Mowat-Wilson Syndrome: \textit{ZEB2} Gene Deletion/Duplication

\textbf{Test Code:} KS  
\textbf{Turnaround time:} 2 weeks  
\textbf{CPT Codes:} 81404 x1

\section*{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 hypertonia 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 \textit{ZEB2} gene located at 2q22 is associated with MWS. In a series of 47 patients with MWS and an identified mutation in \textit{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 \textit{ZEB2} have been reported [2]. \textit{ZEB2} encodes the transcriptional corepressor, Smad Interacting Protein 1 (\textit{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].

\section*{References}


\section*{Genes}

\textit{ZEB2}, \textit{ZFHX1B}

\section*{Indications}

This test is indicated for:

- Patients with clinical features indicative of MWS.

\section*{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.

\section*{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.

\section*{Specimen Requirements}

\textit{Submit only 1 of the following specimen types}

\textbf{Type:} DNA, Isolated

\textbf{Specimen Requirements:}  
Microtainer  
3µg  
Isolation using the Perkin Elmer\textsuperscript{TM}Chemagen\textsuperscript{TM} Chemagen\textsuperscript{TM} Automated Extraction method or Qiagen\textsuperscript{TM} Puregene kit for DNA extraction is
Specimen Collection and Shipping:
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

Type: Whole Blood (EDTA)

Specimen Requirements:
EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old): 3-5 ml
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 72 hours of collection. Do not freeze.

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 EGL Genetics, 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.