Gene Therapy for future application to LOTS and LOS patients

	Activities completed / underway	Funding agencies
2007-present	. Therapeutic efficacy shown in Sandhoff (SD) mice and cats . Therapeutic benefit in Tay-Sachs (TSD) sheep . Pre-IND meeting with FDA . IND-enabling tox studies completed-mice and monkeys . No toxicity noted - green light from FDA for IND for intracranial injections . This therapy uses simultaneous delivery of two different vectors – one for HexA the other for HexB – <u>not ideal</u> for cerebrospinal fluid (CSF) or intravenous (IV) injections. Due to its invasiveness of intracranial injections not planned for LOTS or LOS. Need a less invasive therapy.	NTSAD CTSF NIH UMMS Auburn
2017	. Development of novel bicistronic AAV vector encoding both HexA and HexB genes in same vector – Ideal for LOTS and LOS	
2017-present	. Testing of new bicistronic AAV vector in SD mice (survival 4m). .Intravenous delivery increases survival so far to 1 year, animals are asymptomatic. .CSF delivery increases survival so far to 6 months, also asymptomatic and still ongoing. . Testing also underway in SD cats. . Ultra-large scale of AAV produced to treat TSD sheep . Treated 5 TSD sheep intravenously at human-like doses . Treated 4 TSD sheep by CSF at human-like doses. . TSD Sheep and SD cats will be followed with neurologic, MRI, CSF and other biomarkers for future IND application.	