BENIGN HEREDITARY CHOREA & CHOREOATHETOSIS, HYPOTHYROIDISM, AND NEONATAL RESPIRATORY DISTRESS

NKX2-1 (TITF1) GENE SEQUENCING & DOSAGE

Benign hereditary chorea (OMIM 118700) is an autosomal dominant disorder caused by mutations in the NKX2-1 gene (OMIM 600635). Benign hereditary chorea is characterized by delayed motor development and onset of chorea in childhood, usually before 5 years of age. Dysarthria and gait abnormalities may occur. In contrast with Huntington’s disease, dementia is absent, and there is little to no progression of the disease beyond the second decade of life.

Choreoathetosis, congenital hypothyroidism, and neonatal respiratory distress (OMIM 610978) is an allelic disorder, also known as brain-lung-thyroid syndrome. Inheritance is autosomal dominant. Symptoms are present at birth and may be followed by global developmental delay, hypotonia, ataxia, and dysarthria.

**Testing:** Testing is performed by sequencing the entire coding region of NKX2-1. This will detect point mutations, small deletions, and small insertions. If no heterozygous sites are detected, copy number analysis will be performed to detect a whole or partial gene deletion, since deletions of the entire NKX2-1 gene have been reported in affected individuals.

Some mutations, such as nonsense, splicing, and frameshift mutations, can be clearly identified as disease-causing. Certain missense mutations may be difficult to interpret, as there have been few pathogenic mutations described to date. Novel missense mutations will be compared to previously published mutations, and to available controls. Mutations may also be analyzed by determining the evolutionary conservation of the affected amino acid. Family studies may be helpful, and samples from family members may be requested.

NKX2-1 is the only gene known to be associated with these specific disorders. However, a negative test result does not rule out a genetic cause of early-onset chorea or congenital hypothyroidism. There are other genes associated with other types of movement disorders, as well as with other hypothyroid disorders.

**Turnaround time:** 10 – 14 days

**CPT codes and cost:**

<table>
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<th>Proband: 83891 (x1) 83900 (x1) 83904 (x9) 83909 (x1) 83912 (x1)</th>
<th>$ 550</th>
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<td>Known mutation: 83891 (x1) 83898 (x2) 83904 (x8) 83912 (x1)</td>
<td>$ 235</td>
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**BILLING:** We do not bill third party payers (insurance companies) for samples received from external sources. The person or institution (e.g., Clinical Lab; Send-out Lab; Physician Office) sending the sample is responsible for full payment of the invoices within 30 days of receipt of the invoice. If the patient is on Medical assistance, please contact the lab prior to sample submission. Direct patient billing will be accepted only when a valid credit card form is received with the patient sample.

**On-line Resources:**

**References:**


## Credit Card Billing Information

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<th>Credit Card:</th>
<th>Name of Card holder:</th>
<th>Credit Card Number:</th>
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<th>Expiration Date:</th>
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<tr>
<th>Card holder signature:</th>
<th>Authorized payment amount:</th>
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### For Direct Patient Billing

Prepayment for the testing services is required prior to beginning our testing. Please complete this form and include this paperwork with the shipment of the patient sample.

Billing questions can be addressed to:  
Denise Axsmith  
Senior Budget/Financial Analyst  
Nemours/A.I. duPONT Hospital for Children  
daxsmith@nemours.org  
Phone: 302.651.6802  
Fax: 302.651.6881
Facsimile Verification Form

Name of Facility receiving Fax: ____________________________________________________________

Name of Physician/Lab receiving Fax: _______________________________________________________

Street Address: _______________________________________________________________________

City____________________________ State: _____

Fax Number: ______________________ (to which lab results and/or patient information may be sent)

Phone Number: ______________________

By signing this Facsimile Verification Form, I validate the accuracy of the above information and assume responsibility for assuring that the Fax machine is in a location which will maintain confidentiality of all reports transmitted by the Molecular Diagnostics Laboratory of the Alfred I. duPont Hospital for Children, to the above fax number.

Authorized Contact Person: __________________________________________________________

Signature: ______________________________ Date: ______________

Title: _______________________________________________________________________________

In our continuing efforts to maintain patient confidentiality, the Molecular Diagnostics Laboratory of the Alfred I. duPont Hospital for Children requests you to verify the fax number only once from your medical practice or institution and to assure that all faxes regarding patient information are received in a secure location in accordance with HIPAA regulations.

Please complete this Facsimile Verification Form and fax back to 302.651.6795.
If you have any questions regarding this form please contact Susan Kirwin, Assistant Director of The Molecular Diagnostics Laboratory, at 302.651.6775.

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