Immunol promotes the degradation of HDL Generation-Related Functional Protein ABCA1 through IRS/PI3K/Akt signaling pathway in 3T3-L1 adipocytes

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Objectives: Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of human death. Dyslipidemia is one of the most important risk factors for atherosclerosis. Although the early intensive statin therapy is closely associated with the improved survival in patients with coronary heart disease (CHD), cardiovascular residual risk still exists. Hyperinsulinaemia/insulin resistance is the major risk factor for ASCVD. And decreased high-density lipoprotein (HDL) levels are usually the main changes of blood lipid spectrum of the hyperinsulinaemia/insulin resistance. But the exact mechanism is not fully clearly understood. This study is aimed to discuss effects of high insulin environment on HDL generation-related functional protein ATP binding cassette transporter A1 (ABCA1), and explore mechanisms of its specific signaling pathway so as to provide a new basic medical evidence for the intervention of residual cardiovascular risks.

Methods: In this experiment, 3T3-L1 adipocytes were induced to differentiation and maturation. Mature 3T3-L1 adipocytes were taken as the objects and stimulated by different concentrations of insulin (0 nmol/L, 10 nmol/L, 102 nmol/L, 103 nmol/L) for 12 hours. The endpoint of the experiments was the degradation, whereas the selective inhibitor Raf inhib I of MAPK signaling pathway protein degradation by IRS/PI3K/Akt signaling pathway, which is not conducive to reverse cholesterol transport (RCT). However, Many studies have suggested that the formation of HDL is achieved by related genes. Several cell cholesterol transport genes are played close attention. To investigate ATP binding cassette transporters (ABCA1 and ABCG1) gene expression in peripheral blood leukocytes from subjects with low plasma HDL cholesterol levels.

Results: In the Ad-shRNA-FOXO3a group, the results were counter-productive. (CDK2), cyclin D1 and proliferating cell nuclear antigen (PCNA).

Conclusions: We demonstrate for the first time that insulin promotes the ABCA1 protein degradation by IRS/PI3K/Akt signaling pathway, which is not conducive to ABCA1-mediated cholesterol efflux and nascent HDL generation in 3T3-L1 adipocytes.