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MicroRNA-302c-3p inhibits endothelial cell pyroptosis via directly targeting NOD-, LRR- and pyrin domain-containing protein 3 in atherosclerosis

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Abstract

Inflammation and endothelial dysfunction are important participants and drivers in atherosclerosis. NOD-, LRR- and pyrin domain-containing protein 3 (NLRP3) inflammasome activation and the resulting pyroptosis are involved in the initiation and vicious circle of chronic inflammation, thus playing an indispensable role in atherosclerosis. Accordingly, blocking the activation of NLRP3 inflammasome may be a promising treatment strategy to blunt the progression of atherosclerosis. In this study, it was demonstrated that miR-302c-3p exerted anti-pyroptosis effects by directly targeting NLRP3 in vivo and in vitro. In brief, the expression of miR-302c-3p was down-regulated whereas the expression of NLRP3 was up-regulated in human plaques and in vitro pyroptosis model of endothelial cells. Overexpression of miR-302c-3p suppressed endothelial cell pyroptosis by targeting specific sites of NLRP3. By comparison, down-regulation of endogenous miR-302c-3p led to the opposite results, which were reversed by silencing the expression of NLRP3. Finally, the up-regulation of miR-302c-3p inhibited the inflammation and pyroptosis of atherosclerosis mouse model. In conclusion, miR-302c-3p may be a powerful and attractive target for suppressing endothelial inflammation and pyroptosis, providing a novel strategy for preventing or alleviating the progression of atherosclerosis.

KEYWORDS

atherosclerosis, endothelial cell, miR-302c-3p, NLRP3, pyroptosis

Bai and Yang authors equally contributed to this paper.