MASSACHUSES GENERAL HOSPITAL
Neurogenetics DNA Diagnostic Laboratory
CLIA #22D0882074
New York State #cQP4866

REPORT OF DNA-BASED TEST RESULTS

Test: **Late Infantile Neuronal Ceroid-lipofuscinosis (LINCL,** *CLN2)* **DNA analysis**
Patient Name: Nathan Philip Milto
Patient ID Number: DOB 6/29/94
Sample Submitted: blood
Date of Specimen Collection: 2/26/99
Date of Specimen Receipt: 3/2/99
Accession: #99-225
Date of Report: 3/11/99
Referring Physician/Counselor: Dr. Forrest Ellis
Midwest Eye Institute
Methodist Hospital Plaza North
201 Pennsylvania Parkway
Indianapolis, IN 46280-1381
(800)8224699, (317)817-1329 fax

RESULTS:

Genomic DNA from this individual was analyzed by polymerase chain reaction (PCR) amplification of a segment containing intron 5/exon 6 junction and part of exon 6 in the LINCL gene *(CLN2*). The PCR-amplified product was analyzed by DNA sequencing in both directions. The intron 5 splicing mutation, G3560C, was found on one allele.

INTERPRETATION:

DNA sequence analysis identified heterozygous G to C mutation at 3'- splice acceptor in intron 5 of *CLN2* gene.

Recent research findings have shown that mutations in CLN2 gene result in classical late infantile neuronal ceroid lipofuscinosis (LINCL)[1]. The defective gene in this hereditary disorder encodes a recently identified lysosomal pepstatin-insensitive acid protease[2]. An intronic G to C transversion in the invariant AG of the 3'-splice acceptor of intron 5 and a C to T transition in exon 6 account for more than 60% of all the mutation alleles identified[3]. The exon 6 mutation, C3674T, is a nonsense mutation and predicts a premature translation termination at amino acid codon #208Arg.

Since there are other known mutations in the remaining exons of *CLN2* gene which are associated with LINCL and our detection rate is only 60-70%, we suspect the patient harbors another *CLN2* mutation on the other allele.

Winnie W. Mn, Ph.D. Supervisor
Katherine B. Sims, M.D. Director

References: 1. Sleat, D. (1997) Association of mutations in a lysosomal protein with classical lateAnfantile neuronal ceroid lipofuscinosis. Science 277(5333): 1802-1805.

2. Lin, C. (1998) Structural organization and sequence of *CLN2,* the defective gene in classical late infantile neuronal ceroid lipofuscinosis. Genomics 50:206-212.

3. Sleat, D. (1999) Mutational analysis of the defective protease in classical late-infantile neurotial ceroid