GW23-e0341

PROSTAGLANFIN E RECEPTORS AS INFLAMMATORY THERAPEUTIC TARGETS FOR ATHEROSCLEROSIS

doi:10.1136/heartjnl-2012-302920a.215

[1]Xiuxia Liu, [2]Kui Hong. *[1]Medical Molecular Laboratory, the Second Affiliated Hospital of Nanchang University, Nanchang 330006, P.R., China; [2]Medical Molecular Laboratory; Cardiology, the Second Affiliated Hospital of Nanchang University, Nanchang 330006, P.R., China*

Objectives Atherosclerosis is currently considered to be a chronic inflammatory disease. Prostaglandin E receptors (EPs) are the G-protein-coupled receptors that respond to prostaglandin E_2 (PGE_2). Data has shown that PGE_2 may function as an endogenous anti-inflammatory mediator by suppressing the production of cytokines. However, other studies have demonstrated that PGE_2, a pro-inflammatory mediator produced by various cell types within the wounded vascular wall, plays a crucial role in atherosclerotic development. These contradictory results may be due to the versatility of EPs.

Methods Experimental data suggest an individual role for each PGE_2 receptor in atherosclerosis.

Results The expression of EP_1 was enhanced in the inflammatory region of human atherosclerotic plaques. Activation of the EP_2 receptor and subsequent elevation of cAMP levels by PGE_2 induces monocytes/macrophages to accumulate in the sub-endothelial space. By activating the EP_3 receptors and subsequently inhibiting the cAMP-dependent pathway, pGE_2 promotes platelet aggregation and contributes to atherothrombosis. PGE_2-EP_4 signalling crucially contributes to the anti-inflammatory function of macrophages by inhibiting the NF-$_\kappa$B and MAPK pathways. However, the activation of the EP_4 receptor promotes macrophage survival through the PI_3K/Akt and NF-$_\kappa$B signalling pathways.

Conclusions Regardless of the function of EPs as pro-inflammatory or anti-inflammatory mediators, pGE_2 -EPs signalling has been indicated as a possible therapeutic strategy to modulate the development of atherosclerosis and plaque stability.