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アガロオリゴ糖によるヘムオキシゲナーゼ-1 誘導機構と抗炎症作用

Induction Mechanism of Heme Oxygenase-1 and Anti-inflammatory Activity by Agaro-oligosaccharides

Agaro-oligosaccharides (AGOs) are easily produced from agar under acidic conditions. We previously reported inhibitory action of AGOs on the production of pro-inflammatory mediators, such as nitric oxide, prostaglandin E_2, pro-inflammatory cytokines, in LPS-stimulated monocyte/macrophages. This inhibitory activity is thought to result from the induction of heme oxygenase-1 (HO-1). Here, we further clarified the induction mechanism of HO-1 and its involvement in the anti-inflammatory activity of AGOs. HO-1 expression is known to be regulated by the transcription factor, nuclear factor E2-related factor-2. We verified that siRNA of this transcription factor could attenuate the induction of HO-1 by AGOs. The production of some pro-inflammatory mediators has been associated with mitogenic stimuli (i.e., LPS), followed by activation of transcription factor, nuclear factor-kappa B. We found that AGOs partially suppressed LPS-mediated nuclear factor-kappa B activation, whereas HO-1 siRNA showed no effect on this inhibitory activity. Taken together, AGOs appear to exert their anti-inflammatory effects on activated macrophages through both HO-1-dependent and -independent mechanisms.