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$_2$ 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 PI3K/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.