Rush University Medical Center
Section of Genetics
1750 W. Harrison St. Rm. 1501 Jelke
Chicago, IL 60612
Phone 312-942-6298
CLIA 14D0646609

RUSH UNIVERSITY MEDICAL CENTER

CONGENITAL CENTRAL HYPOVENTILATION SYNDROME (CCHS)*

***PHOX2B* Gene Screening Test:** The *PHOX2B* Screening Test is a PCR-based, fragment-analysis assay which directly amplifies and sizes the second polyalanine-coding triplet repeat sequence in exon 3 of the *PHOX2B* gene. The test is highly sensitive and specific for detection of the triplet repeat polyalanine expansion mutations found in the majority (~92%) of individuals with CCHS[1]. The remaining individuals with CCHS will have either *PHOX2B* coding sequence mutations (~8%), which can be identified by follow-up sequencing, or *PHOX2B* whole or partial gene deletions (<1%), which can be identified by follow-up MLPA testing[2].

Inheritance and Mosaicism: It should be noted that up to 25% of CCHS patients inherited their *PHOX2B* mutation from a parent who has mosaicism, which is a 'lesser dose' of the mutation and explains why the parents are not affected with the CCHS phenotype[1]. Because mosaic parents can pass the same *PHOX2B* mutation on to other children, it is necessary to test *all* parents of CCHS probands for mosaicism. The PCR assay *PHOX2B* Screening Test is the best available assay for identifying and quantifying mosaicism[3].

Testing Recommendations: The American Thoracic Society (ATS) Statement on CCHS[1] recommends a step-wise testing strategy. Children suspected to have CCHS should ideally be tested first by the *PHOX2B* Screening Test, then with follow-up sequencing and MLPA if no mutation is found[4]. All parents of children with identified polyalanine repeat expansion mutations should be screened by the *PHOX2B* Screening Test to determine mosaicism[1,3,4].
For further clarification, please contact Dr. Elizabeth Berry-Kravis at Elizabeth_M_Berry-Kravis@Rush.edu

Specimen Preparation: Three to 6 ml of blood in an EDTA-coated vacutainer are required. Call (312-942-6298), FAX (312-942-2857) or e-mail Kisha Johnson MS, CGC, or Dr. Paul Wong if less than 3 ml of blood are available. Send the blood at room temperature by overnight delivery service like Federal Express. Because of transportation issues, it is best *not* to obtain blood on Friday, Saturday or Sunday. If kept overnight, the blood should be refrigerated. **DO NOT FREEZE**. No refrigeration is needed for same day deliveries. A turnaround time of 1 to 2 weeks is anticipated. **A FULLY COMPLETED REQUISITION *MUST* ACCOMPANY EACH BLOOD SAMPLE**. Please include the requesting physician's complete address, e-mail address, and phone and fax numbers.
For queries on specimen preparation please contact: Kisha_D_Johnson@Rush.edu, or PWong@Rush.edu

Billing Information: Billing information must accompany the blood sample. The patient can pre-pay with a cashier's check or credit card or we can bill the referring institution. Pre-payment is required for all samples from outside the U.S. Rush University Medical Center (RUMC) will not bill third party payors (e.g. insurance, Medicare, Medicaid) for this testing. Payment is the responsibility of the submitting entity. **The cost of the *PHOX2B* Screening Test is USD $399.00**; CPT code is 81479. This pricing is effective as of March 1, 2013 and is subject to change without notice.
Please note: the cost of testing has been reduced to accommodate families with CCHS. More than half of all proceeds are applied directly to CCHS research. These funds have been invaluable to support much needed research into this gene and CCHS.

[1] Weese-Mayer et al. Am J Respir Crit Care Med. 2010. 181(6):626-644.
[2] Jennings et al. Pediatr Pulmonol. 2012. 47(2):153-161.
[3] Jennings et al. Diagn Mol Pathol. 2010. 19(4):224-231.
[4] Weese-Mayer et al. In: Primer on the Autonomic Nervous System (Robertson D, Biaggioni I, Burnstock G, Low PA, and Paton, JFR, editors), Academic Press, Oxford, UK. 2012. pp. 445-450.

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Request for Congenital Central Hypoventilation Syndrome (CCHS) *PHOX2B* Screening Test*

PLEASE THOROUGHLY COMPLETE THIS FORM TO AVOID DELAYING SAMPLE PROCESSING.

☐ **I am ordering the Congenital Central Hypoventilation Syndrome (CCHS) *PHOX2B* Screening Test***

Patient Information: ***If submitting samples from multiple family members, please attach a pedigree and complete one order form for each submitted sample.***

Last Name:_____ **First Name:**_____
DOB: _____, ___ **Year:** **Gender:** ☐**Female** ☐**Male**
Ethnicity: ☐**Caucasian** ☐**African American** ☐**Hispanic** ☐**Asian Pacific Islander**
☐**Native American** ☐**Unknown** ☐**Other**_____
Home phone number: _____ **Cell phone number:** _____
Address: _____
City: _____ **State:** _____ **Zip:**_____ **Country:** _____
Date of blood draw:_____ **Date blood sent:** _____
Reason for ordering test: _____

Diagnoses (check all that apply):

☐ **CCHS**	☐**Asleep ventilator needs**
☐ **Hirschsprung disease**	☐**Mechanical ventilation via tracheostomy**
☐ **Neuroblastoma**	☐ **BiPAP via mask ventilation**
☐ **Other neural crest tumor**	☐**Negative pressure ventilation**
☐ **Apparent life threatening events (ALTEs)**	☐**Diaphragmatic pacers**
☐ **Unresolved apnea of prematurity**	☐**Awake ventilator needs**
☐ **Unresolved apnea of infancy**	☐ **Mechanical ventilation via tracheostomy**
☐**Cardiac pacemaker**	☐ **Diaphragmatic pacers**
☐ **Esotropia** ☐**Exotropia** ☐**Fixed and dilated pupils**	☐ **Tracheostomy**
Age at diagnosis of alveolar hypoventilation: Years ____ Months ____ Days____	
Other pertinent information:	

***All test results will be reviewed by Drs. Weese-Mayer and Jennings (Lurie Children's Hospital, Northwestern University) and Dr. Berry-Kravis (RUMC). Additional information and medical records may be requested.**

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Physician Information: ***(results will be sent to physician)***

Last Name:_____ **First Name:**_____
Phone: _____ **Fax:** _____
Address: _____
City: _____ **State:** _____ **Zip:** _____ **Country:** _____
e-mail: _____

Billing Information: **RUMC will not bill third party payors (e.g. insurance, Medicare, Medicaid) for this testing. Payment is the responsibility of the submitting entity.**

Pre-payment by cashier's check or credit card is r*equired for all samples referred from outside of U.S.*

☐**Check enclosed (payable to Rush University Medical Center)**
☐**Credit Card** ☐**Visa** ☐**MasterCard** ☐**Discover**

Account #: _____ **Expiration date:** ___/___
MM/YY

Card Holder's Name: _____**Phone #:** _____

Signature: _____ **Date:** ___/___/____
MM/DD/YYYY

☐**Institutional Billing**

Contact Person/Title:_____
Name of Institution:_____
Section/Laboratory:_____
Phone: _____ **Fax:**_____
Address: _____
City:_____ **State:**_____ **Zip:**_____ **Country:**_____
e-mail:_____

Shipping Information:

Kisha Johnson
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Rush University Medical Center
1750 W. Harrison Street, Room 1501 Jelke
Chicago, IL 60612
Phone: (312) 942-6298 Fax: (312) 942-2857

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