ATP-binding cassette transporter ABCA1, also known as the cholesterol efflux regulatory protein is a protein which in humans is encoded by the ABCA1 gene. This transporter is a major regulator of cellular cholesterol and phospholipid homeostasis.

In brain, microvascular endothelial cells are exposed to various forces, including shear stress (SS). However, little is known about the effects of high shear stress (HSS) on human brain microvascular endothelial cells (HBMECs) and the underlying mechanism. The cholesterol efflux regulator ATPbinding cassette subfamily A member 1 (ABCA1) has been demonstrated to exert protective effect on HBMECs. However, whether ABCA1 is involved in the mechanism underneath the effect of HSS on HBMECs remains obscure. In a study, a series of experiments were performed to better understand the effect of HSS on cellular processes of HBMECs and the possible involvement of ABCA1 and PI3K/Akt/eNOS in the underlying mechanisms.

HBMECs were subjected to physiological SS (PSS) or high SS (HSS). Cell migration was evaluated using Transwell assay. Apoptotic HBMECs were detected by flow cytometry or caspase3/7 activity. IL-1 $\beta$ , IL-6, MCP-1 and TNF- $\alpha$  levels were measured by ELISA. RT-qPCR and western blotting were used for mRNA and protein expression detection, respectively. ROS and NO levels were detected using specific detection kits. Compared to PSS, HBMECs exhibited decreased cell viability and migration and increased cell apoptosis, increased levels of inflammatory cytokines, and improved ROS and NO productions after HSS treatment. Moreover, HSS downregulated ABCA1 but upregulated the cholesterol efflux-related proteins MMP9, AQP4, and CYP46 and activated PI3K/Akt/eNOS pathway. Overexpression of ABCA1 in HBMECS inhibited PI3K/Akt/eNOS pathway and counteracted the deleterious effects of HSS. Contrary effects were observed by ABCA1 silencing. Inhibiting PI3K/Akt/eNOS pathway mimicked ABCA1 effects, suggesting that ABCA1 protects HBMECs from HSS via PI3K/Akt/eNOS signaling.

These results advanced our understanding on the mechanisms of HSS on HBMECs and potentiated ABCA1/PI3K/Akt/eNOS pathway as therapeutic target for cerebrovascular diseases <sup>1)</sup>.

## 1)

Li Z, Li JN, Li Q, Liu C, Zhou LH, Zhang Q, Xu Y. Cholesterol efflux regulator ABCA1 exerts protective role against high shear stress-induced injury of HBMECs via regulating PI3K/Akt/eNOS signaling. BMC Neurosci. 2022 Nov 5;23(1):61. doi: 10.1186/s12868-022-00748-2. PMID: 36335301.

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