Abstract

The CLUH proteins are highly conserved through evolution. The deletions of the homologues of *Dictyostelium discoideum*, *Saccharomyces cerevisiae* and *Arabidopsis thaliana* led to a perinuclear accumulation, so called clustering, of mitochondria. Null mutants of the CLUH protein in *Drosophila melanogaster* were sterile and had shortened life span.

This is the first analysis of mammalian homologues of the CLUH protein. The mammalian CLUH protein is a cytosolic protein that localizes to stress granules, sites of mRNA storage, under energy deprivation conditions. A conditional knock out mouse model for the murine gene *Cluh* was successfully generated.

Since neurons are highly susceptible to dysfunctional and not properly distributed mitochondria, a Purkinje neuron specific knock out of *Cluh* was analyzed for a potential neurodegenerative phenotype. The mice did not display any phenotype up to the age of 20 weeks.

Cluh$^{-/-}$ embryos developed normally but the pups did not survive the first day of life. Ultrastructure analysis of the liver revealed that autophagy is not taking place when the *Cluh* gene is deleted. Biochemical analysis in *Cluh*$^{-/-}$ mouse embryonic fibroblasts showed that the mTOR pathway, which negatively regulates autophagosome formation, is constitutively active under starvation conditions. In conclusion, the analysis of the full body knock out revealed that the CLUH protein has an essential function during the starvation period after birth.