PALLADACYCLES INDUCE THE OPENING OF AN UNREGULATED MITOCHONDRIAL PERMEABILITY TRANSITION PORE

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The mitochondrial permeability transition (MPT) is classically described as a Ca^{2+}-dependent and CsA-sensitive permeability transition pore (PTP) opening triggered by the assembly of mitochondrial membrane protein frequently promoted thiol cross-linkage. MPT is involved with the triggering of apoptosis or necrosis induced by a wide variety of stimulus. Recently it was described that palladacycles care able to induce apoptosis in a melanoma cell line. In this work, we evaluated the effects of palladacycles derived from N,N-dimethyl-1-phenethylamine (dmpa) and 1,2-bis(diphenylphosphine)ethanebis (dppe) on the MPT to investigate a possible participation of the mitochondria in the pro-apoptotic action of these drugs. Palladacycles induced a Ca^{2+}-independent CsA-insensitive PTP opening that was prevented by pre-incubation with DTT. These effects of palladacycles were accompanied by a decrease in the content of reduced mitochondrial membrane protein thiol groups without the presence of protein aggregates in SDS-PAGE, lipid peroxidation and GSH depletion. Thus, the ability of palladacycles to induce PTP could be assigned to the reaction with the thiol groups of mitochondrial membrane proteins leading to their misfolding and assembly. The studies of palladacycle-induced PTP in isolated rat liver mitochondria will be extended to tumor cell lines. Keywords: TPM, palladacycles, protein thiol groups. Supported by FAPESP, CNPq, PAEP-UMC.