

Methods The normal HMCs and the HMCs were transfected with DNA plasmid or SCAP siRNA by electroporation to overexpress or knockdown SCAP. Intracellular lipid level of HMCs was assessed by Oil Red O staining and quantitative measurement intracellular cholesterol ester. Total cellular RNA was isolated from cells for detecting SCAP, LDLr, HMG-CoAR mRNA levels using real-time PCR; nSREBP-2 (N terminal of SREBP2), LDLr, HMG-CoAR protein expression were examined by western blotting.

Results IL-1b or SCAP overexpression increased intracellular lipid droplets accumulation and cholesterol ester level with a high concentration of LDL. SCAP gene silence decreased intracellular lipid droplets accumulation and cholesterol ester level under inflammatory stress. IL-1b or SCAP overexpression overrode SCAP, nSREBP-2, LDLr, HMG-CoAR suppression induced by a high concentration of LDL. SCAP gene silence decreased LDLr and HMG-CoAR mRNA expression and intracellular lipid level under inflammatory stress.

Conclusions IL-1b or SCAP overexpression disrupts cholesterol mediated LDLr and HMG-CoAR feedback regulation, thereby increasing nSREBP-2, LDLr and HMG-CoAR expression even in the presence of high concentration of LDL. SCAP gene silence decreases LDLr, HMG-CoAR mRNA expression and intracellular lipid droplets accumulation under inflammatory stress. These results suggest SCAP is a key node on lipid accumulation and foam cell formation; it would be a new therapy target under inflammatory stress of glomerular atherosclerosis.

GW23-e2159

INFLAMMATORY STRESS EXACERBATES CHOLESTEROL ACCUMULATION BY DISRUPTING SCAP IN HUMAN MESANGIAL CELLS

doi:10.1136/heartjnl-2012-302920a.163

¹Xu Xue-lian, ²Lei Han. ¹Department of Cardiology, University Town Hospital, Chongqing Medical University, Chongqing, China; ²Department of Cardiology, The First Affiliated Hospital, Chongqing Medical University, Chongqing, China

Objectives We have demonstrated that inflammation play a significant m role in glomerulosclerosis and its similarity to atherosclerosis is well described. The aim of this study was to investigate the dysregulation of SCAP pathway including cholesterol exogenous up taking via LDL receptor, endogenous synthesis via HMG-CoA reductase in human kidney mesangial cell line (HMCs) cells induced by inflammatory cytokines.