Participant Information Sheet

Cardiosome Project

Genes and mechanisms in cardiovascular disease

University of Cambridge & NHS Blood and Transplant, Long Road, Cambridge CB2 0PT

We would like to invite you to take part in a research project. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the project if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the Cardiosome project?

"Cardiosome" is a short term for Cardiovascular Diseasome. We have chosen this acronym for our project because we are carrying out an in-depth investigation to identify the genes and mechanisms underlying heart disease. Heart attacks are the leading cause of death in Western societies, and we aim to understand the interplay between genes and environment in this disease.

Why have I been invited?

You have consented to be enrolled in the NHSBT Research BioResource or the Cambridge BioResource and as part of this to be contacted again for future biomedical and genetic studies, in some cases on the basis of results we have obtained on the samples you have already given.

Do I have to take part?

It is up to you to decide. We have sent you this information to introduce the project to you, and we might give you a phone call to see whether you are interested in taking part. If you decide to take part you will be asked to give informed consent. You are free to withdraw at any time, without giving a reason.

What happens to me if I take part?

If you decide to enrol in the project, then a member of the BioResource team will make an appointment for you via phone or email to come to the NHS Blood and Transplant (NHSBT, formerly National Blood Service) Centre on Addenbrooke's campus. Please indicate your preferred way of contact on the reply slip, otherwise we will use the phone as primary contact.
In some cases, the nurse might ask you not to eat anything after breakfast until you have the appointment. In this instance, the appointment would be scheduled just before lunchtime. During the appointment, you will have the opportunity to get additional information about the project from the Nurse and ask any questions you might have. It is up to you to decide if you wish to take part in the project or not. The Nurse will ask you to sign the consent form if you decide to take part.

After you have given your consent, the Nurse will draw blood samples from you. Usually, the amount of blood we need will be less than 100 ml (7 tablespoons). On rare occasions, and only if you are a registered blood donor, we might ask you to give a full blood donation (approx. 475 ml) for use in research. This would be instead of a routine donation. If you are a blood donor, we might also use waste products that accrue during the processing of your blood donation (e.g. tubes filled with blood or filters used to separate cells) and use these for research. We will ensure at all times that you are not giving too much blood, and in some cases we might defer your next donation for a couple of weeks.

In the future, we might contact you again, e.g. to ask you to complete a questionnaire covering lifestyle and medical history of you and your family. We might also ask you to come back to give further samples. All direct contact with you will be through members of the BioResource team only, and they will also ensure that you are not asked to come back for Cardiosome research studies more than 4 times a year.

How will your blood samples be used?

<u>We will isolate, analyse, amplify, and store your DNA</u>

We want to know how variation in genes influences the behaviour of blood cells in heart disease. Genes are made of DNA. This is why we need to analyse your DNA in detail. As part of this study we will test your DNA for many genes, and this is why we will isolate, analyse, amplify, and store your DNA. In the end, we will obtain a complete genetic fingerprint of your blood cells.

<u>We will isolate, analyse, and store other blood components</u>

Besides the DNA, there are many other molecules in blood and blood cells that contribute to their function and we would like to study these. For example, cells use their genes to produce RNA, and RNA is again used to produce proteins. We will isolate, analyse, and store these and additional components of your blood to obtain detailed information on biomarkers (e.g. cholesterol) and the functional behaviour of your blood cells.

<u>We will isolate, analyse, and store your blood cells</u>

All blood cells can potentially contribute to heart disease. This is why we need to isolate them from your blood, separate the different cells, test their function and store them. This enables us to better understand the relation between genetic variation and blood cell function. We might also use some of your cells to create a new 'long-living' cell line that can be grown in the laboratory for indefinite time and be used in future experiments. This enables us to get unlimited amounts of your DNA and RNA . These 'long-living' cells might even become a standard reference in national and international studies or in diagnostic laboratories. One application of such cell lines is to prepare World Health Organisation International Standards which are used in NHS diagnostic laboratories and other national/international healthcare laboratories.

Will my information be kept confidential?

We will protect your privacy at all times. Your blood samples will be labelled with a unique sample number before being transferred to the research laboratory. Your name and contact details will never appear on the blood sample to ensure that the laboratory researchers never get to know who you are. The consent form will be archived separately by the BioResource team at the University of Cambridge/NHSBT centre or the MRC Epidemiology Unit, respectively.

The test results obtained with your samples will be stored within a laboratory database, which is not connected to the database that contains your contact details. Therefore, information from genetic and other tests will be at all times kept separate from your surname, first name and contact details. The information from your questionnaire, and any information from you that was obtained before, e.g. the first three digits of your postcode, month/year of birth, gender, ethnicity, and any clinical information (e.g. full blood count, blood group, frequency of blood donation if you are a donor, etc.) will be stored on the BioResource database in a non-identifiable fashion and can be linked to the laboratory database where needed for statistical analysis. The database linking the sample number to your identity is kept completely separate, and access is strictly limited. Therefore, researchers working with your sample will never know your identity, and the

BioResource team members who may contact you do not know the test results obtained with your samples.

How can researchers ask for further samples if they do not have my personal details?
The only way researchers can get a further sample is by providing the unique sample number to selected BioResource IT personnel who have access to the table linking your sample number with your contact details. The IT person will then advise the BioResource team to call you back for another sample. The team members calling you back will not know the results obtained with your samples, and the reason why more samples are needed.

Is there something wrong with my blood if I am asked to give another sample?
No. There are many reasons why we might ask you to come again. We might want to reproduce former results, to do more detailed analysis, or even to look at a completely different question related to the mechanism of heart disease. Therefore there is no need to worry if we call you back.

Will any of the results obtained with my sample predict my risk for disease? Unfortunately, we cannot answer this question. The aim of the Cardiosome project is to understand mechanisms of heart disease, and this includes the analysis of variations in the genetic code (called genetic markers) that might predict the risk for heart disease. Every healthy individual carries risk markers and protective markers in their genes. However, it may take years before we can confirm how important or accurate these markers are and determine the associated risk or protection. Also, any predictions will have to take into account environmental factors and lifestyle. We are a long way from understanding how they balance each other and what combination of markers, interacting with other factors such as age, gender, smoking etc. cause heart disease.

Can I know the results you get using my blood sample?
As outlined above, for protection of your privacy, your blood sample will be kept completely separate from your contact details. It is not planned to feed back any genetic testing results to you as it would be of no direct benefit. The Nurses will not know any results obtained with your samples. The only time any laboratory test results would be communicated back to you would be if we discover anything that has an immediate impact on your healthcare, and in this case a NHSBT doctor would be informing you and liaise with your GP.

Who will work with my samples?
The primary laboratories working with your sample are located at the University of Cambridge and within the NHSBT. However, we are collaborating with leading scientists worldwide, and your samples may be transferred in a non-identifiable fashion to those collaborators, including private companies. Again, your identity will never be known to any of these collaborators.

What will happen to the results obtained from my samples?
Results of the Cardiosome project will be made available to the public through scientific publications, including placing information on the internet, in press articles and project leaflets. Your identity will never be disclosed in any publication.

Will I be reimbursed for taking part?
We will cover reasonable expenses for travelling to Addenbrooke's Campus.

What are the possible risks of being enrolled in the Cardiosome project?
The risk is mainly the risk associated with a venepuncture. Every venepuncture has a potential for minor problems including bruising, inflammation and fainting. However, the research nurses carrying out the venepuncture are experienced ensuring that any risk is minimised.

If you are a registered blood donor and give regularly, there is a small risk of iron deficiency (anaemia) developing as a consequence of frequent blood donation. To prevent this, the NHSBT monitors your level of haemoglobin at every donation. At the same time, we will only ask you to give a research sample if you have not yet given the maximum volume of blood in the past 12 months.

What is the benefit of being involved in the Cardiosome project?

There will be no direct benefit to you if you choose to participate. However, there will be a benefit to the future development of healthcare provision, and the long-term prevention and treatment of heart disease.

What happens if the funding for the Cardiosome project stops?

The Cardiosome project is currently funded by NHS Research & Development and the European Union. If the funding ceases, the samples and data will be safeguarded by the NHSBT.

Who has approved the Cardiosome project?

All research in the NHS is reviewed by an independent group of people, called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. This project has been reviewed and was given a favourable opinion by the Cambridgeshire 1 Research Ethics Committee.

What happens if an invention is made using my sample?

You are giving your sample as an absolute gift. An “absolute” gift is a gift which is given as a donation, i.e. without receiving a payment and without conditions. In the future, your sample may help us to make an invention, e.g. develop a new product to diagnose or treat disease. If an invention results from the research undertaken with your sample, you will not receive any compensation or payment. Cardiosome project partners in the public sector may work together with commercial companies to develop inventions for the benefit of patients; and we hope that such products are brought into use by the NHS to improve healthcare in the future. Part of the profits earned by marketing such products may be returned to Cardiosome project partners and can be invested in further research.

How can I withdraw my consent?

If you wish to withdraw, please contact the NHSBT Research BioResource team on freephone 0800 085 3650 or the Cambridge BioResource study team on 01223 740024, respectively, and a withdrawal form will be sent to you. Please note that we will not be able to remove results of any tests already obtained with your sample from the computer. Your samples cannot be destroyed and will remain in the original arrays of 96 samples per plate, as it is not feasible to pick out single samples. However, we can assure you that no new data will be added, and the stored data will not be used after we have received your written notification.

What arrangements have been made for indemnity?

The NHSBT is the sponsor of the Cardiosome project and therefore cover is provided under the NHSBT indemnity scheme.

Whom do I contact if I have further questions?

If you have a question or wish to complain about any aspect of the Cardiosome project, please contact the project leader Dr Willem Ouwehand MD PhD FRCPath, Honorary Consultant Haematologist, University of Cambridge/NHS Blood and Transplant, Long Road, Cambridge CB2 0PT or contact the NHSBT Research BioResource under freephone 0800 085 3650 or the Cambridge BioResource study team under 01223 740024.