NEU1 Gene Analysis in Sialidosis (Mucolipidosis I)

Clinical Features:
Sialidosis is a rare lysosomal storage disease with two distinct clinical phenotypes. Type I sialidosis 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. The frequency of diagnosed sialidosis in the general population is estimated at approximately one in four million live births.

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.

References: (12 pt bold)