The metabolic effects of a CREBRF gene variant in NZ Women

PARTICIPANT INFORMATION SHEET

We invite you to participate in an observational study aimed to assess how a small difference in genes may influence how we store and use energy that we get from food (kai).

The information you gift us in this study will be used to better understand how genetics effects the risk of developing diseases like gout, obesity, diabetes and heart disease, and in the long-term lead to better treatment and prevention options for these diseases. Your participation in the research is entirely voluntary (your choice).

If you do agree to take part, you may contact the investigators to withdraw from the research at any time, without having to give a reason. You can also request that any samples or data you provide for this research be withdrawn at any time prior to their analysis.

PLEASE READ THE FOLLOWING INFORMATION CAREFULLY – THANK YOU

Who can take part?

You can take part if you are:

- A woman aged 18-50 years of age
- If you do not have diabetes or any other long-term or serious health issues.

You must be willing to provide:

- A saliva sample before you go to bed and in the morning when you wake
- Attend a 4-5 h testing session at the Centre for Translational Physiology at the University of Otago, Wellington
- Provide information on your diet over the phone on 1-2 additional days.

We will:

- Take a detailed scan of your body to measure the amount of muscle, bone and fat
- Analyse your breath to determine how you use your energy
- Take blood tests to see how well your body clears sugar and measure your genes (DNA).

You may also be invited to attend a second laboratory session for up to 7 hours on a different day, for a measurement of how well your body clears sugar. Also, 1-10 years after your study visit, you may be invited to attend our laboratory again for a follow up visit that will be similar to our first visit and between 1-4 h in duration. You can choose not to attend any of these additional visits.

The study investigators understand that in Māori worldview, the body is considered tapu and therefore such sampling should be treated with special consideration and respect.

Whilst individuals have the right to choose whether or not to participate in this study, we encourage you to discuss this project with your whanau and friends, especially with regards to the collection of your samples before agreeing to participate.

If you have any cultural requirements or questions that relate to your potential participation in this project, please ask the research team before signing this document. It is the role of the investigators to ensure that you understand all procedures and risks: please feel free to ask any questions.

Who designed the trial?

This trial was designed by research staff at the Universities of Auckland and Otago in a partnership with Ngāti Porou Hauora and the Moko foundation. The researchers conducting this trial are interested in understanding how certain genes affect metabolism.

Background

The research team conducting this study are interested in understanding how certain genes affect how the body handles kai (metabolism). Some of the kai we eat can be stored in our body as fat, and body fat rather than body weight is the greatest risk factor for type 2 diabetes.

Body mass index (BMI: calculated by height divided by weight squared) is often used as a measure of body fat. However, in some people it does not accurately reflect the amount of fat. This is interesting because it has recently been found that people with a small change (variant) in a gene called CREBRF have a higher BMI, but a LOWER risk of developing type 2 diabetes.

In this study we are further investigating how gene variants may affect body composition (muscle and fat mass), and the risk of developing metabolic diseases like type 2 diabetes, gout, obesity and heart disease.

What is the aim of the research?

The aim of this research is to assess how variants in our genes effect our body composition, how we respond to a meal and risk of developing metabolic diseases.

What happens if I decide to take part?

This research requires **one visit of up to 5 hours** and start before 9 am.

You will be asked not to drink any coffee in the 12 hours prior, and no alcohol or any vigorous activity in the 24 hours prior to visit. You will also be asked to not eat anything after 9pm the night before and have arrived in the morning only having consumed water (not coffee, tea or juice).

You will be given a meal during your visit. We will also send out saliva tubes with instructions on how to provide samples to bring on the morning of your visit.

Because some test results change over the month in women who have periods, we will need to ask you some questions about periods, pregnancies and breastfeeding to help schedule the right time for these tests. You may also be invited to undertake a urine pregnancy test.

- **Discussion and consent forms**
  On arrival, we will discuss this participant information sheet with you and if you wish to participate you will be asked to sign informed consent forms.

- **Anthropometric measurements**
  We will ask to take measurements of your height, weight, blood pressure and circumference measurements of your neck, waist and hip area.

- **Metabolic rate**
  We will measure your resting metabolic rate which will indicate how much energy you use during the day. This is carried out in a hood calorimetry room where you will sit on a reclined chair and have a clear mask/hood covering your head which will allow us to sample the air you breathe in and out normally for 45 minutes. You will be provided with an iPad and headphones during this time.

- **Body composition**
  You will undergo a whole body DXA scan which will give information about bone mass, whole body fat and fat free mass or muscle in your body. This will take approximately 15 minutes.

- **Mixed meal test**
  You will be provided with a standard meal to eat and drink. Additionally, a very small plastic tube (cannula) which will be placed inside a vein in your arm. We will ask to take blood samples from the cannula in your arm before the meal and every 30 minutes for 2.5 hours following this meal. For the whole day the total volume of blood taken will be <200 ml, this is less than 1 cup and less than half the volume of a blood donation.

- You will be asked to provide a urine sample and complete some questions about your health, your usual exercise habits and dietary habits.

Invited second visit

Based on the results from your first visit, you may be invited to attend a second testing session. If you are interested in taking part in this test, you will be given a separate information sheet to read and a consent form to sign. You do not have to take part in these visits of you do not want to.

One to ten years after this visit, you may have the opportunity to attend for an additional follow-up visit. This is not compulsory. This visit will be a shorter **one-two hour** visit with start before 9am. At this visit, we will ask to take anthropometric measurements and perform a body composition scan, similar to your first visit. We will also ask to take a one-off blood test.

If you are asked to undertake a metabolic clamp then you will be moved to a chair/bed and have a very small plastic tube (cannula) placed in the vein of an arm and hand. One will be used blood sampling and the other the infusion of sugar (glucose) and you may also receive an infusion of a natural hormone that lowers blood sugar levels (insulin), or an amino acid the is found in your diet (L-arginine). You will be told before and during

your visit which infusions are to be used. This infusion and sampling will take place over 1.5-3 h, during which time you can rest in a chair or bed. We will collect less than 1 cup of blood during this time.

The risk and benefits of the research

Overall there are no major risks associated with taking part in this research. We are exposed to very low amounts of radiation all the time from the sun and other sources in our everyday lives. You will be exposed to low levels of radiation through the DEXA that are less than what you would experience on an international flight.

There are slight risks associated with blood sampling. These are minimised by having all procedures undertaken by a person experienced at taking blood using accepted antiseptic (very clean) technique. There is a small chance of minor bruising as a result of insertion of the venipuncture needle. Very occasionally, however, there can be infections. We consider the risk extremely low given the aseptic techniques used.

The research will be stopped should any harmful effects appear or if research investigators feel that it is not in your best interest to continue. Any symptoms that you may experience will be recorded as part of the trial and you will be encouraged to inform the investigator of these as soon as possible.

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 2001. ACC cover is not automatic, and your case will need to be assessed by ACC according to the provisions of the Injury Prevention, Rehabilitation, and Compensation Act 2001. 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. You are also advised to check whether participation in this study would affect any indemnity cover you have or are considering, such as medical insurance, life insurance and superannuation.

The genetic testing

Studying genes involves looking at the DNA which is the genetic code that is found inside the body's cells. We are investigating how differences in DNA may affect how the body responds to kai (food), and how this might determine the risk of developing metabolic diseases like gout, diabetes, heart disease and obesity.

DNA is prepared from a sample of your blood. If you would like, we can arrange for a karakia when your left-over blood or DNA is disposed of. Please indicate this in the Consent Form.

From the DNA, we will compare the genes which control how you use and store energy from your food. As part of this study, we may need to read your complete genetic code. This means that we may decode and record your **entire** genetic code.

When DNA is made, it is a clear liquid in a test-tube. Your genetic code is inside the DNA. In the past we have used labour intensive laboratory methods to look at certain genes in the liquid DNA. However, by using the latest technology we can now 'decode'

the DNA in the liquid into a ‘sequence’ which is stored on a computer. We can then more easily look at the genes we are interested in, and we can also uncover versions of genes that are specific to you and your family.

Your genetic information is protected on sequence computers at The University of Otago and The University of Auckland. We would look for and study only the genes which are related to how you use and store kia (food), and related metabolic diseases as explained above.

It is important to know that there is no one gene that determines your health or metabolism, but a number of small changes which contribute to response to a meal. We will NOT be testing other genetic diseases that you could be carrying. Our genetic testing will NOT provide any information on heritage.

What will happen with my blood samples?

In addition to genetic testing, we will analyse your blood, spit and Urine samples for small molecules that tell us about how your body responds when you eat kai (food), and how your body stores and uses this food. Blood samples will be stored in secure freezers in an access-restricted area at the University of Auckland or Otago, until analysis is completed. Samples may be stored in the same facility (freezer) as animal tissue.

DNA samples, or molecules from them may be sent overseas for expert analysis. There will be no future research made on your samples without your prior approval. After completion of the study, we will keep your contact details for at least 10 years but you will only be contacted in the unlikely event that we would like to perform further unspecified analysis.

If we cannot contact you at this time we will not perform this analysis. After analyses have been performed on your samples, it will not be possible to return any unused samples to you, although you are welcome to request their return prior to any analysis.

Your samples will be kept until the end of the analysis for at least 10 years. At the end of this time, a medical waste contactor will dispose of your samples. If you would like a karakia performed at this time, please indicate so in the consent portion of this form.

Any samples for disposal following karakia will be clearly marked. It is possible that the entire sample may be used for analysis, in that case there will be no need for disposal and a karakia is not possible.

What will happen if the research finds any results which could impact my health?

If any of the testing procedures or analysis of any samples produces findings which could have an adverse impact on your health status (such as blood glucose levels outside the normal range) the principal investigator will discuss with clinicians at the University who will decide what information to feed back (if any) and you may be advised to contact your health professional. If we make any findings which may adversely impact on your health you and, with your permission, your GP will be informed.

Confidentiality

Research files, data and all other information that you provide will remain strictly confidential. When the analysis is completed the researchers will analyse the whole group's data and report on averages, however it is a requirement that individual data be reported in a public data-base.

You will not be able to be identified from this data and this data will be used for scientific publication and presentations. No material that could personally identify you will be used in any reports on this research. All computer records will be password protected. Upon completion of the research your records will be stored for at least 10 years in a secure place, before being destroyed by the principle investigator or co-investigators.

If this is not possible for any reason the head of the principle investigators department or otherwise designated research will take responsibility for this process. A copy of your results will be given to you upon completion of the research at your request.

Trial Payments

There will be no financial cost to you for taking part in the trial. If you are completing all testing procedures, you will receive a gratuity of $100 per visit in the form of a Prezzy voucher. Free parking will also be provided.

Finally

Thank you for considering your participation in this study

Ngā Tāngata hei whakapānga atu - For more information please contact:

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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@hdc.org.nz

You can also contact the health and disability ethics committee (HDEC) that approved this study on:
Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

This research has received Ethical Approval from the Health and Disability Ethics Committee, approval number 17/STH/79/AM15

The Wellington-based investigators of the research are:

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In addition to collaborators at the Maurice Wilkins Centre (University of Auckland); the Moko Foundation (Kaitaia) and the Ngati Porou Hauora Charitable Trust

Please keep this information sheet for your records