Public Abstract
First Name:Christopher
Middle Name:Joseph
Last Name:Tracy
Adviser's First Name:Martin
Adviser's Last Name:Katz
Co-Adviser's First Name:
Co-Adviser's Last Name:
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Title:Ex vivo gene therapy for the preservation of retinal and central nervous system structure and function in a canine model of CLN2 neuronal ceroid lipofuscinosis

CLN2 neuronal ceroid lipofuscinosis is an inherited neurodegenerative disorder that affects both the retina and brain, resulting in progressive vision loss, loss of motor function and cognitive faculties, seizures, and eventual death in preadolescence. No treatments are currently available for the disease. CLN2 is caused by mutations in the TPP1 gene, which results in little to no functional TPP1 enzyme being produced. Using a dog model of CLN2, we endeavored to develop a treatment method that would continuously supply the TPP1 enzyme to the retina and central nervous system, thereby preserving both structure and function. We injected transgenic stem cells capable of producing the deficient TPP1 enzyme into the eye and the brain, and then monitored the dogs for any therapeutic benefits. Retinal degeneration was delayed in treated dogs relative to controls, indicating that the enzyme produced by the cells exerted a protective effect upon the retina. Central nervous system studies are still ongoing, but no adverse effects as a result of the treatment have been observed, indicating that the approach itself should be safe for use in treating the brain. This therapeutic approach should also be effective in treating other similar diseases that affect either the retina or the brain and with which can treated by the application of a soluble protein or biological therapeutic molecule.