



Uniparental Disomy (UPD)

Service Description

1 Background

UPD is defined as the inheritance of both homologues of a pair of chromosomes from only one parent. The presence of both homologues is termed heterodisomy while the presence of two copies of one homologue is termed isodisomy. A mixture of both types is possible. UPD may arise through the following mechanisms:

- Chromosome loss in trisomy (trisomic rescue) to generate a disomic foetus. This is the most common mechanism for UPD
- Gamete complementation in which both gametes are coincidentally abnormal, one disomic and the other nullisomic, where one parent has contributed both members of a homologous pair to the zygote and the other parent has contributed none.
- Duplication in monosomy in which one chromosome from a normal gamete from one parent has nothing to pair with from a nullisomic gamete from the other parent - monosomic rescue describes duplication of the chromosome in the foetus and restoration of euploidy (complete set of chromosomes)
- Post fertilisation error in which there is mitotic loss of 1 homologue of a chromosome pair and reduplication of the remaining one

UPD does not necessarily involve a whole chromosome; segmental UPD occurs due to somatic recombination between parental chromosomes before one of the events above.

The phenotypic consequences of UPD for several chromosomes are still unknown or poorly understood. UPD for some chromosomes e.g. chromosomes 13, 21, 22, 16, seems to have no effect or no constant effect on phenotype. Placental/foetal mosaicism is usually due to trisomy rescue and can cause severe growth retardation and possible developmental delay. UPD can cause reduction to homozygosity of autosomal recessively inherited mutations e.g. CF in UPD 7. However, most diseases associated with UPD are due to loss of the active homologue of an imprinted gene e.g. Prader Willi and Angelman syndromes, Beckwith Wiedemann syndrome. UPD in many cases is correlated with advanced maternal age (35 years and over), evidence that this is the result of meiotic non-disjunction.

Referrals are usually as a result of cytogenetic findings in a patient e.g. chromosomal missegregations including confined placental mosaicism (CPM) and apparently balanced Robertsonian translocations or where unexpected homozygosity for a recessive allele is found. Referrals are usually made by a clinical geneticist.

2 Standard service

A Essential referral information

In addition to supplying standard patient identification and referral information (see Section I below), the following should be clearly indicated:

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Revision Number: 4	Page 1 of 3	



National Centre for Medical Genetics

Dublin, Ireland

Division of Molecular Genetics

- Patient's symptoms
- Any family history, including names / dobs relationship, and genetic test results if available.
- Copy of cytogenetic report where relevant

It is the responsibility of the referring clinician to ensure consent has been obtained for testing and storage.

B Samples required

Blood (3-5ml) in EDTA from the patient and both parents is required. Sample identification policy is detailed at (see Section I below).

Blood specimens must be appropriately packaged (see Section I), and preferably sent by courier to arrive as soon as possible. Do not freeze prior or during postage.

Please note that extracted DNA is stored from patient's samples at the National Centre for Medical Genetics, and kept indefinitely unless a written request for its disposal is received from the patient or their parent/guardian.

C Restrictions on testing

Testing would not normally be considered for asymptomatic children under age 16. A referral to a clinical geneticist may be suggested prior to testing.

D Tests offered

Diagnostic tests are performed for patients where clinical symptoms and / or cytogenetic findings indicate the possibility of UPD. Analysis of polymorphic DNA markers distributed along the length of the chromosome under investigation is performed on DNA extracted from the proband and both parents.

Prenatal testing must be arranged in advance with the laboratory, through a Clinical Genetics department if possible.

E Diagnostic Sensitivity of tests

The sensitivity of such analysis is dependent on factors which are unique to each family assessed. As each polymorphic marker only tests a single point on the chromosome, it is never possible to exclude the presence of UPD at other points along the chromosome.

F Interpretation:

Following laboratory analysis, a report is prepared indicating the presence or absence of uniparental disomy and an interpretation of the result. Results are given in the form of a written interpretative report to the referring clinician.

G Target reporting times:

As reporting times are constantly evolving, please refer to www.genetics.ie/molecular, or contact the molecular genetics laboratory, to receive up-to-date information on anticipated reporting times for your referral. The following are current target reporting times for each category of test offered (information correct as of 16/12/09):

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Revision Number: 4	Page 2 of 3	



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- Urgent samples (newborns and PNDs): 2 weeks.
 - UPD: 3 months.
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- Please contact the laboratory if you have not received a report within a week of your patient being due back in clinic.
 - Please note it is our policy not to issue verbal results.
 - Request for copies of reports on the day that your patient is in clinic cannot normally be accommodated. We usually require 24 hours notice in which to fax a copy of a report.

H Further tests

Samples may be sent to an external lab (Karin Buiting, Essen) for further analysis of the 14q32 imprinted region.

I Web Links to Related Documents

Standard referral information/NCMG request form
Sample/Patient identification policy
Packaging of specimens for transport

http://www.genetics.ie/pir/2006_NCMG_Referral_Form.pdf
<http://www.genetics.ie/pir/SampleIdentificationPolicyWeb.pdf>
http://www.genetics.ie/pir/sending_samples.pdf

Please note that hard copies of the above documents may be requested from:

Division of Molecular Genetics, National Centre for Medical Genetics, Our Lady's Children's Hospital, Crumlin, Dublin 12. Tel: 01 4096733; Fax: 01 4096971

The NCMG Molecular Genetics laboratory participates in external QA schemes run by the UK NEQAS for Molecular Genetics, the European Molecular Genetics Quality Network (EMQN), and the Cystic Fibrosis European Network. Results of assessments are available for inspection upon request.

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Page 3 of 3