

East Midlands Regional Molecular Genetics Laboratory

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Service information: Angelman / Prader-Willi syndromes (AS/PWS)

Gene/Locus: 15q11-13

OMIM: #105830(AS) / #176270(PWS)

Referrals: Clinical Geneticists, Paediatricians, Other Relevant Specialties

Testing: Diagnostic testing offered in clinically affected patients

Target Reporting Times:

- Diagnostic 28 calendar days
- Diagnostic testing in neonates 14 calendar days
- Uniparental Disomy (UPD)15 28 calendar days (requires parental DNA)
- Urgent testing* 3 calendar days

***Please contact the laboratory for urgent testing, e.g. prenatal diagnosis**

Test Details:

- **Methylation and copy number analysis of the *SNRPN* gene region**, using methylation-specific multiplex ligation-dependent probe amplification (MS-MLPA) (Me028 kit MRC Holland) to detect 15q11-13 deletions and abnormal imprinting.
- PCR analysis of **microsatellite markers** to distinguish between UPD and imprinting defects in cases with an abnormal imprinting pattern (this testing requires parental samples).

Service Details:

Diagnostic testing using MS-MLPA will detect pathological deletions and the abnormal imprinting associated with deletions, UPD and imprinting defects of the 15q11-q13 region causing Angelman and Prader-Willi syndromes. This testing will detect more than 99% of individuals with PWS and ~75-85% of individuals with AS. Patients suspected of having AS with normal methylation patterns can be tested for *UBE3A* mutations at another centre, but the cost of this testing is the responsibility of the referring clinician.

Sample Requirements:

- **EDTA** blood sample (1-4 ml), labelled with patient's **full name**, **date of birth** and **NHS number**, or genomic DNA (50µl at ≥100ng/µl)
- Samples should be accompanied by a **fully** completed referral card which should include the patient's full name, date of birth and NHS number
- Please also include details of the test, relevant clinical details and full details of the referring clinician and centre
- Maternal and paternal samples are required in cases of prenatal diagnosis to exclude maternal cell contamination and for informativeness testing in microsatellite analysis.

Consent:

Please note that in submitting a sample, it is the responsibility of the clinician to ensure that consent has been taken i) for testing, ii) for storage, and iii) for the use of this sample and the information generated to be shared with the patient's relatives and their health professionals. Following testing, a sample of the patient's DNA may also be used anonymously to validate new tests and for internal quality control purposes.