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97) Novel missense mutation M185V in exon 7 of the TAZ (G4.5) gene in a patient with atypical Barth syndrome

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Barth Syndrome (BTHS) is an X-linked inherited disorder characterized clinically by cardiac and skeletal myopathy, short stature and neutropenia. While such features generally vary in presentation and severity, they often prove fatal during childhood. Multiple genetic mutations in the TAZ gene, located on Xq28, have been identified in association with BTHS, and we describe a novel missense mutation 553A>G (M185V) in the TAZ gene through bidirectional sequencing of a 4-month-old proband of Irish/German decent. He first presented with respiratory distress, neutropenia, and dilated cardiomyopathy with reduced ejection fraction of 10% by echocardiogram. 3-Methylglutaconic aciduria was not detected on three urine organic acid analyses. Family studies revealed that his maternal uncle died of endocardial fibroelastosis and dilated cardiomyopathy at 26 months old, and that the proband's mother, maternal aunt, and grandmother all carry the same missense mutation. Bioinformatic analysis predicted that this sequence alteration is deleterious by PolyPhen-2 algorithm. This missense mutation was not present in 115 X chromosomes from 81 ethnically-matched control subjects (47 males and 34 females). The identification of TAZ gene mutations is important for the diagnosis and genetic counseling in this family with atypical Barth syndrome that is not associated with 3-methylglutaconic aciduria.