

Research study checklist

1. Samples from all affected family members and parents (and unaffected siblings where available)

DNA (5-10ug)

OR

Blood - EDTA

2. Clinical information

Completed Clinical data sheet including pedigree

Photos

3. Consent *

Consent obtained using Scottish MREC forms, enclosed

OR

Consent obtained under local research ethics approval and
Copy of research ethics committee approval enclosed

4. Transportation:

No risk factors for blood-borne viral infections (HIV/Hepatitis B, C)

Commercial invoice, 6 copies (International samples)

*As a requirement of our European Research Council funding for international patients we are asked to submit a copy of your local research ethics committee approval before starting work on samples consented using local ethics forms. If this is not possible, we have approval by the Scottish NHS Multicentre Research Ethics Committee for use of research samples from international collaborators who have used our research consent forms and information sheets. All consent should be taken in accordance with local professional and regulatory standards.

**Clinical Data Sheet
Microcephalic Primordial Dwarfism**



Name: _____

Date of birth: _____

Male / Female

Hospital record/Pedigree Number _____

Clinician (to send report to): _____

Email: _____

Is this patient enrolled in the DDD study (UK)? Yes/No DDD ref: _____

Required Information: Please note we are unable to commence sequencing until growth information is provided

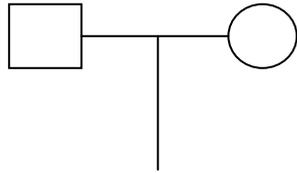
		Date	Weight/kg	OFC/cm	Height/cm
At Birth	Gestation:				
At Recent assessment	Age:				

MENTAL RETARDATION	None/Mild/Moderate/Severe, or IQ:
CONSANGUINITY	Yes/No Degree:
PATELLA SMALL OR ABSENT?	Yes/No Examination: Palpation/USS/Xray Please note patella are not visible on Xray prior to 6 years of age
EARS	Normal/Small Please provide photo if abnormal

Additional Information (please continue overleaf if required)

MEDICAL HISTORY (Please circle or tick box if present)	Teratogen Exposure/Drug Use Yes/No Skin/Hair/Teeth/Nails Normal/Abnormal Deafness <input type="checkbox"/> Cytopenia <input type="checkbox"/> Recurrent Infections <input type="checkbox"/> Diabetes <input type="checkbox"/> Seizures <input type="checkbox"/> Details.....
EXAMINATION	Malformations <input type="checkbox"/> Neurological Deficit <input type="checkbox"/> Details.....
INVESTIGATIONS	Array-CGH Y/N/In progress MRI/MRA <input type="checkbox"/> Skeletal Survey <input type="checkbox"/> Results.....

PLEASE SUPPLY COPY OF PEDIGREE OR DRAW OVERLEAF



Consent Form (6/3/12. Version 3)

Genetic disorders of growth, development and the brain

Adult Consent Form

Name:

Date of Birth:

Please keep a copy of this signed form in the patient record

I have read *Information for families: Genetic disorders of growth, development and the brain*: **Yes / No**

I give permission:

To: (name of clinician or genetic counsellor)

Of: (insert Departmental address)

To perform genetic tests on our DNA samples to try to establish a cause for my condition
(specify name/description of condition):

Yes / No

I would like to receive the result of any genetic finding relating to my genetic condition via the referring clinician:

Yes / No

I understand that:

- My name will not be published.
- Any clinical information and photographs relating to me will be stored securely in the MRC Human Genetics Unit and will be used only for research purposes
- Only genetic information likely to relate directly to the cause of your condition will be reported back to your doctor.
- Anonymised clinical and genetic data from you/your family may be made accessible to other researchers.

Signature of patient Date

Signature of clinician Date

Thank you for taking the time to read and complete this form. Please return it to your doctor.

Consent Form (6/3/12. Version 3)

Genetic disorders of growth, development and the brain

Adult (unable to consent for themselves) Consent Form

Patient's Name:

Date of Birth:

Please keep a copy of this signed form in the patient record

I have read *Information for families: Genetic disorders of growth, development and the brain*: **Yes / No**

I give permission:

To: (name of clinician or genetic counsellor)

Of: (insert Departmental address)

To perform genetic tests on _____'s DNA sample to try to establish a cause for his/her condition (specify name/description of condition):

Yes / No

I would like to receive the result of any genetic finding relating to his/her genetic condition via the referring clinician: **Yes / No**

I understand that:

- _____'s name will not be published.
- Any clinical information and photographs relating to him/her will be stored securely in the MRC Human Genetics Unit and will be used only for research purposes
- Only genetic information likely to relate directly to the cause of his/her condition will be reported back to his/her doctor.
- Anonymised clinical and genetic data from his/her family may be made accessible to other researchers.

Signature of person consenting* Date

Signature of clinician Date

Thank you for taking the time to read and complete this form. Please return it to your doctor.

* This should be the patient's legal proxy or equivalent in your country. (eg. Scotland:- welfare guardian/attorney or nearest relative).

Consent Form (6/3/2012. Version 3)

Genetic disorders of growth, development and the brain

Parent/Guardian Consent Form

Please keep a copy of this signed form in the patient record

I/We have read *Information for families: Genetic disorders of growth, development and the brain*: **Yes / No**

I/We give permission on behalf of my/our child

Named:

Date of Birth:

And myself/ourselves:

Mother (Full Name):

Father (Full Name):

To: (name of clinician or genetic counsellor)

Of: (insert Departmental address)

To perform genetic tests on our DNA samples to try to establish a cause for my/our child's condition (specify name/description of condition):

Yes / No

I would like to receive the result of any genetic finding relating to my child's genetic condition via the referring clinician: **Yes / No**

I/We understand that:

- My child's name will not be published.
- Any clinical information and photographs relating to my child will be stored securely in the MRC Human Genetics Unit and will be used only for research purposes
- Only genetic information likely to relate directly to the cause of your child's condition will be reported back to your doctor.
- Anonymised clinical and genetic data from your family may be made accessible to other researchers.

Signature of mother Date

Signature of father Date

Signature of legal guardian Date

Signature of clinician Date

Thank you for taking the time to read and complete this form. Please return it to your doctor.

**STUDY TITLE: Genetic disorders of growth, development and the brain
Family information sheet (primordial dwarfism)
(Version 4, date 1-8-14)**

We would like to invite you to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study?

The aim of this study is to identify genes that cause reduced growth. In particular we are studying conditions in which growth is reduced from early on in development. The conditions we are studying include diagnosis such as Microcephalic Dwarfism, MOPD II, MOPD I/III, Seckel syndrome, Meier Gorlin syndrome and Dubowitz syndrome. Finding such genes will help make genetic testing possible for these disorders. This knowledge may eventually help in the management and treatment of these or other illnesses. Our research can also help understand how these genes normally work in the human body and brain.

Why has my family been chosen?

You have been approached about this research because you have a family member/relative whose reduced growth could be caused by changes in such a gene.

Do we have to take part?

It is up to you to decide whether or not to take part. If you decide to take part you are free to withdraw from the study at any time and without giving a reason. This will not affect the standard of care you receive in any way.

What will happen to me if our family takes part?

If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. Your doctor will also take into consideration children's views, according to their age and intellectual ability, in the consent process. We will ask your doctor to take a sample of blood from your affected family member. We may also ask for samples from unaffected family members. Occasionally, it could be helpful to also have a very small piece of skin, and if so this will be discussed with you. Likewise, very occasionally, it may be useful to study a spare tissue left over from an operation or medical procedure, and if so this will be discussed with you.

These samples will provide us with DNA which can then be used to identify and test genes. Cells from these samples will be stored in the laboratory and may be used to create cell lines. Cell lines provide a renewable supply of DNA and a source of cells for study. Studying cells will help with understanding how these conditions occur as well as the normal role of these genes in the body. We may also convert cell lines into other cell types to grow cells and small amounts of tissue most relevant to the disorder being studied.

The sample will be used for research purposes only and will be stored indefinitely. The sample will be treated as a gift from you, and will be under the custodianship of the MRC Human Genetics Unit at the University of Edinburgh.

We will also ask your doctor for clinical information about your family member, relevant to their condition (that may include photos, if these are part of their clinical record). Any personal data and information given to us will be kept confidential.

What are the possible benefits of taking part?

A gene change could be identified in your family during the research which would provide an explanation for the reduced growth and make gene testing for family members possible. However, there may be no direct benefit from this research to you or your family. There would not be any financial benefit to you if this research led to the development of a new treatment or medical test.

What are the possible disadvantages and risks of taking part?

There is a risk of some minor discomfort and bruising from the blood or skin sample. Your doctor will make sure that any distress caused to children is kept to a minimum, for instance by using local anaesthetic cream to numb the area, before the sample is taken. For those with needle-phobia samples of saliva, can be taken instead to obtain DNA.

How will my information be kept confidential?

Names and dates of birth along with clinical information will be stored securely at the MRC Human Genetics Unit. Each individual in the study is given a unique code number which is held securely at the Human Genetics Unit, and is used to label all samples stored.

DNA samples and cell lines will be stored and analysed in the MRC Human Genetics Unit. Anonymised (coded) samples and cell lines may also be sent to other research labs for analysis (such as the Wellcome Trust Sanger Institute, Cambridge for high throughput genome sequencing).

Anonymised data generated from the analyses may also be shared with other research teams performing similar work, to increase the chance of important discoveries. Likewise, results of whole genome sequencing will be shared with the wider research community by storing the information in an archive called EGA (www.ebi.ac.uk/ega). The genetic data that is deposited will be identified only by a code number and will only be accessible to bona fide researchers who have agreed to use the data for research and to keep the data confidential and safe.

What if new information becomes available?

Information relevant to the condition being studied in your family may be discovered. This may mean that gene testing became possible for your family. You will be given the option on the consent form to say if you would like to be re-contacted in that case. A diagnostic test would require discussion with your doctor. A new DNA sample might be needed for the diagnostic test that is then arranged.

Will any genetic tests be done for any other diseases?

No. The analyses that are done during the project will examine the DNA at very high resolution to determine the cause of condition being studied. Because the approaches are genome-wide, these techniques could also identify other genetic problems that are not related to this condition, but only in rare cases. This would be termed an incidental finding. We will NOT look for or follow up on such possible changes in the DNA sequence.

What happens when the research study finishes?

DNA and tissue samples will continue to be stored at the MRC HGU after the study is ended. These samples may be used for future related research studies. Every care will be taken to prevent misuse of your sample by other researchers, and such future studies will require approval by an Ethics Committee. If a future study will provide information useful to you the samples will be anonymised by coding. Otherwise, such samples will be completely anonymised. Completely anonymous cell lines may be deposited at the end of the research in a European or International cell-line bank so that they could be available to other qualified researchers to increase the possibility of future important discoveries. Such researchers would generally be academic researchers at other Universities, but could possibly include those working for companies.

How long will the study take and what will happen to the results of the research study?

The study is currently funded until 2017. Gene sequencing of an already identified gene(s), may identify the cause your condition in 6-12 months, however, it may take much longer to identify the responsible gene, and we plan to continue working on your sample until we do so. The results from the study will be published in scientific medical journals during the study and after its completion.

Who is funding the research?

The Medical Research Council and European Research Council are funding this research.

Contacts for Further Information

In this leaflet we have tried to answer any questions you may have about the project. If you have more questions, please ask your clinical geneticist or specialist for further explanation. If you still have queries after speaking with them, please contact:

Dr Andrew Jackson
MRC Programme Leader and Hon. Consultant Clinical Geneticist
MRC Human Genetics Unit,
Institute of Genetics and Molecular Medicine at the University of Edinburgh
Western General Hospital
Edinburgh EH4 2XU
Tel: 0131 332 2471

If you have any concerns or complaints arising from this research study please contact:
Stephen Lissaman, IGMM Business Manager, MRC Human Genetics Unit, IGMM at the University of Edinburgh, Edinburgh, EH4 2XU.

DNA and Blood Sample Sending Instructions

Blood samples

Please send 5-10ml EDTA blood sample from the affected child and parents. For small children please send 5ml, or no more than 1ml/kg body weight. DNA samples (or blood) from unaffected siblings are also appreciated where available.

Send samples at room temperature, ideally to arrive within 48 hours. So that we can receive and process samples during weekdays, we would prefer samples to be collected and shipped as early in the week as possible (i.e. Monday/Tuesday).

DNA samples

please send 5-10ug DNA from affected child and parents.

Please send to:

Andrea Robertson/Louise Bicknell
Andrew Jackson Lab
MRC Human Genetics Unit
MRC IGMM
University of Edinburgh
Crewe Road
Edinburgh
EH4 2XU
UK
Tel: +44 (0) 131 332 2471

For blood samples please notify us of the expected arrival date, together with the tracking number - email:

louise.bicknell@igmm.ed.ac.uk, andrea.robertson@igmm.ed.ac.uk

Sending samples from abroad, please complete and enclose 5 copies of the commercial invoice form (also in the information pack) with the blood samples to ensure clearance through customs into the UK. Blood and skin samples should be shipped at room temperature. With longhaul flights, samples may be exposed to very low temperatures. Therefore, insulation by wrapping the blood sample tubes in tissue/paper, and if at all possible placing them in a polystyrene box, will ensure they are preserved as well as possible.

Samples should be packed in accordance with IATA regulations.

Infection Risk

Finally, for our lab workers, please ensure there are no risk factors in the family for blood-borne viral infections (ie. HIV/hepatitis B, C). We can not accept high risk samples.

Do please let us know if you need any further information or clarification - louise.bicknell@igmm.ed.ac.uk, andrew.jackson@igmm.ed.ac.uk,.

Skin Biopsy Sample Sending Instructions

Skin biopsies should be taken using standard aseptic technique, eg. using a 3mm punch biopsy. Prior to biopsy the site should be thoroughly washed with an antiseptic soap (eg chlorhexidine) and this washed off with PBS (or wiped with 70% ethanol, which is allowed to dry before the biopsy is taken). Iodine and Mercurochrome-like antiseptics (eg Betadine) should be avoided.

The skin biopsy sample should be placed in a sterile tube containing cell culture media or PBS. This should be shipped immediately to us at room temperature. We would prefer samples to be collected and shipped as early in the week as possible to ensure they arrive as quickly as possible. Ideally we would like to receive samples within 2-3 days. Please use a tracked-delivery method (ie courier) and notify us of the tracking number on sending the sample. Our FedEx number is: 5412 7866 4

Disposable biopsy punches and sterile sample containers with culture media can be provided if needed.

Please send to:

Andrea Robertson/Louise Bicknell
Andrew Jackson Lab
MRC Human Genetics Unit
MRC IGMM
University of Edinburgh
Crewe Road
Edinburgh
EH4 2XU
UK
Tel: +44 (0) 131 332 2471

Please email: louise.bicknell@igmm.ed.ac.uk and andrea.robertson@igmm.ed.ac.uk, with the expected arrival date and tracking number.

Sending samples from abroad, please complete and enclose 5 copies of the commercial invoice form (also in the information pack) with the skin samples to ensure clearance through customs into the UK. Skin samples should be shipped at room temperature. With longhaul flights, samples may be exposed to very low temperatures. Therefore, insulation by wrapping the sample tubes in tissue/paper, and if at all possible placing them in a polystyrene box, will ensure they are preserved as well as possible. Samples should be packed in accordance with IATA regulations.

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INSTITUTE OF GENETICS
& MOLECULAR MEDICINE

Commercial Invoice

From:

To:

Sean O'Neil / Dr Andrew Jackson
MRC Human Genetics Unit
MRC Institute of Genetics and Molecular Medicine
University of Edinburgh
Western General Hospital
Crewe Road
Edinburgh
EH4 2XU

AWB # -

Tel: +44 (0) 131 332 2471

VAT No: 592950700

The Shipment contains:

Human Blood Samples- for medical research purposes only.

The sample is being supplied free of charge with no commercial transaction involved to be used for medical research and laboratory use only.

Value for custom purposes only £1.00

I can confirm –

1. That this material is not known or suspected to contain an etiological agent, host, or vector of human disease.
2. The material is non-hazardous, non-contagious and non-toxic.
3. The material does not come from a facility where work with exotic viruses affecting livestock and avian species is conducted.
4. The material is not recombinant.
5. The contents are for research purposes only.
6. Being supplied free of charge with no commercial transaction involved for medical research purposes only.

I hereby certify that the contents of this consignment are fully and accurately described above by the proper shipping name and are classified, packed, marked and labelled, and in proper condition for carriage by air according to applicable national regulations and IATA regulations.

Certified true and correct,



MRC Human Genetics Unit
MRC IGMM, University of Edinburgh,
Western General Hospital, Crewe Road,
Edinburgh EH4 2XU United Kingdom
T: +44 (0)131 332 2471 F: +44 (0)131 467 8456
E: enquiries@igmm.ac.uk
www.igmm.ac.uk www.hgu.mrc.ac.uk

The University of Edinburgh is a charitable body, registered in Scotland, with registration number SC005536

Height and Head circumference charts
Primary Microcephaly and Primordial Dwarfism
research projects

Research Use Only

Derived from British Birth Cohort data, using LMSgrowth and
With thanks to Prof Tim Cole and Huiqi Pan for their help.

These charts have not been extensively validated, and so to be used at the user's
own risk. Please let me know if there any improvements I can make.

Andrew Jackson

November 2009

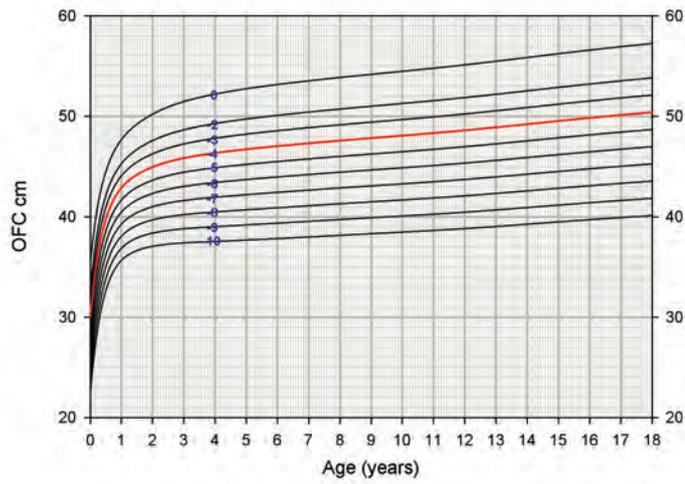
Male HC- standard deviations below mean



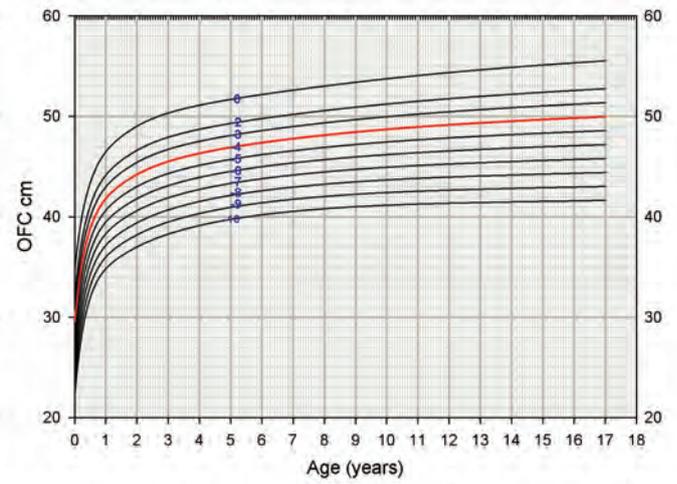
Female HC- standard deviations below mean



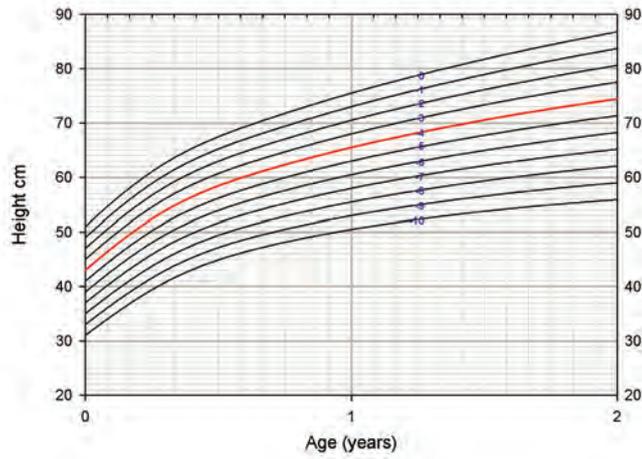
Male HC- standard deviations below mean



Female HC- standard deviations below mean



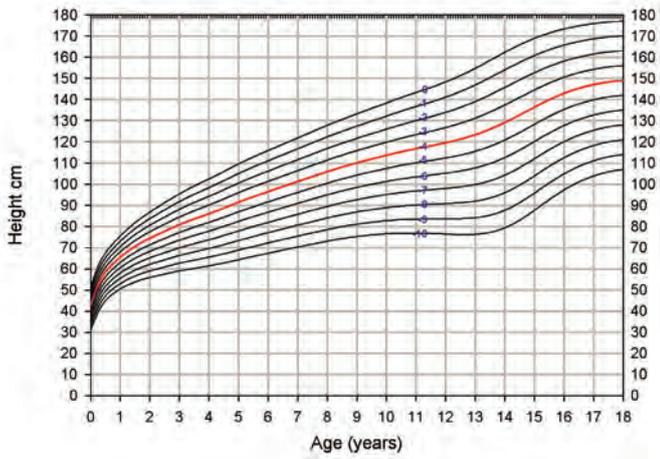
Male height - standard deviations below mean



Female height - standard deviations below mean



Male height - standard deviations below mean



Female height - standard deviations below mean

