FAMILIAL ISOLATED HYPOPARATHYROIDISM

GCM2 GENE SEQUENCING

Familial isolated hypoparathyroidism (FIH; OMIM 146200) is characterized by hypocalcemia and hyperphosphatemia due to insufficient or abnormal parathyroid hormone activity, in the absence of syndromic features. FIH is heterogeneous with X-linked, autosomal dominant, and autosomal recessive inheritance patterns reported.

Clinical symptoms of FIH are variable and are predominantly due to hypocalcemia. Individuals may present with seizures in the neonatal period. Other acute symptoms include muscle spasms and tingling of the lips, tongue, fingers and toes. Chronically, hypocalcemia can be asymptomatic or cause mild neuromuscular irritability, calcification of the basal ganglia, extrapyramidal disorders, cataracts, alopecia, abnormal dentition, coarse brittle hair, mental retardation, or personality disorders.

Homoyzogous mutations in GCM2 (OMIM 603716) have been shown to cause autosomal recessive FIH in several families. Previously reported homozygous mutations include nonsense mutations in exon 2 of GCM2, affecting the DNA-binding domain of the GCM2 gene, as well as a large deletion affecting exons 1 through 4 of GCM2.

Heterozygous mutations in GCM2 have been identified in two families with autosomal dominant FIH. These mutations are thought to cause FIH by exerting a dominant-negative effect on the wild-type GCM2 protein and/or downstream targets of GCM2. Heterozygous mutations associated with autosomal dominant FIH have been reported in exon 5, affecting the second transactivation domain of the protein.

Testing: Testing is performed by sequencing the entire coding region of the GCM2 gene. This will detect point mutations, small deletions, and small insertions. It will not detect a partial or whole gene deletion or duplication.

Turnaround time: 10 - 14 business days

CPT code and cost:  
Full Gene Sequencing 81479 $ 500
Known mutation testing 81479 $ 200

BILLING: We do not bill third party payers (insurance companies) for samples received from external sources. The person or institution (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:

References:


Ding, C; Buckingham, B; Levine, M. Familial isolated hypoparathyroidism caused by a mutation in the gene for the transcription factor GCMB. J Clin Invest. 2001; 108(8):1215 -1220

Mannstadt M; Bertrand G; Muresan; Weryha, G; et al. Dominant-negative GCMB mutations cause an autosomal dominant form of hypoparathyroidism. J Clin Endocrinol Metab. 2008; 93(9):3568-3576

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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.

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Signature: ___________________________ Date: ______________________

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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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### Credit Card Billing Information

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<th>Patient Name:</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