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

CONGENITAL CENTRAL HYPOVENTILATION SYNDROME*

The Molecular Diagnostic Laboratory at Rush University Medical Center (RUMC) is pleased to offer a clinical DNA *PHOX2B* Screening Test for Congenital Central Hypoventilation Syndrome (CCHS) to physicians and medical institutions. The *PHOX2B* Screening Test is a PCR 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. This triplet repeat is expanded in the majority (about 90%) of individuals with CCHS. The remaining individuals with CCHS (10%) will have mutations that can be identified by follow-up sequencing of the coding regions of the *PHOX2B* gene.

It should be noted that 5-10% of CCHS patients inherited their *PHOX2B* mutation from a parent who has mosaicism or a 'lesser dose' of the mutation (which explains why the parents are not affected with the CCHS phenotype). 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 (and not sequencing) is the best available assay for identifying and quantifying mosaicism.

Therefore, children suspected to have CCHS should ideally be tested by the PCR assay *PHOX2B* Screening Test, with follow-up sequencing if no mutation is found. All parents of children with identified polyalanine expansion mutations should be screened by the PCR assay *PHOX2B* Screening Test to determine mosaicism. For further clarification of testing indications, please contact Dr. Elizabeth Berry-Kravis at Elizabeth_M_Berry-Kravis@rush.edu.

Three to 9 cc of blood in an EDTA vacutainer is required. Call the (312-942-6298), FAX (312-942-2857) or e-mail Nancy Becker or Dr. Paul Wong if less than 3cc of blood is 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. Please include the requesting physician's complete address, e-mail address and phone and fax numbers.

For queries, please use e-mail contact:

Nancy_R_Becker@rush.edu, pwong@rush.edu, or DWeese-Mayer@ChildrensMemorial.org

Diagnosis, clinical information and 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 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 codes are 83891, 83894, 83898, 83912. This pricing is effective as of July 1, 2008 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 previous proceeds were applied directly to CCHS research. CCHS is a very rare disease, and like all rare diseases, it is difficult to obtain funding from public sources since it is not considered a major public health issue. The funds previously generated from *PHOX2B* testing have been invaluable to support much needed research into this gene and CCHS.

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

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

PLEASE THOROUGHLY COMPLETE THIS FORM TO AVOID DELAYING THE PROCESSING OF THE SAMPLE.

❑ 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.***

Name of patient: _____
last *first*

Date of Birth: ___/___/____ **Gender:** ❑ **Male** ❑ **Female**
MM/DD/YYYY

Ethnicity: ❑**Caucasian** ❑**African American** ❑**Hispanic** ❑**Asian Pacific Islander** ❑**Native American** ❑**Other**_____

Home phone number: _____ **Cell phone number:** _____

Address: _____

City: _____ **State:** _____ **Zip:**_____ **Country:** _____

Date of Blood Draw: ___/___/____ **Date Blood sent:** ___/___/____
MM/DD/YYYY *MM/DD/YYYY*

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: _____	
Other pertinent information:	

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

Name: (last)_____ (first)_____
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:_____
Address: _____
City:_____ State:_____ Country:_____ Zip:_____
Phone: _____ FAX:_____
e-mail:_____

Shipping Information:

Nancy Becker
Section of Genetics
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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