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Characterization of degeneration in the retina, brain and spinal cord of the Cln1 knockout mouse

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The neuronal-ceroid lipofuscinoses (NCLs; often referred to as Battens Disease) are a group of hereditary disorders of childhood. Symptoms of NCLs are characterized by neurodegeneration with progressive neural cell death in the retina and central nervous system (CNS). The infantile form of NCL results from a deficiency in the protein, palmitoyl protein thioesterase-1 (PPT-1). PPT-1, encoded by the Cln1 gene, removes long chain fatty acids from modified cysteine residues in proteins. Mutations in the Cln1 gene are associated with an accumulation of autofluorescent lysosomal lipopigments in various tissues such as the retina and CNS. In the current study, we use a transgenic mouse model in which the gene for Cln1 has been mutated, i.e., 'knocked out'. Our goal is to perform histological experiments to assess the functional progression of neurodegenerative changes in the retina, brain and spinal cord as the subject ages. The retina, brain and spinal cord of the mice at different ages were fixed and embedded in plastic resin and/or paraffin. Thick sections (1 mm or 10 mm, respectively) were stained with toluidine blue or propidium iodide to detect neuronal loss and/or apoptosis as a result of the PPT-1 deficiency. Fluorescent images of the stained sections were obtained to document changes in tissue structure and the extent of degeneration. These studies provide information that will aid future studies in which stem cell transplants will be made into the Cln1 knockout mouse model. Ultimately, this approach will determine whether combined gene and stem cell therapies can be applied to patients with Battens Disease.