Cincinnati Children's
Heart Institute

Heart Institute Diagnostic Lab
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TBX5 Sequencing

The *TBX5* gene is a transcription factor important for heart and limb development. Mutations in *TBX5* cause Holt-Oram syndrome, an autosomal dominant genetic condition. Holt-Oram syndrome is characterized by upper limb defects of the radial ray, congenital heart disease, and arrhythmias. There is significant variability in limb defects within and between families ranging from an abnormal carpal bone to phocomelia. Congenital heart disease is highly penetrant in individuals with Holt-Oram syndrome. Atrial septal defects and ventricular septal defects are the most common heart abnormality. Conduction system disease may include first-degree atrioventricular block or complete heart block with and without atrial fibrillation.

The *TBX5* gene contains 10 exons and is located at chromosome 12q24.1. Up to 70 percent of individuals meeting strict clinical diagnostic criteria of Holt-Oram syndrome have *TBX5* mutations (1). *TBX5* mutations are inherited in an autosomal dominant manner. Approximately 85 percent of individuals with Holt-Oram syndrome have a *de novo* mutation.

Indication

TBX5 testing is used for molecular confirmation of a diagnosis of Holt-Oram syndrome. We recommend testing the most clearly affected individual in the family whenever possible.

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:

All 8 coding exons of the *TBX5* 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 references 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 98.5% of the mutations in exon 3-10 of *TBX5* are detectable by sequence based methods. Sequencing does not detect deletions or duplications. Mutations in *TBX5* account for up to 70 percent of cases of Holt-Oram syndrome.

References:

1. McDermott DA, Bressan MC, He J, Lee JS, Aftimos S, Brueckner M, Gilbert F, Graham GE, Hannibal MC, Innis JW, Pierpont ME, Raas-Rothschild A, Shanske AL, Smith WE, Spencer RH, St John-Sutton MG, van Maldergem L, Waggoner DJ, Weber M, Basson CT. *TBX5* genetic testing validates strict clinical criteria for Holt-Oram syndrome. *Pediatric Research*. 2005;58:981-986.

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