BMC Pharmacology

Oral presentation

Open Access

Regulation of PKG expression in vascular smooth muscle cells

Ying Zeng and Renate B Pilz*

Address: University of California at San Diego, USA

Email: Renate B Pilz* - rpilz@ucsd.edu

* Corresponding author

from 2nd International Conference of cGMP Generators, Effectors and Therapeutic Implications
Potsdam, Germany, 10–12 June, 2005

Published: 16 June 2005

BMC Pharmacology 2005, **5**(Suppl 1):S16 doi:10.1186/1471-2210-5-S1-S16

Type I cGMP-dependent protein kinase (PKG I) plays a major role in vascular homeostasis mediating smooth muscle relaxation in response to nitric oxide, but relatively little is known about the regulation of PKG I expression. Rho family GTPases (including RhoA and Rac1) are regulated by growth factors and cell adhesion molecules and modulate cell proliferation and motility as well as gene expression. We found opposing effects of RhoA and Rac1 on PKG I expression: (i) cell density-induced increases in PKG I expression occurred under conditions of high Rac1 activity and low RhoA activity in post-confluent cells; (ii) activation of RhoA by calpeptin suppressed PKG I, whereas down-regulation of RhoA by siRNA increased PKG I expression; and (iii) PKG I promoter activity was suppressed in cells expressing active RhoA or Rho-kinase, but was enhanced in cells expressing active Rac1, a dominant negative RhoA, or p120 catenin. Sp1 consensus sequences in the PKG I promoter were required for Rho regulation and bound nuclear proteins in a cell density-dependent manner, including the Krüppel-like factor 4 (KLF4). KLF4 was identified as the major trans-acting factor at two proximal SP1 sites; active RhoA suppressed KLF4 DNA binding and transactivation potential on the PKG I promoter. We propose a novel mechanism for cell density-dependent regulation of gene expression involving Rho and Rac; moreover, suppression of PKG I expression by RhoA may explain the decrease in vascular smooth muscle cell PKG I levels found in some models of hypertension and vascular injury.