GW23-e0812 **INCREASED ABCG1 EXPRESSION PROTECTS AGAINST ENDOTHELIAL INJURY INDUCED BY TNFα**

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Objectives Endothelial dysfunction is a key feature of early atherosclerosis lesions. ATP binding cassette transporter G 1(ABCG1), a regulator of reversing cholesterol efflux, is highly expressed in endothelial cells. It has been shown that ABCG1 deficiency in mice promotes endothelial activation and upregulation of ABCG1 seems to preserve endothelial function. The study was to further determine the role of ABCG1 in endothelial injury induced by TNF-a.

Methods Human Umbilical Vein endothelial cells (HUVECs) were incubated in the presence of 10 ng/ml TNF-α and/or liver X receptor (LXR) agonist T0901317 for 0, 12 and 24 h. Real-time PCR and western blot were used to measure ABCG1 expression. The nitric oxide synthase (NOS) activity was determined by quantifying the rate of the conversion of [3H] l-arginine to [3H] l-citrulline and NO concentration in cultured media was measured by nitrate reeducates assay. Intracellular malonaldehyde (MDA) content and reactive oxygen species (ROS) were measured to show oxidative stress levels in TNF-α treated HUVECs.

Results 10ng/mL TNF-α decreased both ABCG1 expression and NOS activity, and induced intracellular oxidative stress in a time-dependent manner in cultured endothelial cells. Moreover, T0901317, a LXR agonist, significantly increased the ABCG1mRNA expression by 3 times when 5 μg/ml T0901317 treated HUVECs for 24 h. With upregulation of ABCG1, decreased NOS activity induced by TNF-α was reversed about 47%, and concomitant NO levels was reversed by 30% when treatment of the cells with the T0901317. In addition, increased MDA content by TNF-α was abolished by 30% and increased intracellular ROS was significantly decreased with the use of T0901317.

Conclusions These results suggest that increased ABCG1 expression play an important role in preventing from oxidative stress and endothelial injury induced by TNF-α. Upregulation of ABCG1 has a protective effect on endothelial function.

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