Arthrogryposis, Distal, Type 2B: 7NNI2 Gene Deletion/Duplication

Test Code: DTNNI
Turnaround time: 2 weeks
CPT Codes: 81228 x1

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, downsloping palpebral fissures, small mouth, and high arched palate. Other common clinical features can include prominent nasolabial folds, attached earlobes, mild cervical webbing, 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: TNNI2, TNNI3, and 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 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.

References:
- OMIM #601680 Arthrogryposis, Distal, Type 2B

Genes

TNNI2

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.

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. Please note that a "backbone" of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

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.

Specimen Requirements

Submit only 1 of the following specimen types
* Preferred specimen type: Whole Blood

Type: Whole Blood

Specimen Requirements:

In EDTA (purple top) or ACD (yellow 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, 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 Emory Genetics Laboratory, 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.