Increased dosage of p44 causes memory loss, neurodegeneration and premature death

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Abstract

The tumor suppressor p53 has been recently shown to regulate longevity and aging independently of its tumor suppressor activity. Specifically, the longevity-assurance activity of p53 depends on the levels of p44, a short and naturally occurring isoform of p53. As such, increased dosage of p44 in the mouse leads to accelerated aging and short lifespan. Here we show that mice with increased dosage of p44 (p44+/+)

INTRODUCTION

The communication between a cell and its environment is achieved by the use of cellular receptors. Molecules attach to their specific receptors located in the cell surface, and the receptors in turn send signals to the interior of the cell to induce a change. IGF-1R is one of these receptors, and it has been shown to regulate the life span of several organisms.

RESULTS

The increases in p44+/+ mice show memory impairment and synaptic defects

Double-IGF-1R knockout mice do not exhibit memory deficits

Reduced IGF-1R signaling improves the synaptic deficits caused by the accumulation of Aβ in APP695/swe mice.

CONCLUSION

In transgenic mice, increased IGF-1R signaling accelerates Alzheimer's Disease-like pathology, whereas reduced IGF-1R signaling prevents it.

By regulating IGF-1R signaling, p53 may play a role in the cognitive decline associated with both normal aging and late-onset Alzheimer's Disease.

Our results suggest that IGF-1R could be a valid pharmacological target for the treatment and/or prevention of both the memory loss that accompanies aging and the neuropathology that characterizes Alzheimer's Disease.

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