FEINGOLD SYNDROME

MYCN and miR17HG GENE ANALYSIS

Feingold syndrome is an autosomal dominant disorder that includes Feingold syndrome 1 and Feingold syndrome 2. Feingold syndrome 1 (OMIM 164280) is caused by mutations in the MYCN gene (OMIM 164840), and Feingold syndrome 2 (OMIM 614326) is caused by a 13q31.3 deletion encompassing the MIR17HG gene (OMIM 609415).

Feingold syndrome 1 is characterized by microcephaly, short palpebral fissures, gastrointestinal atresia, and digital abnormalities (brachymesophalangy 2 and 5, thumb hypoplasia, and 2-3 or 4-5 toe syndactyly). Six individuals from three families who had skeletal abnormalities consistent with Feingold syndrome, but had no mutations in MYCN, were found to have deletions encompassing MIR17HG (de Pontual et al. Nat Gen 43:1026-30, 2011). None of the individuals with this deletion had gastrointestinal atresia. Since gastrointestinal atresia is not a completely penetrant finding in individuals with MYCN mutations, it is unclear if these six individuals represent true cases of Feingold syndrome or a distinct disorder.

MIR17HG is the host gene for the miR17-92 cluster, which encodes a polycistronic primary transcript that yields at least six mature microRNAs, or miRNAs. MicroRNAs are small regulatory RNAs that control gene expression at the level of translation by binding to messenger RNAs. Current data suggests that the deletion of the miR17-92 cluster is responsible for the key features observed in individuals with Feingold syndrome 2.

Testing: Testing is performed by sequencing exon 1, coding exons 2 and 3, and the surrounding intronic regions of the MYCN gene. This will detect point mutations, small deletions, and small insertions. Gene dosage by capillary electrophoresis will be performed (on mutation negative samples) to detect a whole or partial gene deletion, since deletions of the entire MYCN gene have been reported in affected individuals.

Gene deletion testing of the miR17-92 cluster region will be performed by capillary electrophoresis to determine copy number within the MIR17HG gene.

Sequence analysis of MYCN detects mutations in 65% of individuals with a clinical suspicion of Feingold syndrome. Deletion testing of MYCN detects another 10%. Deletion of MIR17HG accounts for additional cases of Feingold syndrome, but specific detection rate is unknown. MYCN and MIR17HG are the only genes known to be associated with Feingold syndrome. A negative test for both genes does not rule out a diagnosis of Feingold syndrome, since there may be other genes involved.

Turnaround time: 10-14 days
CPT codes and cost:

MYCN:  
- 83891 x 1  
- 83898 x 4  
- 83900 x 1  
- 83904 x 4  
- 83912 x 1

MIR17HG:  
- 83891 x 1  
- 83900 x 1  
- 83901 x 2  
- 83912 x 1

Cost:  
- $450  
- $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:
- Feingold syndrome 1 on OMIM - [http://omim.org/entry/164280](http://omim.org/entry/164280)
- MYCN gene on OMIM - [http://omim.org/entry/164840](http://omim.org/entry/164840)
- Feingold syndrome 2 on OMIM - [http://omim.org/entry/614326](http://omim.org/entry/614326)
- MIR17HG on OMIM - [http://omim.org/entry/609415](http://omim.org/entry/609415)
Facsimile Verification Form

Name of Facility receiving Fax: ____________________________________________

Name of Physician/Lab receiving Fax: ____________________________________________

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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: ____________________________

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the Alfred I. duPont Hospital for Children requests you to verify the fax number only once from your
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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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immediately by telephone, and return the original message to us at the above address via the U.S. Postal Service.
**Credit Card Billing Information**

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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