Beta-Galactosidase Deficiency: Beta-Galactosidase Activity, Leukocytes

**Condition Description**

Beta-galactosidase deficiency is associated with three distinct autosomal recessive lysosomal storage disorders: GM1 gangliosidosis (GM1), mucopolysaccharidosis type IVB (MPS IVB), and galactosialidosis. GM1 and MPS IVB are referred to as GLB1-related disorders as they are the result of biallelic mutations in GLB1. Galactosialidosis is caused by mutations in CTSA (cathepsin A) and results in decreased activity of beta-galactosidase and neuraminidase.

Deficiency of beta-galactosidase leads to the accumulation of sphingolipid intermediates in lysosomes of neuronal tissue, resulting in the CNS deterioration typical of GM1. Deficiency of this enzyme also leads to accumulation of the glycosaminoglycan (GAG) keratan sulfate in cartilage which is suspected to cause the skeletal findings associated with MPS IVB.

Patients with GM1 have a characteristic abnormal pattern of oligosaccharide elevations in urine detectable by TLC and MALDI-TOF mass spectrometry. Patients with MPS IVB have detectable bands of keratan sulfate by GAG analysis with TLC. Keratan sulfate is also present in MPS IVA and the clinical presentation of MPS IVB is not distinguishable from that of MPS IVA. Patients with galactosialidosis also have characteristic oligosaccharide elevations and decreased neuraminidase 1 enzyme levels. Neuraminidase testing and molecular analysis of CTSA is recommended to confirm a diagnosis of galactosialidosis. Determination of beta-galactosidase levels is not recommended for carrier detection.

GM1 gangliosidosis has been classified into three major clinical forms according to the age of onset and severity of symptoms: type I (infantile), type II (late infantile/juvenile) and type III (adult). Type I is the most common and most severe form with developmental arrest observed within 3 to 6 months of birth, macular cherry red spots, skeletal dysplasia and death usually within the first 2 years of life. Corneal clouding, diffuse cerebral atrophy, and developmental delay characterize type II. Type III is the mildest of the three types and can present with gait and speech impairment.

Compared to other types of MPS, most individuals affected by type IV do not have coarse facial features or mental retardation. Skeletal manifestations include: odontoid hypoplasia, a striking short trunk dwarfism, and genu valgum. Compared to other patients with MPS, those with type IV tend to have greater spine involvement with scoliosis, kyphosis, and severe gibbus as well as platyspondyly, rib flaring, pectus carinatum, and ligamentous laxity. Odontoid hypoplasia is the most critical skeletal feature to recognize in any patient with MPS IV. In earlier clinical descriptions, MPS Type IVA was considered to have more severe manifestations than type IVB. However, with the ability to differentiate between types A and B by enzyme analysis, it is understood that significant variability in clinical expression exists within both groups. No clear clinical differentiation between MPS type IVA and IVB exists.

Galactosialidosis is also classified into three subtypes according to age of onset and progression. Common features of early-infantile type are hydrops fetalis, inguinal hernia, growth delay and hepatosplenomegaly. In addition, coarse facial features, corneal clouding, cherry red spot, renal failure, and cardiomegaly have been associated. Death usually occurs by the end of the first year. The late-infantile type includes many of the features of the early-infantile form and can also include hearing loss and short stature. Age of onset of the juvenile/adult form varies and can include ataxia, seizures, corneal clouding, progressive intellectual impairment, cherry red spot, vision and hearing loss, and spinal abnormalities. Life expectancy varies within the late-infantile and juvenile/adult forms.

For questions about testing for beta-galactosidase deficiency, call EGL Genetics at 470-378-2200 or 855-831-7447. For further clinical information about lysosomal storage diseases, including management and treatment, call the Emory Lysosomal Storage Disease Center at (404) 778-8565 or (800) 200-1524.

**Indications**

This test is indicated for children or adults with symptoms of GM1 gangliosidosis (GM1), Morquio syndrome, Type B (MPS IVB) or galactosialidosis. Not valid for carrier testing.

**Methodology**

Fluorometric Enzyme Assay using artificial 4-MU substrate. Beta-galactosidase is evaluated to confirm a diagnosis of GM1 or MPS IVB.

**Specimen Requirements**

**Type: Whole Blood**

Specimen Requirements:

In sodium heparin (green top) tube: 3-5 ml

Specimen Collection and Shipping: Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

**Related Tests**
Mucopolysaccharidosis: Glycosaminoglycans (GAG's), Quantitative and Qualitative, Urine (GA)
Oligosaccharidosis and Congenital Disorders of Glycosylation: High Resolution Oligosaccharide (Free Glycan) Profile, Urine (OS)
Lysosomal Storage Disease: Glycosaminoglycans (GAG's) and Oligosaccharide Profile, Urine (BLSDS)
Lysosomal Storage Disease: Panel Enzyme Activity (13 Enzymes), Leukocytes (LS)
GM1 Gangliosidosis: GLB1 Gene Sequencing (DU)
GM1 Gangliosidosis: GLB1 Deletion/Duplication (KZ)
Mucopolysaccharidosis Type IVB: GLB1 Gene Sequencing (BV)
Mucopolysaccharidosis Type IVB: GLB1 Gene Deletion/Duplication (LY)