PUS1 Gene Analysis in Mitochondrial Myopathy, Lactic Acidosis and Sideroblastic Anemia (MLASA)

Clinical Features:
Mitochondrial myopathy, lactic acidosis and sideroblastic anemia (MLASA) is a rare disorder of oxidative phosphorylation that presents in childhood and is characterized by muscle weakness, normocytic anemia and lactic acidemia. Other features that have been described in affected individuals include microcephaly, micrognathia, high philtrum, high palate, mental retardation and growth hormone deficiency.[1] Variability in clinical features has been described even within members of the same family.[1]

Inheritance Pattern/Genetics:
Autosomal recessive

Test Methods:
Variant analysis of the PUS1 gene is performed on genomic DNA from the submitted specimen using bi-directional sequence analysis of coding exons and corresponding intron/exon boundaries. If sequencing identifies a variant on only one allele of the PUS1 gene, and if clinically indicated, reflex deletion/duplication testing (ExonArrayDx) will be performed at no additional charge to evaluate for a deletion/duplication of one or more exons of this gene. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis or another appropriate method.

Test Sensitivity:
In a study of 60 probands with congenital sideroblastic anemia, one novel homozygous nonsense variant in the PUS1 gene was identified in one individual and a homozygous founder variant in the PUS1 gene was identified in another proband.[2] To our knowledge, a large study of the frequency of PUS1 variants in patients recognized as having MLASA has not been published.

References:

1. Fernandez-Vizarra et al., (2007) J Med Genet 44:173-180.
2. Bergmann et al., (2010) Pediatr Blood Cancer 54:273-278.
3. Bykhovskaya et al., (2004) Am J Hum Genet 74:1303-1308.
4. Riley et al., (2010) Am J Hum Genet 87:52-59.