عنوان مقاله:

Contribution of toll-like receptor ۲ and nicotinamide adenine dinucleotide phosphate oxidase to the trimethylamine N-oxide-induced inflammatory reactions in U۹۳۷-derived macrophages

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خلاصه مقاله:

BACKGROUND: Trimethylamine N-oxide (TMAO) is emerging as a new generation of metabolites related to the activation of inflammatory reactions in the macrophages during atherosclerosis. Stress-activation of cell surface toll-like receptors (TLRs) as well as nicotinamide adenine dinucleotide phosphate (NADPH) oxidases (NOX) is also assumed to be involved in TMAO-induced inflammatory reaction in the macrophages. To elucidate the possible contribution of TLRs and NOX to the mentioned signaling pathway, we aimed to simultaneously evaluate the expression level of TLR۲, TLR۶, and NOX۲ in TMAO-treated macrophages.METHODS: ۲.۵ × ۱۰۶ cells of U۹۳۷-derived macrophages were treated in triplicates with different concentrations (۳۷.۵, ۷۵, ۱۵۰, and ۳۰۰ μM) of TMAO for ۲۴ hours. The cells were also treated with tunicamycin (TUN), as a positive control of stress. Normal control group (CTR) cells received no treatment. The viability of treated cells was checked by ۳-(۴,۵-dimethylthiazol-۲-yl)-۲,۵-diphenyltetrazolium bromide, a tetrazole (MTT) assay. Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was also used to evaluate the relative expression (fold change) of TLR۲, TLR۶, and NOX۲ at messenger ribonucleic acid (mRNA) levels. One-way analysis of variance (ANOVA) with post-hoc Dunnett's test was performed to compare every mean with that of the control.RESULTS: No cell death occurred because of treatments. Dose of ۳۰۰ μM of TMAO significantly increased the relative expression of both TLR۲ and NOX۲ compared to the CTR cells ($P < ۰.۰۰۱$ for both). The elevation of TLR۶ was not statistically significant in all groups of TMAO-treated cells ($P > ۰.۰۵۰$).CONCLUSION: Our results provide documentation supporting contribution of TLR۲ and NOX۲ to previously described inflammatory reactions induced by TMAO in macrophages. In addition, they may clarify the proatherogenic role of TMAO in foam cell formation as well as abnormal activation of macrophages during atherosclerosis.

کلمات کلیدی:

Toll-Like Receptors, Atherosclerosis, Trimethylamine N-Oxide, Macrophages