## Condition Description

Cohen syndrome, an autosomal recessive condition, is characterized by failure to thrive, obesity, hypotonia, and developmental delays. Common features of Cohen syndrome include retinal dystrophy that appears by mid-childhood, progressive high myopia, acquired microcephaly, non-progressive intellectual disability, global developmental delay, hypotonia, and joint hypermobility. Less common features include short stature, small or narrow hands and feet, truncal obesity (which appears during or after mid-childhood) friendly disposition, and non-cyclic granulocytopenia.

Mutations in the VPS13B gene (8q22-q23) (also known as COH1) cause Cohen syndrome and can be detected in 88% of individuals with typical clinical features of Cohen syndrome.

### References:
- GeneReviews
- OMIM #607817: VPS13B gene
- OMIM #216550: Cohen syndrome

## Genes

**VPS13B**

## Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of Cohen Syndrome.
- Carrier testing in adults with a family history of Cohen Syndrome.

## Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

## 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 clinical and/or 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.

### Related Tests

- Deletion/duplication analysis of the VPS13B gene by CGH array is available for those individuals in whom sequence analysis is negative.
- 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 only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.
- X-Linked Intellectual Disability panels are available for 30, 60, and 90+ genes.