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ARTICLES

A comparison of the effects of concanavalin-A and tetradecanoylphorbol acetate on the modulation of parathyroid function by extracellular calcium and neomycin in dispersed bovine parathyroid cells

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Ca2+ and other polyvalent cations as well as polycations, such as neomycin, produce similar effects on intracellular second messengers and PTH release in dispersed bovine parathyroid cells, but it is unclear whether all of these agents share the same mechanism of action. The lectin Concanavalin-A (Con-A) and the activator of protein kinase-C tetradecanoylphorbol acetate (TPA) blunt the effects of elevated extracellular calcium (Ca2+) concentrations on several aspects of parathyroid function, including PTH release, the cytosolic calcium concentration, and the accumulation of cAMP and inositol phosphates. In the present studies we used these two agents as well as pertussis toxin as probes to investigate further whether neomycin acts on parathyroid cells through the same receptor-like mechanism used by extracellular Ca2+ to regulate parathyroid function. Con-A and TPA both enhanced PTH release by about 2-fold at 0.5-1 x 10(-4) M neomycin, concentrations that inhibited PTH release to an extent (40-50%) similar to that seen with high (1.5-2 mM) Ca2+. Con-A also reduced the inhibition of agonist-stimulated cAMP accumulation by the same concentrations of neomycin. Conversely, Con-A and TPA produced 70-80% decreases in the cytosolic calcium concentration transient and the accumulation of inositol phosphates stimulated by neomycin. The effects of these two agents on neomycin-regulated parathyroid function were similar in magnitude to their actions on the modulation of these same parameters by extracellular Ca2+. Pertussis toxin, however, which we have previously shown to block the inhibitory effects of high Ca2+ and neomycin on cAMP accumulation, had no effect on the inhibition of PTH release by these two agents. These results provide further indirect evidence that polyvalent cations and polycations act on the parathyroid cell through related pathways, which probably involve cell surface moieties containing carbohydrate(s).