Lab Dept: Anatomic Pathology

Test Name: HOLT ORAM (TBX5) KNOWN MUTATION

General Information

Lab Order Codes: TBXK (Blood or Buccal Swab)

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

CPT Codes: 81479 – Molecular Pathology Unlisted procedure

Test Includes: Testing of a relative for a specific known mutation (carrier testing) where testing was previously done by GeneDx. Using genomic DNA, the exon or exons of interest are screened by bi-directional sequence analysis and/or by non-sequence methods such as heteroduplex analysis or restriction enzyme digestion. The previously tested proband DNA serves as a positive control.

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.

Carrier testing reasons for referral:
1. Testing parents of a child with a specific dominant mutation, in order to determine if the mutation in the child is new or inherited.
2. Carrier testing in parents of a child with apparently homozygous recessive mutations, to rule out the possibility that the child has one mutated allele and one allele that is deleted or refractory to amplification.
3. Carrier testing in the parents of a child with recessive mutations, to confirm that all four parental alleles can be detected prior to prenatal diagnosis.

	4. Pre-symptomatic testing in siblings of the index case. 5. Carrier testing in the extended family.
Lab Testing Sections:	Anatomic Pathology - Sendouts
Referred to:	GeneDx, Inc. (GDX#: 9011, Specify gene/mutation)
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:	2-4 weeks
Special Instructions:	A GeneDx signed 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 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)
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 in warm weather, 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 7 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

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Interpretive

Reference Range:	Interpretive report
Critical Values:	N/A
Limitations:	Buccal specimens are not acceptable on children under 6 months of age.
Methodology:	Bi-directional sequence analysis or other methods as required
References:	GeneDx, Inc. March 2012 (301) 519-2100 Fax (301) 519-2892
Updates:	2/6/2013:CPT update