University of Otago, Christchurch

Gene Structure and Function Laboratory
Department of Pathology
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NEW ZEALAND

CARNEY CENTRE FOR PHARMACOGENOMICS

INFORMATION SHEET

Understanding Adverse Drug Reactions or Responses Using Genomic Sequencing (UDRUGS)

If an interpreter is requested
Participants will need to be reasonably fluent in English; however an interpreter may be available.

English	I wish to have an interpreter	Yes	No
Deaf	I wish to have a NZ sign language interpreter	Yes	No
Māori	E hiahia ana ahau ki tetahi kaiwhaka Māori/kaiwhaka pakeha korero	Ae	Kao
Cook Island Māori	Ka inangaro au i tetai tangata uri reo	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu	E	Nakai
Sāmoan	Ou te mana'o ia i ai se fa'amatala upu	Ioe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea	Io	Ikai

You are invited to take part in this study, which is part of a PhD research project, to help us identify genes that may influence a person's response to medications. This study has received ethical approval from the Southern Health and Disability Ethics Committee (formerly known as Upper South A Regional Ethics Committee).

Investigators
Professor Martin Kennedy, molecular geneticist
Assoc. Professor Matt Doogue, clinical pharmacologist
Professor Murray Barclay, clinical pharmacologist/gastroenterologist
Dr Simran Maggo, pharmacologist

Background of this study
To some degree, every person has a different response to their medications. While drugs prescribed by a doctor for treatment of a medical condition usually work for most people, some patients fail to get relief from the drugs, and others may suffer a bad side effect (adverse drug reaction). These situations can be really distressing when they occur. This study will help us find out whether individual genetic make-up is linked to these rare situations. By identifying genes that may change a person's response to certain drugs, medical treatment can be fine-tuned. Where the person is genetically prone to a drug's side effects, the drug can be avoided; where we know that the person would not get benefits from a drug, another drug can be used at the beginning of treatment. Knowledge from this research may, in the long run, help us to improve drug treatments and make them safer.

Who will take part in this study?

- People who get a very bad or unusual side effect after taking their medications.
- People who have an unusual response to their medications.
- In some cases, family members of such people may be asked to participate.

Where will this study be held?

The study will take place at the University of Otago, Christchurch (Christchurch Medical School).

What does this study involve?

Your participation in the study is entirely voluntary (your choice).

This study involves the following:

- Completing a questionnaire so we are able to collect demographic, medical and lifestyle information. The questionnaire will take around ½ hour to complete.
- Allowing us to review your medical notes and collect relevant medical information such as laboratory test results.
- Providing up to 20 mL of blood (less than two tablespoons full) for DNA. Blood is definitely preferred, but if you are unable or unwilling to contribute blood, we can collect a saliva sample instead.
- Agreeing to have your DNA and blood stored for future research into rare and serious adverse drug reactions or unusual drug responses. Any subsequent use of your sample will be subject to approval from a Health & Disability Ethics Committee.

In some situations we may wish to contact members of your family to ask for their involvement, for reasons described below. However, you can choose whether or not we do approach any relatives, and you can also specify who we may or may not contact. .

If you do agree to take part in this study, you are free to withdraw at any time, without having to give a reason, and this will in no way affect your future health care.

What will happen to the blood sample?

The blood sample will be sent to the University of Otago, Christchurch, where a portion of blood will be frozen and from the other portion DNA will be extracted. Both the DNA and remaining blood will be stored in a secure freezer (-20 °C) for analysis in the future. The sample will be stored for up to 10 years, before it will be disposed of. At various times during this period, the sample may be studied further as new tests or new knowledge becomes available.

It is possible that the investigators may need to collaborate with overseas researchers to carry out some specific gene studies. This would involve sending a small amount of your DNA overseas. In this situation, your DNA would still be under the custodianship of the investigators and any DNA not used up in the study will be returned to New Zealand.

We cannot be specific about what tests might be done on the stored DNA in the future except that the tests will be relevant to unusual treatment side effects or responses. If you withdraw consent at any time in the future, your DNA and blood will be destroyed. If you withdraw consent for the study, any information about you will not be used in the future but some information may have already been published as part of the study. We are unable to retract this information at this point. You have the option of choosing a standard disposal method for your samples, or disposal with karakia (blessing).

How will the DNA be used?

Each person has a DNA make-up (their genes) which is unique except in the case of identical twins. This genetic make-up is a mixture of the genes of our parents. The precise way they are mixed varies from child to child within the same family, so having the same parents does not mean that two children will have exactly the same genes. We already know that some drug effects are linked to genetic make-up and tests are now available to identify certain genes before treatment is

started. However, some drug effects that are not often seen are still poorly understood. We do not know whether these are influenced by genetic factors.

The genes found in our DNA contain information that "instructs" the body how to make proteins, which are important for many functions of our body. These functions include breaking down the drugs we take or changing them to the forms that work well in our body (active forms). Thus if any errors occur in these kinds of genes, the proteins that are made may not work properly. For example, a person may not respond well to a drug treatment if a protein that changes the drug to its active form is faulty.

In this study, we may apply a range of genetic analyses. The first, and simplest, involves looking at a single gene, if there is clear evidence that gene might be important. At the other end of the spectrum, new methods now enable us to look at *all* of your genes simultaneously, a process called "exome" or "whole genome" sequencing. This will enable us to find variations in genes we may not realise are important in the response to various drugs, which is quite possible for very rare reactions or responses. In some situations we may wish to introduce small parts of your DNA into a bacterium called *E.coli*, to help us better understand how genetic variations can impact on drug responses. Finally, we may need to occasionally perform these kinds of genetic analyses on some of your family members. This is to determine how combinations of variants are inherited from parent to child. Such inheritance patterns cannot be determined from the analysis of your sample alone, and these patterns can influence how a person responds to their drug treatment.

The information we obtain will be confidential and will not be disclosed or used in any way without your informed consent. In particular, the researchers will not claim any right, ownership or property in your individual genetic information or that of your kinship group, *hapu* or *iwi*, without your having first sought and obtained informed consent to the transfer of any such right, ownership or property. Your consenting to participate in DNA sampling for the proposed study will not be construed as creating any right or claim on the part of the researcher to your genetic information.

How will the information and samples collected in this study help identify genetics factors for rare drug responses?

The samples we collect will be used to help us identify changes in DNA, which are called variants, that may alter a person's risk of getting a bad drug side effect or make that person unresponsive to treatment by certain drugs. Information we collect using the questionnaire will help us confirm the nature of the side effect or unusual drug response as well as rule out any other factors that are not gene-related. For example, by determining how often a specific genetic variant occurs in a group of affected people and comparing it with existing data will help us to pinpoint which variations in DNA influence drug response and which do not.

What are the risks of this study?

Apart from the mild and temporary discomfort associated with a blood test there are no risks from contributing the blood samples. Blood will only be taken by trained medical staff. However, because we may carry out quite extensive analysis of all of your genes, it is possible we could discover something not related to the research question, which is relevant to your health or your family's health. If this situation (called "incidental findings") arises, we will seek advice via a medical geneticist about the need for confirmatory testing and appropriate feedback to you. You have a choice whether or not you wish to be informed of these findings if they occur. Any unexpected finding may vary considerably in the implications for you and your family. If the testing reveals a condition that is not likely to be of serious health or reproductive importance or whose likely health or reproductive importance cannot be ascertained then you will not be informed of the 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 potentially impact on your right to receive cover for the medical condition through any private medical insurance scheme to which you belong.

What are the benefits of this study?
It is possible that this information may be useful for your family to know, in case they are also at risk of suffering similar outcomes if given the same drugs. It is also possible that the knowledge discovered though this research will help us to improve drug treatments in the future, making them safer and more effective for other patients.

Expenses
There will be no payment for taking part in the study. However if you require assistance with travel or parking costs in order to participate this will be reimbursed.

Confidentiality
The data and samples collected from participants will only be used for the study of unusual cases of treatment side effects or responses. No material that could personally identify you will be used in any reports on this study. Results of all testing will be coded by a system known only to the researchers. If you decide to withdraw from the study, the DNA sample would then be destroyed before the sample analysis is performed; or if the testing has already been performed, then the information would be destroyed.

Results
We aim to have the results published in the international medical literature, although individual patients will not be identified in any such publications. It may take some time for the results to be completed after you have taken part in the study, and we will inform you by letter of any findings that may relate to your adverse drug reaction or unusual response. Because this research uses new methods there is also a risk that it may not yield useful findings, and if that is the case, we will also inform you of this by letter.

Your rights
If you have any queries or concerns regarding your rights as a participant in this study you may wish to contact a Health and Disability Advocate. This is a free service provided under the Health and Disability Commissioner Act.

- Telephone: (NZ wide) : 0800 555 050
- Free Fax (NZ wide) : 0800 2787 7678 (0800 2 SUPPORT)
- Email (NZ wide) : advocacy@hdc.org.nz

Compensation
In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2001 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. If you have any questions about ACC, contact your nearest ACC office or the investigator.

Contacts
Please feel free to contact the researcher if you have any questions about this study.

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