Differential Activation of C6 Glioma Protein Kinase C Isoforms by a Phorbol Ester and Trimethyltin [MAS]

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Trimethyltin (TMT) is a potent neurotoxin that produces delayed, irreversible damage. Damage is usually not evident for 48 hours. Activation of Protein Kinase C (PKC) has been implicated in the neurotoxicity produced by TMT. In a neuronal cell line, TMT causes translocation and activation of PKC within 30 minutes. We used a rat C6 glioma cell line to determine the ability of PKC to translocate in the presence of phorbol 1 2-myristate 1 3-acetate (PMA) or TMT. Further studies were conducted to differentiate specific isozyme involvement. Isoforms were separated by gel electrophoresis and identified by Western blotting with specific monoclonal antibodies. We have identified the presence of the α, β, γ, δ, ε, θ, ζ, λ, and μ isozymes

in our C6 cell line. These isozymes of PKC were evaluated on their responses to PMA and TMT exposure. All of the cPKC and nPKC isoforms translocated to the cell membrane following PMA exposure. The aPKC isozymes were not translocated by this treatment. TMT exposure for up to 1 hour did not translocate any of the PKC isoforms. PKCs α, δ, and ζ were also evaluated after 24 hours of treatment with PMA and TMT. PKCs a and d had down-regulated with the PMA treatment, while no translocation was detected with TMT treatment on any isoform.