UCL INSTITUTE OF CHILD HEALTH

Great Ormond Street Hospital for Children NHS Foundation Trust

# INFORMATION FOR PATIENTS WITH SUSPECTED GENETIC DISEASE (AGE 14+)

**(GOSH Research Ethics Committee project name: Molecular Genetics of Human Birth Defects – mapping and gene identification)**

You are invited to take part in a study being carried out in the "Genes Development and Disease Theme" at the Institute of Child Health, London. The Institute is part of University College London, but works in partnership with Gt. Ormond St. Hospital for Sick Children.

**Aim of the study:** We are trying to understand the reasons why some children are born with "congenital malformations". All this means is that when you were in the womb, the body did not build itself correctly, sometimes due to faulty genes. If a gene gives a faulty instruction this is often referred to as a mutation. These can run in families, or they may occur "out of the blue". We are now studying a variety of conditions affecting formation of the brain, heart, limbs, kidneys, skin, bones, and immune system. This should help us understand the problems that happen in patients, and in some circumstances can lead to a diagnostic test (which tells you and the doctor what the disease is), or improved prognosis (which is having an idea about how the disease progresses with time).

We now have the technical ability to look at *all* of a person's genes. Although we are only interested in which gene causes the birth defect or syndrome in your family, we will generate information about all of the genes, even those we are not specifically investigating. It is possible that we may find a faulty gene with nothing to do with your/your child's condition, but which could affect general health in the future. The clinician who has responsibility for your care will decide which information will be of benefit to you or your family, after carefully considering his/her own professional guidelines, and may ask for another sample from you to confirm the laboratory results. We will give you the option of receiving this sort of information but some people may not want to have information of this sort, and it is fine if you tell us that you don't want any feedback apart from information about the gene causing the birth defect or syndrome in your family.

As we will not be examining all genes in detail, it is also possible that you may have a change in a gene which is significant for your health but which we do not detect. It would be unwise to assume that there is a 'clean bill of health' if someone has had whole genome analysis of this sort.

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**What the study would involve for you?** If you agree, we would first ask your doctor for medical details so that we can see exactly what is wrong. We might ask to take your photograph. This is because the face is often a very good way of spotting patients with the same problem. We would then ask your clinician to send us a sample of your blood, which we can use in our search for faulty genes. Alternatively, a buccal mouth wash kit (saliva sample) may be requested. In some cases, samples from unaffected relatives may be helpful. We might request permission to study biopsy material (very small pieces of tissue already taken during the course of routine care). Blood samples could be taken at your GP's surgery, rather than at your local hospital, if that were more convenient for you. There is a special cream that numbs the skin before the blood samples are taken, to reduce discomfort to a minimum. Occasionally, a second blood sample may be required where samples run out, or a check is required. If it proves impossible to obtain blood, there are alternatives such as mouthwash or brushings from the inner cheek lining.

In order to investigate the function of identified gene variants in patients, examination of different tissue samples may help us understand the disease better. For these investigations a patient cell line can be required. This means the cells are kept alive indefinitely in a test tube (immortalized) to avoid us having to ask for another sample. These immortalized cells, and the original samples we obtain from you, could potentially be shared with other scientists around the world for research purposes, and may be obtained from the samples listed below. Depending on the disease being studied, we may ask for the following samples:

***Blood sample for DNA:*** This is the standard way we collect DNA for most diseases and will apply to most patients as mentioned above. We may also use the blood sample for other laboratory studies (biochemical and immunological) if relevant to better understand the disease in question. These can usually be done on very small volumes of blood and where possible at the same time as a routine blood test taken for monitoring of the disease to minimise extra needle pricks.

***Skin biopsy*** which involves removal of a small circular piece (about the size of the blunt end of a pencil) of skin after the skin has been numbed with a local anaesthetic to minimise discomfort. This does not impose a significant health risk to the patient but may lead to a small scar, therefore is performed on less exposed skin areas.

***Nasal brushing:*** We may request a nasal brushing, which involves placing a small clean brush into the opening of the nose (about 1 centimeter) and gently brushing the surface to collect some of the cells lining the nose. Side effects are minor and occur rarely (<1%), including “minor blood staining of snot”. This is a standard method and has been performed safely on many children and babies before.

***Hair follicles:*** We may request taking 4-5 hairs from the head, since this contains genetic material. This doesn’t impose a significant health risk and will not cause significant pain or injury.

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***Urine:*** We may ask you to provide a urine sample to undertake research laboratory testing and to isolate kidney cells naturally shed into your urine. This does not impose any health risks or discomfort.

**Storage of your sample(s):** All samples will be stored securely in compliance with the Data Protection Act, and Human Tissue Act. This means that we should not have to trouble you for additional samples in the future (research projects can take many years to complete). The routine clinical records which are managed under the confidentiality rules of the NHS, will contain a note that stored material in the form of DNA or a cell line is available. This material may be used for several purposes: future investigations that may be useful for your routine clinical care or counselling; sharing of the samples with others so that research may be carried out by researchers around the world;; and using the stored material for future research projects. As we will be sharing the stored material with other researchers, it may be used in medical research studies that are unrelated to human birth defects.

**Storage of the results of the study:** We will store the anonymous results of the genetic analysis of your samples, DNA and cell lines indefinitely in electronic archives (databases) and will make these data available to other researchers around the world for many different studies - some studies may not connected to human birth defects. We will also share your anonymous samples, DNA and the cell lines we make with other researchers around the world. These other researchers will be able to carry out genetic analysis on these materials and may publish the results of their studies, or store the data on electronic archives (databases) where it can be accessed by many researchers.

**It might be several years before we eventually find the gene or genes that cause(s) the birth defects in you.** Once we do find a genetic change, your clinician will probably want to arrange to see you again, in order to discuss the significance of the finding for yourself and your family with you. However, unless something is found which your clinician decides you should know about and you have agreed to receive results, there will not be a "test result" to communicate back to you as with other investigations you may have had. If there are other members of your family who are affected or who might have the same genetic change, your clinician will decide whether or not to ask you for your permission to contact these other people, so that we can check to see whether or not they have the same genetic change.

You should understand that if samples, DNA, cell-lines or data are shared with other researchers, then we will not necessarily hear about the results from these research studies, neither will we be able to share the results with you.

**What are the potential disadvantages and risks of taking part?** The clinician responsible for your care may decide to tell you that you are a carrier for or are at high risk of developing a genetic disorder, other than the original condition for which you/your child are being investigated, and some people may find this information stressful. If so, you will be offered genetic counselling to discuss this in depth with a genetic counsellor, so that you are fully informed about what the findings mean for

you and your family. Discomfort from the procedures required to obtain DNA and other tissue samples are dealt with above.

The only other, although very unlikely, risk that we need to tell you about is a risk that you may be identified from genetic data. We would like to stress that this is highly unlikely, but we do need to tell you about it. Identification could occur if someone matched your anonymous genetic data from this study with another set of genetic data which was linked to details such as your name and address.

**What are the potential benefits of the study?** If the study succeeds in discovering a genetic change, we will be able to confirm to you that this is the cause of your problems and that the diagnosis made by your clinician is correct. This may mean that other family members can be tested for the disorder and offered genetic counselling. More broadly, better understanding of genes that cause birth defects may well help in the long term with the prevention, diagnosis and treatment of other disorders. Your clinician may decide to tell you that you are a carrier for or are at high risk of developing a genetic disorder, other than the original condition for which you/your child are being investigated, and you may be glad to have this information. Many people find this useful information for the purposes of family planning or health screening. However it is of note that we are investigating your sample primarily only for changes in genes we believe to be related to the disease you came to see us/your clinician for. Therefore we might not recognize changes in genes not related to your primary purpose of enrolling in this study.

**Who will have access to the case/research records?** Only the researchers will have access to the data collected during this study. The use of some types of personal information is safeguarded by the Data Protection Act 1998 (DPA). The DPA places an obligation on those who record or use personal information, but also gives rights to people about whom information is held. If you have any questions about data protection, contact the Data Protection officer via the switchboard on 020 7405 9200 extension 5217.

In some cases, the research may be undertaken in collaboration with industrial partners (e.g. a pharmaceutical company) where the intention is to develop new drug therapies based on genetics findings or to develop tests to determine if an individual may or may not respond to a drug. Anonymised genetic information only will be used in these studies so that no-one will know of your identity. Unless you say otherwise, your G.P. may be copied into communications relating to this work. Involvement or non-involvement in this research does not affect your routine care.

**Are there any other long term implications?** This research test does not affect health insurance (make it cheaper or more expensive), but we have no control over future government policy in this area.

**What are the arrangements for compensation (UK only)?** This project has been approved by an independent research ethics committee who believe that it is of minimal risk to you. However, research can carry unforeseen risks and we want to be

informed of your rights in the unlikely event that any harm should occur as a result of taking part in this study. No special compensation arrangements have been made for this project but you have the right to claim damages in a court of law. This would require you to prove fault on the part of the Hospital and/or any manufacturer involved.

**Do I have to take part in the study?** No. If you decide, now or at a later stage, that you do not wish to take part in this research project, that is entirely your right, and will not in any way affect any future offer of treatment or genetic counselling. Any samples will be destroyed upon your request. However, any DNA extracted or cell lines already made from your samples, or any results of the analysis of these materials, will be kept and used in research, and will be shared with other researchers around the world.

**Who do I speak to if problems arise?** If you have any complaints about the way in which this research project has been, or is being conducted, please discuss them in the first instance with the researchers in charge. If the problems are not resolved, or you wish to comment in any other way, please contact Mr Luke Murphy, Head of PALS unit, by post at PALS Department, Great Ormond Street Hospital NHS Foundation Trust London WC1N 3JH or if urgent, by telephone on 02078297862, or by emailing pals@gosh.nhs.uk.

**How to contact the researcher at ICH, 30 Guilford Street, London WC1N 1EH.** Please do not hesitate to contact him/her if you have any questions or comments about the study. You can write/email to:

***Co-I:***

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| Prof. Philip Beales: | p.beales@ucl.ac.uk |
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***PCD Project:***

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Or telephone 020 7242 9789 ICH switchboard.