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## Activation of toll-like receptor signaling by polysaccharide isolated from cell culture of Acantopanax senticosus

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We investigated the mechanism of immunomodulatory action of polysaccharide isolated from cell culture of Acanthopanax senticosus (ASP). ASP was found to increase directly proliferation and differentiation of B cells, and cytokine production of macrophages, but not proliferation and cytokine production of T cells. Since ASP cannot penetrate cells due to its large molecular mass, cellular activation may be caused by the surface binding of this molecule to receptors expressed on B cells and macrophages. Blocking antibodies to TLR2 and TLR4 strongly inhibited ASP activity in B cell and macrophages, suggesting the possible binding sites of ASP. Especially, the role of TLR4 as a ASP receptor was confirmed by the result that ASP activity in cells from C3H/HeJ, known to have a defective TLR4, was decreased in comparison with that in control cells from C3H/HeN mice. Ligation of TLRs by ASP induced the activation of a transcription factor NF-kB and mitogen-activated kinase (Erk1/2, p38, and JNK). Although ASP was shown to activate TLR signaling cascades in a similar way with LPS, they were differentiated by the results that polymyxin B, a specific inhibitor of LPS, did not affect ASP activity in B cells and macrophages. In addition, ASP was heat-stable, but LPS was heat-unstable. Taken together, our results demonstrated that ASP isolated from cell culture of Acanthopanax senticosus activated TLR signaling cascades, resulting in subsequent enhancement of immune response of macrophages and B cells.

Keyword: Acanthopanax senticosus; Polysaccharide; B cells; Macrophages; T cells