

## Congenital Generalized Lipodystrophy Type 1 via *AGPAT2* Gene Sequencing (Test #462)

**Brief Description of Clinical Features:** Congenital generalized lipodystrophy (CGL) is a group of disorders characterized by altered body fat distribution and insulin resistance. CGL type 1 (CGL1, OMIM #608594), also known as Berardenelli-Seip congenital lipodystrophy type 1, results from mutations in the *AGPAT2* gene (OMIM #603100; Agarwal et al. *Nat Genet* 31:21-23, 2002). Generalized lipodystrophy disorders demonstrate near absence of body fat at birth or in early infancy and severe insulin resistance leading to diabetes mellitus. Patients have hypertriglyceridemia and low levels of HDL cholesterol. Absence of adipose tissue results in a hypermuscular appearance. Bone age is advanced in early childhood and patients have an accelerated growth rate and a voracious appetite (Agarwal et al. *J Clin Endocrinol Metab* 88:4840-4847, 2003). Fatty infiltration of the liver may lead to hepatic disease including cirrhosis. Other complications include acanthosis nigricans and hypertrophic cardiomyopathy (Van Maldergem et al. *J Med Genet* 39:722-733, 2002).

**Genetics:** Congenital generalized lipodystrophy type 1, like CGL2, is inherited as autosomal recessive disorder. Mutations that result in null alleles are the most frequent pathogenic changes in the *AGPAT2* gene, although missense mutations have also been reported.

**Description of This Particular Test:** 1-acyl-glycerol-3-phosphate acetyltransferase is encoded by the *AGPAT2* gene located on chr 9q34. Testing is accomplished by amplifying the six coding exons and ~50 bp of adjacent noncoding sequence, then determining the nucleotide sequence using standard dideoxy sequencing methods and a capillary electrophoresis instrument.

**Reference Sequences:**

Gene:	Genomic:	mRNA:	Protein:	CCDS:
<i>AGPAT2</i>	NC_000009.11	NM_006412.3	NP_006403.2	7003.1

**Indication for Testing:** Individuals with clinical features of a generalized lipodystrophy with congenital or early infancy onset and insulin resistance.

**Sensitivity of Test:** Among a cohort of 45 congenital generalized lipodystrophy patients, 26 were found to have *AGPAT2* gene mutations and 11 to have *BSCL2* gene mutations (Agarwal et al. 2003). Linkage to the *AGPAT2* and *BSCL2* loci was ruled-out in three of the remaining patients suggesting further genetic heterogeneity exists. Among a cohort of 94 CGL patients, (Magré et al. *Diabetes* 52:1573-1578, 2003) found *BSCL2* mutations in 62 patients and *AGPAT2* mutations in 30 of the remaining 32 unrelated subjects.

**Turn Around Time:** Maximum of 40 days, although many tests are completed in 2-3 weeks.

**Specimen Requirements:** See page 4 of Requisition Form.

**Price: Sequencing of the *AGPAT2* Gene \$640**

CPT Codes							
Gene	83890	83891	83898	83904	83894	83912	Totals
<i>AGPAT2</i>	\$ 30 x1	\$ 40 x1	\$ 170 x9	\$ 260 x9	\$ 60 x1	\$ 80 x1	<b>\$ 640</b>

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

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