**CHARGE Syndrome: CHD7 Gene Sequencing**

**Test Code:** UH  
**Turnaround time:** 4 weeks  
**CPT Codes:** 81407 x1

### Condition Description

CHARGE is a mnemonic that stands for coloboma, heart defects, choanal atresia, retarded growth and development, genital abnormalities, and ear anomalies. CHARGE syndrome is characterized by unilateral or bilateral coloboma of the iris, retina-choroid, and/or disc with or without microphthalmos (80%-90% of individuals); unilateral or bilateral choanal atresia or stenosis (50%-60%); cranial nerve dysfunction resulting in hyposomia or anosmia, unilateral or bilateral facial palsy (40%); impaired hearing, and/or swallowing problems (70%-90%); abnormal outer ears, ossicular malformations, Mondini defect of the cochlea, and absent or hypoplastic semicircular canals; cryptorchidism in males and hypogonadotropic hypogonadism in both males and females; developmental delay; cardiovascular malformations (75%-85%); growth deficiency (70%-80%); orofacial clefts (15%-20%); and tracheoesophageal fistula (15%-20%). Neonates with CHARGE syndrome often have multiple life-threatening medical conditions. Feeding difficulties are a major cause of morbidity in all age groups.

The diagnosis of CHARGE syndrome is based on clinical findings and temporal bone imaging. The CHD7 gene (8q12.1) is the only gene currently known to be associated with CHARGE syndrome; it encodes the chromodomain helicase DNA binding protein. Sequence analysis of the CHD7 coding region detects mutations in approximately 60%-65% of individuals with CHARGE syndrome. While one study suggested that individuals with CHARGE syndrome caused by a mutation in CHD7 were more likely to exhibit cardiovascular malformations, coloboma of the eye, and facial asymmetry, another study found no genotype-phenotype correlations in this cohort and noted that there were differences in clinical presentation even in sib pairs with identical mutations. Most individuals diagnosed with CHARGE syndrome represent simplex cases (i.e., a single occurrence in a family), although CHARGE syndrome caused by mutation of CHD7 can be inherited in an autosomal dominant manner. CHARGE syndrome has an estimated birth incidence of 1 in 10,120.

Mutations in CHD7 have also been shown to cause Kallmann syndrome-5, an allelic disorder with a less severe but overlapping phenotype. Patients with anosmia and/or hypogonadotrophic hypogonadism, therefore, should be screened for additional clinical features of CHARGE syndrome.

*Click here* for the GeneTests summary on this condition.

### Genes

**CHD7**

### Indications

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of CHARGE 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:** 60-65%. 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**

**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 cannot provide a blood sample.

**Specimen Collection and Shipping:**

- Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**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.

Type: DNA, Isolated

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

Specimen Collection and Shipping:
Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample 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.

Related Tests
- 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 individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.