HSN-1 and sphingolipids

Hereditary sensory neuropathy type 1 (HSN1), the most common inherited peripheral neuropathy, is clinically defined by severe sensory loss that leads to painless injuries, skin ulcers, and distal amputation. The gene that is defective in persons with HSN1 regulates the production of the sphingolipid serine palmitoyltransferase (SPT),

Sphingolipids are essential components of cells in the body. They give cell membranes important structural properties and may play a part in organizing the movement of proteins in and out of cells.

Sphingolipids are formed when a fatty acid bonds with an amino acid. The resulting product is called a metabolite. These metabolites regulate processes within cells. Sphingolipid metabolites are formed when sphingolipids are created or broken down.

Last year The Deater Foundation sponsored an HSN1 Symposium in Charlestown (Boston). Many scientists shared their theories of how the sphingolipid process may cause the clinical symptoms seen in HSN1. Ideas shared since that meeting, and research generated from those ideas, have resulted in new discoveries about what may cause the damage to nerves in HSN1.

Diane McKenna-Yasak from Dr. Brown's laboratory collected blood samples from family members at the Deater Reunion last year. These samples show high levels of certain sphingolipid metabolites.

Studies on the HSN1 mouse models at Massachusetts General Hospital show high levels of the same metabolites. This is very encouraging and supports the notion that these metabolites play a role in the disease.

Pursuing this further, the mice were given a supplement of an amino acid in their diet. After two weeks on this special diet, the blood levels of the metabolites decreased.

The researchers are now interested in determining if dietary supplements of amino acids will reduce the levels of the metabolites in people with HSN1. The research study would involve persons with HSN1 taking a dietary supplement and keeping a food diary for a specified period of time (probably 3 months). Blood samples taken at the start, mid-point, and end of the experiment may reveal important data concerning the use of supplements and their effect, if any, on patients with HSN1.

Many people in the family affected with HSN1 have already volunteered to be a part of the study when the study protocol is finalized and approved. Dr. Robert H.

Brown, Jr., Director of the Day Neuromuscular Laboratory now at the University of Massachusetts, and Dr. Florian Eichler at Massachusetts General Hospital are collaborating in this research.

It is anticipated that the blood samples can be taken in Noxen. The largest numbers of persons in the Deater family affected with HSN1 live within reasonable driving distance of this location. A gathering of the family would also be valuable for the doctors, who are both neurologists as well as experts in genetics.

Drs. Brown and Eichler both have expressed support for a second HSN1 Symposium sometime this year, after the results of the proposed study are known. This would be a worthwhile project for The Deater Foundation to support.

We look forward to contributing to this important work.