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Anti-inflammatory effects of Cobrotoxin in LPS induced astrocytes.

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Cobrotoxin (venom of Vipera lebetina turanica) binds with high affinity to both muscular type nicotinic acetylcholine receptor (AchRs) and neuronal α7-AchRs. Cobrotoxins are a group of basic peptides, in two main groups; short peptides composed of 60~62 residues with four disulfide bonds and long peptides composed of 71 amino acids with five disulfide bonds. Cobrotoxin also has been known to produce nerve growh factor (NGF). NF-kB binding site has been identified within the promoter region of the choline acetyltransferase, the enzyme that synthesizes acetylcholine. This binding site is also located within the NGF responsive enhancer element. Therefore, we questioned that cobrotoxin may be involved in neuronal cell servival through inhibition of NF-kB, an implicated inflammatory transcription factor. However, the cobrotoxin-induced anti neuroinflammatory effect has been not reported yet. Therefore, in the present study we investigated anti-inflammatory effect of cobrotoxin in astrocyte, which is the major glial cell in the central nervous system and influence many aspects of inflammation and immune reactivity within the brain. Cobrotoxin (0.1, 0.5, 1.0 ug/ml) increased cell survival dose dependently. The present data also showed that cobrotoxin has a preventive effect on lipopolysaccharide (LPS, 100 ng/ml) induced expression of COX-2, cPLA2 and iNOS. Cobrotoxin also inactivated LPS-induced NF-kB, an important transcription factor regulating expression of COX-2, cPLA2 and iNOS, and inhibited NF-kB dependent luciferase activity. Cobrotoxin also inhibited LPS-induced nitric oxide release. Target disrupting ability of cobrotoxin on the NF-kB subunit is being under investigated.

Keyword : cobrotoxin, astrocyte, LPS