Congenital Central Hypoventilation Syndrome: Sequencing Panel

**Test Code:** MM244
**Turnaround time:** 6 weeks
**CPT Codes:** 81479 x1, 81404 x1, 81406 x1

### Condition Description

Congenital central hypoventilation syndrome (CCHS) is a disorder of respiratory and autonomic regulation typically presenting in newborns. It is characterized by hypoventilation with monotonous respiratory rates and shallow breathing. Some individuals present with altered development of neural crest-derived structures and/or tumors of neural crest origin (neuroblastoma, ganglioneuroma and ganglioneuroblastoma). A milder later-onset presentation of the syndrome can be seen in toddlers, children and adults.

**References:**
- Genereviews
- OMIM

### Genes

- ASCL1
- BDNF
- EDN3
- GDNF
- HOXA1
- PHOX2B
- RET

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of congenital central hypoventilation 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

**Next Generation Sequencing:** Clinical Sensitivity: Unknown. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element pathogenic variants 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**

**Type: Saliva**

**Specimen Requirements:**
Oragene™ Saliva Collection Kit
Orangene™ 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 24 hours of collection. Do not refrigerate or freeze.

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**Type:** DNA, Isolated

**Specimen Requirements:**
- Microtainer
- 8µg

Isolation using the Perkin Elmer™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.

**Related Tests**
- Pulmonary Disease: Comprehensive Sequencing Panel
- Bronchiectasis Panel
- Cystic Lung Disease Panel
- Pulmonary Fibrosis - Hermansky-Pudlak Syndrome Panel
- Pulmonary Arterial Hypertension Panel
- Congenital Central Hypoventilation Syndrome: Deletion/Duplication Panel