The DES gene encodes desmin, the main intermediate filament protein expressed in skeletal, cardiac, and smooth muscle, which forms a cytoskeletal network with additional proteins to provide maintenance of cellular integrity, force transmission, and mechanochemical signaling (1, 2, 3). Mutations in DES cause Desmin myopathy, part of the group of myofibrillar myopathies. Desmin myopathy is characterized by skeletal myopathy and cardiac abnormalities, which may occur in conjunction with each other or in isolation. The skeletal myopathy typically involves muscle weakness in the lower limbs which spreads proximally with slow progression and may include respiratory dysfunction (1). Dilated, restrictive, and hypertrophic cardiomyopathies have all been seen in association with DES mutations. Atrioventricular conduction abnormalities are also a common feature, as the cardiac conduction system is rich in desmin (1, 4). Genotype-phenotype correlations have been described with mutations in DES, and are dependent on the location of mutations in the three different domains of the gene (3).

Mutations in DES exhibit autosomal dominant and recessive inheritance. Cases with autosomal recessive inheritance may present with more severe forms of Desmin myopathy and present at earlier ages than seen with autosomal dominant cases (2). Fourteen percent of mutations occur de novo and cause disease with a wide range of variability (1, 2). DES is located at chromosome 2q35 and contains nine exons. The majority of mutations are missense (3).

**Indication**

DES sequencing is utilized to confirm a clinical diagnosis of Desmin myopathy. Due to the variability associated with this condition, Desmin myopathy may be considered in cases of isolated skeletal myopathy, cardiomyopathy, or atrioventricular conduction abnormality. We recommend testing the most clearly affected individual in the family whenever possible.
Methodology:

All 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 1-9 of DES are detectable by sequence based methods.

References:


Specimen:

Peripheral blood in EDTA tube
Adult: 3-5mL
Child: 3-5mL
Infant: 1-3mL
For other specimen types, please contact us at 513-636-4474

Turnaround Time:

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

CPT Codes:

Full Gene Sequencing 81405
Additional Family Members 81403