

**ROLE OF PROTEIN KINASE C IN THE REGULATION OF PUMPING
ACTIVITY IN BOVINE MESENTERIC LYMPHATIC VESSELS****H. Rodela, Z. Yuan, M.G. Johnston**

Trauma Research Program and Department of Pathology, Sunnybrook Health Science Centre,
University of Toronto, Canada

ABSTRACT

We investigated the role of protein kinase C (PKC) in regulating the lymphatic myogenic response. Bovine mesenteric lymphatics were suspended in an organ bath with inflow and outflow ends cannulated. Input was provided from a reservoir filled with Krebs solution. The PKC activator phorbol 12-myristate 13-acetate (PMA) inhibited pumping significantly whether tested at a fixed pressure or as pressures were raised in 2 cm H₂O increments (50% inhibition achieved at $4.6 \times 10^{-8}M$). The inactive phorbol ester (4- α -PMA) had no effect. The specific PKC inhibitors calphostin (10^{-9} to $10^{-7}M$) or chelerythrine (10^{-8} to $10^{-6}M$) had no significant effect on pumping. However, chelerythrine ($10^{-6}M$) was capable of reversing the inhibitory effects of PMA ($5 \times 10^{-8}M$). PKC activation is believed to inhibit nitric oxide (NO) production in some blood vessels, and previous work from our laboratory has demonstrated that NO is important in facilitating pumping activity in bovine lymphatics. We observed that sodium nitroprusside (sNP, $10^{-7}M$) or L-arginine ($10^{-4}M$), reversed the depressor effects of PMA. These results suggest that PKC may not be involved in regulating the vessel's contractile response to pressure-induced stretch. However, the data with PMA suggest that these ducts contain PKC. PKC activation depresses lymphatic pumping and this effect may be mediated in part, by inhibition of