Lab Dept: Anatomic Pathology

Test Name: ANOPHTHALMIA, MICROPHTHALMIA (SIX6) KNOWN MUTATION

General Information

Lab Order Codes: SIXK

Synonyms: Developmental Eye Disorders Gene Testing

CPT Codes: 81479 – Unlisted Molecular Pathology procedure (SIX6 Known Mutation)

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: Several developmental eye disorders have a known genetic basis including microphthalmia and anophthalmia. Anophthalmia is the complete absence of the globe, or bulb, of the eye and hence the most structural eye malformation. A milder form is microphthalmia, where total axial length of the eye globe is the least two standard deviations below the mean for age. Simple microphthalmia refers to a structurally normal eye with short total axial length. In each of these conditions, the eyelids, conjunctiva and lacrimal apparatus are normal. In complex microphthalmia, additional abnormalities are present and may include anterior segment dysgenesis, cataract, persistent hyperplastic primary vitreous, chorioretinal coloboma and/or retinal dysplasia. In addition, anophthalmia and microphthalmia may be seen in association with various genetic syndromes or chromosome abnormalities. Mutations in the SOX2 and SIX6 genes leading to haploinsufficiency may be associated with hearing loss, developmental delay, esophageal atresia, genitourinary abnormalities, myopathy, and spastic diplegia. Hemizygosity for SIX6 has been seen in some cases of bilateral anophthalmia due to interstitial chromosome deletions. Homozygosity for PAX6 mutation has also been associated with anophthalmia..

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.

Specimen

Specimen Type:	Whole blood
Container:	Lavender top (EDTA) tube
Draw Volume:	1 - 5 mL blood
Processed Volume:	Same as Draw Volume
Collection:	Routine venipuncture for blood specimens, invert gently to mix
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). Include a cool pack when shipping during warm weather. 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.
Patient Preparation:	None
Sample Rejection:	Unrefrigerated specimens older than 48 hours; clotted or hemolyzed for blood; frozen specimens; mislabeled or unlabeled specimens

Interpretive

Reference Range:	Interpretive report
Critical Values:	N/A
Limitations:	Buccal specimens are not acceptable for this testing.
Methodology:	Bi-directional sequence analysis or other methods as required
References:	GeneDx, Inc. February 2012 (301) 519-2100 Fax (301) 519-2892
Updates:	1/29/2013: CPT 2013 update