National Niemann-Pick Disease Foundation Grant #48
Six-month Progress (May 2009): Edward H. Schuchman, PhD
Lay Summary

We have used funds from this NNPDF grant to generate a new mouse model of Type A NPD. These mice express a specific human Type A mutation (R496L) on the background of mice that are "null" for ASM activity* (i.e., ASMKO mice). Thus, the only ASM that is produced in these animals is the mutant R496L. These mice express normal amounts of the ASM protein, but the enzyme is functionally inactive, as is the case in human patients with Type A NPD. Our primary goal for these animals is to use them to evaluate new ways to enhance the residual ASM activity, particularly in the brain. This may include small molecule "chaperones", and/or dietary supplementation. This is an important step towards our long-term goal of developing a treatment for Type A NPD, and we are thankful to the NNPDF for the funds that permitted us to accomplish these studies.

*An ASMKO mouse is one in which the ASM (acid sphingomyelinase) genes have been "Knocked-Out, or made non-functional. Thus, they have "null," or zero ASM activity unless a gene or genes are re-introduced into the animals to make ASM. This is what Dr. Schuchman did with the R496L mutation–carrying gene.