Pathogenic role of BECN1/Beclin 1 in the development of amyotrophic lateral sclerosis

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Pharmacological activation of autophagy is becoming an attractive strategy to induce the selective degradation of aggregate-prone proteins. Recent evidence also suggests that autophagy impairment may underlie the pathogenesis of several neurodegenerative diseases. Mutations in the gene encoding SOD1 (superoxide disumutase 1) trigger familial amyotrophic lateral sclerosis (ALS), inducing its misfolding and aggregation and the progressive loss of motoneurons. It is still under debate whether autophagy has a protective or detrimental role in ALS. Here we evaluate the impact of BECN1/Beclin 1, an essential autophagy regulator, in ALS. BECN1 levels were upregulated in both cells and animals expressing mutant SOD1. To evaluate the impact of BECN1 to the pathogenesis of ALS in vivo, we generated mutant SOD1 transgenic mice heterozygous for Becn1. We observed an unexpected increase in life span of mutant SOD1 transgenic mice haploinsufficient for Becn1 compared with littermate control animals.