

## Farber Lipogranulomatosis via *ASAHI* Gene Sequencing -- Test #481

**Brief Description of Clinical Features:** Farber Lipogranulomatosis or Farber Disease (OMIM 228000) is a rare lysosomal storage disorder due to deficiency in the lysosomal enzyme acid ceramidase (Farber, AMA Am J Dis Child 84:499-500, 1952; Sugita et al Science 178:1100-1102, 1972). The enzymatic deficiency results in the accumulation of ceramide and ganglioside in various tissues including the skin, kidney, and brain. Symptoms usually begin during infancy and death occurs within the first years of life. Patients with milder forms, later onset and longer life span have been reported. Farber disease is characterized by a hoarse cry, difficulty in feeding and subcutaneous nodules (lipogranuloma), usually near the interphalangeal, wrist, elbow and ankle joints. These manifestations are painful and lead to progressive joint deformations. Additional features may include variable degrees of nervous system, lung, heart, lymph node, spleen and liver impairment (Moser et al. In The Metabolic and Molecular Bases of Inherited Disease:3573-3585, 2001; Edited by Scriver et al).

**Genetics:** Farber disease is inherited in an autosomal recessive manner. Mutations in the *ASAHI* gene are responsible for the acid ceramidase deficiency and subsequent development of the disease (Koch et al. J Biol Chem 271:33110-33115, 1996). To date, about 20 mutations, distributed along the entire coding region of the gene, have been detected in patients with Farber disease from various populations. Nearly all reported mutations were missense, although a frameshift and two splicing mutations were also reported (<http://www.biobase-international.com>). Most mutations are private (Muramatsu et al. J Inherit Metab Dis 25:585-592, 2002). In mice, deletion of the entire gene leads to embryonic lethality (Li et al. Genomics 79:218-224, 2002).

**Description of This Particular Test:** The *ASAHI* gene encodes a heterodimeric protein consisting of a nonglycosylated alpha subunit and a glycosylated beta subunit that is cleaved post-translationally to form the mature enzyme. The ceramidase enzyme catalyzes the degradation of ceramide into sphingosine and fatty acid. This test involves bidirectional DNA sequencing of all 14 coding exons and splice sites of the *ASAHI* gene. The full coding sequence of each exon plus ~ 50 bp of flanking DNA on either side are sequenced. As indicated, 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\_000008.9** mRNA: **NM\_004315.4**  
 Protein: **NP\_004306.3** mRNA and Protein: **CCDS 6005.1**

**Indications for Test:** Patients with clinical features of Farber disease and their biological relatives are candidates.

**Sensitivity of Test:** Unknown at this time

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

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

**Price:** Sequencing of all coding exons of the *ASAHI* Gene: \$ 820

**CPT Codes:**

Sample Ascertainment x1	83890	\$ 30	DNA Isolation x1	83891	\$ 40
Amplification x15	83898	\$ 220	Sequencing x15	83904	\$ 340
Separation x1	83894	\$ 70	Interpretation/Report x1	83912	\$ 120

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

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