PCSK9 and inflammation: A review of experimental and clinical evidence

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Proprotein convertase subtilisin/kexin Type 9 (PCSK9) is now identified as an important and major player in hypercholesterolaemia and atherosclerosis pathophysiology. PCSK9, through promoting lysosomal degradation of hepatic low-density lipoprotein (LDL) receptor, can decrease the clearance of plasma LDLs, leading to hypercholesterolaemia and consequent atherosclerotic plaque formation. Hypercholesterolaemia has been found to promote systemic and vascular inflammation, which can cause atherosclerotic lesion formation and progression and subsequent incidence of cardiovascular disease. Recent studies have shown the involvement of PCSK9 in the inflammatory pathway of atherosclerosis. Although trials with PCSK9 inhibitors have not shown any alteration in plasma C-reactive protein levels, there is accumulating evidence showing lessened inflammatory response in the arterial wall that could attenuate atherosclerotic plaque development beyond the established LDL-lowering effect of PCSK9 inhibition. In this review, we represent mounting evidence indicating that PCSK9 can locally increase vascular inflammation and contribute to atherosclerotic plaque progression in patients with hypercholesterolaemia.

Atherosclerosis

Inflammation

LDL-C

LDLR

PCSK9

bococizumab

C reactive protein

cytokine

fibrinogen

hydroxymethylglutaryl coenzyme A reductase inhibitor

low density lipoprotein cholesterol

oxidized low density lipoprotein

placebo

proprotein convertase 9

rg 7652

serine proteinase inhibitor

unclassified drug

antiinflammatory agent

autacoid

C reactive protein

cytokine

hypocholesterolemic agent

PCSK9 protein, human

proprotein convertase 9

serine proteinase inhibitor

atherogenesis

atheroma

atherosclerotic plaque

cardiovascular disease

coronary artery disease

cytokine production

enzyme activity

enzyme analysis

gene expression

human

hypercholesterolemia

inflammation

leukocyte count

nonhuman

outcome assessment

pathophysiology

priority journal

protein blood level

protein function

Review

sepsis

signal transduction

vasculitis

animal

atherosclerosis

atherosclerotic plaque

enzymology

inflammation

metabolism

pathology

Animals

Anti-Inflammatory Agents

Anticholesteremic Agents

Atherosclerosis

C-Reactive Protein

Cytokines

Humans

Inflammation

Inflammation Mediators

Plaque, Atherosclerotic

Proprotein Convertase 9

Serine Proteinase Inhibitors

Signal Transduction