XLMR with Growth Hormone Deficiency: SOX3 Gene Sequencing

Test Code: YU  
Turnaround time: 4 weeks  
CPT Codes: 81479 x1

Condition Description

Duplicationsof and in the SOX3 gene (Xq26.3) havebeen associated with X-linked recessive mental retardation with growth hormonedeficiency. Mental retardation is mild to moderate and growth hormone levelscan vary between affected individuals even within families. Some affected maleshave died during the first day of life and exhibited postmortem findings ofhypoadrenalism, presumably due to hypopituitarism. Others have variablecombinations of hypothyroidism, delayed pubertal development, and short staturedue to growth hormone deficiency. All surviving affected individuals exhibitedmild to moderate mental retardation. Behavior in affected individuals has beenconsidered infantile.

Variablecraniofacial dysmorphism has also been reported, including hypertelorism,epicanthus, synophrys, broad nasal bridge, high-arched palate, long philtrum,cup helices, and coarse facies. In one study, male patients continued to grow untilwell into their twenties and reached a height ranging from 135 to 159 cm. BrainMRI in some affected males showed anterior pituitary hypoplasia, ectopicposterior pituitary, and absent infundibulum.

For patients with suspected XLMR with growth hormone deficiency, sequence analysis is recommended as the first step in mutation identification. Forpatients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

Click here for the OMIM summary on this condition.

Genes

SOX3

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of XLMR with growth hormone deficiency
- Carrier testing in adult females with a family history of XLMR with growth hormone deficiency

Methodology

PCR amplification of 1 exon contained in the SOX3 gene is performed on the patient's genomic DNA. Direct sequencing of amplification products isperformed in both forward and reverse directions, using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are thencompared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations ofunknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assaydoes 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 thepatient's 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 cannotprovide a blood sample.

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

Type: DNA, Isolated

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

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

Submit copies of diagnostic biochemical test results with the sample, if appropriate. 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

- Deletion/duplication analysis of the *SOX3* gene by CGH array is available for those individuals in whom sequence analysis is negative (YV).
- X-Linked Intellectual Disability panels are available for 30, 60, and 90+ genes.
- **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 to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.