The NKX2.5 gene is a homeodomain transcription factor important for cardiac, conduction system, and thyroid development. Mutations in NKX2.5 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.
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.

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.


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

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

Full Gene Sequencing 81479
Additional Family Members 81403