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Service information: Rett Syndrome (RTT)

Gene/Locus: *MECP2* (Xq28) **OMIM:** #312750; *300005 (*MECP2* gene)

Referrals: Clinical Geneticists, Paediatricians, Neurologists, Other Relevant Specialties
Testing: Diagnostic testing offered in clinically affected patients (Rett syndrome or *MECP2* duplication syndrome). Carrier testing in females with a family history of RTT/*MECP2* mutation.
Target Reporting Times:

• Diagnostic	40 working days	10 working days for MLPA only
• Carrier testing	10 working days	
• Urgent testing*	3 working days	Prenatal diagnosis/carrier testing in pregnant women

***Please contact the laboratory for urgent testing**

Test Details:

- **Mutation screening for *MECP2* mutations:** includes bidirectional Sanger sequencing of the coding region and the adjacent splice donor/acceptor sites of the *MECP2* gene and MLPA (multiplex ligation-dependent probe amplification) analysis to detect exonic deletions/duplications of the *MECP2* gene (MRC Holland P015 kit).
- **Testing for known mutations** in individuals with a family history of Rett syndrome/*MECP2* mutations, by Sanger sequencing or MLPA, as appropriate.

Service Details:

Bidirectional sequencing should detect 85-90% of mutations found in classic Rett syndrome (RTT) and 30-40% of mutations in atypical RTT (Fukuda et al Brain & Development 27 (2005) 211-217). Large *MECP2* deletions detected using MLPA can account for approximately 8% of classic RTT cases. However, deletions and duplications only account for 3% of mutations in atypical RTT (MECP2 Related disorders Gene Reviews). Mutation screening of the *CDKL5* gene can also be considered in patients with atypical RTT. This testing is available at another centre, however the funding for this testing will need to be provided by your department. It is estimated that the prevalence of MECP2 duplication syndrome is ~1% in males with moderate to severe learning disabilities (MECP2 Duplication Syndrome – Gene Reviews).

Sample Requirements:

- **EDTA** blood sample (1-4 ml), labelled with patient's **full name**, **date of birth** and **NHS number**, or genomic DNA (≥40μl at ≥50ng/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.
- A maternal sample is required in cases of prenatal diagnosis.

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.

We are here for you