Title: **Neuroprotection of minocycline via inhibition of EMMPRIN expression following intracerebral hemorrhage in mice**

Author / Authors: Mengzhou Xue, Yang Liu
The Second Affiliated Hospital of Zhengzhou Universit Zhengzhou / China

Abstract

Background: Neuroinflammation is an important host defense response to secondary brain injury after intracerebral hemorrhage (ICH). Extracellular matrix metalloproteinase inducer (EMMPRIN) has been shown to be a vital inflammatory mediator in some neurological diseases. Minocycline has the neuroprotective effect in ICH brain injury by inhibiting the MMPs expression. We hypothesize that neuroprotection of minocycline is via inhibition of EMMPRIN following ICH in mice.

Methods: Male adult C57BL/6 mice were injected with collagenase type VII or saline into the right basal ganglia. Minocycline (45 mg/kg) was administered intraperitoneally 2 h after ICH and then every 12 h until euthanasia. Immunofluorescence, western blot analysis, Fluoro-Jade C (FJC) staining, terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL), and HE staining were used to evaluate the EMMPRIN, MMP-9 expression, brain inflammation, and hematoma volume. The neurobehavioral tests were used to determine the functional recovery.

Results: The outcomes of western blot and immunofluorescence analysis revealed that EMMPRIN expression significantly decreased in the perihematomal area at 3 days after ICH with minocycline treatment. Meanwhile, the animals with minocycline treatment significantly reduced the expression of MMP-9, elevated the expression of ZO-1 and occludin, inhibited activation of microglia/macrophages and infiltration of neutrophils in perihematomal tissue, reduced neuronal death and neuronal degeneration and promoted the neurological recovery after ICH.

Conclusion: Our findings demonstrated that inhibition of EMMPRIN expression by minocycline reduced neuroinflammation and neuronal injury after ICH, which may be mediated by activation of the EMMPRIN/MMP-9 pathway. Therefore, inhibition of EMMPRIN may be a potential therapeutic strategy for ICH patients.

Keywords: Intracerebral hemorrhage, EMMPRIN, Minocycline, Matrix metalloproteinase-9