

Cardiovascular Diseases Genetic Testing Program

DES Sequencing

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.

Molecular Genetics Laboratory

Shipping Instructions

Please enclose a test requisition form with sample. All information must be complete before sample can be processed. Samples may be shipped at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship to:

Molecular Genetics Lab
Cincinnati Children's Hospital
3333 Burnet Ave. NRB 1042
Cincinnati, OH 45229

Phone: 513-636-4474
Fax: 513-636-4373

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:

1. Goldfarb, L.G., and Dalakas, M.C. (2009). Tragedy in a heartbeat: malfunctioning desmin causes skeletal and cardiac muscle disease. *The Journal of Clinical Investigation*. 119: 1806-1813.
2. Goldfarb, L.G., Vicart, P., Goebel, H.H., Dalakas, M.C. (2004). Desmin myopathy. *Brain*. 127: 723-734.
3. Van Spaendonck-Zwarts, K.Y., Van Hessem, L., Jongbloed, J., et al. (2010). Desmin-related myopathy: a review and meta-analysis. *Clinical Genetics*. no. doi: 10.1111/j.1399-0004.2010.01512.x.
4. Kostera-Pruszczyk, A., Pruszczyk, P., Kaminska, A., et al. (2008). Diversity of cardiomyopathy phenotypes caused by mutations in desmin. *International Journal of Cardiology*. 131: 146-147.

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