
Lab Dept: Anatomic Pathology

Test Name: HOLT ORAM SYNDROME (TBX5) SEQUENCING

General Information

Lab Order Codes: TBX5 (Blood or Buccal Swab)

Synonyms: Heart band disease; HOS; Holt-Oram Syndrome; Atrioidigital hypoplasia; cardiac-limb syndrome; upper limb cardiovascular syndrome

CPT Codes: 81405 – Molecular Pathology, Level 6

Test Includes: Analysis is performed bi-directional sequencing of the coding regions and splice sites of the exons 2-9 of the TBX5 gene. Mutations found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method.

Logistics

Test Indications: Holt-Oram syndrome is a malformation syndrome characterized by upper limb abnormalities and heart defects. Affected individuals may present in infancy with obvious limb malformations and/or signs of cardiac failure secondary to cardiac malformations and/or cardiac conduction disease. Although the condition is considered to be fully penetrant, subtle limb involvement may not become clinically apparent without radiographic studies. The spectrum of limb defects ranges from severe (phocomelia) to mild (slight carpal bone abnormalities), the most common limb abnormalities being either triphalangeal (finger-like) or absent thumbs. Upper limb deformities are usually bilateral and are frequently asymmetrical. Cardiac abnormalities occur in approximately 75% of patients with HOS (95% of familial cases). The most common cardiac abnormality is an atrial septal defect (ASD) or ventral septal defect (VSD). Strict diagnostic criteria for HOS are met with personal and/or positive family history of cardiac septation and/or conduction defects in combination with preaxial radial ray deformity. Atypical characteristics thought to exclude a diagnosis of HOS include: ulnar or lower limb involvement, renal anomalies, syndactyly involving digits other than thumb, polydactyly, and craniofacial abnormalities.

Reasons for referral:

1. Confirmation of a clinical diagnosis
2. Genetic counseling and risk assessment

Lab Testing Sections: Anatomic Pathology - Sendouts

Referred to: GeneDx, Inc. (GDX Test: 2361)

Phone Numbers: MIN Lab: 612-813-6280

STP Lab: 651-220-6550

Test Availability: Daily, 24 hours (Preferred draws are Sunday - Thursday as specimens can only be received at the reference lab Monday - Friday. Specimens collected Friday or Saturday will be held for shipment on Monday.)

Turnaround Time: 8 - 10 weeks for new patients

Special Instructions: A GeneDx [request form](#) must be sent with any patient or specimen to the laboratory.

TBX5 can be tested using cells obtained by swabbing the buccal mucosa (inside of cheek). Buccal specimens can only be used for sequencing and are not accepted on children under 6 months of age. Buccal swab collection kits are available from GeneDx (ph. 301-519-2100).

Specimen

Specimen Type: Whole blood

Buccal cell swab (preferred specimen) – Sequencing only

Container: Blood: Lavender top (EDTA) tube

Buccal Smear: Cytobrush Plus Cell Collector® kit

Draw Volume: 1 - 5 mL blood

2 swabs from the Cytobrush Plus Cell Collector® kit

Processed Volume: Same as Draw Volume

Collection: Routine venipuncture for blood specimens, invert gently to mix

Buccal swab kit for buccal swabs:

Buccal Cell Collection procedure:

1. Remove a swab from the Buccal swab kit touching only the “stick” end.
2. **Do Not** rinse mouth before starting. Have the individual open his/her mouth. Twirl the swab on the inner cheek for 30 seconds. **Do Not** scrape so hard that the cheek bleeds.
3. Place the swab end in the labeled tube. Cut the “stick” with scissors at the level of the top of the tube. Replace cap and close completely.
4. Repeat the process with another swab on the opposite cheek.
5. Send the kit to the lab for processing and mailing.

Special Processing: Lab Staff: Send whole blood in original collection container labeled with patient name, date of birth and medical record number, including signed consent form and requisition, with a cool pack, via overnight or second-day courier so that the sample will arrive at GeneDx, Inc. on a weekday (Monday through Friday). Samples drawn on Friday or Saturday should be held at refrigerated temperatures for shipment on Sunday. **Do not** freeze. **Note:** Specimens may be stored at refrigerated temperatures for up to 3 days prior to shipping.

Mail the Cytobrush Plus Cell Collector® kit, including signed consent form and requisition, by regular mail to GeneDx in the included envelope.

Patient Preparation: For buccal cell collection, **Do Not** have the patient rinse his/her mouth.

Sample Rejection: Unrefrigerated specimens older than 48 hours; clotted or hemolyzed for blood; frozen specimens; mislabeled or unlabeled specimens

Interpretive

Reference Range: No mutations detected

Critical Values: N/A

Limitations: Buccal specimens can only be used for sequencing and are not accepted on children under 6 months of age.

Methodology: Bi-directional sequence analysis

References: [GeneDx, Inc.](#) March 2012
(301) 519-2100 Fax (301) 519-2892

Updates: 2/6/2013: CPT update
3/26/2014: CPT update