MOLECULAR NEURODEGENERATION

MEETING ABSTRACT Open Access

Retrovirus mediated hypoxia-responsive element-regulated neurotrophin-3 transduction attenuates brain injury following focal cerebral ischemia in rats

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From 2011 International Conference on Molecular Neurodegeneration
Shanghai, China. 22-24 September 2011

Background

Exogenous delivery of Neurotrophin-3 (NT-3) gene may provide a potential therapeutic strategy for ischemic stroke. But uncontrolled expression of NT-3 may cause deleterious side effects. Recently, hypoxia-specific gene expression systems have been developed in various ischemic diseases. To explore ischemia/hypoxia-controlled expression of NT-3 in rats, we constructed a recombinant retrovirus vector with 5HRE and NT-3 and delivered it to rat brain to investigate the neuroprotective effects of hypoxia induced NT-3 overexpression on focal cerebral ischemia.

Methods

Three groups of rats received RV-5H-NT3, RV-5H-EGFP or saline injection, respectively. 3 days after gene transfer, the rats underwent 90 minutes of transient middle cerebral artery occlusion (tMCAO) and followed by 1 to 14 days reperfusion. Expression of NT-3 was detected by immunohistochemical staining and Western blot; neurological function was assessed by sensorimotor behavioral tests; infarct volume was determined by TTC staining; neuronal injury was examined by TUNEL.

Results

NT-3 expression was significantly increased in RV-5H-NT3 transduced rat brain compared with RV-5H-EGFP or saline group 3 days after tMCAO ($P < 0.05$). Infarct volume was smaller in RV-5H-NT3 transduced rat brain than RV-5H-EGFP or saline group ($P < 0.05$) with reduced percentage of TUNEL positive cells ($P < 0.05$). Furthermore, functional recovery in RV-5H-NT3 transduced rats was better than RV-5H-EGFP or saline transduced group from 1 day to 2 weeks after tMCAO ($P < 0.05$).

Conclusions

After RV-5H-NT3 gene transfer, NT-3 expression was up-regulated by five copies of HRE in response to hypoxia/ischemia, and hypoxia-regulated NT-3 expression attenuates ischemic brain injury and promotes functional recovery in cerebral ischemia rats.

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Published: 7 February 2012

doi:10.1186/1750-1326-7-S1-S16
Cite this article as: Zhang *et al.*: Retrovirus mediated hypoxia-responsive element-regulated neurotrophin-3 transduction attenuates brain injury following focal cerebral ischemia in rats. *Molecular Neurodegeneration* 2012 **7**(Suppl 1):S16.

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