[P-51]

Activation of NF-κB and mitogen-activated protein kinases by polysaccharide isolated from Platycodon grandiflorum in RAW 264.7 macrophages

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In our previous study, we reported that PG, a polysaccharide isolated from Plyatycodon grandiflorum, activated macrophages and B cells, but not T cells. Here, we investigated in more detail the mechanism of action of PG in macrophage activation. Since PG cannot penetrate cells due to the large molecular mass, it should bind to membrane receptors of macrophages. We showed that some antibodies to cell surface molecules (CD14, CD11b, TLR2, and TLR4) inhibited RAW264.7 macrophage activation, suggesting the possible binding sites of PG. The role of TLR4 as the PG receptor was also confirmed by the results that PG activity in macrophages from C3H/HeJ, known to have a defective TLR4, was completely inhibited. Ligation of TLR2/4 by PG also resulted in the activation of JNK, p38 and ERK1/2 MAPKs, which was examined by immunoblotting and kinase assays. It also resulted in the phosphorylation of IkBs, the translocation NF-κB into the nucleus and the initiation of gene transcriptions of IL-1β, IL-6, TNF-α and iNOS. In spite of the similarity in their mode of action, PG and LPS were differentiated by using polymyxin B, which only inhibited macrophage activation by LPS, but not PG. Taken together, our results indicated that PG, as a plant-derived polysaccharide, activated macrophages by mediating TLR signaling cascades and might accelerate the innate immunity against to infectious pathogens and cancers.

Keyword : Platycodon grandiflorum;TLR signaling;innate immunity;macrophages