Title	Endothelium-selective activation of AMP-activated protein kinase improves re-endothelialization and vascular function via induction of heme oxygenase-1 in diabetic mice
Author(s)	Li, FYL; Lam, KSL; Wang, Y; Vanhoutte, PM; Xu, A
Citation	The 10th Anniversary EDHF Meeting (EDHF 2012), Vaux-de-Cernay, France, 27-30 June 2012. In Journal of Vascular Research, 2012, v. 49 suppl. 2, abstract no. 32
Issued Date	2012
URL	http://hdl.handle.net/10722/165452
Rights	Creative Commons: Attribution 3.0 Hong Kong License

ENDOTHELIUM-SELECTIVE ACTIVATION OF AMP-ACTIVATED PROTEIN KINASE IMPROVES RE-ENDOTHELIALIZATION AND VASCULAR FUNCTION VIA INDUCTION OF HEME OXYGENASE-1 IN DIABETIC MICE

Francois Y L Li, Karen S L Lam , Yu Wang, Paul M Vanhoutte, and Aimin Xu
Medicine and Pharmacology and Pharmacy, University of Hong Kong, China

Reduced number and impaired function of endothelial progenitor cells (EPCs) exacerbate vascular injury in diabetes. As AMP-activated kinase (AMPK) is a target of several anti-diabetic and cardiovascular drugs, this study investigated whether endothelium-selective activation of AMPK prevents diabetes-induced impairment in endothelial repair and vasoreactivity by improving EPC functions. Transgenic mice with endothelium-selective expression of a constitutively-active (CA-) AMPK were generated and rendered diabetic with streptozotocin. Relaxation and re-endothelialization of carotid arteries and circulating EPC numbers were examined after wire-induced denudation. Bone marrow-derived EPCs were isolated to monitor their in vivo and in vitro functions. In comparison to wild type (WT) littermates, the CA-AMPK transgenic mice were resistant to diabetes-induced impairment in re-endothelialization and endothelium-dependent relaxation in injured carotid arteries. These changes in the transgenic mice were accompanied by increased mobilization of EPCs and enhanced incorporation of EPCs into injured vessel walls. Furthermore, EPCs from the transgenic mice exhibited augmented adhesion, migration and tubule formation capacities. At the molecular level, the expression of heme oxygenase (HO)-1 and secretion of stromal cell-derived factor (SDF)-1α were up-regulated in EPCs derived from the transgenic mice, whereas AMPK-mediated elevations of serum SDF-1α levels and circulating EPC numbers were abrogated by pharmacological inhibition of HO-1 in mice. Thus, endothelium-specific AMPK activation is sufficient to protect against diabetes-induced vascular injury by promoting EPC functions and re-endothelialization via up-regulation of HO-1 and SDF-1α.