Understanding more about Niemann-Pick C disease

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Dr. Melanie Dobson and her research team are investigating Niemann-Pick C disease, a rare, inherited neurodegenerative disease affecting children. Currently, there is no effective treatment. Their research into the basic science underlying this disorder may aid the cluster of Nova Scotians of Acadian descent affected by the condition.

There are three types of Niemann-Pick: A, B and C. They are each characterized by the inappropriate accumulation of fats (lipids) within cells, particularly within the liver, spleen and brain. Types A and B of the disease result from a deficiency of an enzyme, ASM, required to break down sphingomyelin, a fatty substance found in the brain and nervous system. Type C, which is always fatal, involves accumulation of cholesterol. Cholesterol is an essential building block of cell membranes and is required for synthesis of steroid hormones, key cell-to-cell signaling molecules within our bodies. Three hundred to 400 cases of Niemann Pick C have been diagnosed worldwide, but it is thought to be under-reported.

Since the early 1990s, research into treatments for types A and B has focused on bone marrow transplants, enzyme replacement therapy and gene therapy. Currently there is no specific treatment for Type C. In 1997, researchers identified the gene responsible for Niemann-Pick Type C – NPC1 on chromosome 18. Mutations or changes to this gene account for 95% of all cases of the disease. NPC1 includes a protein important to the trafficking and storage of cholesterol.

We do not yet understand the role that NPC1 plays in regulating the production and movement of lipids and sterols, such as cholesterol, within cells. Dr. Dobson's approach to determining the function of human NPC1 is to analyze the yeast version of the gene. Yeast, single-celled fungi, are useful for genetic studies. They have an NPC1-related gene and synthesize and regulate fat production in a similar manner to human cells.

Dr. Dobson and her colleagues have constructed yeast strains in which they deleted or mutated this gene. Through biochemical and molecular genetic analyses, they are examining the effects mutations have on fat metabolism and cell physiology. They are also identifying where and how the normal protein functions within the cell.

Support from the Nova Scotia Health Research Foundation for this basic science research triggered additional funding from other sources, including a grant from the National Niemann-Pick Disease Foundation (NNPDF), an American charitable organization funding research on this family of diseases. Association with other groups involved in NPC research allows Dr. Dobson to bring research advances on this disease to the Nova Scotians families affected by Niemann-Pick. The findings from Dr. Dobson's research will also have broader relevance because a better understanding of lipid transport and regulation is important for many human diseases.

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Research Results