TPM1-related Disorders: TPM1 Gene Deletion/Duplication

**Condition Description**

Pathogenic variants in the *TPM1* gene (15q22.2), inherited in an autosomal dominant manner, cause dilated cardiomyopathy and hypertrophic cardiomyopathy.

**Dilated Cardiomyopathy**

Hereditary dilated cardiomyopathy (DCM) may be inherited in an autosomal dominant, autosomal recessive, or X-linked manner, depending on the gene involved. DCM is characterized by left ventricular enlargement and reduced myocardial contraction force. Typically, DCM presents with one of three features: heart failure, thromboembolic disease, or arrhythmias and/or conduction system disease. Approximately 20-50% of idiopathic dilated cardiomyopathy (those cases not due to acquired causes) are thought to have a genetic cause.

**Hypertrophic Cardiomyopathy**

Hereditary hypertrophic cardiomyopathy (HCM) is characterized by left ventricular hypertrophy in the absence of a predisposing cardiac or cardiovascular condition. The manifestation of HCM is extremely variable, even within the same family, and can range from asymptomatic to progressive heart failure. Other features include syncope, presyncope, shortness of breath, chest pain, orthostasis, and palpitations. The onset of HCM is usually during adolescence or young adulthood; however, it can range from infancy to much later in adult life.

References:
- GeneReviews
- OMIM #191010: *TPM1* gene
- OMIM #611878: Dilated Cardiomyopathy 1Y
- OMIM #115196: Familial Hypertrophic Cardiomyopathy 3

**Genes**

*TPM1*

**Indications**

This test is indicated for:
- Confirmation of a clinical diagnosis of *TPM1*-related disorders in an individual in whom sequence analysis was negative.
- Carrier testing in adults with a family history of *TPM1*-related disorders in whom sequence analysis was negative.

**Methodology**

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

**Detection**

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic pathogenic variants. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

**Type: DNA, Isolated**

**Specimen Requirements:**
- Microtainer 3µg Isolation using the Perkin Elmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

**Specimen Collection and Shipping:**
- Refrigerate until time of shipment in 100 ng/µL in TE buffer. Ship sample at room temperature with overnight delivery.

**Type: Whole Blood (EDTA)**

**Specimen Requirements:**
EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

**Special Instructions**
Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**
- Sequence analysis of the *TPM1* gene is available and is required before deletion/duplication analysis.
- A cardiomyopathy panel and other single cardiac genes are available.
- Custom diagnostic mutation analysis (KM) is available to family members if mutations are identified by targeted mutation testing or sequencing analysis.
- Prenatal testing is available only for known familial mutations to individuals who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.