HOTLINE: Effective May 20, 2019

New Test **3001395** ***SHOX*-Related Disorders, Deletion/Duplication** **SHOX DD**

Patient History for *SHOX*-Related Disorders

Additional Technical Information

Methodology: Multiplex Ligation-dependent Probe Amplification
Performed: Varies
Reported: 12-14 days

Specimen Required: Collect: Lavender (EDTA), Pink (K_2EDTA), or Yellow (ACD).
Specimen Preparation: Transport 3 mL whole blood. (Min: 2 mL)
Storage/Transport Temperature: Refrigerated.
Stability (collection to initiation of testing): Ambient: 1 week; Refrigerated: 1 month; Frozen: 6 months

Reference Interval: By Report

Interpretive Data:
Background Information for *SHOX*-Related Disorders, Deletion/Duplication:
Characteristics of *SHOX*-related disorders (*SHOX* deficiency): Short stature, mesomelia, and abnormal alignment of the radius, ulna, and carpal bones at wrist (Madelung deformity). Variable expressivity results in some affected individuals with syndromic short stature and additional findings (eg, Leri-Weill dyschondrosteosis (LWD) or Langer mesomelic dysplasia (LMD)), while others have isolated short stature (ISS).
Prevalence of *SHOX* deficiency: 1 in 1,000
Inheritance: *SHOX* is located in pseudoautosomal region 1 (PAR1) on the X and Y chromosomes and escapes X inactivation. Thus, inheritance is pseudoautosomal dominant for ISS and LWD, and pseudoautosomal recessive for LMD.
Penetrance: High, with variability in expression.
Cause: One pathogenic variant (haploinsufficiency) of the *SHOX* gene causes ISS and LWD. Two pathogenic variants in *SHOX* (complete loss of *SHOX*) causes LMD.
Clinical Sensitivity: Approximately 80-90 percent of disease-causing *SHOX* variants are deletions.
Methodology: Multiplex Ligation-dependent Probe Amplification (MLPA) to detect large deletions/duplications in the *SHOX* gene and surrounding *SHOX* region, which includes upstream and downstream enhancer elements in the pseudoautosomal 1 region (PAR1).
Analytical Sensitivity and Specificity: Greater than 99 percent.
Limitations: Diagnostic errors can occur due to rare sequence variations. Deletion/duplication breakpoints are not determined. Contiguous gene syndromes, complex rearrangements, chromosome translocations, inversions or aneuploidy affecting the sex chromosomes are not detected by this assay; additional testing may be required in such cases. *SHOX* sequence variants, and deep intronic and promoter variants are not detected.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online at www.aruplab.com.

See Compliance Statement C: www.aruplab.com/CS

CPT Code(s): 81479

New York DOH approval pending. Call for status update.

HOTLINE NOTE: Refer to the Test Mix Addendum for interface build information.