THE PROTECTIVE PROPERTIES OF NEW AGONISTS OF FPR2 ON THE EVOKED BY BACTERIAL ENDOTOXIN CHANGES IN MICROGLIA CELLS

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Introduction

Neuroinflammation is a complex multicellular process that plays an important role in the onset and progression of neurodegenerative disorders, including Alzheimer's disease (AD). It is believed that a short-term inflammation, as a beneficial phenomenon, guarantees repair and restoration of homeostasis, whereas failure in resolution of inflammation (RoI) results in long-lasting, chronic inflammation. Recently, it has been shown that RoI is regulated by endogenous molecules, called specialized pro-resolving mediators (SPMs) like lipoxins, resolvins, protectins and others. SPMs modulate RoI by interacting with specific membrane receptor, such as Formyl peptide receptor 2 (FPR2).

Aim of the study

The aim of this study was to determine, whether specialized pro-resolving mediators (SPMs) such as endogenous - lipoxin A4 (LXA₄), its analog - aspirin triggered lipoxin (AT-LXA) as well as new non-peptidic agonists with ureidopropanamide scaffold (MR-39 and AMS) are able to affect the cell death processes evoked by lipopolysaccharide (LPS) treatment in primary microglia cells.

Fig. 3. New non-peptidic agonist – MR-39

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Methods

Female Sprague-Dawley rats were paired with males. Pregnancy was confirmed the next morning. Primary microglia cultures were prepared from cortices of 1-2 day old offspring. Microglia cells were pretreated with each compound (1-500 nM) and next exposed to nonspecific immune system activator – LPS in the concentration of 100 ng/ml. Time-dependent (3-24 h) cell death was determined by lactate dehydrogenase release (LDH test).

Results

Fig. 1. Lipoxin A4

Fig. 2. Aspirin triggered lipoxin

Fig. 4. New non-peptidic agonist – AMS

Fig.1,2,3,4. The effects of LPS and SPMs on microglia death parameters measured by the LDH assay. * $p < 0.05$ vs non-stimulated control group, # $p < 0.05$ vs LPS-stimulated control group

Conclusions

Our results expanded our current understanding of the role of FPR2 in neuroprotection. Moreover, the agonists of FPR2 can be considered as an attractive target for protective therapies.