A novel Porcine model of CLN2 Batten disease recapitulates clinical phenotypes

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CLN2 Batten disease is a lysosomal storage disorder in which mutations in the *CLN2* gene result in the reduced activity of the lysosomal enzyme, tripeptidyl peptidase 1. The disease is typically diagnosed at 2 to 4 years of age following onset of developmental delays. Other early symptoms include ataxia and seizures, and patients eventually lose the ability to speak and walk. CLN2 Batten disease has no cure, and most patients succumb to the disease between 6 to 12 years of age. Multiple *CLN2* mouse models have been generated to better understand the etiology of the disease, however these models are unable to adequately recapitulate the disease due to differences in anatomy and life history (e.g., metabolism, brain structure, life span), limiting their utility for therapeutic testing. Pigs have a gyrencephalic brain with similar anatomical, physiological, and immunological characteristics to humans, making this model ideal for preclinical testing of therapeutics. Additionally, large animals such as pigs can be readily scanned on current human neuroimaging scanners (such as MRI) to model changes within the CNS longitudinally. Recently, we have developed a novel *CLN2*$^{R208X/R208X}$ porcine model of CLN2 Batten disease. Herein we present initial characterization results showing behavioral, pathological, and visual phenotypes that recapitulate those seen in CLN2 patients. The *CLN2*$^{R208X/R208X}$ pigs develop multiple, severe symptoms of CLN2 Batten disease, making this an excellent model for testing therapies.