

## **Barth Syndrome; X-linked Dilated Cardiomyopathy; Left Ventricular Noncompaction, and Endocardial Fibroelastosis via *TAZ* Gene Sequencing (Test #149)**

**Brief Description of Clinical Features:** Barth syndrome (BTHS, OMIM 302060) is a rare X-linked disorder of lipid metabolism. Symptoms typically present within the first year of life. Boys with BTHS generally present with skeletal myopathy and abnormal mitochondria along with either dilated cardiomyopathy (DCM, OMIM 115200), left ventricular noncompaction (LVNC, OMIM 300183) or endocardial fibroelastosis (EFE, OMIM 305300) (Barth et al. *Neurol Sci* 62:327-355, 1983). Additional features include growth delay and elevated urinary 3-methylglutaconic acid and 2-ethylhydracrylic acid. Patients with BTHS are also at risk for bacterial infection due to neutropenia. See also the Barth Syndrome Foundation (<http://www.barthsyndrome.org>).

**Genetics:** BTHS is inherited in an X-linked recessive manner and primarily affects boys with carrier females being asymptomatic. BTHS results from mutations in *TAZ*, which encodes for the protein tafazzin. Tafazzin is important for the synthesis of cardiolipins and mitochondrial function. Mutations in *TAZ* can result in a wide-spectrum of cardiomyopathies, including DCM and LVNC without other symptoms associated with Barth Syndrome. (Bione et al. *Nat Genet* 12:385-389, 1996; D'Adamo et al. *J Hum Genet* 61:862-867, 1997; Bleyl et al. *Am J Med Genet* 72:257-265, 1997; Ichida et al. *Circulation* 103:1256-1263, 2001). Over 100 mutations in *TAZ* have been identified throughout the entire coding region. The majority of causative variants are missense, nonsense, and splice site mutations. Small insertions and deletions have also been found in patients with BTHS, DCM or LVNC.

**Description of This Particular Test:** This test involves bidirectional DNA sequencing of the 11 coding exons and splice sites of the *TAZ* gene. The full coding sequence of each exon plus ~50 bp of flanking non-coding DNA are sequenced. As indicated, we will sequence any single exon (Test #100, \$190) in family members of patients with known mutation, or to confirm research results.

**Reference Sequences:** Genomic: NC\_000023.10 mRNA: NM\_000116.3 Protein: NP\_000107.1 (CCDS 14748.1)

**Indications for Test:** Patients with symptoms suggestive of Barth Syndrome. *TAZ* testing should be considered when males present with cardiomyopathy (DCM or LVNC) along with neutropenia or skeletal muscle weakness.

**Sensitivity of Test:** The majority of Barth Syndrome patients have mutations in *TAZ*.

**Turnaround Time:** Maximum of 40 calendar days, although many tests are completed in 3-4 weeks.

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

**Price:** Sequencing of coding exons of the *TAZ* Gene: \$ 640

**CPT Codes:**

Sample Ascertainment x1	83890	\$ 30	DNA Isolation x1	83891	\$ 40
Amplification x9	83898	\$ 175	Sequencing x9	83904	\$ 260
Separation x1	83894	\$ 40	Interpretation/Report x1	83912	\$ 95

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

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