CHARGE Syndrome: CHD7 Gene Deletion/Duplication

**Test Code:** DCHD7  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 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 hyposmia 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 hypogonadotrophic 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 10-12,000.

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 hypogonadotropic 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 diagnosis of CHARGE syndrome in individuals who have tested negative for sequence analysis

### 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

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

- Sequence analysis of the CHD7 gene is available and 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.