Fibrillin-1 is an extracellular matrix glycoprotein protein that is the main component of the microfibrils. Fibrillin-1 is initially synthesized as profibrillin, which is cleaved near the carboxy-terminus to form the mature peptide. After maturation, fibrillin-1 forms homodimers. Fibrillin-1 is expressed in multiple connective tissues, where it provides force-bearing structural support, and it is encoded by the \textit{FBN1} gene, which is composed of 65 exons and is located at 15q21.1.

Multiple autosomal dominant mutations in \textit{FBN1} have been described for a wide spectrum of disease including complete and incomplete forms of Marfan syndrome, which is characterized by cardiovascular, skeletal, and/or ocular manifestations with possible involvement of other systems (pulmonary, dura, integument, and skin). \textit{FBN1} mutations have also been identified in patients with severe neonatal Marfan syndrome, isolated skeletal features of Marfan syndrome, autosomal dominant ectopia lentis, and aortic aneurysm. With the exception of severe neonatal Marfan syndrome, which is typically caused by mutations in exons 24-32 of the \textit{FBN1} gene, strong genotype/phenotype correlations have not been identified. In addition, \textit{FBN1} mutations have been noted to demonstrate broad variable expressivity.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for \textit{FBN1} mutations. Individuals will be tested by automatic fluorescent DNA sequencing of all 65 exons of the \textit{FBN1} gene. Genetic counseling is recommended for all individuals in order to identify additional at-risk family members and to discuss reproductive issues.

\begin{itemize}
    \item Molecular confirmation of the diagnosis of Marfan syndrome, severe neonatal Marfan syndrome, isolated skeletal features of Marfan syndrome, autosomal dominant ectopia lentis, or aortic aneurysm
\end{itemize}

\section*{METHODOLOGY}

Genomic DNA will be analyzed for \textit{FBN1} mutations by automatic fluorescent DNA sequencing of all 65 exons of the \textit{FBN1} gene, as well as the exon/intron junctions and a portion of the 5’ and 3’ untranslated regions. Patient DNA will be sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members will be analyzed only for the familial mutation(s) by automatic fluorescent DNA sequencing.

\section*{SERVICE FEES}

\begin{center}
\begin{tabular}{|l|c|c|}
\hline
\textbf{Index Case (Full Gene)} & \textit{Direct and Institutional Billing} & \textit{CPT Codes} \\
\hline
& $1650$ per sample & 83891, 83898x58, 83904x116, 83912 \\
\hline
\textbf{Index Case – Neonatal MFS} & \textit{Exons 24-33} & $750$ per sample \\
\hline
& & 83891, 83898x7, 83904x14, 83912 \\
\hline
\textbf{Additional Family Members} & & $200$ per sample; known familial mutation only \\
& & 83891, 83898, 83904x2, 83912 \\
\hline
\end{tabular}
\end{center}

\section*{SENSITIVITY}

DNA Sequencing Analysis: Approximately 98.4% detection of mutations in exons 1-65 of \textit{FBN1}

\section*{SPECIMEN REQUIREMENTS}

\begin{itemize}
    \item \textbf{Blood (preferred):} EDTA (purple-top) tubes: \textit{Adult:} 5 cc \textit{Child:} 5 cc \textit{Infant:} 2-3 cc
    \item \textbf{Tissue:} Frozen (preferred), RNA\textit{later}, Formalin-fixed, Paraffin embedded
    \item \textbf{Other Body Fluids:} Call to inquire
\end{itemize}