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KNOCKDOWN OF REPRESSOR ACTIVATOR PROTEIN 1 FACILITATED FOAM CELL FORMATION BY AUGMENTING CHOLESTEROL UPTAKE

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OBJECTIVES: Repressor activator protein 1 (Rap1) is a telomere-associated protein with telomeric-regulating functions, but it also displays non-telomeric functions and regulates metabolism. The expression of Rap1 is enhanced in atherosclerotic plaques. Presence of foam cells is an indicator of plaque buildup. This study aims to investigate if Rap1 knockdown has an effect on foam cell formation and cholesterol transport.

METHODS: Knockdown of Rap1 was established in macrophage cells derived from the human monocytic leukemia cell line (THP-1) using small interfering ribonucleic acid (RNA). Knockdown and wild-type cells were transformed into foam cells by incubating with 50 μg/mL acetylated low-density lipoprotein for 72 hours. Then the cells were stained with oil red O to assess the efficiency of foam cell formation, or subjected to RNA extraction to study the expression of key genes involved in cholesterol transport by quantitative polymerase chain reaction.

RESULTS: Rap1 knockdown cells accumulated 40.9%±14.7% more intracellular lipids ($P<0.05$). The mRNA expression of peroxisome proliferator-activated receptors alpha (PPARα) increased by 3.04-fold ($P<0.05$), while peroxisome proliferator-activated receptor-gamma coactivator (PGC1α) was significantly reduced by 89%±2.2% ($P<0.03$) in Rap1 knockdown cells as compared with wild-type cells. The mRNA expression of scavenger receptor A (SR-A) in Rap1 knockdown increased by 4.79-fold ($P<0.02$), while there is no significant change in the expression of another cholesterol uptake receptor − cluster of differentiation 36 (CD36), and other efflux-associated genes − including ATP binding cassettes A1 and G1 (ABCA1 and ABCG1) and scavenger receptor B1 (SR-B1) was observed.

CONCLUSIONS: Rap1 knockdown enhanced foam cell formation and significantly affected the mRNA expression of master transcriptional regulators − PPARα and PGC1α. Effective foam cell formation is accounted by increased SR-A expression and hence enhanced cholesterol uptake, which warrants further studies to confirm such postulation.