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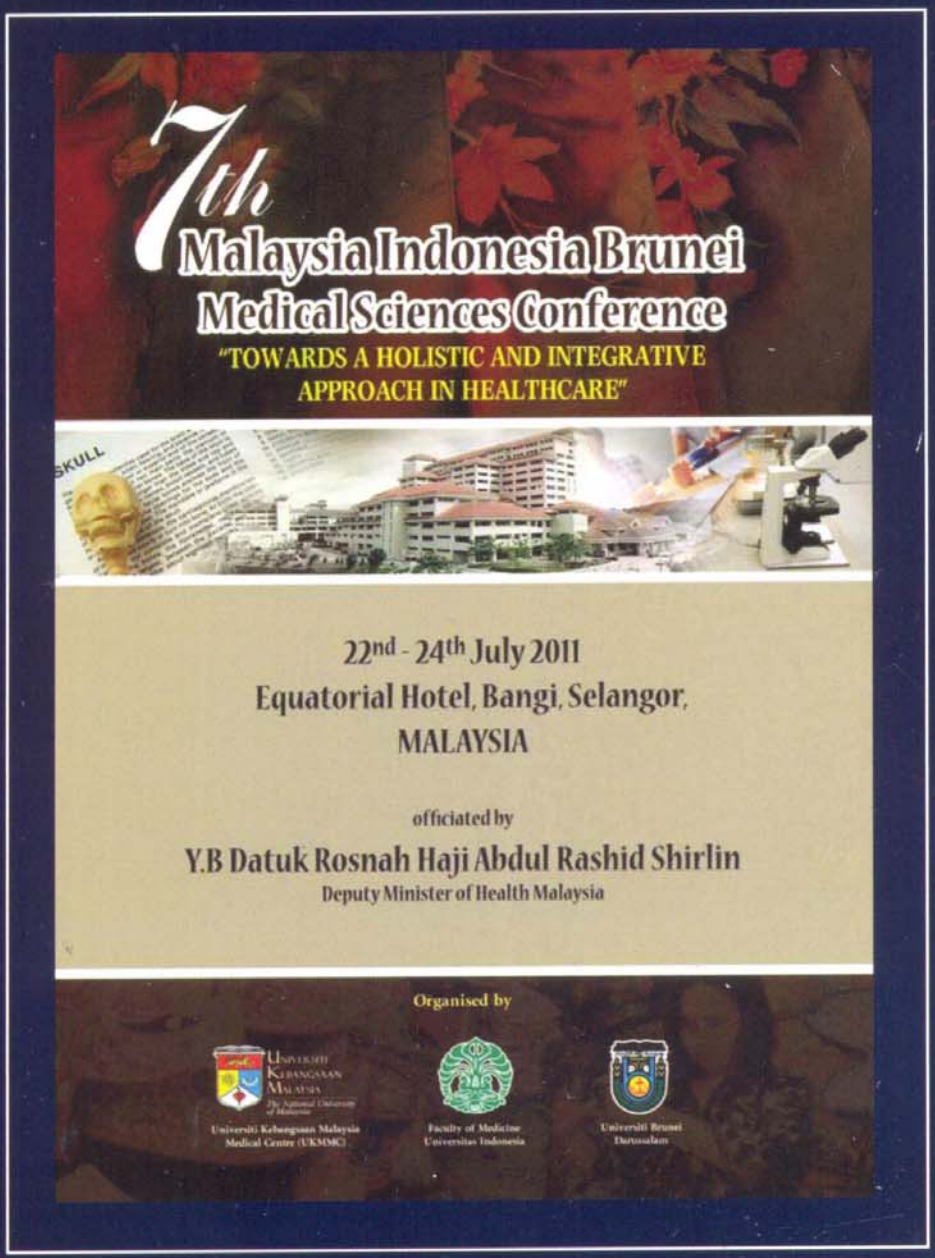

THE CONTRIBUTION OF PROTEIN KINASE C IN P2Y RECEPTOR-EVOKED VASOCONSTRICTION OF RAT PULMONARY ARTERY

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Background:
P2Y receptors are a family of G protein-coupled receptors that are activated by endogenous nucleotides, such as UTP and UDP. In the vascular system these agonists induce vasodilation via endothelial P2Y receptors and vasoconstriction via P2Y receptors located on arterial smooth muscle cells. The intracellular signalling mechanisms by which vasoconstriction is induced are poorly characterised, so the aim of this study was to determine the role of protein kinase C (PKC) in nucleotide-evoked vasoconstriction of rat small intrapulmonary artery (SPA) and whether this kinase mediates via Ca^{2+}-sensitisation of the contractile proteins.

Materials and Methods:
Both intact and membrane-permeabilised SPAs were used in this study. Membrane-permeabilisation was achieved by incubating the arteries with 50μg/mL α-toxin. The endothelium of the arteries were removed by rubbing the vessel lumen gently with a thread, and were mounted under isometric conditions in 1ml baths at 37°C and a resting tension of 0.5g. Tension was recorded by Grass FT 03 transducers connected to a Powerlab/4e system (AD Instruments). Contractions were elicited by addition of agonists to the bath.

Results:
In intact arteries, UTP and UDP (both 300 □M) evoked slowly developing contractions, which reached a peak within 5 minutes and decayed slowly in the continued presence of agonist until the tension reached a plateau. PKC have been implicated in Ca^{2+}-sensitisation of smooth muscle, therefore we investigated the effects of its selective inhibitor, GF109203X. Pre-incubation for 15 minutes or post-addition (after contractions reached its peak) with GF109203X (10 □M) had caused moderate inhibition of UTP- and UDP-evoked contractions. In membrane-permeabilised preparations, UTP and UDP also induced vasoconstriction, but were unaffected by GF109203X.

Conclusion:
These results indicate that PKC is involved in P2Y receptor-mediated contraction of rat pulmonary artery, via non-Ca^{2+} sensitisation and how it contributes to UTP- and UDP-induced contractions remains to be determined.

Keywords:
P2Y receptors, vasoconstriction, arterial smooth muscle