Isolated Nonsyndromic Congenital Heart Disease: NKX2-5 Gene Sequencing

**Condition Description**

Mutations in the *NKX2-5* gene have been associated with atrioventricular (AV) conduction block, septal defects, conotruncal abnormalities (particularly Tetrology of Fallot), and AV valve formation defects. Mutations in *NKX2-5* have been observed in autosomal dominant pedigrees and isolated cases of congenital heart disease. Studies suggest that *NKX2-5* mutation may be a frequent cause (up to 4%) of sporadic and familial congenital heart defects.

*NKX2-5* mutation analysis is appropriate for patients with an atrioventricular conduction block or structural heart defects with or without a family history of congenital heart defects. Analysis includes sequencing the entire *NKX2-5* coding region (2 exons) and immediate exon/intron boundaries. Mutations in other regulatory regions and large deletions will not be detected by this assay. Variants of unknown clinical significance may be detected. Custom mutation detection is available for known familial mutations. For patients with mutations not identified by full gene sequencing, a separate deletion/duplication assay is available using a targeted CGH array KP.

**Genes**

*NKX2-5*

**Indications**

This test is indicated for:

- Confirmation of a clinical diagnosis of *NKX2-5*-related congenital heart disease.
- Carrier testing in adults with a family history of *NKX2-5*-related congenital heart disease.

**Methodology**

The 2 exons and flanking regions of *NKX2-5* are amplified by PCR and sequenced in both the forward and reverse directions. Custom mutation detection is available for known familial mutations.

**Detection**

Over 95% of mutations in the coding regions or splice sites will be detected by this assay. This assay will detect sequence variants in the coding region and splice junctions. Mutations in the promoter region, some mutations in the introns, and other regulatory elements cannot be detected by this analysis. Large deletion and insertion mutations will not be detected by this assay. It is possible that some patients with a typical presentation may not carry a mutation detected by this analysis. This analysis may detect novel variants of unclear effect, which may require further studies.

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample. Sequence analysis is required before deletion/duplication analysis by targeted
CGH array. If sequencing is performed outside EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.