Mucopolysaccharidosis IIIA (MPS IIIA), also known as Sanfilippo syndrome A, is an autosomal recessive lysosomal storage disorder. The disease is characterized by severe and progressive loss of cognitive and motor functions, behavioral deficits and eventually death in the second decade of life, although the severity and progression of the disease varies widely. MPS IIIA is caused by mutations in the SGSH gene that result in deficiency of the N-sulfoglucosamine sulfohydrolase enzyme and subsequent accumulation of undegraded heparan sulfate, lysosomal enlargement as well as cellular and organ dysfunction. To model the disease, a MPS IIIA mouse strain with spontaneous Sgsh mutation, resulting in an almost complete loss of N-sulfoglucosamine sulfohydrolase activity, was characterized. Male MPS IIIA mice (JAX#003780) were analyzed at an age of 28 to 30 weeks for body weight changes, activity, social interaction and cognition. Afterwards, neuropathology was evaluated by using a LIMP2 antibody, labeling lysosomal and endosomal membranes, and GFAP and IBA1 antibodies to analyze neuroinflammation.

In summary, these results confirm that MPS IIIA mice present a similar phenotype as observed in Sanfilippo syndrome A patients. The mouse is therefore a valuable model for preclinical research.