Lab Dept: Anatomic Pathology

Test Name: PHOX2B FULL GENE SEQUENCE

General Information

Lab Order Codes: P2B

Synonyms: Congenital Central Hypoventilation Syndrome (CCHS); NBLST2; NB Phox; PMX2B

CPT Codes: 81404 – Molecular Pathology, Level 5

Test Includes: Full gene sequence analysis performed by PCR-based double-stranded automated sequencing in the sense and antisense directions for exons 1-3 of the PHOX2B gene, plus at least 20 bases into the 5' and 3' ends of all the introns. Alanine repeat numbers for the commonly-expanded region in exon 3 are determined and reported in all cases

Logistics

Test Indications: Diagnostic confirmation in patients suspected to have congenital or late-onset CHS

Define level of suspicion for other autonomic dysfunction and tumors

Parental testing to rule out risk for late-onset symptoms

Individuals with Congenital Central Hypoventilation Syndrome (CCHS) generally have adequate ventilation when awake and hypoventilation with normal respiratory rates and shallow breathing during sleep.

Some affected children show symptoms of a generalized autonomic nervous system dysfunction including Hirschsprung Disease in 20%. Neural crest tumors are found in 6%. The condition is increasingly recognized in older children and adults.

In a few cases, CCHS is inherited in an autosomal dominant pattern, but the majority of cases are de novo. Approximately 92% of affected individuals have an in-frame expansion of a polyalanine repeat in exon 3 of the PHOX2B gene from the normal 20 repeats to 25-33 repeats. The remaining ~8% of patients have other mutations at the end of exon 2 or within exon 3.

Lab Testing Sections: Anatomic Pathology - Sendouts

Referred to: Ambry Genetics (Ambry Test: 1580)

Phone Numbers: MIN Lab: 612-813-6280

	STP Lab: 651-220-6550
Test Availability:	Daily, 24 hours
Turnaround Time:	2-4 weeks
Special Instructions:	Include Required Forms: Ambry Pulmonology Test Request Form and History. Please send completed form with the specimen or patient to the laboratory. Clearly label each specimen with patient name, DOB, and collection date. All Requisition and Consent form requirements must be met prior to processing. Incomplete forms will result in the delay of sample processing.

Specimen

Specimen Type:	Whole blood
Container:	Lavender top (EDTA) top tube Alternate ACD yellow-top tube
Draw Volume:	3-5 mL (Minimum 2 mL) EDTA whole blood
Processed Volume:	Same as Draw Volume
Collection:	Routine Venipuncture
Special Processing:	Lab Staff: Do Not centrifuge. Store specimen at room temperature or refrigerate. Ship at room temperature. 2 Day delivery preferred. Protect from freezing. Note: Stable for 7 days refrigerated. Stability may be affected if patient samples are stored at room temperature for more than 3 days. (Please contact Ambry if your sample is more than 7 days old)
Patient Preparation:	None
Sample Rejection:	Mislabeled or unlabeled specimens; incorrect preservative; incorrect storage

Interpretive

Reference Range:	No mutations found.
Critical Values:	N/A
Limitations:	Approximately 99% of PHOX2B mutations are detectable by this test. It is recommended that patients wait at least 2 weeks after a packed cell or platelet transfusion, and at least 4 weeks after a whole blood transfusion

procedure prior to blood draw for testing at Ambry Genetics. Testing quality may be affected if patients have received chemotherapy within the last 120 days. For patients who have had a bone marrow transplant, please send cultured fibroblasts.

Methodology: PHOX2B full gene sequence analysis performed by PCR

References:

Berry-Kravis EM et al. Congenital central hypoventilation syndrome: PHOX2B mutations and phenotype. *Am J Respir Crit Care Med*. 2006;174:1139-1144. [PMID:16888290]

Trochet D et al. Molecular consequences of PHOX2B missense, frameshift and Alanine expansion mutations leading to autonomic dysfunction. *Hum Mol Genet*.2005;14:3697-3708. [PMID: 162492188]

Trochet D et al. PHOX2B genotype allows for prediction of tumor risk in congenital central hypoventilation syndrome. *Am J Hum Genet*. 2005;76;421-426. [PMID: 15657873]

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