S37-5 Ligand function of J2-type prostaglandins

◯Koji UCHIDA[1]

[1]Graduate School of Bioagricultural Sciences, Nagoya University

Cyclooxygenase-2 (COX-2), an inducible isoform responsible for high levels of prostaglandin (PG) production during inflammation and immune responses, mediate a variety of biological actions involved in vascular pathophysiology. Based on the observation that a major serum component, human serum albumin (HSA), was detected in human atherosclerotic aorta, we searched a COX-2 inducer in human serum and found that HSA actually acted as an inducer of COX-2 gene expression in macrophages. In addition, we established a mechanism by which HSA activates COX-2 expression through a signaling pathway involving Toll-like receptors. Moreover, we identify one of the PGD_2 metabolites, Δ^{12}-PGJ_2, as an endogenous enhancer and ligand of HSA. Our data suggest that, since HSA is also involved in the enzymatic conversion of PGD_2 to Δ^{12}-PGJ_2, the COX-2-inducing effect of HSA may be reinforced by its own product, Δ^{12}-PGJ_2, which initiates a positive feedback loop that enhances the albumin-dependent COX-2 gene expression. These results suggest that serum albumin may be a key regulator of inflammatory response.