Arthrogryposis, Distal, Type 2B: \textit{TNNI2} Gene Deletion/Duplication

\textbf{Test Code: DTNNI}
\textbf{Turnaround time: 2 weeks}
\textbf{CPT Codes: 81228 x1}

\section*{Condition Description}

Distal arthrogryposis type 2B is an autosomal dominant congenital contracture syndrome. Characteristics include contractures primarily in the distal joints of the limb, a triangular face, downslanting palpebral fissures, small mouth, and high arched palate. Other common clinical features can include prominent nasolabial folds, attached earlobes, short stature, severe camptodactyly, ulnar deviation, and vertical talus and/or talipes equinovarus. Primary neurological defects and muscle abnormalities are absent.

Contractures tend to be most severe at birth and are non-progressive. While distal joints are primarily affected, more proximal joints may also be affected. The severity of the contractures can vary between the upper and lower limbs and between the left and right sides of the body. Growth, development, cognitive abilities, and life expectancy are in the normal range. Clinical presentation is highly variable both between and within families.

Approximately half of the reported cases of distal arthrogryposis type 2B are inherited, and half are sporadic. Gene mutations can be identified in about 50\% of individuals with a clinical diagnosis. Germline mosaicism has been reported. Three genes are currently known to be involved: \textit{TNNI2}, \textit{TNNI3}, and \textit{MYH3}. While diagnosis is based on clinical criteria, mutation analysis can help distinguish distal arthrogryposis type 2B from other arthrogryposis syndromes.

This testing is for mutations in the \textit{TNNI2} gene (11p15.5) only.

For patients with suspected distal arthrogryposis type 2B, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

\section*{References}

- OMIM #601680 \textit{Arthrogryposis, Distal, Type 2B}

\section*{Genes}

\textit{TNNI2}

\section*{Indications}

This test is indicated for:

- Confirmation of a clinical diagnosis of distal arthrogryposis type 2B in an individual in whom sequence analysis was negative.

\section*{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.

\section*{Detection}

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

\section*{Specimen Requirements}

\textit{Submit only 1 of the following specimen types}

\textbf{Type: Whole Blood (EDTA)}

\textbf{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

\textbf{Specimen Collection and Shipping:}
Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.
Type: DNA, Isolated

Specimen Requirements:
- Microtainer
- 3µg
- Isolation using the Perkin Elmer™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.

Special Instructions
- Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.
- 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 TNNI2 gene is available and is required before deletion/duplication analysis.
- 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 for known familial mutations only. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.