Ginkgo biloba Extract Inhibits Astrocytic Lipocalin-2 Expression and Alleviates Neuroinflammatory Injury via the JAK2/STAT3 Pathway after Ischemic Brain Stroke

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Background: Astrogliosis has the potential to lead to harmful effects, namely, neuroinflammation, and to interfere with synapse sprouting. Previous studies have suggested that Lipocalin-2 (LCN2) acts as a key target in regulating the neuroinflammatory response. However, the underlying molecular mechanisms are still unknown. In the present study, we examined the anti-inflammatory and neuroprotective effects of Ginkgo biloba extract (EGB), a well-known compound with potential immunoregulatory properties in the nervous system.

Methods: Triphenyltetrazolium chloride staining, hematoxylin-eosin staining, electron microscopy, and neurological assessments were performed in a microsphere-embolized rat model. Human astrocytes exposed to oxygen glucose deprivation (OGD) were used for in vitro experiments. Inflammatory cytokines, multi-labeling immunofluorescence, and Western blotting were also used to investigate the molecular mechanisms underlying the EGB-mediated anti-inflammatory effects in vivo and in vitro.

Results: EGB markedly attenuated cerebral infarction and neuronal apoptosis, reduced the inflammatory cytokine level, and alleviated neurological deficiencies in cerebral ischemic rats. After surgery, EGB significantly inhibited astrocyte activation, reduced the phosphorylation of STAT3 and JAK2 and decreased LCN2 expression. In vitro, EGB blocked OGD-induced STAT3 activation and the generation of pro-inflammatory cytokines in human astrocytes, and these effects were significantly enhanced by LCN2 overexpression. EGB downregulated these effects enhanced by LCN2 overexpression.

Conclusions: This study demonstrates that EGB activates astrocytic LCN2 and thereby suppresses neuroinflammation via the JAK2/STAT3 pathway, providing insight into a promising therapeutic strategy for ischemic stroke.