Increased mammalian target of rapamycin signaling contributes to the accumulation of protein oxidative damage in a mouse model of down's syndrome

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Background: Neurodegenerative diseases are characterized by increased levels of oxidative stress and an altered mammalian target of rapamycin (mTOR)/autophagy axis; however, the mutual relationship between these two events is controversial. Previous studies in Down's syndrome (DS) and Alzheimer's disease (AD) suggested that the accumulation of protein oxidative damage results from the increased free radical production, mainly related to metabolic alterations, mitochondrial degeneration and amyloid-? deposition, and aberrant activity of protein degradative systems. Summary: This study analyzed mTOR signaling in Ts65Dn mice, a model of DS, at 6 and 12 months of age compared with euploid mice showing the early aberrant hyperphosphorylation of mTOR coupled with the reduction of autophagosome formation. Moreover, the evaluation of protein oxidation shows an increase in protein nitration and protein-bound 4-hydroxynonenal in 12-month-old Ts65Dn mice suggesting the potential involvement of altered autophagy in the buildup of protein oxidative damage. In addition, data obtained on cell culture support the protective role of autophagy in reducing protein oxidation. Key Messages: Overall, this study provides further evidence for the role of mTOR hyperactivation and reduced autophagy in the accumulation of protein oxidative damage during DS and AD pathologies.Background: Effective therap.

Alzheimer's disease

Autophagy

Down's syndrome

Mammalian target of rapamycin

Protein oxidation

4 hydroxynonenal

mammalian target of rapamycin

rapamycin

MTOR protein, human

mTOR protein, mouse

target of rapamycin kinase

animal cell

animal experiment

animal model

autophagosome

autophagy

cell viability

Conference Paper

controlled study

Down syndrome

female

male

mouse

MTT assay

neuroblastoma cell

nonhuman

oxidation

oxidative stress

priority journal

protein phosphorylation

reciprocal chromosome translocation

signal transduction

trisomy

Western blotting

animal

C3H mouse

C57BL mouse

disease model

Down syndrome

hippocampus

human

metabolism

oxidation reduction reaction

phosphorylation

signal transduction

transgenic mouse

tumor cell line

Animals

Blotting, Western

Cell Line, Tumor

Disease Models, Animal

Down Syndrome

Hippocampus

Humans

Mice, Inbred C3H

Mice, Inbred C57BL

Mice, Transgenic

Oxidation-Reduction

Phosphorylation

Signal Transduction

Sirolimus

TOR Serine-Threonine Kinases