PENDRED SYNDROME and DFNB4 AUTOSOMAL RECESSIVE DEAFNESS

SLC26A4 GENE SEQUENCING

Pendred syndrome (OMIM 274600) and DFNB4 (OMIM 600791) are autosomal recessive disorders caused by mutations in the SLC26A4 gene (OMIM 605646). Pendred syndrome is characterized by sensorineural hearing loss, temporal bone abnormalities, and development of euthyroid goiter in early adulthood. Hearing loss is typically bilateral and severe to profound with onset at birth or in early childhood. Temporal bone abnormalities include enlarged vestibular aqueduct (EVA) with or without cochlear hypoplasia. There is considerable variability of findings, even within the same family.

DFNB4 is characterized by nonsyndromic sensorineural hearing impairment and temporal bone abnormalities (typically EVA). Thyroid defects are not seen in DFNB4.

Testing:
Testing is performed by sequencing all exons and the surrounding intronic regions of the SLC26A4 gene. This assay will detect point mutations, small deletions, and small insertions. It will not detect a partial or whole gene deletion or duplication.

Molecular testing of the SLC26A4 gene should be considered for individuals with hearing loss and EVA. SLC26A4 mutations are identified in 80% to 90% of familial cases of Pendred syndrome, and in about 30% of cases with no family history. Mutations have been identified throughout the SLC26A4 gene and include point mutations, small insertions or deletions, and splice site mutations. Deletions of single and multiple exons have also been reported.

The detection of two pathogenic mutations in SLC26A4 is consistent with a diagnosis of Pendred syndrome or DFNB4. However, single heterozygous mutations have been identified in SLC26A4 in 20% to 30% of individuals who meet criteria for Pendred syndrome or DFNB4. It is hypothesized that a second unidentified mutation is present in SLC26A4 or in another gene. There is some evidence to suggest that individuals with one identified mutation in SLC26A4 are less likely to develop thyroid manifestations than individuals with two identified mutations.

Turnaround time: 10-14 business days

CPT codes and cost: 83891 (x1) 83900(x1) 83901(x4) 83904 (x38) 83912 (x1) $1500

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.
Online resources:

National Institute on Deafness and Other Communication Disorders:
Genetics of EVA - [http://www.nidcd.nih.gov/health/hearing-genetics.html](http://www.nidcd.nih.gov/health/hearing-genetics.html)

OMIM entries:

References:

Facsimile Verification Form

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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 Nemours/Alfred I. duPont Hospital for Children, to the above fax number.

Authorized Contact Person: _____________________________________________

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In our continuing efforts to maintain patient confidentiality, the Molecular Diagnostics Laboratory of the Nemours/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 302.651.6777.

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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

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