CAV3 Sequencing

The CAV3 gene encodes caveolin-3, a protein which forms caveolae and is expressed in cardiomyocytes and skeletal muscle (1). Caveolae are flask-shaped invaginations of the plasma membrane and function in membrane integrity, vesicular trafficking, and signal transduction (2). Traditionally, mutations in CAV3 genes have been linked to a group of muscle diseases, Caveolinopathies, with four distinct phenotypes: limb girdle muscular dystrophy-1C, rippling muscle disease, hyperCKemia, and distal myopathy (2). However, recent studies have shown mutations in CAV3 to cause cardiac disease in the absence of skeletal muscle findings. Cardiac ion channels have been localized to caveolae in cardiomyocytes, and although the exact mechanism has not been identified, CAV3 mutations have been shown to modify the kinetics of closely associated ion channels (1, 2). A loss of caveolin-3 in mice has been shown to cause hyperactivation of the p42/44 mitogen-activated protein kinase cascade that plays a role in cardiac hypertrophy (5, 6). Mutations have been identified in individuals with Long QT Syndrome, Sudden Infant Death Syndrome, and Familial Hypertrophic Cardiomyopathy (1, 3, 4, 5).

The CAV3 gene is mapped to chromosome 3p25 and contains two coding exons. The mutations in CAV3 that have caused traditional Caveolinopathies have been inherited in an autosomal dominant manner although rare autosomal recessive mutations have been described. The majority of these mutations are missense (2).

Indication

Molecular confirmation of a suspected Caveolinopathy. In the absence of skeletal muscle disease, can be considered in cases of LQTS, Sudden Infant Death Syndrome, or Hypertrophic Cardiomyopathy.
Methodology:
Both coding exons as well as the exon/intron boundaries and a portion of untranslated regions of the gene(s) 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 members.

Sensitivity & Accuracy:
Greater than 98.5% of the mutations in exons 1 and 2 of CAV3 are detectable by sequence based methods.

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 2-4 weeks
Known Mutation Analysis 1-2 weeks

CPT Codes:
Full Genome Sequencing 81404
Additional Family Members 81403