Cincinnati Children's
Heart Institute

Heart Institute Diagnostic Lab
CAP#: 7518730
CLIA#: 36D2003208
Phone: (513) 803-1751
Fax: (513) 803-1748
Email: HeartDx@cchmc.org

Barth Syndrome Testing- *TAZ* Sequencing

Barth Syndrome is rare and the prevalence is unknown as the disease is thought to be under diagnosed (1). The *TAZ* gene codes for taffazin, a protein important for normal cardiolipin production and mitochondrial function. Cardiolipin is an important component of the inner mitochondrial membrane and is closely associated with the electron transport chain (2). Mutations in the *TAZ* gene can result in cardiomyopathy (dilated cardiomyopathy and/or left ventricular non-compaction), neutropenia, skeletal myopathy, growth deficiency, and 3-methylglutaconic aciduria. Female carriers of *TAZ* mutations do not have features of Barth syndrome. The *TAZ* gene contains 11 exons and is located at chromosome Xq28.

The majority of individuals with a clinical diagnosis of Barth syndrome have *TAZ* mutations (3,4). *TAZ* mutations are inherited in an X-linked recessive manner. Approximately 2/3 of males with Barth have a confirmed or suspected family history of the condition (4).

Indication

TAZ testing is utilized to confirm a diagnosis of Barth syndrome in patients with clinically evident disease. Barth syndrome should be considered when males present with cardiomyopathy, especially when associated with left ventricular noncompaction, neutropenia, skeletal muscle weakness, or family history suggestive of X-linked inheritance. We recommend testing the most clearly affected individual in the family whenever possible.

Shipping Instructions

Please enclose a test requisition form with sample. All information must be complete before sample can be processed. Samples may be shipped at room temperature by overnight Federal Express to arrive Monday through Friday.

Ship To:

Cincinnati Children's
Hospital Medical Center
Attn: Heart Institute Diagnostic Lab
240 Albert Sabin Way,
Room S4.381
Cincinnati, OH 45229-3039

Methodology:

All 11 exons of the *TAZ* gene, as well as the exon/intron boundaries and a portion of untranslated regions of the gene are amplified by PCR. Genomic DNA sequences from both forward and reverse directions are obtained by automatic fluorescent detection using an *ABI PRISM® 3730 DNA Analyzer*. Sequence variants different from National Center for Biotechnology Information GenBank references are further evaluated for genetic significance. If a mutation is identified, a known familial mutation analysis will be available for additional family members.

Sensitivity & Accuracy:

Greater than 98.5% of the mutations in exon 1-11 of *TAZ* are detectable by sequence based methods. Sequencing does not detect deletions or duplications in carrier females but may detect these changes in affected males. Mutations in *TAZ* account for the majority of cases of Barth syndrome.

References:

1. Cantlay AM, Shokrollahi K, Allen JT, Lunt PW, Newbury-Ecob RA, Steward CG. Genetic analysis of the G4.5 gene in families with suspected Barth syndrome. *The Journal of Pediatrics*. 1999;135:311-315.

2. Valianpour F, Wanders RJ, Overmars H, Vreken P, Van Gennip AH, Baas F, Plecko B, Santer R, Becker K, Barth PG. Cardiolipin deficiency in x-linked cardioskeletal myopathy and neutropenia (Barth syndrome, mim 302060): A study in cultured skin fibroblasts. *The Journal of Pediatrics*. 2002;141:729-733.

3. Bione S, D'Adamo P, Maestrini E, Gedeon AK, Bolhuis PA, Toniolo D. A novel x-linked gene, G4.5. Is responsible for Barth syndrome. *Nature Genetics*. 1996;12:385-389.

4. Spencer CT, Bryant RM, Day J, Gonzalez IL, Colan SD, Thompson WR, Berthy J, Redfearn SP, Byrne BJ. Cardiac and clinical phenotype in Barth syndrome. *Pediatrics*. 2006;118:e337-346.

Specimen:

Peripheral blood in EDTA tube
Adult: 5-10mL
Child: 3-5mL
Infant: 1-3mL
For other specimen types, please contact Amy Shikany at 513-803-3317

Turnaround Time:

Full Mutation Analysis 2-4 weeks
Known Mutation Analysis 1-2 weeks

CPT Codes:

Full Gene Sequencing	81406
Additional Family Members	81403