we can arrange for you to see an independent genetic counsellor. If your child has already turned 18 by the time results are available, we will write to them directly. We also encourage your child to contact us when they are older to talk to us, or a genetic counsellor, about what the results mean.

Any changes found in your child's DNA sequence may not be the only cause of their seizures or related disorder and we may not be able to predict accurately if the epilepsy could be passed on to other generations of your family. It may take years of research before we can be clear about the nature of the genetic change and its effects. If you would like to have results from the research passed on to others, for example your child's local doctor, this can be arranged. We will not pass personal information between family members.

If your child has an unusual test result that is likely to have health implications for your child or your family, we can arrange for you to see a neurologist associated with this study or we can refer you to see a specialist in your local area who can discuss the results with you.

Each year we send a newsletter to all of our research participants with general information about the results obtained from this project and about the work we are doing. These results may not be directly applicable to the type of seizures seen in your family.

12. What else do I need to know?

What will happen to information about my child?

Any information obtained in connection with this research project that can identify your child will remain confidential and will only be used for the purpose of this research project. It will only be disclosed with your permission, except as required by law. The information will be stored in a locked facility under the supervision of Prof Scheffer and Prof Berkovic, and/or in a digital form on a secure computer network. We are obliged to store your child's records safely for at least 7 years, but they may be stored for longer if this project continues beyond that time.

Information about your child may be obtained from their health records held at this, and other, health services for the purposes of this research.

In any publication and/or presentation, information will be provided without any identifying details such as names or dates of birth. However, when our research findings are published in medical and scientific journals, we may include family trees and detailed medical information. Such information may make it possible for someone who knows your child well, such as a family member, to identify your child and their medical information. This is unlikely but the possibility needs to be acknowledged.

Information about your participation in this research project may be recorded in their health records.

How can I access my child's information?

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to access the information collected and stored by the researchers about your child. You also have the right to request that any information, with which you disagree, be corrected. Please contact one of the researchers named at the end of this document if you would like to access your child's information.

What happens if my child is injured as a result of participating in this research project?

If your child suffers an injury as a result of participating in this research project, hospital care and treatment will be provided by the public health service at no extra cost to you if you elect for your child to be treated as a public patient.

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Is this research project approved?

The ethical aspects of this research project have been approved by the Human Research Ethics Committee of Austin Health.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

13. Who can I contact?

The person you may need to contact will depend on the nature of your query.

If you want further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctors on (03) 9035 7330 or (03) 9035 7344 or any of the following people:

Clinical contact:

Prof Sam Berkovic	Role: Principal Researcher	Telephone: (03) 9035 7093
Prof Ingrid Scheffer	Role: Principal Researcher	Telephone: (03) 9035 7344
A/Prof Piero Perucca	Role: Principal Researcher	Telephone: (03) 9035 7372
Dr Saul Mullen	Research Fellow/Neurologist	Telephone: (03) 9035 7330

Research Assistants:

Caitlin Bennett	- (03) 9035 7144	Amy Schneider	- (03) 9035 7349
Alisha Ryan	- (03) 9035 7326	Rebekah Harris	- (03) 9035 7336
Sophie Russ-Hall	- (03) 9035 7299	Kate Esnault	- (03) 9035 7355

Neuropsychology team

Dr Genevieve Rayner	Neuropsychology Fellow	Telephone: (03) 9035 7045

For complaints:

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Complaints contact person

Position	Complaints Officer
Telephone	(03) 9496 4090 or (03) 9496 3248
Email	ethics@austin.org.au

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Human Research Ethics Committee

LIST OF QUESTIONS FOR POTENTIAL PARTICIPANTS TO ASK INVESTIGATORS ABOUT RESEARCH INVOLVING GENETIC TESTING

You have been invited to participate in research involving genetic materials.

You may be interested in asking the researcher these questions after you have looked over the written information, and before you consent to be involved in the research project.

1. What do you think you might find out in this research?
2. Will I be able to get my results?
3. Who else will get a copy of my results?
4. If I choose to find out the results, what will this mean to me?
5. If I agree to participate what arrangements have been made for my independent counselling and who is the independent counsellor?
6. How might the results affect my family?
7. If I choose to get the results, how long will it be before I get them?
8. If I choose to get the results, who will help me to understand what they mean for my family and I?
9. What will happen to my specimen or sample? Will it be used in other studies?
10. Will my results have any effect upon my job, my being able to get insurance, or my status in legal matters?
11. What will happen if this research leads to the manufacture of commercial products?

For more information about ethical issues concerning this research you may contact

Complaints contact person

Position	Complaints Officer
Telephone	(03) 9496 4090 or (03) 9496 3248
Email	ethics@austin.org.au

There is more general information about research ethics issues at:
http://www.nhmrc.gov.au/your_health/egenetics/index.htm