Mowat-Wilson Syndrome: ZEB2 Gene Deletion/Duplication

Test Code: KS
Turnaround time: 2 weeks
CPT Codes: 81404 x1

Condition Description

Mowat-Wilson syndrome (MWS) is a clinically recognizable syndrome characterized by mental retardation, dysmorphic features, and multiple congenital anomalies. All patients are reported with moderate to severe mental retardation. Distinct facial features evolve with age. In young children the facial features are characterized by:

- prominent chin
- deep-set eyes
- broad nasal bridge
- open mouth with a full lower lip
- hypertelorism
- broad eyebrows
- posteriorly rotated ears with uplifted earlobes and a central depression

In older children, the chin becomes more prominent, the face elongates, and the nasal tip becomes more prominent extending below the ala nasi. Individuals often have a smiling expression. Nearly all individuals have microcephaly and seizures. Many individuals have hypotonia with delayed motor milestones. Speech may be absent or delayed. Hirschsprung disease is present in ~60% of patients. Other reported congenital anomalies include heart defects (~45%), genitourinary anomalies, and agenesis of the corpus callosum [1, 2].

De novo deletion or mutation of the ZEB2 gene located at 2q22 is associated with MWS. In a series of 47 patients with MWS and an identified mutation in ZEB2, 39 (83%) had a mutation identifiable by gene sequencing and 8 (17%) had a chromosome deletion or rearrangement detectable by FISH [3]. A small number of patients with a clinical diagnosis of MWS but no identified mutation in ZEB2 have been reported [2]. ZEB2 encodes the transcriptional corepressor, Smad Interacting Protein 1 (SIP1). It is suggested that haploinsufficiency of this gene leads to a gene dosage effect early in development. All reported cases are sporadic, and recurrence risk in families is thought to be low, however, parental mosaicism and germline mosaicism have been reported [4].

References:

Genes
ZEB2, ZFHX1B

Indications

This test is indicated for:

- Patients with clinical features indicative of MWS.

Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

Detection

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations.

Results of molecular analysis must be interpreted in the context of the patient’s clinical and/or biochemical phenotype.

Specimen Requirements

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood
Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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.

Special Instructions

Please submit copies of diagnostic biochemical test results along with the sample. Contact the laboratory if further information is needed. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of Emory Genetics Laboratory, please submit a copy of the sequencing report with the test requisition.

Related Tests

- Chromosome Analysis and Telomere FISH are indicated for patients with mental retardation or congenital anomalies.
- Sequence analysis of the ZEB2 gene is available and is required before deletion/duplication analysis.