MYCN is a member of the Myc family of oncogenes which regulate cell proliferation and apoptosis. The MYCN protein, with a basic helix-loop-helix (bHLH) domain, plays an important role in the formation of tissues and organs during embryonic development. MYCN gene contains 2 coding exons and spans 6.44 kb genomic distance on chromosome 2p24.3. Mutations in the MYCN gene have been found to cause Feingold syndrome, an autosomal dominant disorder characterized by variable combinations of esophageal and duodenal atresias, microcephaly, learning disability, syndactyly, and cardiac defect. Amplification of this gene is associated with a variety of tumors, most notably neuroblastomas. MYCN mutations demonstrate autosomal dominant inheritance with a broad range of clinical severity both within and between families. Definitive genotype/phenotype correlations have not been described.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for MYCN mutations. Individuals are tested by DNA sequencing of the coding exons of the MYCN gene. We strongly recommend initial testing of a clearly affected individual, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent family members. Genetic counseling is recommended for all individuals.

REASONS FOR REFERRAL
Molecular confirmation of the diagnosis of Feingold syndrome, a developmental disorder characterized in part by congenital heart defects (CHDs).

METHODOLOGY
Genomic DNA is analyzed for MYCN mutations by DNA sequencing of the coding exons of the MYCN gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated region. Patient DNA is sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members are analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

SERVICE FEES

<table>
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<tr>
<th>Description</th>
<th>Direct and Institutional Billing</th>
<th>CPT Codes</th>
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<tbody>
<tr>
<td>Index Case (Male or Female)</td>
<td>$500 per sample</td>
<td>81404</td>
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<tr>
<td>Additional Family Members</td>
<td>$300 per sample; known familial mutation only</td>
<td>81403</td>
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SENSITIVITY
DNA Sequencing Analysis: Approximately 99 percent detection of mutations in the coding exon 2-3 of MYCN.

SPECIMEN REQUIREMENTS

Blood (preferred): EDTA (purple-top) tubes: Adult: 5 cc  Child: 5 cc  Infant: 2-3 cc
Tissue: Frozen (preferred), RNA later
Other Body Fluids or Formalin-fixed, Paraffin-embedded Tissue: Call to inquire