XLMR with Growth Hormone Deficiency: SOX3 Gene Sequencing

**Condition Description**

Duplications of and in the SOX3 gene (Xq26.3) have been associated with X-linked recessive mental retardation with growth hormone deficiency. Mental retardation is mild to moderate and growth hormone levels can vary between affected individuals even within families. Some affected males have died during the first day of life and exhibited postmortem findings of hypoadrenalism, presumably due to hypopituitarism. Others have variable combinations of hypothyroidism, delayed pubertal development, and short stature due to growth hormone deficiency. All surviving affected individuals exhibited mild to moderate mental retardation. Behavior in affected individuals has been considered infantile.

Variable craniofacial 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 until well into their twenties and reached a height ranging from 135 to 159 cm. Brain MRI in some affected males showed anterior pituitary hypoplasia, ectopic posterior pituitary, and absent infundibulum.

For patients with suspected XLMR with growth hormone deficiency, sequence analysis is recommended as the first step in mutation identification. For patients 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 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 biochemical phenotype.

Analytical Sensitivity: ~99%

**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

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 Emory Genetics Laboratory, 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.