Angiotensin II Inhibits Inward Rectifier K^+ Channels in Rabbit Small-diameter Coronary Arterial Smooth Muscle Cells through Ca^{2+}-dependent Protein Kinase C

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We investigated the effects of the vasoconstrictor angiotensin (Ang) II onthe whole cell inward rectifier K^+ (Kir) currents of smooth muscle cells that were isolated enzymatically from rabbit small-diameter (<100 μm) coronary artery. Ang II inhibited Kir currents in a dose-dependent manner (half inhibition value: 154 nM). Pretreatment with the phospholipase C (PLC) inhibitor (U73122) and protein kinaseC (PKC) inhibitors (GF 109203X and staurosporine) prevented the Ang II-induced inhibition of Kir currents. The PKC activator, PDBu reduced Kir currents. The inhibitory effect of Ang II was reduced by both intra- and extracellular Ca^{2+} free conditions and Gö6976 (1 μM), which is selective for Ca^{2+}-dependent isoforms (α and β) of PKC. However, the inhibitory effect of Ang II was unaffected by a selective peptide inhibitor of the translocation of the isoform of PKC (PKC_ζ TIP, 40 μM). The AT1-receptor antagonist CV-11974 (Candesartan, 1μM) prevented the Ang II-induced inhibition of Kir currents. From these results, we conclude that Ang II inhibits Kir channels through AT_1 receptor by activation of PKC (α and/or β).

Key Words : angiotensin II, protein kinase C, coronary artery