Autosomal Dominant Mental Retardation 1: MBD5 Gene Sequencing

**Test Code:** SMBD5  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81479 x1

### Condition Description

Talkowski et al. (2011) mapped the MBD5 gene (2q23.1) to the critical region of the 2q23.1 deletion syndrome. Haploinsufficiency of the MBD5 gene causes Autosomal Dominant Mental Retardation syndrome type 1. Overall, of the features evaluated in individuals with 2q23.1 deletion syndrome and MBD5-specific deletions, approximately 84% were observed in both groups. Features associated with the haploinsufficiency of the MBD5 gene include intellectual disability, developmental delay, motor delay, significant speech impairment, craniofacial manifestations, seizures, constipation, and behavioral problems.

For patients with suspected Autosomal Dominant Mental Retardation syndrome type 1, deletion/duplication analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by deletion/duplication analysis, full gene sequencing is appropriate.

**References:**
- OMIM #611472: MBD5 gene  
- OMIM #156200: Autosomal Dominant Mental Retardation Syndrome Type 1  

### Genes

**MBD5**

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of Autosomal Dominant Mental Retardation syndrome type 1 in whom deletion/duplication analysis was negative.  
- Carrier testing in adults with a family history of Autosomal Dominant Mental Retardation syndrome type 1 in whom deletion/duplication analysis was negative.

### Methodology

PCR amplification of 10 exons contained in the MBD5 gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

### Detection

Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

Analytical Sensitivity: ~99%

### Specimen Requirements

Submit only 1 of the following specimen types

**Type: Saliva**

**Specimen Requirements:**  
Oragene™ Saliva Collection Kit  
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**  
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**  
EDTA (Purple Top)  
Infants and Young Children (2 years of age to 10 years old): 3-5 ml

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Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
8µg
Isolation using the Perkin Elmer™Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping:
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Special Instructions
Deletion/duplication analysis is required before sequence analysis. If deletion/duplication analysis is performed outside of EGL Genetics, please submit a copy of the deletion/duplication report with the test requisition.

Related Tests
- Deletion/duplication analysis of the MBD5 gene by CGH array is available and is required before sequence analysis.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.