

TAZ (G4.5) MUTATION ANALYSIS

JOHN WELSH CARDIOVASCULAR
DIAGNOSTIC LABORATORY



Barth syndrome, originally described in 1979 by Neustein *et al.* and later by Barth *et al.* as an X-linked cardioskeletal myopathy with abnormal mitochondria and neutropenia, is a severe disorder which classically presents in infancy with heart failure, sepsis, and may be associated with 3-methylglutaconic aciduria. Growth retardation, abnormalities of carnitine and cholesterol, and mitochondrial respiratory chain deficiency, particularly cytochrome C, are also notable. A high percentage of affected children reportedly succumb early in life from this disorder.

Bione *et al.* identified the disease-causing gene as *TAZ (G4.5)*, a novel gene containing 11 alternatively spliced exons. The gene, which is located on the X chromosome at Xq28, encodes a protein family called tafazzins, whose function remains unknown. Multiple mutations in *TAZ* have been identified including missense, nonsense, and splicing mutations, as well as small deletions and insertions. However, phenotype-genotype correlations have not been identified. Further, it has been shown that mutations in *TAZ* not only result in classic Barth syndrome but also in left ventricular noncompaction (LVNC), X-linked infantile cardiomyopathy, X-linked endocardial fibroelastosis (EFE), and dilated cardiomyopathy (DCM). Thus, mutations in *TAZ* can result in a broad spectrum of clinical diseases, including but not limited to classical Barth syndrome.

The John Welsh Cardiovascular Diagnostic Laboratory offers molecular genetic testing for *TAZ* mutations. Symptomatic males will be tested by automatic fluorescent DNA sequencing of all 11 exons of the *TAZ* gene. We strongly recommend initial testing of an affected male, if available, in order to provide the greatest test sensitivity and clearest interpretation of results for subsequent carrier female testing. If an affected male is unavailable for testing, testing of females at high risk is offered. Genetic counseling is recommended for all individuals in order to identify additional at-risk family members and to discuss reproductive issues.

REASONS FOR REFERRAL

- Molecular confirmation of the diagnosis of Barth syndrome, X-linked infantile cardiomyopathy, left ventricular noncompaction, and X-linked endocardial fibroelastosis (EFE) in affected males
- Carrier testing in females with a family history of Barth syndrome, X-linked infantile cardiomyopathy, left ventricular noncompaction, and X-linked endocardial fibroelastosis (EFE)
- Carrier testing is not offered for asymptomatic minor females. Please call for additional information.

METHODOLOGY

Genomic DNA will be analyzed for *TAZ* mutations by automatic fluorescent DNA sequencing of all 11 exons of the *TAZ* gene, as well as the exon/intron junctions and a portion of the 5' and 3' untranslated regions. Patient DNA will be sequenced in both the forward and reverse orientations. If a mutation is identified, additional family members will be analyzed only for the familial mutation by automatic fluorescent DNA sequencing.

SERVICE FEES

	<i>Direct and Institutional Billing</i>	<i>CPT Codes</i>
Index Case (Male or Female)	\$600 per sample	83891, 83898x6, 83904x12, 83912
Additional Family Members	\$180 per sample; known familial mutation only	83891, 83898, 83904x2, 83912

SENSITIVITY

DNA Sequencing Analysis: Approximately 99% detection of mutations in exons 1-11 of *TAZ*

SPECIMEN REQUIREMENTS

Blood (preferred): EDTA (purple-top) tubes: **Adult:** 5 cc **Child:** 5 cc **Infant:** 2-3 cc
Tissue: Frozen (preferred), RNAlater, Formalin-fixed, Paraffin embedded
Other Body Fluids: Call to inquire