

Effects of PKC α activation on Ca $^{2+}$ pump and K(Ca) channel in deoxygenated sickle cells

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We have previously shown that a pretreatment with phorbol 12-myristate 13-acetate (PMA), an activator of protein kinase C (PKC), reduced deoxygenation-induced K $^{+}$ loss and Ca $^{2+}$ uptake and prevented cell dehydration in sickle anemia red blood cells (SS cells) (H. Fathallah, E. Coezy, R.-S. De Neef, M.-D. Hardy-Dessources, and F. Giraud. *Blood* 86: 1999- 2007, 1995). The present study explores the detailed mechanism of this PMA- induced inhibition. The main findings are, first, the detection of PKC α PKC β in normal red blood cells and the demonstration that both isoforms are expressed at higher levels in SS cells. The α -isoform only is translocated to the membrane and activated by PMA and by elevation of cytosolic Ca $^{2+}$. Second, PMA is demonstrated to activate Ca $^{2+}$ efflux in deoxygenated SS cells by a direct stimulation of the Ca $^{2+}$ pump. PMA, moreover, inhibits deoxygenation-induced, charybdotoxin-sensitive K $^{+}$ efflux in SS cells. This inhibition is partly indirect and explained by the reduce