Lowe Syndrome: OCRL Gene Deletion/Duplication

Condition Description

Lowe syndrome (oculocerebrorenal syndrome) is an X-linked intellectual disability condition characterized by:

- hydrophthalmia
- dense congenital cataracts (found in all affected boys)
- infantile glaucoma (in approximately 50% of affected boys)
- intellectual disability
- vitamin D-resistant rickets
- amino aciduria
- reduced ammonia production by the kidney

Generalized hypotonia is noted at birth which may slowly improve by age. Affected males are delayed in their motor milestones. Approximately 95% of carrier females over age 15 years have characteristic findings in the lens of the eye when the lens is evaluated by slit-lamp examination. Most carrier females show numerous irregular, punctate, smooth, off-white (white to gray) opacities, present in the lens cortex, more in the anterior cortex than the posterior cortex and wrapping around the lens equator.

The OCRL gene (Xq26.1) encodes the protein inositol polyphosphate 5-phosphatase OCRL-1, an enzyme that is present in the trans-Golgi network and the endosomal compartment of a variety of cell types, including brain, skeletal muscle, heart and kidney. The loss of inositol polyphosphate 5-phosphatase OCRL-1 causes a defect in intracellular protein trafficking. Affected males have less than 10% normal activity of the enzyme in cultured skin fibroblasts. Peripheral blood samples cannot be used for enzyme analysis because the enzyme is not present in lymphocytes. Measurement of enzyme activity is not accurate for carrier detection in females because of a wide range of "normal" activity due to random X-chromosome inactivation.

New mutations have been reported in 32% of affected males with Lowe syndrome. A high risk of germline mosaicism (4.5%) has been identified. Sequence analysis of the OCRL gene identifies mutations in approximately 95% of males with Lowe syndrome. There are no common mutations. Although a few mutations have been noted in more than one affected individual, most mutations are unique to a family. Penetrance is complete, with similar phenotype in affected males within any given family. Lowe syndrome is an uncommon, pan ethnic disorder with the prevalence of only a few individuals per 100,000 births.

For patients with suspected Lowe syndrome, 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.

Please [click here](#) for the GeneReviews summary on this condition.

Genes

OCRL

Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of Lowe syndrome in an individual in whom sequencing analysis was negative.
- Carrier testing in adult females with a family history of Lowe syndrome in whom sequencing analysis was negative.

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 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

- Lyme Syndrome: OCRL Gene Sequencing (RO) is required before deletion/duplication analysis.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.