

## Lymphedema-Distichiasis Testing via *FOXC2* Gene Sequencing (Test #280)

**Brief Description:** Lymphedema-distichiasis (LD) Syndrome (OMIM 153400) presents with lymphedema of the lower extremities, a double row of eyelashes and a variable age of onset (Mansour et al. GeneReviews, 2007, www.genetests.org). Patients may also have cleft palate, extradural cysts, cardiac defects, or photophobia. Other ocular findings may include: exotropia, ptosis as well as congenital ectropion and cataracts.

**Genetics:** LD is inherited in an autosomal dominant manner, although approximately one quarter of cases are the result of *de novo* mutations. Researchers in the laboratory of Dr. Thomas Glover at the University of Michigan (Fang et al., Am J Hum Genet. 67:1382-1388, 2000) identified mutations in the *FOXC2* (Forkhead Box C2) gene as a cause of LD Syndrome. The single exon, 1.5 kb *FOXC2* gene is a member of the 'forkhead' (or winged helix) gene family, originally identified in *Drosophila*, which encode transcription factors with a conserved 100-amino acid DNA binding motif. About 50 different causative *FOXC2* mutations have been reported. Nearly all are frameshift or nonsense. Cases of Lymphedema Type II (OMIM 153200) and Lymphedema with ptosis (OMIM 153000) have also been linked to mutations in the *FOXC2* gene (Feingold et al. Hum Molec Genet 10:1185-1189, 2001).

**Description of This Particular Test:** This particular test involves bidirectional DNA sequencing of the entire single *FOXC2* exon in four overlapping sequence reads along with ~100 bases of non coding flanking DNA. We also perform sequencing of any single portion this gene for family members of patients with known mutations and to confirm research results (\$190 charge).

**Indications for Test:** Candidates for this test are patients with symptoms consistent with LD and the family members of patients with known mutations.

**Sensitivity of Test:** In a patient with clearly clinically delineated Lymphedema-distichiasis, we estimate that the sensitivity of this test to be 90%.

**Turn Around Time:** Maximum of 40 days, although many tests are completed in 2-3 weeks.

**Specimen Requirements:** See page 4 of the Requisition Form.

**Price:** *FOXC* Gene Sequencing **\$390**

**CPT Codes:**

Sample Ascertainment	83890 \$ 30	DNA Isolation	83891 \$ 40
Amplification x4	83898 \$ 80	Sequencing x4	83904 \$ 120
Separation	83894 \$ 40	Interpretation/Report	83912 \$ 80

**Accreditation Info.** CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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