NEU1 Gene Analysis in Sialidosis (Mucolipidosis I)

Clinical Features:
Sialidosis is a rare lysosomal storage disease with two distinct clinical phenotypes. Type I sialadosis is the milder form with onset of gait abnormalities, progressive vision loss, bilateral macular cherry-red spots, and myoclonus in the second or third decade. Ataxia and seizures have also been reported in type I patients. Type II has an earlier onset with coarse facial features, dysostosis multiplex, short stature, developmental delay, mental retardation and hepatosplenomegaly. Type II patients may also present with a congenital-onset form associated with ascites and hydrops fetalis prenatally, an infantile-onset form with the absence of symptoms at birth or a juvenile form that has onset in late childhood and a relatively milder phenotype. Seizures, myoclonus and renal involvement have also been documented in type II cases.[1] The frequency of diagnosed sialidosis in the general population is estimated at approximately one in four million live births.[2]

Genetics:
Autosomal Recessive. Sialidosis is caused by pathogenic variants in the *NEU1* gene that encodes the lysosomal alpha-*N*-acetyl neuraminidase-1 (NEU1) enzyme that removes terminally linked sialic acid residues from gangliosides, oligosaccharides, and glycoproteins and is part of a multi-enzyme complex containing □-galactosidase and protective protein cathepsin A. Deficiency of neuraminidase 1 results in lysosomal accumulation and urinary excretion of sialylated glycoconjugates. The *NEU1* gene is located on chromosome 6p21.3 and has 6 exons.

Test Methods:
Variant analysis of the *NEU1* 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 *NEU1* 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 three small studies each including between 3 and 10 patients with sialidosis, sequencing identified all variants in the *NEU1* gene.[2, 3,]

References: (12 pt bold)

1. Caciotti et al., (2009) J Neurol 256:1911-1915.
2. Bonten et al., (2000) Hum Mol Genet 9:2715-2725.

3. Coutinho et al., (2012) Clin Genet 2012) Clin Genet 81:379-393.
4. Pattison et al., (2004) Hum Mutat 23:32-39.
5. Seyrantepe et al., (2003) Hum Mutat 22:343-352.