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PROSTAGLANDIN E RECEPTORS AS INFLAMMATORY THERAPEUTIC TARGETS FOR ATHEROSCLEROSIS

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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 E₂ (PGE₂). Data has shown that PGE₂ may function as an endogenous anti-inflammatory mediator by suppressing the production of cytokines. However, other studies have demonstrated that PGE₂, 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 PGE₂ receptor in atherosclerosis.

Results The expression of EP₁ was enhanced in the inflammatory region of human atherosclerotic plaques. Activation of the EP₂ receptor and subsequent elevation of cAMP levels by PGE₂ induces monocytes/macrophages to accumulate in the sub-endothelial space. By activating the EP₃ receptors and subsequently inhibiting the cAMP-dependent pathway, pGE₂ promotes platelet aggregation and contributes to atherothrombosis. PGE₂-EP₄ signalling crucially contributes to the anti-inflammatory function of macrophages by inhibiting the NF- κ B and MAPK pathways. However, the activation of the EP₄ receptor promotes macrophage survival through the PI₃K/Akt and NF- κ B signalling pathways.

Conclusions Regardless of the function of EPs as pro-inflammatory or anti-inflammatory mediators, pGE₂-EPs signalling has been indicated as a possible therapeutic strategy to modulate the development of atherosclerosis and plaque stability.