Information leaflet - for adults/parents with imprinting disorders
V5 - 21/12/2012

Research Study: Imprinting disorders, finding out why?

You are being invited to take part in a genetic research study to understand more about why some medical problems occur.

What are genes?

Genes are passed on from father and mother to their children and they are made up of DNA, sometimes called the molecule of life. Genes contain the essential information to allow a baby to develop and grow from a very simple cell into a person with eyes, a brain, a heart etc... Our genes, therefore, come in pairs because we inherit one from each parent. Usually both copies are turned on and work equally. However, there are a special group of genes which are designed so that only one of the copies is turned on, while the other is turned off. For some genes it is the one from the mother that is turned off and for others it is the gene copy that comes from the father that is turned off. The genes with only one copy working are called imprinted genes.

Sometimes genes don't work correctly either because they are not made correctly or because they are not turned on and off correctly. This is a study to look at how genes are turned on and off and this is called epigenetics. In the study we are looking at the special group of genes called imprinted genes which are very carefully controlled.

Switching on a gene is rather like switching on an electric light. For a light to work the light bulb has to be made correctly, but also the light switch has to be working. An epigenetic study is all about the switch.

Why are we carrying out this study?

People with medical problems sometimes have a difficulty with the way genes are controlled but we have only recently developed a way of testing for this. We hope that this method will show changes that cannot be seen using other techniques. This research project may help to explain why some people have been born with medical and developmental problems.

Why have I been chosen?

You have been chosen because the medical problems that you/your child have suggest to the doctors looking after you that they are due to a problem with the control of imprinted genes.

What will happen to me/my child if I/they take part?

You may decide to participate simply by filling out and returning the enclosed consent form. Alternatively, you might wish to phone to discuss it in more detail. Whether a blood sample is needed will depend on which blood tests you/your child has already had. Many will already have a sample of blood stored in the hospital laboratory. However if this is not the case it will involve having a blood test. Approximately 2 teaspoonfuls of blood (a small amount) would be needed. The sample will usually be taken at the blood taking unit in the hospital; or, sometimes samples may be taken at your GP surgery. The study involves us doing genetic tests on the sample.

Because you are already known to have an imprinting disorder, you/your child will be invited for a clinic visit in Southampton. A medical history, clinical examination and

photos will be taken and where possible questions answered. This will last about 1 hour. If this is not possible we will ask your clinical genetics consultant to arrange a similar visit and send us details and photos. We may need blood samples from parents to determine the significance of the results and you/your child will be asked for urine and spit samples.

What tests will be performed on the sample?

In this study we are looking at the way imprinted genes are controlled. We currently know that imprinted genes are controlled by regulatory factors working on DNA sequences known as genetic control centres. We will examine in great detail all the known genetic control centres to see if they are abnormal. We will also check that the codes of some of the imprinted genes and regulatory factors are normal. In some cases it may be necessary to carry out DNA sequencing (reading the genetic code of a large number of genes, or all of the genetic code). This is known as genome-wide sequencing. This will be done in the Wessex Regional Genetics Laboratory in Salisbury and in collaboration with scientists working with us; some of whom are working in other parts of the United Kingdom or abroad. However it must be noted that clinical information and patient details will only be stored at the Wessex Genetics Service and part of the sample only will be sent to collaborators.

Will any genetic tests be done for any other diseases?

The test that will be run as part of the IDFOW research study will look at the DNA of both your child and you in great detail. It is hoped that this will allow us to find the cause of the imprinting/growth disorder in many cases. These techniques can also sometimes find other genetic problems that are not related to the imprinting disorder. However these other genetic problems may still be of medical importance. We call this an 'incidental finding', as it does not relate to the imprinting disorder being studied. Often we are unsure what an incidental finding might mean for the person concerned. Since these findings are not related to the cause of your child's imprinting disorder and we may be uncertain as to their meaning, we will NOT pass these results back to you.

What clinical information will be collected?

A simple clinical questionnaire will be completed recording the main clinical problems, pregnancy and family history if known. The examination findings will be stored in research notes in Southampton. Results about known genetic and medical investigations will be requested.

What are the possible risks of taking part?

There are no physical risks to taking part, over and above those of attending your hospital outpatient clinic, and giving a small blood sample for testing, if that is needed. Blood sampling and spit sampling is considered to be a safe procedure without significant risk. As with any genetic test, there is the possibility of a result which may be difficult to interpret or has long-term implications that are not known about at the time of the study. The opportunity for full discussion of the results will be given to you. It is also important to realise that genetic tests may give information that is important for relatives.

What are the advantages of taking part?

We may be able to shed light on why you/your child have a problem with imprinted genes. Understanding why a genetic problem has occurred is the key to determining what medical management is most likely to be required. We may be able to give you

information on risks for other family members. Careful analysis of the molecular changes in the light of clinical findings will help us in the future to tell other families what genetic findings mean.

What if you discover something new about the way my imprinted genes are controlled from the study?

If you decide to participate, you will be asked whether you would like to know the results of the research or not. If we do find out something new we will be happy to see you again in clinic to explain the results. We may ask you for a further urine and spit sample and perhaps a further blood sample. It may also involve finding out whether other family members have the same change although this will depend on their consent.

Publication of findings in medical journals

If the study is successful the findings may be of interest to other doctors and scientists and we will wish to publish them. If you tick the box relating to point 8 on the consent form, this will give us permission to publish limited information relating to yourself (test result and very brief medical information, which will not allow you/your child to be identified). If we wish to publish photographs, we will first ask you for your separate consent.

Data Protection Act,

Handling of patient information within the research project will comply with the Data protection Act, 1998.

Complaints

Any complaints relating to the conduct of the research project should be directed in the first instance to the Study Coordinator (full contact details are given below).

Indemnity

In the very unlikely event of a claim arising through an act of medical negligence: all research personnel with whom the research subject may come into contact are indemnified, that is to say, they are covered against the possibility of an act of medical negligence, through the Hospital Trust and University that employs them; or, through an independent agency such as the Medical Defense Union.

Please feel that you can contact us on the number below if you wish to discuss any aspect of this. If you wish to participate then please return the consent form. You are under no obligation to take part and if you decide not to, this will not alter your normal medical care.

Contact details of Study Coordinator:
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This study has been reviewed by the Southampton and South West Hampshire Research Ethics Committee A. The ethics approval number is 07/H0502/8