

Characterising the Pre-diabetic Asian and Caucasian Phenotype: The 'TOFI' Profile

PARTICIPANT INFORMATION SHEET

We invite you to participate in a clinical study where we aim to assess your current risk of diabetes and then investigate whether this is related to your body composition and/or other newly discovered markers that circulate in your blood.

Your participation in this research is entirely voluntary (your choice). If you do agree to take part, you are free to withdraw from the research at any time, without having to give a reason.

Who can take part?

You can take part if you are of Asian (mainland Chinese; Hong Kong, Taiwan, Singapore or Malaysian Chinese; or Korean) or Caucasian European ethnicity, aged 18-70 years old, normal weight or overweight with a body mass index (BMI=weight/height²) of between 20-50kg/m², but are otherwise healthy.

To take part in the study you need to be available for 1 clinic visit of about 4 hours, which will take place at the University of Auckland Human Nutrition Unit (HNU) in Mt Eden and the Body Composition Unit of Auckland City Hospital in Grafton. Occasionally, if it is more convenient for you, we can split this long visit into 2 shorter visits.

Background to the study

Perhaps surprisingly, people of Asian descent are at much greater risk of poor metabolic health and diabetes at a younger age and a lower body weight than Europeans, Maori or Pacific people. The reason why some individuals are more susceptible than others and what controls their diabetes risk may lie in the storage of body fat. Gaining even small amounts of body weight can lead to the fat 'spilling over' from adipose tissue and into important organs such as the muscle, liver and pancreas, which in turn may significantly increase risk of disease. Often known as **the TOFI profile – 'Thin on the Outside, Fat on the Inside'** – people who appear quite slim can develop diabetes whilst those who are very overweight and/or obese may not. As part of the National Science Challenge, our research team is conducting clinical studies to ask questions such as 'who is most at risk and why?', 'is the TOFI profile important?', and 'what are the early blood markers of diabetes?'

Who designed the trial?

This trial is part of the National Science Challenge High Value Nutrition program. It is designed by the research staff at the University of Auckland Human Nutrition Unit, in collaboration with Ag Research and Plant & Food Research Ltd. You can find out more about the HNU by visiting our website at www.hnu.auckland.ac.nz. To know more about the High Value Nutrition program, visit www.highvaluenutrition.co.nz.

What is the aim of the research?

The main aim of the study is to compare the diabetic risk profile, body composition and blood markers between a group of normal healthy weight/overweight Chinese/Korean adults (healthy vs prediabetic) and normal healthy weight/overweight Caucasian adults (healthy vs prediabetic):



1. Characterise the healthy vs prediabetic profile for diabetes based on blood biomarkers (Hb_{A1c} blood sampling, and metabolomics markers) and body composition (DeXA and MRI scanning)
2. Identify any ethnic differences in risk profile for diabetes based on blood biomarkers and body composition.

How many and what type of people will be in the research?

We are looking for 200 Chinese/Korean adults and 200 Caucasian adults aged 18-70 years, overweight with BMI of 20-50 kg/m², and either healthy or prediabetic. We will ask everybody to come to the HNU clinic for a blood sample and diabetes assessment; and also to have a whole body DeXA scan. In addition, up to 100 people will be asked if they would also like to have an MRI organ scan, to assess whether any fat has 'spilt over' into their organs (liver and pancreas), and a short fitness test using an exercise cycle, to assess their physical fitness which can also affect diabetes risk. 40 participants that have undergone the MRI scan and fitness test, will also be asked if they would also like to undergo a routine clinical test that looks at how well their pancreas is secreting the important anti-diabetes hormone insulin, in a test called the intravenously glucose tolerance test (IVGTT). Furthermore these participants will also be asked to collect a stool/faecal sample, using a kit provided by HNU, so that the gut 'microbiome' (protective bacteria in your gut) can be determined

What happens if I decide to take part?

To enrol in this study we ask you to come in to the Human Nutrition Unit in Mt Eden, Auckland for a short screening visit where we will explain the study and ask you to consent to take part (in writing). We will record your age, gender, ethnicity, waist circumference, height, weight, and BMI; and ask you questions about your medical history and medications. You will also be asked to provide us with your GP contact details so that should there be any unexpected findings, such as diabetes at the blood test, we give you the information and also send it to your GP.

If you are eligible after the screening and would like to participate, you would then continue to stay in the HNU where we will collect an early morning fasting (before breakfast) venous blood sample for the Hb_{A1c} test which identifies your current risk of diabetes. We will also store a blood sample to look for new blood markers of diabetes, using a method known as metabolomics which will be conducted in the research laboratory at AgResearch, Palmerston North.

Your blood sample will also be used to measure the number and types of microRNAs circulating in your blood. miRNAs are produced by plants and animals, and are present in most of the foods that we eat. Our own bodies produce over a thousand different miRNAs that play an important role in regulating the activity of our genes and in regulating various biological activity such as glucose metabolism. miRNAs are non-encoding molecules that represent only a small percentage of your genome (estimated <0.1%) and will be sequenced from cells in we collect from your blood sample. Additionally, we will run analyses on your DNA, as small variations in the genetic code may explain the variability in T2D risk across a population. These are commonly called single nucleotide polymorphisms or SNPs. We aim to identify SNPs that are associated with differing levels of fat stored in the body, especially that surrounding the organs, such as pancreas and liver. None of the SNPs that we will measure in your blood are associated with any known hereditary diseases or health outcomes. Importantly, there is no one gene that determines health. We will NOT be testing for genetic diseases that you could be carrying. Importantly, the testing will NOT provide



any information on heritage. You will not be informed of the results of the SNP and miRNA analyses. You are free to decline that your blood samples be analysed for SNP and miRNA, your decision to withdraw consent for these analyses will not affect your participation in the study.

Some of you may also further have a routine ivGTT and be asked to provide a stool/faecal sample. You will be given a faecal sample kit at your study visit to the Human Nutrition Unit and explained how to collect a small faecal sample. You can return the sample to us on the day you come for your scheduled MRI scan.

After that our research staff will take you to the Auckland City Hospital and University of Auckland Grafton Campus (both located in Park Road, Grafton) for a body composition DeXA scan and, if you would like to, also an MRI scan and a simple fitness test.

What is Dual energy X-ray Absorptiometry (DeXA)?

DeXA is a scanning method, to measure body composition (bone, fat, muscle). The scan takes about 10 minutes. You lie quietly on an open bed and a scanning arm passes quickly over the top of you. You have to lie quietly without moving, but it is not an unpleasant measurement. As the scanning arm passes over you it emits 2 types of very low dose x-ray, similar to the radiation dose that you would receive if you took a 1 hour flight – perhaps between Auckland and Wellington. The DeXA then measures the density of the different tissues in your body. Bone is very dense so it appears bright white on the scan. Muscle is less dense and so it is less white, and fat even less dense and so it is the least white of all. At the end of the 10 minute scan we will print a picture of you showing an image of the bone, fat and lean tissue in your body for you to take home with you.

What is Magnetic Resonance Imaging (MRI)?

MRI is a body scanning method that has been used in hospitals worldwide for many years. It uses a magnetic field and radio frequency pulse to obtain detailed images of your organs without the use of x-rays. It will identify if any fat has been stored in your liver, pancreas, or muscle. You will be asked to lie down in a relaxed state, without movement if possible, within the chamber of the machine whilst it scans your abdomen and legs. The scan will take around 30 minutes.

What is a Cardiorespiratory fitness Test (CRF)?

This is a short and simple bicycle test that assesses how quickly your heart rate increases when you do some exercise. It is not a difficult test, with the amount of exercise similar to you climbing a flight of stairs. Before you take the test we will ask you to complete a questionnaire to confirm that you do not have any cardiovascular risks that prevent you from exercising, and we will also check your blood pressure. For the test we will ask you to cycle slowly on a stationary bike in the clinic for between 3-12 minutes. You will be asked to cycle at a specific speed and resistance for *3 minutes, and then to repeat this several times* (maximum 3 repeats) so that your heart rate slowly increases. The exercise begins at a very low level and will increased in stages depending on your personal fitness level. During the whole test we will record your heart rate using a monitor that is attached to on your index finger. A researcher will be with you throughout the test and will stop the test at any time because of signs of fatigue or changes in your heart rate or any other symptoms you may experience. You could of course stop at any time if you have any feelings of fatigue or any other discomfort. This test is approved by the American College of Sports Medicine for older adults, and most people find the test quite easy to do.

What is an intravenous glucose tolerance test (ivGTT)?



In this test you will be given a small dose of glucose (a sugar that is found in many foods/beverages) directly into a vein in your arm, and we will measure how well your pancreas (which secretes the important hormone insulin) is working. This is called an intravenous glucose tolerance test (ivGTT). Bloods samples will then be collected at regular intervals over the next 70 minutes. The ivGTT is a routine test which takes approximately 1 ½ hours in total to conduct, and will be conducted by our Research Nurse and an investigator from our team. You will receive the glucose infusion slowly via a small line (cannula) that our Research Nurse will insert in one of your arms. After the glucose infusion we will then collect blood samples at intervals from another cannula that our Research Nurse will insert into your other arm. Collecting bloods using the cannula ensures that you will only feel the needle prick once and that subsequent blood samples can be collected conveniently without any discomfort or pain during the procedure. Towards the end of the test, you will be given an arginine dose via the cannula. Arginine is an amino acid and is given routinely during the test to see how much more insulin the pancreas can produce. You will be continuously monitored by the Research Nurse and investigators during the whole procedure, during which you will relax in the clinical suite of the Human Nutrition Unit. This test is used very frequently in diabetes testing and is simple and quite easy to perform. Should you feel uneasy or experience any discomfort you could of course stop the procedure at any time.

What is the microbiome?

Our gut contains many millions of bacteria (gut bugs) which recent research have shown to possibly be associated with good or poor health. These bacteria are known as the 'microbiome'. There may be bugs which are associated with being either lean or overweight, and healthy or diabetic. This is a very new area of research and the TOFI study will help to determine whether your microbiome does affect your health. The test can be done on a very small stool sample which we would ask you to collect at home and bring to your MRI measurement session at Auckland Hospital.

Incidental findings

It is possible that you may be diagnosed with abnormal blood results, such as pre-diabetes or diabetes, during the study. If so you will be informed, provided with the results, and advised to contact your GP directly. Our research staff will discuss with you the significance of any abnormal result and will also make contact with your GP or specialist to ensure adequate follow-up is in place, since these disorders can have significant impact on your health. MRI scans may also pick up incidental findings that could result in a new diagnosis or require further investigation. Again our research staff will discuss with you the significance of the results and will also make contact with your GP or specialist to ensure adequate follow-up is in place. However, follow-up investigations would not be paid for by the researchers.

The risk and benefits of the research

Overall there is low risk associated with taking part in this research study. The main risk is due to the dose of X-ray involved in the DeXA scan, which is similar to the radiation exposure on a flight from Auckland to Wellington, and completion of the low level exercise test. Prior to the exercise test, we will ask you for any information you possess about your health status or previous experience of heart related symptoms (e.g. shortness of breath with low-level activity, pain, pressure, tightness, heaviness in the chest, neck, jaw, and/or arms). If you have had any of these symptoms then you would not be allowed to participate in the exercise test. Therefore your prompt reporting of these and any other unusual feelings



with effort during the exercise test is very important. It is also important to explain to the Research Nurse if you feel and uncomfortable during the ivGTT Research personnel will monitor you during the trial. 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.

Trial Gratuity

All participants in this study will receive a \$50 voucher as a gratitude for participating in the study and for travel expenses. Those that further complete the ivGTT and provide a stool sample for microbiome analyses will receive an additional \$50 voucher. Participants who complete the MRI scan and fitness test will also receive \$100 voucher.

Compensation

If you were injured in this study, which is unlikely, 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.

Confidentiality

Research files and all other information that you provide will remain strictly confidential. No material that could personally identify you will be used in any reports on this research. Upon completion of the research your records will be stored for 10 years in a secure place at the HNU. All computer records will be password protected and available only to research staff at HNU, Auckland City Hospital, and AgResearch.

Finally

Thank you for considering taking part in this study

For more information please contact:

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This research has received Ethical Approval from Auckland Health and Disabilities Committee (HDEC), Auckland, New Zealand, Ethics ref: 16/STH/23

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Please keep this information sheet for your records.

Characterising the Pre-diabetic Asian and Caucasian Phenotype: The 'TOFI' Profile

INFORMED CONSENT FORM (ICF)

I have read and I understand the Patient Information Sheet dated _____ and wish to take part in the research entitled "*Characterising the Pre-diabetic Asian and Caucasian Phenotype: the 'TOFI' Profile*"

I have had the opportunity to discuss this research with the investigator. I am satisfied with the answers I have been given.

1. I have had the opportunity to use support from a family (whanau) member or a friend to help me ask questions and understand the research.
2. I understand that taking part in this research is voluntary (my choice), and that I may withdraw from the research at any time and this will in no way affect my future or continuing health care.
3. I understand that my participation in this research is confidential and that no material which could identify me will be used in any reports on this research. I understand that the sponsor of the research, others working on the sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current research and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published
4. I also agree for my blood samples to be processed and analysed for microRNA and DNA sequencing. I understand that data generated from microRNA and DNA sequencing will be used in reports, publications, and other research outputs (such as accessible online scientific databases) but that any information shared will preserve my confidentiality and I will not be identified.
5. I understand that if I consent to such analysis, no rights will be created for the researcher to get my genetic information.
6. I understand that the treatment, or investigation, will be stopped if it should appear harmful to myself.
7. I understand the compensation provisions for this research.
8. I have had time to consider whether to take part.
9. I know whom to contact if I have any side effects from the research.
10. I know whom to contact if I have any questions about the research.
11. I agree not to restrict the use of any data or results that arise from this research provided such a use is only for scientific purpose(s)

Participant to complete: Please circle as appropriate			Participant Signature:
I consent to participate in the "TOFI profile: Asian vs Caucasian" study	Yes	No	
I consent to having a MRI, cardiorespiratory fitness test, intravenous glucose tolerance test and a microbiome test in addition to blood and DEXA scan.	Yes	No	



I also agree for my blood samples to be processed for small RNA and DNA sequencing. I understand that no information that may identify me personally will be provided.	Yes	No	
I wish to receive a copy of the results. This will not include the results from the miRNA and SNP analyses. I understand that there may be a specific delay between data collection and the publication of the research results.	Yes	No	
I consent for research staff at HNU to contact me at a later date if there are future studies for which I am eligible.	Yes	No	

INFORMED CONSENT FORM (ICF)

Participant to complete:

I _____ Print full name

of _____ Print address

hereby consent to take part in this research which is designed to characterise prediabetic phenotype and identify potential biomarkers.

_____ Signature of Participant

_____ Date

Research Personnel to complete:

_____ Full name of Investigator

(on behalf of the PI)

_____ Signature of Investigator

_____ Contact telephone number

_____ Date

A copy of this consent form is to be given to the participant and a copy is to be kept in their research file at the Human Nutrition Unit.