PKCbI mediates the inhibition of P2Y receptor-induced inositol phosphate formation in endothelial cells

陳炳常

Chen BC and Lin WW

摘要

Abstract

1 Bovine pulmonary artery endothelium (CPAE) expresses phospholipase C (PLC)-linked P2Y(1) and P2Y(2) receptors, for them 2-methylthio-ATP (2 MeSATP) and UTP are respective agonists. Here, we have investigated the particular protein kinase C (PKC) isoform(s) responsible for the inhibition of P2Y(1) and P2Y(2) receptor-evoked inositol phosphate (IP) formation by phorbol 12-myristate 13-acetate (PMA).2 Although short-term (20 min) pretreatment of cells with PMA attenuated 2MeSATP- and UTP-induced phosphoinositide (PI) breakdown, this inhibition was lost after 15 h. Preincubation with PMA for 24 h, on the contrary, potentiated 2MeSATP and UTP responses. The TP formation stimulated by NaF was unaltered by PMA pretreatment.3 Western blot analysis showed that treatment of CPAE with PMA resulted in a rapid translocation of PKC isoform beta I, epsilon and mu, but not lambda, from the cytosol to the membrane fraction.4 Pretreatment of the selective PKC inhibitor Ro 31-8220 attenuated the inhibitory effect of PMA on IP formation. Go 6976 (an inhibitor of conventional PKC alpha, beta and gamma) and LY 379196 (a selective PKC beta inhibitor) also dose-dependently inhibited the PMA-mediated desensitization.5 Transfection of PKC beta-specific antisense oligonucleotide reduced PKC beta I protein level and inhibited PMA- mediated PI reduction.6 RT-PCR analysis showed that PMA treatment for 4-24 h up-regulated P2Y(1) and P2Y(2) receptors at the mRNA levels.7 These results suggest that PKC beta I may exert a negative feedback regulation on endothelial P2Y(1) and P2Y2 receptor-mediated PI turnover. The down- regulation of PKC beta I and enhanced P2Y receptor expression together might contribute to the late PI enhancing effect of PMA.