Cincinnati Children's
Heart Institute

TBX1 – Velo-cardio-facial Syndrome (VCFS) or DiGeorge syndrome

22q11.2 deletion syndrome (also known as velo-cardio-facial syndrome and DiGeorge syndrome) is a well-known continuous gene syndrome that can be characterized by many abnormalities. Common features include: Congenital heart disease (75% of individuals), most commonly tetralogy of Fallot, interrupted aortic arch, ventricular septal defects, and truncus arteriosus; palatal abnormalities (69%), developmental delays (70-90%), immune deficiency (77%), hyopcalacemia (50%), feeding problems (30%), renal anomalies (37%), hearing loss, growth hormone deficiency, seizures, psychiatric illness, and skeletal anomalies.

Approximately 95% of cases of velo-cardio-facial syndrome are caused by a microdeletion of chromosome 22q11.2, which can be detected by fluorescence in situ hybridization (FISH) using most commonly the TUPLE1 probe, or through chromosome microarray technology. The typical 3Mb deletion includes approximately 30 genes. One of the typically deleted genes, *TBX1*, is thought to cause many of the phenotypic findings, especially congenital heart defects. In a small number of cases, velo-cardio-facial syndrome is caused by a mutation in the *TBX1* gene rather than a deletion.

The *TBX1* gene encodes a transcription factor that belongs to the T-box family. This transcription factor is expressed in early embryonic development, and is known to have an essential role in cardiac and pharyngeal development.

Indication

TBX1 gene testing is utilized to confirm a diagnosis of Velocardiofacial syndrome in patients with clinically evident disease. This test should only be done in individuals for whom there is a high clinical suspicion of velo-cardio-facial syndrome, when no chromosome deletion of 22q11.2 can be identified by FISH or microarray.

Heart Institute Diagnostic Lab
CAP#: 7518730
CLIA#: 36D2003208
Phone: (513) 803-1751
Fax: (513) 803-1748
Email: HeartDx@cchmc.org

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 10 coding exons of the *TBX1* gene, as well as the exon/intron boundaries and 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 GeneBank reference 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 2-9 of *TBX1* are detectable by sequence based methods. Sequencing does not detect large DNA rearrangements, deletions or low level mosaicism.

References:

1. Yagi, H., Y. Furutani, et al. (2003). "Role of *TBX1* in human del22q11.2 syndrome." *Lancet* 362(9393): 1366-1373.

2. Torres-Juan, L., J. Rosell, et al. (2007). "Mutations in TBX1 genocopy the 22q11.2 deletion and duplication syndromes: a new susceptibility factor for mental retardation." *European Journal of Human Genetics.* 15(6): 658-663.

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 4-6 weeks
Known Mutation Analysis 1-2 weeks

CPT Codes:

Index Case (Full Gene Sequencing)	81478
Additional Family Members	81403