Neuropathology of a novel knock–in mouse model for mucolipidosis II alpha/beta (MLII)

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M6P-dependent transport of lysosomal proteins

Phenotype of Gntptab−/−C3082InC mice.

Pathological alterations in the brain of 9-month-old Gntptab−/−C3082InC mice.

N-glycans and cholesterol accumulations in Gntptab−/−C3082InC brain

Ultrastructural analysis of storage material in Gntptab−/−C3082InC brain.

Conclusion

Loss of M6P residues on lysosomal enzymes resulted in a progressive neurodegeneration in Gntptab−/−C3082InC mice. Neurodegeneration was accompanied by accumulation of storage material ranging from floccular and electron-opaque to electron-dense material, membranous and zebra bodies and curvilinear and fingerprint inclusions, as have been described for the neuropathology of patients and cats with mucolipidosis II (Martin et al., 1984; Bosshard et al., 1996).

The further identification and compositional analysis of mucolipidosis II-associated storage material in the Gntptab−/−C3082InC mouse brain allow conclusions by which specific mannos 6-phosphate-containing proteins are limiting for overall function of lysosomes.