

## **Familial Rhabdomyolysis / Childhood Recurrent Acute Myoglobinuria, Autosomal Recessive via *LPINI* Gene Sequencing --Test #369**

**Brief Description of Clinical Features:** Childhood Recurrent Acute Myoglobinuria, also known as Familial Paroxysmal Paralytic Rhabdomyolysis with Myoglobinuria (OMIM 268200), is a rare and life-threatening disease of young children, in which prompt diagnosis and treatment are critical (Tein et al. *Adv Pediatr* 37:77-117, 1990). Early symptoms typically begin before the age of seven years and consist of generalized weakness, inability to walk, myalgia, and dark urine. Recurrent episodes of myoglobinuria are frequent features of the disease. Additional features include cardiac abnormalities, marked sensitivity over the thighs and calf muscles, muscle hypotonia and renal failures. The episodes are triggered by febrile illnesses and persist for several days; they are characterized by concomitant elevated levels of plasma creatine kinase and aspartate aminotransferase (Ramesh and Gardner-Medwin, *Dev Med Child Neurol* 34:73-79, 1992; Zeharia et al. *Am J Hum Genet* 83:489-494, 2008).

**Genetics:** Familial cases of Childhood Recurrent Acute Myoglobinuria have been reported (Christensen et al. *Danish Med Bull* 30:112-115, 1983; Ramesh and Gardner-Medwin, *Dev Med Child Neurol* 34:73-79, 1992). In these families the disease appeared to be transmitted as an autosomal recessive trait. More recently, Zeharia et al. (2008) reported six mutations in the *LPINI* gene in children with Recurrent Acute Myoglobinuria. Both homozygous and compound heterozygous mutations were found, confirming the autosomal recessive inheritance. The mutations were: nonsense (3), missense (1), splicing (1), and one 2-kb deletion including exons 18 and 19.

**Description of This Particular Test:** The *LPINI* gene encodes Lipin-1, phosphatidic acid phosphatase, which catalyzes the conversion of phosphatidic acid to diacylglycerol in the triacylglycerol synthesis pathway. This test involves bidirectional DNA sequencing of all coding exons and splice sites of the *LPINI* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. We will sequence any single or double exons in family members of patients with known mutation or to confirm previous results.

**Reference Sequences:** Genomic: **NC\_000002.10** mRNA and Protein: **CCDS 1682.1**

**Indications for Test:** Patients with Recurrent Acute Myoglobinuria and biological relatives.

**Sensitivity of Test:** Currently unknown.

**Turn Around Time:** Maximum of 40 calendar days.

**Specimen Requirements:** See bottom of page 2 of Requisition Form.

**Price:**                      **Sequencing of all 19 coding exons of the *LPINI* Gene:**                      **\$1090**

**CPT Codes:**

|                      |       |        |                       |       |        |
|----------------------|-------|--------|-----------------------|-------|--------|
| Sample Ascertainment | 83890 | \$ 30  | DNA Isolation         | 83891 | \$ 40  |
| Amplification x 21   | 83898 | \$ 340 | Sequencing x 21       | 83904 | \$ 510 |
| Separation           | 83894 | \$ 80  | Interpretation/Report | 83912 | \$ 90  |

**Accreditation Info. CLIA ID #: 52D1027685** (expires 1/18/11) (CAP#: 7185561, AU ID: 1407125 expires 12/20/10)

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