Cincinnati Children's Heart Institute

Heart Institute Diagnostic Lab
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NKX2.5 Sequencing

The *NKX2.5* gene is a homeodomain transcription factor important for cardiac, conduction system, and thyroid development. Mutations in *NXK2.5* cause isolated, nonsyndromic cardiovascular malformations occurring in an autosomal dominant inheritance pattern with reduced penetrance and variable clinical expressivity. Secundum atrial septal defects, ventricular septal defects, and tetralogy of Fallot are the most common cardiovascular malformations. Heterotaxy syndrome and double outlet right ventricle cardiovascular malformations also result from heterozygous *NKX2.5* mutations. Atrioventricular (AV) block is the classic conduction system disease associated with *NKX2.5* mutations, although other arrhythmias have also been described.

The *NKX2.5* gene contains 2 exons and is located at chromosome 5q34. *NKX2.5* mutations are the major cause of cardiovascular disease in families with autosomal dominant congenital heart disease with AV block. In cases of sporadic cardiovascular malformations, *NKX2.5* mutations account for up to 4% of secundum ASD and 4% of tetralogy of Fallot cases (1).

Indication

Molecular confirmation of non-syndromic cardiovascular disease including atrial septal defect with AV conduction defects, ventricular septal defects, tetralogy of Fallot, heterotaxy, and double outlet right ventricle.

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:

Cincinnati Children's
Hospital Medical Center
Attn: Heart Institute Diagnostic Lab
240 Albert Sabin Way,
Room S4.381
Cincinnati, OH 45229-3039

Methodology:

Both coding exons of the *NKX2.5* 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 reference are further evaluated for genetic significance. If a mutation is identified, known familial mutation analysis will be available for additional family members.

Sensitivity & Accuracy:

Greater than 99% of the mutations in exons 1-2 of *NKX2.5* are detectable by sequence based methods. Sequencing does not detect deletions or duplications.

References:

1. McElhinney DB, Geiger E, Blinder J, Benson DW, Goldmuntz E. *NKX2.5* mutations in patients with congenital heart disease. *Journal of the American College of Cardiology*. 2003;42:1650-1655.

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 Gene Sequencing	81479
Additional Family Members	81403