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SR-BI Associates with ABCG1 and Inhibits ABCG1-mediated Cholesterol Efflux from Cells to HDL3

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Reverse cholesterol transport (RCT) is assumed to play a critical role in the pathogenesis of atherosclerosis. Cellular cholesterol efflux, by which cholesterol is transported from peripheral cells to high-density lipoprotein (HDL) acceptor molecules, is the first step of RCT. ATP-binding cassette transporter (ABC) A1, G1 and scavenger receptor-BI (SR-BI) are three important mediators of cholesterol efflux. ABCA1 exports cholesterol and phospholipid to lipid-poor apolipoproteins and initiates HDL formation by lipidating apolipoproteinA-I (apoA-I). A great line of reports have indicated a synergistic relationship between ABCA1 and ABCG1 in peripheral tissues, where ABCA1 lipidates any lipid-poor/free apoA-I to generate nascent or pre - β-HDL. These particles in turn may serve as substrates for ABCG1-mediated cholesterol export. However, the relations between SR-BI and two ABC transporters are not well understood. The current study was undertaken to compare the roles of SR-BI and two ABC transporters in promoting mass cholesterol efflux and determine a possible interaction between the SR-BI- and ABC transporter-mediated cholesterol efflux pathways in vitro. The single and combined effects of scavenger receptor-BI (SR-BI), ATP-binding cassette transporter (ABC) A1 and G1 on cholesterol efflux from Chinese Hamster Ovary (CHO) cells were investigated. When apolipoproteinA-I (apoA-I) was used as an acceptor, ABCA1 overexpression led to an increase in total cholesterol (TC) in medium which attributable to a 2-fold increase in free cholesterol (FC) content. When high-density lipoprotein 3 (HDL3) was used as an acceptor, SR-BI overexpression not only promoted FC efflux, but also promoted the uptake of cholesteryl ester (CE) into cells, resulting in no TC varieties in medium. Overexpression of ABCG1 increased both the FC and CE levels in medium. However, when apoA-I and HDL3 were both used as acceptors, coexpression of SR-BI has no effect on ABCA1-mediated increased FC and TC accumulation in medium. Interestingly, coexpression of SR-BI with ABCG1 blocked the ABCG1-mediated cholesterol efflux to HDL3, mostly by promoting the reuptake of CE from the medium. Furthermore, co-immunoprecipitation experiments revealed that SR-BI interacted with ABCG1 in BHK cells overexpressing ABCG1 and SR-BI. In conclusion, we found SR-BI associates with ABCG1 and inhibits ABCG1-mediated cholesterol efflux from cells to HDL3.

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