

Glycogen Storage Disease Type IX via *PHKB* Gene Sequencing (Test #233)

Brief Description of Clinical Features: Glycogen Storage Disease (GSD) resulting from glycogen phosphorylase kinase deficiency (sometimes called GSD Type IX) has several genetic causes. This is because the phosphorylase kinase (Phk) enzyme is comprised of four subunits ($\alpha\beta\gamma\delta$) and because there are tissue-specific forms of the subunits. GSD Type IX is one of the most common types of GSD involving ~25% of all GSD patients (Hendrickx et al. Am J Hum Genet 64:1541-1549, 1999). Patients typically present in the first few months of life with hepatomegaly, growth retardation, elevated liver and/or muscle glycogen, and elevated serum triglycerides and cholesterol. In some patients, symptoms gradually subside with age, while in others cirrhosis develops. For more information see www.agsdus.org.

Genetics: The *PHKB* gene on chromosome 16 encodes the β subunit of the phosphorylase kinase enzyme. GSD Type IX due to *PHKB* mutations (OMIM 261750) is an autosomal recessive disorder (there are also X-linked recessive forms). Nearly all of the ~15 reported pathogenic *PHKB* mutations have been nonsense, frameshift or splicing (Burwinkel et al. Hum Mol Genet 6:1109-1115, 1997; van den Berg et al. Am J Hum Genet 61:539-546, 1997; Beauchamp et al. Mol Genet Metab 92:88-99, 2007). One larger intragenic deletion which would not be detectable in the heterozygous state by our genomic DNA sequencing test was reported (Burwinkel et al. 1997). Some residual Phk enzyme activity may remain even after complete loss of functional *PHKB* protein. *PHKB* mutations have not been found in patients with only muscle disease and no liver involvement (Burwinkel et al. Eur J Hum Genet 11:516-526, 2003).

Description of This Particular Test: This test involves bidirectional sequencing using genomic DNA of exons 1, 3-26, and 28-33 of the *PHKB* gene (isoform α). The full coding region of each exon plus ~50 bp of flanking non-coding DNA on either side are sequenced. We will also perform sequencing of any single or pair of exons for family members of patients with known mutations and to confirm previous results (\$190-340).

Reference Sequences: Genomic: NC_000016.8 mRNA and Protein: CCDS 10729.1

Indications for Test: Patients with clinical features of (liver) GSD Type IX and patients with Phk deficiency are candidates for this test. Female patients, male patients with negative results for *PHKA2*, or male patients with consanguineous parents are preferred candidates.

Sensitivity of Test: Out of 12 GSD Type IX families, Beauchamp et al. (2007) reported 8 with mutations in the *PHKA2* gene, 2 with mutations in the *PHKG2* gene, and 1 or 2 with mutations in the *PHKB* gene.

Turn Around Time: Maximum of 40 calendar days.

Specimen Requirements: See page 4 of the Requisition Form.

Price: Sequencing of *PHKB* Gene Exons 1-33 \$ 1690

CPT Codes:

Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1	83891 \$ 40
Amplification x30	83898 \$ 570	Sequencing x30	83904 \$ 850
Separation x1	83894 \$ 80	Interpretation/Report x1	83912 \$ 120

Accreditation Info. CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

Contact for info: Dr. Keith Nykamp, keith.nykamp@preventiongenetics.com, www.preventiongenetics.com