



## Russell Silver (RSS) UPD7

## Service Description

### 1 Background

Russell Silver Syndrome (RSS) is a malformation syndrome characterised by pre- and post-natal growth retardation. Genetic alterations can be identified in approximately 50% of RSS patients: 7–10% carry a maternal uniparental disomy of chromosome 7 [mUPD(7)] that is, the patient has inherited both copies of chromosome 7 from the mother and none from the father, a further 38–63% show a hypomethylation of the H19/IGF2 DMR mapping to chromosome 11p15. If present, mUPD(7) contributes to diagnosis and indicates a low recurrence risk. Specific clinical features of RSS include; pre and post natal growth retardation, cerebral haemorrhage, feeding difficulties (at 16 months) triangular face, downturned mouth, micrognathia (unusually small jaw), broad high forehead, pointed chin, low prominent dysplastic ears, clinodactyly (inward bending) of little fingers and toes and mild psychomotor developmental delay. There is some evidence to suggest that mUPD(7) patients are less likely to have the triangular face, downturned mouth and micrognathia. 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:

- Patient's symptoms
- Any family history, including names / dobs relationship, and genetic test results if available.

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. If paternal sample not available, testing can proceed with the maternal sample.

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 and where the patient has not been seen by a clinical geneticist. Referrals are only accepted from Clinical Geneticists.



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**Division of Molecular Genetics**

***D Tests offered***

Diagnostic tests are performed for patients where clinical symptoms are suggestive of RSS and where the patient has been seen by a clinical geneticist. Microsatellite analysis of markers distributed along the length of chromosome 7 is performed on DNA extracted from both parents and the proband.

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:***

Results are given in the form of a written interpretative report to the referring clinician. Following laboratory analysis, a report is prepared indicating the presence or absence of maternal uniparental disomy of chromosome 7 [mUPD(7)] and an interpretation of the result. Absence of mUPD(7) neither supports nor refutes a diagnosis of Russell Silver Syndrome (RSS), as less than 10% of sporadic RSS result from mUPD of chromosome 7. The analysis does not exclude the possibility of segmental mUPD(7).

***G Target reporting times:***

As reporting times are constantly evolving, please refer to [www.genetics.ie/molecular](http://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):

- Urgent samples (newborns and PNDs): 2 weeks.
  - RSS - UPD7: 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***

If a clinical diagnosis of Russell Silver syndrome is still considered, DNA samples can be sent to an external laboratory (M. Mannens, Amsterdam) for High-resolution melting (HRM) analysis to determine methylation of the H19 gene. Please note if samples are to be sent to AMC the lab requires their questionnaire to be completed and please ensure the H19 methylation box only is ticked.



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**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/2006_NCMG_Referral_Form.pdf)  
<http://www.genetics.ie/pir/SampleIdentificationPolicyWeb.pdf>  
[http://www.genetics.ie/pir/sending\\_samples.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.*