Adipokine omentin-1 enhances atherosclerotic plaque stability by binding to macrophage integrin receptor

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Topic(s):
Atherosclerosis, Cerebrovascular Diseases, Aneurysm, Restenosis

Backgrounds:
Omentin-1 is a novel cytokine which is primarily released by epicardial adipose tissues, and the molecule structure analysis revealed that it contained a fibrinogen-like domain. Clinical studies considered that the expression of omentin-1 is tightly associated with the development of cardiovascular diseases. In this research, we sought to investigate the effect of omentin-1 on already-established atherosclerotic lesion in ApoE−/− mouse and find out the cellular receptor of omentin-1 in macrophages.

Methods:
We investigated the effect of omentin-1 on the plaque phenotype by implanting the ALZET minipump (which can continuously inject omentin-1 solution into mice’s jugular vein) in western diet-treated ApoE−/− mice. To validate the conjugation of omentin-1 to integrin receptor αvβ3 and αvβ5, we performed immunoprecipitation experiment. Confocal microscopy was used to verify the spatial co-localization of omentin-1 and integrin receptors.

Results:
In vivo studies showed that the administration of omentin-1 increased the collagen content and the average fibrous cap thickness of atherosclerotic plaque in ApoE−/− mice. Omentin-1 mitigated the formation of necrotic cores within the plaque, and reduced the foam cell infiltration concomitantly. Immunohistochemistry analysis of the atherosclerotic lesion from the aorta of mice revealed that the intravenous infusion of omentin-1 can suppress expression of inflammatory cytokines in vivo. Immunoprecipitation experiment and confocal microscopy analysis confirmed the binding of omentin-1 to integrin receptor αvβ3 and αvβ5. To further study the mechanism by which omentin-1 had exerted its protective function, we used human myeloid leukemia mononuclear cell line (THP1) and oxidized low density lipoprotein (ox-LDL) to establish macrophage-derived foam cell model in vitro. Cell studies demonstrated that omentin-1 can attenuated the apoptosis and inflammatory cytokines secretion in ox-LDL-induced macrophages. Besides, omentin-1 can promote the phosphorylation of integrin-relevant signaling pathway in macrophage. After adding the cilengitide (inhibitor of integrin receptor αvβ3 and αvβ5) or intervening the expression of integrin subunit αv, the phenomenon induced by omentin-1 were potently suppressed. Moreover, flowcytometry analysis provided the evidence that omentin-1 had a negative effect on macrophage efferocytosis ability.

Conclusions:
The administration of adipokine omentin-1 can inhibit the necrotic cores formation and pro-inflammatory cytokines expression within the atherosclerotic lesion. The mechanism might be the inhibition of apoptosis and the secretion of pro-inflammatory cytokines in macrophage by binding to integrin receptor αvβ3 and αvβ5.
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