Activation of cGKI in primary vascular smooth muscle cells promotes adhesion

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Nitric oxide (NO) regulates many cellular functions via the cGMP/cGMP-dependent protein kinase type I (cGKI) pathway. The analysis of isolated vascular smooth muscle cells (VSMCs) suggested that activation of cGKI can promote cell “growth”, in contrast to many studies on passaged smooth muscle cell lines that reported an anti-proliferative role for cGKI. Stimulation of primary but not subcultured wild type VSMCs with 8-Br-cGMP strongly promotes “growth”. This effect depends on cGKI since it is absent in cGKI-deficient cells. Confirming the previous results by others, cGKI was found to mediate an anti-proliferative effect in repeatedly passaged VSMCs. To resolve the underlying mechanism of the growth promoting effect of cGKI, the detailed analysis of proliferation, apoptosis, and cytoskeletal dynamics indicated that 8-Br-cGMP increased cell adhesion in primary wild type VSMCs. This pro-adhesive effect of cGKI is mediated via an inhibition of the RhoA/Rho kinase pathway. The inhibition of the RhoA/Rho kinase pathway enhanced b1 and b3 integrin mediated adhesion. In conclusion, a yet unknown effect for cGKI-signalling in primary VSMCs was revealed. Furthermore, these results show that the opposing effects of cGK-signalling depend on the phenotypic context of VSMC.

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