Role of protein kinase C in BSA-AGE- mediated inducible nitric oxide synthase expression in RAW 264.7 macrophage

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摘要

Abstract

In the present study, the roles of protein kinase C (PKC) in BSA-derived advanced glycosylation end products (BSA-AGEs)-induced nitric oxide (NO) production and inducible nitric oxide synthase (iNOS) expression were investigated. Treatment of RAW 264.7 cells with BSA-AGEs caused dose- and time-dependent increases in NO release and iNOS expression in RAW 264.7 cells, whereas BSA alone had no effect on iNOS induction. The tyrosine kinase inhibitor (genistein), the phosphatidylinositol-specific phospholipase C inhibitor (U-73122), the phosphatidylcholine-specific phospholipase C inhibitor (D-609), and the PKC inhibitors (staurosporine, Ro 31-8220, and Go 6976) all inhibited BSA-AGE-induced NO release and iNOS expression in RAW 264.7 cells. Stimulation of RAW 264.7 cells with BSA-AGEs resulted in the formation of inositol monophosphate; the response was attenuated by U-73122 and genistein. BSA-AGEs stimulated PKC-alpha, -betaI, -delta, and -eta but not -zeta translocation from the cytosolto the membrane. However, incubation of RAW 264.7 cells with BSA-AGEs increased phosphorylation of PKC-zeta at threonine-410, which reflects activation of PKC-zeta, indicating the possible involvement of these PKC isoforms in AGE-mediated effects. Pretreatment of RAW 264.7 cells with U-73122, D-609, and genistein reduced the AGE-stimulated translocation of PKC-alpha, -betaI, -delta, and -eta and activation of PKC-zeta. Taken together, these data suggest that BSA-AGEs might activate PKC and subsequently induce iNOS expression and NO release.