Marfan Syndrome (MS) is relatively common, with a prevalence of 1 in 5-10,000 individuals. The FBN1 gene codes for fibrillin-1, a structural component of microfibrils. Microfibrils provide mechanical stability and elastic properties to connective tissues. Mutations in the FBN1 gene can affect multiple organ systems with primary involvement of the skeletal, ocular and cardiovascular systems. The FBN1 gene contains 65 exons and is located at chromosome 15q21.

Up to 90% of individuals with a clinical diagnosis of MS have FBN1 mutations (1). FBN1 mutations are inherited in an autosomal dominant manner. Approximately 75% of individuals with MS have an affected parent, and 25% have a de novo mutation.

Five to 21% of individuals with a known or suspected diagnosis of MS who did not have mutations in FBN1 had mutations in TGFBR2 (2,3). Loeys-Dietz syndrome (LDS) has been associated with mutations in both TGFBR1 and TGFBR2. LDS is an autosomal dominant condition that has many vascular and skeletal features in common with MS. Craniofacial and cutaneous manifestations are also frequently present in individuals with LDS.

**Indication**

FBN1 testing is utilized to confirm a diagnosis of MS in patients with clinically evident disease. Genetic testing also allows for early identification and diagnosis of individuals at greatest risk prior to the expression of typical clinical manifestations and can be used for prenatal diagnosis. If a mutation is identified in an asymptomatic individual, regular and routine outpatient follow up is indicated. If clinically unaffected members of a family with an identified mutation for MS are found not carry that mutation, they can be definitely diagnosed as unaffected and reassured that neither they nor their children will be at higher risk compared to the general population to develop symptoms related to MS. A negative test result in an individual with a known familial mutation also eliminates the need for routine follow up.
Methodology:

All 65 exons of the FBN1 gene, as well as the exon/intron boundaries and a portion of untranslated regions of the gene are amplified by PCR. Genomic DNA sequences from both forward and reverse directions are obtained by automatic fluorescent detection using an ABI PRISM® 3730 DNA Analyzer. Sequence variants different from National Center for Biotechnology Information GenBank references are further evaluated for genetic significance. If a mutation is identified, a known familial mutation analysis will be available for additional family member.

Sensitivity & Accuracy:

Greater than 98.5% of the mutations in exon 1-65 of FBN1 are detectable by sequence based methods. Sequencing does not detect deletions or duplications. Mutations in FBN1 account for up to 90% of cases of Marfan syndrome.

References:


Specimen:

Peripheral blood in EDTA tube
Adult: 5-10mL
Child: 3-5mL
Infant: 1-3mL
For other specimen types, please contact Amy Shikany at 513-803-3317

Turnaround Time:

Full Mutation Analysis 4-6 weeks
Known Mutation Analysis 1-2 weeks

CPT Codes:

Full Gene Sequencing 81408
Additional Family Members 81403