Rett Syndrome: MECP2 Gene Sequencing

Test Code: SR
Turnaround time: 4 weeks
CPT Codes: 81302 x1

**Condition Description**

Rett syndrome is one of the leading causes of mental retardation and developmental regression in girls. Mutations in the MECP2 gene are found in approximately 80% of affected girls. Rett syndrome is inherited as an X-linked dominant trait. Though usually lethal in males, males meeting the clinical criteria for Rett syndrome have been identified. Some of them survive into adulthood with moderate to severe mental retardation, impaired language development, and movement disorders. MECP2 gene mutations may also present as atypical Rett syndrome. Patients previously diagnosed with autism, mild learning disability, clinically suspected but molecularly unconfirmed Angelman syndrome, or mental retardation with spasticity or tremor have been found to carry MECP2 mutations. The MECP2 gene consists of four exons. Over 200 mutations have been reported in this gene that account for approximately 80% of the causes. About 64% of all MECP2 mutations are caused by C>T transitions at eight CpG dinucleotides. The C-terminal domain is prone to larger multi-nucleotide deletions that account for ~15% of all mutations. Although these deletions tend to affect the same region, completely identical deletions are rare. These may not be detectable in females by sequencing. For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array (KT).

Click here for the GeneReviews summary on this condition.


**Genes**

MECP2

**Indications**

This test is indicated for:
- Confirmation of a clinical diagnosis of Rett syndrome.
- Carrier testing in adults with a family history of Rett syndrome.

**Methodology**

The 4 exons and flanking regions of MECP2 are amplified by PCR and sequenced in both the forward and reverse directions. Custom mutation detection is available for known familial mutations.

**Detection**

This assay will detect over 85% of sequence variants in the coding region and splice junctions. Mutations in the promoter region, some mutations in the introns, and other regulatory elements cannot be detected by this analysis. Large deletion and insertion mutations will not be detected by this assay. It is possible that some patients with a typical presentation may not carry a mutation detected by this analysis. This analysis may detect novel variants of unclear effect, which may require further studies.

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

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**Special Instructions**

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

**Related Tests**

- Custom Diagnostics Known Mutation Analysis (KM) is available to family members if mutations are identified by sequencing.
- Rett Syndrome Deletion/Duplication of MECP2 Gene (KT) is available separately for individuals where mutations are not identified by sequence analysis. Refer to the test requisition or contact the laboratory for more information.