

P53 Inhibition Provides a Pivotal Protective Effect Against Spine Cord Ischemia-reperfusion Injury in Vitro

via mTOR Signaling

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Introduction

Tumor suppressor p53 has recently been reported to have numerous functions independent of tumorigenesis, including neuronal survival during ischemia. The mammalian target of rapamycin (mTOR) signaling pathway plays a central role in the regulation of metabolism, cell growth, development, and cell survival. The aim of our research is to further clarify the role of p53 and the mTOR signaling pathway in neuronal ischemic-reperfusion injury in vitro.

Methods

Mouse primary mixed cultured spine cord neurons with an oxygen glucose deprivation (OGD) model was used to mimic an ischemic-reperfusion injury in vitro. A lentiviral system was also used to inhibit or overexpress p53 to determine whether p53 alteration affects OGD and reperfusion injury.

Results

Our results show that activated p53 was induced and it suppressed mTOR expression in primary mixed cultured neurons after OGD and reperfusion. Inhibiting p53, using either a chemical inhibitor or lentiviral-mediated shRNA, exhibited neuroprotective effects in primary cultured neurons against OGD and reperfusion injury through the upregulation of mTOR activity. Such protective effects could be reversed by rapamycin, an mTOR inhibitor. Conversely, p53 overexpression tended to exacerbate the detrimental effects of OGD injury by down-regulating mTOR activity.

Conclusions

p53 inhibition has a pivotal protective effect against an in vitro ischemia-reperfusion injury via mTOR signaling and provides a potential and promising therapeutic target for spine cord ischemia treatment.

Learning Objectives

To further clarify the role of p53 and the mTOR signaling pathway in neuronal ischemic-reperfusion injury in vitro.

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