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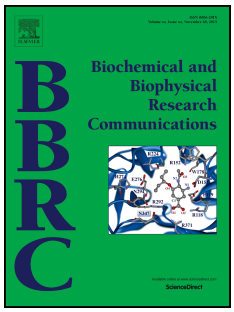

Sevoflurane prevents lipopolysaccharide-induced barrier dysfunction in human lung microvascular endothelial cells: Rho-mediated alterations of VE-cadherin

Yiran Huang, Qindong Tan, Rui Chen, Biao Cao, Wenhong Li

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Sevoflurane prevents lipopolysaccharide-induced barrier dysfunction in human microvascular endothelial cells: Rho-mediated alterations of VE-cadherin

Yiran Huang[1]*, Qindong Tan[2], Rui Chen[1], Biao Cao[1], Wenhong Li[1]

1. Department of Anesthesiology, the 157 Affiliated Hospital, General Hospital of Guangzhou Military Command of PLA, Guangzhou 510510, P.R. China.
2. Department of Anesthesiology, Xiangya Hospital, Central South University, Changsha, 410008, Hunan, P.R. China.

*Corresponding author at: Department of Anesthesiology, 157th Hospital Affiliated to Guangzhou General Hospital of Guangzhou Military Command of PLA, Guangzhoudadaobei Road, Guangzhou 510510, P.R. China
E-mail addresses: Hyr88955@163.com, huangyiran.gz@gmail.com

Abstract:
Acute lung injury (ALI) mainly occurs as increased permeability of lung tissue and pleural effusion. Inhaled anesthetic sevoflurane has been demonstrated to alleviate lung permeability by upregulating junction proteins after ischemia-reperfusion. However, the exact mechanisms of its protective effect on reperfusion injury remain elusive. The aim of this study was to assess possible preconditioning with sevoflurane in an *in vitro* model of lipopolysaccharide (LPS)-induced barrier dysfunction in human lung microvascular endothelial cells (HMVEC-Ls). In this study, HMVEC-Ls were exposed to minimum alveolar concentration of sevoflurane for 2 h. LPS significantly increased the permeability of HMVEC-L. Moreover, the distribution of junction protein, vascular endothelial (VE)-cadherin, in cell-cell junction area and the total expression in HMVEC-Ls were significantly decreased by LPS treatment. However, the abnormal distribution and decreased expression of VE-cadherin and hyperpermeability of HMVEC-Ls were significantly reversed by pretreatment with sevoflurane. Furthermore, LPS-induced activation of the RhoA/ROCK signaling pathway was significantly inhibited with sevoflurane. Such activation, abnormal distribution and decreased expression of VE-cadherin and hyperpermeability of HMVEC-Ls were significantly inhibited with sevoflurane pretreatment or knockdown of RhoA or ROCK-2. In conclusion, sevoflurane prevented LPS-induced rupture of HMVEC-L monolayers by suppressing the RhoA/ROCK-mediated VE-cadherin signaling pathway. Our results may explain, at least in part, some beneficial effects of sevoflurane on pulmonary dysfunction such as ischemia-reperfusion injury.

Key words: Acute lung injury, permeability, human lung microvascular endothelial cells, sevoflurane, RhoA/ROCK signaling pathway, VE-cadherin

1. Introduction: