Participant Information Sheet and Consent Form

Understanding Modifiers of TRPC6 kidney disease (UMoT Study)

Sponsor: University of Otago

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Study Sites:
University of Otago, Christchurch, New Zealand.
Nephrology Department, Te Whatu Ora Southern, Dunedin
Department of Nephrology, Te Whatu Ora Waitaha Canterbury, Christchurch
New Zealand Clinical Research, 3/264 Antigua St, Christchurch

Ethics committee reference: 2024 EXP 15283

INTRODUCTION

You are invited to participate in a research study that aims to better describe the range of clinical experiences in individuals who have inherited the *TRPC6* gene variant associated with focal segmental glomerulosclerosis (FSGS), and to seek genetic factors that modify the clinical course of this disease.

If you choose to participate, we will collect information about your health, lifestyle, family relationships (i.e. grandparents, parents, siblings, and children etc.), and if relevant, the course of your disease. We will also ask you to provide a blood (or saliva) sample and we may ask you to provide a sample of your urine. A caregiver or support person may help you complete the questionnaire if you feel you are not able to.

Your survey information and DNA will be retained and analysed in our University of Otago and Te Whatu Ora laboratories. However, some genetic analyses may need to be carried out via overseas service providers, and we will ask your permission to send samples overseas as appropriate. Your sample will remain confidential and be identified by a study code, the key to which will only be accessible to the UMoT Study investigators and will not be shared with anyone outside this team.

If you are interested in learning more about this study, please continue reading below.

VOLUNTARY PARTICIPATION AND WITHDRAWAL FROM THIS STUDY

This Participant Information Sheet for the UMoT study will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. It is important that you understand this information so that you can make an informed choice about being in this study.

You do not have to decide today whether or not you will participate in this study. Feel free to talk about the study with other people, such as family, whānau, friends, or healthcare providers, or contact us if you have any questions. You may choose not to participate or withdraw your consent to be in the study for any reason.

This document is 8 pages long, not including the Consent Form. Please make sure you have read and understood all the pages.

If you agree to take part in this study, please complete the consent form; you will be provided a link to this once you finished reading this information sheet. You can save a copy of the Participant Information Sheet and the Consent Form online, or ask the researchers to provide it to you.

WHAT IS THE PURPOSE OF THE STUDY?

Over the past few decades, researchers and doctors looking after patients with genetic illnesses have observed that the way in which a disease presents, i.e. the age at which it occurs, the severity of the illness, and other features of the condition, can be quite variable. This variability may at least in part be due to differences in the wider genetic makeup (the genome) of affected family members. In order to properly investigate this, we wish to better understand the clinical presentation, as well as general health and lifestyle, of members of the *TRPC6* FSGS family (including people who have very mild disease who may not even currently be aware they are affected), and then analyse both the *TRPC6* gene and other genes

in family members with different presentation of the disease (such as young, severe disease or older, with less severe disease).

We will carry out a range of analyses on your DNA to try to understand whether genetic factors (in addition to the *TRPC6* mutation) are influencing the way FSGS occurs for each family member who carries the mutation.

WHO CAN TAKE PART IN THE STUDY?

We are seeking members of the *TRPC6* FSGS family aged 16 years and over as study participants. This will include people with and without obvious symptoms of FSGS kidney disease.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

In order to participate in this study, you will be asked to complete an online consent form (or a paper option if preferred). You will then be asked for your contact details so we can contact you about the study should we need more information, and to update you on any outcomes from it, as well as invite you to be involved in any future research studies.

After giving your consent, you will be asked to complete a short online questionnaire about your family relationships (i.e. the names and dates of birth of your close relatives, if you know them) and health related information. Completing the online questionnaire may take up to 20 minutes, depending on how much information you know or have on hand, and a paper version can be made available if preferred.

We will also ask for your permission to access your health records held electronically or in other forms at your GP, at hospitals and/or at private specialists in New Zealand, to collect information about your health now and in the past as it relates or may relate to kidney disease and other conditions. If you have been looked after in other countries, we will ask you for permission to approach your doctors in those countries for similar information.

Depending on your responses to the questionnaire, you may be asked to donate a blood sample, from which we will extract your DNA and RNA (a related substance which is useful for understanding gene function) to investigate genetic factors that may influence the age and severity of presentation of FSGS. If giving a blood sample is difficult or not possible, we will provide a specialised saliva collection kit for you to use instead. The kit is easy to use, and the sample can be collected in your own home at your convenience. You will be asked to return this sample via pre-paid New Zealand Post bag to our laboratory at no cost to you. Where possible, we may also request a sample of your urine which can provide information that will aid this research.

It is possible you may have already given a blood sample in order to have a test for the *TRPC6* mutation. If DNA from this blood sample is still held at Canterbury Health Laboratories, we may instead request your permission to retrieve this sample for our research so you do not have to provide another sample. However, we may still ask you to provide a urine sample, for measurement of biomarkers.

All samples will be stored in our University of Otago laboratories, in a secure freezer on a floor which can only be accessed by authorized personnel.

Participation is entirely voluntary and if you choose not to take part this will not affect any future care or treatment. If you do agree to take part you are free to withdraw from the study at any time, without having to give a reason.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

Possible benefits:

This study is unlikely to be of immediate and specific benefit to you. Extensive research is required to find answers to the questions we are studying and we may not discover any information that helps take care of people affected with *TRCP6* gene changes. However, future medical or scientific discoveries may come from the research in which you participate. These discoveries may improve our understanding of genetic factors that influence presentation of FSGS in your family, and perhaps more widely in other families. Some of the genetic factors we find may give us clues about normal kidney function, and other kidney diseases, so the findings may be of wider benefit.

Possible risks:

Providing a blood sample may cause some bruising and slight discomfort.

Inadvertent release of genetic data (through a security breach or accidentally) is a risk to participants in research of this nature. To reduce this risk, all samples and survey data will be identified, handled and stored with a study code rather than identifying information (for example, name, date of birth or hospital number). All data will be stored on a secure University of Otago server, accessible only to authorised personnel with a valid University login and knowledge of the appropriate password. Information gathered from hospital records will be stored within the health system at Te Whatu Ora Waitaha Canterbury and/or Southern's system which is secured by passwords and multifactor authentication.

When we produce research reports or communicate with collaborators about the information you have provided or we have collected with your permission, no identifying information about participants will be shared. Information generated from the research intended to be available to other people (for example, information we provide back to study participants about our research, presentations at conferences and journal articles) will not include any identifying information about you.

Another risk relates to the chance of making an unexpected genetic discovery regarding your health status (called an incidental finding). In this study we are performing a comprehensive evaluation of your genes. It is possible we could discover something not related to the kidney disease under the study, but which is still relevant to you or your family's health and can be acted upon by you in a practical way to reduce the potential for harm. The chances of an incidental finding like this being discovered are quite low. If this situation arises, we will consult with a medical genetics doctor about the need for more testing to confirm this finding. That doctor will then discuss this information with you and together you will decide on a course of action. Incidental findings may vary considerably in their implications for you or your family. If the analysis reveals a possible risk for a condition that is not of clear and serious health importance then you will NOT be informed of such findings.

If we do inadvertently discover something of major health significance that is reported back to you, it is important to note that this information could be considered "prior knowledge" of a

medical condition. This knowledge may then potentially impact on subsequent ability to obtain life or medical insurance.

Cultural issues statement:

For Māori participants, there may be cultural issues associated with the collection and storing of your samples/specimens. These issues should be discussed with your family/whānau as appropriate, citing the protection of whakapapa. Controlling access to your samples/specimens and data, and limiting unauthorised use of those, are important questions that you may need to think about before consenting to research. It is also acknowledged that individuals have the right to choose whether they participate or not in a research study. We encourage you to consider the benefits and risks that this research may have for yourself, your whānau, and for Māori as a people. Participants may wish to consult with their whānau prior to consenting to participate in a research study.

ACC statement:

If you were injured in this study, you would be eligible to apply for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

In the very unlikely event that ACC determines that their cover did not apply to your injury, then the University of Otago's clinical trial insurance would apply. This cover would provide you with compensation equivalent to that you would otherwise have been entitled to under the Accident Compensation Act 2001. By signing the Consent Form for this study, should ACC decline cover, you are explicitly agreeing that compensation for any injury will be as per the terms of University's then current clinical trials insurance cover, the full terms and conditions of which are freely available on request.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

WHO IS FUNDING THE STUDY?

This study is to be conducted by staff (or postgraduate students) from the University of Otago (on both Christchurch and Dunedin campuses) and/or staff of Te Whatu Ora or New Zealand Clinical Research. The study will be supported by internal research funds (a University of Otago PhD Scholarship, and University research support funding to Prof Kennedy), and Dr Cross has some initial funding to cover genetic consultations for family members. However, we also plan to seek external grant funding from health research funding bodies to provide longer term support of the research.

WILL ANY COSTS BE REIMBURSED?

There are no direct costs associated with participating in this research project, nor will you receive any payment for participating. If you incur costs in relation to the research study, such as transport or parking charges, we will reimburse these.

WHAT HAPPENS TO MY SURVEY DATA AND BIOLOGICAL SAMPLES?

During this study, the research team will use surveys or interviews to collect information about you and your study participation. You cannot take part in this study if you do not consent to the provision of this information. Your DNA/RNA and urine samples will be analysed in the course of this study to find and understand genetic factors that may influence onset and progression of the disease.

The personal details you provide in the online questionnaire and the genetic data will be stored separately. The only link between your information provided in this way and your genetic data is your study code, which will be assigned after you have completed the questionnaire. The ability to link your personal details and other data using this code is restricted to authorised members of the New Zealand research team.

Results of this research project may be presented in scientific papers in medical literature, or in public talks, but your identity will not be revealed. The data collected as part of this study will be combined at analysis with the data from many other people, and as such there will be no way of identifying you as a participant.

Survey data:

All survey information will be stored on password-protected files on a secure University of Otago computer system. Access to this data is restricted to authorised members of the New Zealand research team. After the study ends the data will be maintained within a secure archive site at the University and stored for up to 10 years after the study is completed, and then it will be destroyed.

Biological samples and genome data:

We will either ask you to provide a blood sample during a clinic visit, or provide a barcoded saliva sample kit with instructions for sample collection at home. This can be returned to our laboratory in a pre-labelled, pre-paid courier bag.

Your blood or saliva sample will be used to extract DNA and the related compound RNA. Each sample will be registered and stored frozen in a secure location at the University of Otago, Christchurch. Samples will be identified only by a study number, not by name.

After DNA and RNA is extracted, it will be used for a range of genetic analyses. This will include analysis targeted at one or a few genes in particular, but it is also likely to involve analyses including “genotyping” across the genome (testing >600,000 sites for genetic differences), and full sequencing of your genome (which permits examination of all your genes). Finally, we also plan to examine so called “epigenetic” marks in the DNA, as this can point to regions of the genome which may contribute to disease processes. This work will be undertaken locally or in collaboration with other similar research laboratories.

It is possible that small amounts of anonymised data (but not tissue) collected in the study will be submitted to international genetic databases such as dbSNP (NCBI) or ClinVar (NCBI). These databases record human genetic variants that are discovered through research or clinical tests, and can help guide future research or clinical testing. The submitted data would consist of tiny regions of DNA sequence containing any novel variants, and no identifying information would be included with any submission.

Your urine sample may help us to identify or confirm factors that modify the way FSGS develops, and we will be able to test for some of these factors as we discover them. This will usually involve biochemical analysis of proteins and other molecules in your urine.

In order to permit ongoing analysis, we would store these samples for up to 10 years from the end of this study before disposing of them. Disposal can be either by standard methods (usually incineration), but you can also opt to have them disposed of after a karakia (blessing) has been performed. It will not be possible to return samples to participants.

You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/ whānau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult before participating in research where this occurs. However, it is acknowledged that individuals have the right to choose.

What are my rights?

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason with no disadvantage to you. If you withdraw consent, we will remove your data and sample from the study from that point forth. However, if the data has already been processed into group summary form or has been published, we are unable to retract that information.

You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected. If you have any questions about the collection and use of information about you, you should contact the investigators.

If you consent to participate, you will be donating your survey and genetic data for research purposes and waive any claim to commercial or intellectual property rights arising from this work. If you wish to withdraw from the study please contact the investigators.

Can I access my data?

You are able to download your responses at the end of the survey, however we cannot provide personalised interpretation of those survey questions. Similarly, it will not be possible to return individual genetic data or provide meaningful interpretations of genetic information on an individual basis. We do not have sufficient resources to provide interpretation of such data, and the data are being generated in a research setting, not a diagnostic laboratory.

You have the right to receive the general results of the study for participants as a group. It will take some time, however, before the main findings will be available.

How will we protect your confidentiality?

Your personal details will be securely stored in a password protected file at the University of Otago, Christchurch. Information collected about your health will be provided by you in an online survey, and drawn from your medical records (if you consent to that), and interviews with clinical staff. Your health information and genetic data will be given a unique study code to ensure your confidentiality. Only the New Zealand research team will hold the key that links your health information data and your biological samples (DNA, RNA, urine) to your personal

details. No identifying information about you will be sent overseas, or used in any publication related to this project.

Although very unlikely, information from this study may lead to discoveries and inventions or the development of a commercial product. The rights to these will belong to the lead investigators, and your family will not receive any financial benefits or compensation, nor have any rights in any developments, inventions, or other discoveries that might come from this information.

WHO HAS APPROVED THE STUDY?

This study has been approved by an independent group of people called a Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards. The Central Health and Disability Ethics Committee has approved this study.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study, you can contact:

Professor Martin Kennedy – Lead investigator
+64 (3) 244 1147
Martin.Kennedy@otago.ac.nz

Dr Nick Cross - Lead investigator and Nephrologist (Canterbury)
+64 (3) 364 0640
Nick.Cross@nzcr.co.nz

Dr Frederiek Vos – Investigator and Nephrologist (Southern)
+64 (3) 218 1949
Frederiek.Heenan-Vos@southerndhb.govt.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@advocacy.org.nz
Website: https://www.advocacy.org.nz/

For Māori cultural support please contact:

Kaitohutohu Rangahau Hauora Māori – Māori Health Research Advisor
University of Otago, Christchurch
Email: mailto:maoriresearchconsult.uoc@otago.ac.nz

Alternatively, you can directly contact the Associate Dean Māori Dr Christina McKerchar:

Phone: +64 (3) 364 3638

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHIC

Email: hdecs@health.govt.nz

Consent Form

Understanding Modifiers of TRPC6 kidney disease (UMoT Study)

Please check the optional consent boxes below to indicate your consent to the following in relation to the UMoT Study.

I have read and understood the Participant Information Sheet.

I have been given sufficient time to consider whether or not to participate in this study.

I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand this study, as appropriate.

I know who to contact if I have any questions about this study in general.

I understand that taking part in this study is voluntary (my choice).

I understand that I may withdraw from this study at any time.

I know who to contact if I wish to withdraw from this study.

I understand that my participation in this study is confidential and that no material which could identify me personally will be used in any reports on this study.

I consent to giving information about my health and family in the survey.

I consent to giving a blood (or saliva) sample for DNA and RNA analysis.

I consent to giving a urine sample for analysis (if requested).

I understand the compensation provisions in case of injury during this study.

I am aware that my DNA/RNA may be sent for analysis overseas in approved facilities.

I am aware that any DNA/RNA sample remaining after such genetic processing or analysis will be destroyed using standard disposal methods and that a karakia is available prior to disposal.

I am aware that my survey and genetic data, and my biological samples, will be stored for up to 10 years after this study has ended.

I am aware that genetic analysis may discover something of major health significance not related to the kidney disease under this study, and that if this occurs I will be contacted by a doctor to discuss the implications of this and any further investigations required.

I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant survey for the sole purpose of checking the accuracy of the information recorded for this study.

Yes ☐ No ☐

(Continued over…)

I give consent for my medical records to be accessed through the National Health Index (NHI) database	Yes ☐	No ☐
I have had a genetic test previously for *TRPC6* genetic testing in New Zealand and give my permission to obtain this from Canterbury Health Laboratories, if it is still available	Yes ☐	No ☐
If I decide to withdraw from this study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during this study.	Yes ☐	No ☐
I consent to being contacted in future to ask about participating in related research.	Yes ☐	No ☐
I request that any of my biological samples remaining after completion of this study be destroyed after a karakia (blessing) ceremony	Yes ☐	No ☐
I wish to receive a summary of the results from this study	Yes ☐	No ☐

FOR PAPER BASED FORM:

Declaration by the participant:

I hereby consent to take part in this study.

Participant's full name: Date of Birth:

Signature: Date:

Declaration by member of research team:

I have given a verbal explanation of the research project to the parent/guardian of the proposed participant and have answered their questions about it.

I believe that the above-signed understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date: