Co-administration of TiO2 nanowired mesenchymal stem cells with cerebrolysin potentiates neprilysin level and reduces brain pathology in alzheimer?s disease

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Neprilysin (NPL), the rate-limiting enzyme for amyloid beta peptide (A?P), appears to play a crucial role in the pathogenesis of Alzheimer?s disease (AD). Since mesenchymal stem cells (MSCs) and/or cerebrolysin (CBL, a combination of neurotrophic factors and active peptide fragments) have neuroprotective effects in various CNS disorders, we examined nanowired delivery of MSCs and CBL on NPL content and brain pathology in AD using a rat model. AD-like symptoms were produced by intraventricular (i.c.v.) administration of A?P (1-40) in the left lateral ventricle (250 ng/10 ?l, once daily) for 4 weeks. After 30 days, the rats were examined for NPL and A?P concentrations in the brain and related pathology. Co-administration of TiO2-nanowired MSCs (106 cells) with 2.5 ml/kg CBL (i.v.) once daily for 1 week after 2 weeks of A?P infusion significantly increased the NPL in the hippocampus (400 pg/g) from the untreated control group (120 pg/g; control 420 ± 8 pg/g brain) along with a significant decrease in the A?P deposition (45 pg/g from untreated control 75 pg/g; saline control 40 ± 4 pg/g). Interestingly, these changes were much less evident when the MSCs or CBL treatment was given alone. Neuronal damages, gliosis, and myelin vesiculation were also markedly reduced by the combined treatment of TiO2, MSCs, and CBL in AD. These observations are the first to show that co-administration of TiO2-nanowired CBL and MSCs has superior

neuroprotective effects in AD probably due to increasing the brain NPL level effectively, not reported earlier.

Alzheimer?s disease (AD)

Amyloid-beta peptide (a?P)

Cerebrolysin (CBL)

Mesenchymal stem cells (MSCs)

Nanodelivery

Neprilysin (NPL)

TiO2 nanowires

amyloid beta protein[1-40]

cerebrolysin

glial fibrillary acidic protein

membrane metalloendopeptidase

myelin

nanowire

titanium dioxide

amino acid

cerebrolysin

membrane metalloendopeptidase

nanowire

titanium

titanium dioxide

Alzheimer disease

animal experiment

animal model

animal tissue

Article

blood brain barrier

brain edema

controlled study

gliosis

hippocampus

male

mesenchymal stem cell transplantation

nerve cell lesion

neuroprotection

nonhuman

rat

Alzheimer disease

animal

biosynthesis

brain

drug effect

mesenchymal stem cell transplantation

metabolism

pathology

procedures

Sprague Dawley rat

Alzheimer Disease

Amino Acids

Animals

Brain

Male

Mesenchymal Stem Cell Transplantation

Nanowires

Neprilysin

Rats

Rats, Sprague-Dawley

Titanium