

Public Abstract

First Name:Douglas

Middle Name:N.

Last Name:Sanders

Adviser's First Name:Martin

Adviser's Last Name:Katz

Co-Adviser's First Name:

Co-Adviser's Last Name:

Graduation Term:SS 2007

Department:Pathobiology Area Program

Degree:PhD

Title:AUTOLOGOUS BONE MARROW-DERIVED MESENCHYMAL STEM CELL TRANSPLANTATION AS A THERAPY FOR NEURONAL CEROID LIPOFUSCINOSIS

The neuronal ceroid lipofuscinoses (NCLs) are a rare set of genetically inherited diseases with childhood onset. They are characterized by the buildup of autofluorescent material in neural tissues and neurodegeneration which leads to blindness, seizures, mental and physical deterioration, coma and eventually death. These problems are the result of defective or absent enzymes within the cells of affected patients. Currently, no effective clinical treatment is available for NCLs.

Autologous (i.e. - self-derived) mesenchymal stem cells offer great promise as a potential treatment for NCLs and a number of other diseases. MSCs can be easily isolated from the bone marrow and have the ability to engraft in and differentiate into numerous tissue types. Because they are derived from the patient being treated, autologous cells do not suffer from the same technical difficulties (such as immune rejection) or ethical concerns that embryonic or fetal cells do. Using animal models of NCL we demonstrate that MSCs can be genetically modified to repair defective NCL-specific genes and that, when transplanted into tissue affected with NCL they can engraft, survive for up to 5 weeks and correct the enzymatic deficit in surrounding cells as demonstrated by the reduction in autofluorescent storage material. Further experiments in these animal models will determine the extent to which transplanted cells are able to reduce neurodegeneration and other symptoms of NCL. Developing effective methods of autologous MSC therapy has implications for numerous diseases other than the NCLs. Such therapy could readily be applied to common disorders such as stroke, heart disease, diabetes and Parkinson's and numerous other rare genetically inherited diseases.