

Understanding the disorders of the RAS-MAPK pathway: Information sheet for parents and carers

This leaflet gives information about a research study into a group of conditions called the RAS-MAPK pathway disorders. These disorders arise due to changes in genes, the instruction manuals for the body's cells. RAS-MAPK pathway disorders include cardio-facio-cutaneous, Noonan and Costello syndromes (CFC, NS and CS). We hope that this leaflet will help you to understand why the research is being done and what it will involve. Please ask if there is anything that is not clear, or if you would like more information to help you decide whether or not your child should take part.

What is the purpose of the study?

We want to know more about how the gene changes that are responsible for CFC, NS and CS result in the problems that people with these conditions may have. People with each of these conditions can have similar problems to one another, and this is because all of the disorders involve changes in the way that a particular pathway, called the RAS-MAPK pathway, works in the cells of the body. Affected people may have a wide variety of problems including heart disease, poor growth, skin changes and learning problems. The underlying gene changes that cause these are now clear in many, but not all, cases.

This study has 2 aims:

1. to identify what particular features individuals with these conditions have, so that they can be most effectively managed.
2. to try to identify the genetic cause of the condition in affected people who do not currently have a known gene change.

Who is carrying out the research?

The study is being conducted by Dr Emma Burkitt Wright and Dr Bronwyn Kerr from the Genetic Medicine department at St Mary's Hospital, Manchester. Dr Burkitt Wright is doing this study as part of a PhD at the University of Manchester, and the project will be carried out over the next three years. Dr Kerr is the Educational Supervisor. The project has been funded by the Wellcome Trust, and the North West Ethics Committee has reviewed it (application number 10/H1003/77).

Why have I been chosen?

We are contacting you because you have a child with cardio-facio-cutaneous, Noonan or Costello syndrome, or a condition with similarities to this group of disorders.

What will taking part involve?

If you agree to involvement in the research project, we will ask your permission to allow the doctor looking after your child to provide us with information about his or her medical history and any tests performed to date. This information will focus on growth, health problems and development. With your permission, we would like to contact your child's teacher to provide us with information about your child's concentration at school.

We will ask permission to use a sample of blood or saliva from your child to check for genetic changes which may give rise to their condition. If a sample has been taken previously for genetic testing, this may be used, if you consent to this. If no stored sample is available, then a new sample can be taken at the same time as the appointment for other aspects of the study. If you prefer, arrangements could be made for this to be done locally with any other tests that are being done, and sent on to us. If your child is having an operation, we will ask if a tiny piece of tissue could be taken for us to analyse in the study. This is because we think that there may be important differences in how the RAS-MAPK pathway acts in different body tissues. No tissue other than that being operated upon would be taken, and there would be no differences to the operation or recovery from it as a result. If a fresh blood sample is being taken, or if a skin biopsy is taken at the time of an operation, we may ask if you would be prepared for a cell line to be made from this and gifted to us for use in the research. This means that cells with the DNA of the affected person could be frozen down and stored securely (like their DNA sample) and available for further studies in the University of Manchester.

The study assessment itself involves taking a clinical history and doing a physical examination of your child (as happens when you attend other specialist doctors). We would then like to do some tests that assess learning and memory, which are laptop computer programs (like simple games). We would also like to interview a parent to find out more about your child's social development. This is because we think that there are some important differences in how children with these disorders think and learn. Understanding these better could lead to improved ways of teaching and supporting the learning of your child and other children with these conditions in the future. The total time taken for these tests is variable, but overall the time taken by these assessments should not exceed three hours. If you or your child need a break in this time then just ask, this is fine.

We might also ask if you, as parents, could provide blood samples too, so that any possible changes found in your child's sample could be further assessed. This is helpful because when changes have arisen newly in the individual, rather than having been inherited from one of their parents, these are more likely to be important in explaining their pattern of differences.

We will ask you if we can take photographs of your child, or use pictures that have been sent to us by their clinical geneticist. All information and photographs will be stored securely on a computer database that is only accessible to members of our research team. Personal, identifying, details will be stored separately, also on a secure database or in a locked filing cabinet.

We will ask you to sign a consent form for the study and forward a copy to us. If you decide to take part, and give us permission to contact them, we will let your family doctor know that your child is taking part in the study.

Do I have to take part in the study?

You have a completely free choice about whether to enter the study. If you do not want your child to take part, you do not have to give a reason. Deciding not to take part will not affect the medical care that your family receive. You can also choose to stop taking part in the study at any time. This would not affect anyone's medical care in any way.

Are there any benefits to taking part?

There may be no direct benefits to your family, but we hope that you find taking part worthwhile. The findings of this study will help us to understand better the causes and effects of RAS-MAPK pathway disorders. This could improve the care of people with these conditions in the future. When the work is complete, we will send you a summary of the results. We will also be able to provide you with a report summarising the results of your child's learning and behaviour assessments.

Are there any disadvantages to taking part in the research?

For anyone having a new blood sample taken, then there is a small risk of bruising or discomfort at the skin site. This can be minimised by using local anaesthetic spray. A further possible risk of this study is that testing might reveal a gene change which is either unexpected or which has implications for your child or other family members. If this situation were to arise, we would arrange for all relevant individuals to be seen by a clinical geneticist within their local genetic service, so that this can be explained fully and any important findings acted upon. Similarly, if anyone were to become distressed in the course of taking part in the study, we would arrange for an appointment for genetic counselling regarding this.

What if something goes wrong?

It is very unlikely that any participant will come to any harm as a result of taking part in this research. If taking part causes you any worries, we can arrange for you to discuss these with a research nurse or with your local clinical geneticist.

Complaints

If you have a concern about any aspect of this study, you should speak to us, the researchers, and we will do our best to answer your questions. If we are unable to resolve your concern, or you wish to make a complaint regarding the study, please contact a University Research Practice and Governance Co-ordinator on 0161 2757583 or 0161 2758093 or by email to research-governance@manchester.ac.uk.

Harm

In the event that something does go wrong and you are harmed during the research, you may have grounds for a legal action for compensation against The University of Manchester and Central Manchester Foundation Trust, but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in the study be kept confidential?

Yes. The names of participants will not be used in any publication or shown to any person. All information will be kept strictly confidential. Any information will have names and addresses removed so that no-one can be recognised from it. Any information that is used in a presentation or publication will have all names, dates of birth and other identifiers removed. Notes and computer files will not be shown to anyone outside the research team, except for individuals representing the Research Sponsor or Regulatory authorities (for the purpose of monitoring or auditing the study).

Will I be paid for participation?

We will not be able to offer any payment for helping with this study, but we will happily refund any extra costs, such as travel expenses (mileage costs, or public transport costs, on production of receipts), that you incur as a result of taking part.

Further Information

If you require any further information, please contact:

For Information about the Learning Studies:

Amy Burns
Research Assistant
Social Development Research Group
Mobile: 07919 528164

Ami Brooks
Research Assistant
Social Development Research Group
Telephone: 0161 306 7953

For Information about the Clinical Studies:

Dr Emma Burkitt Wright
emma.burkitt-wright@manchester.ac.uk
Genetic Medicine, St Mary's Hospital,
Manchester M13 9WL
Tel: 0161 901 2335 Fax : 0161 276 6145

Dr Bronwyn Kerr
bronwyn.kerr@cmft.nhs.uk
Genetic Medicine, St Mary's Hospital
Manchester M13 9WL
Tel: 0161 901 2335 Fax : 0161 276 6145

What happens now?

If you are happy to help with the research, please can you return the consent form to us in the reply paid envelope provided.

Thank you for taking the time to read about this study