TPPS derivatives induce apoptosis on A375 human melanoma cells

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The incidence of malignant melanoma, one of the most aggressive and lethal type form of cutaneous cancer, is increasing more rapidly than any other tumours among Caucasians in most countries. Indeed, these cancer cells often acquire the capacity to evade the cytotoxic action of the current available chemotherapeutic drugs treatments. The study of the porphyrin derivatives, as potential anti-tumour drugs, based on the peculiarity of the porphyrin themselves to be accumulated in large amounts and to be retained for prolonged periods of time by a variety of malignant lesions, has been an interesting field of investigation in the last years. Therefore, we analysed the effects of TPPS derivatives treatment on the death of A375 human melanoma cells and we demonstrated that the $(Bu_2Sn)_2$TPPS and the $(Bu_3Sn)_4$TPPS complexes are clearly cytotoxic for melanoma cells. To examine the pathway of A375 cell death induced by the treatment with $(Bu_2Sn)_2$TPPS or $(Bu_3Sn)_4$TPPS compounds, DNA fragmentation analysis, Annexin V binding and PI uptake as well as caspases activation analysis by Western blot, were carried out. Both the $(Bu_2Sn)_2$TPPS and the $(Bu_3Sn)_4$TPPS compounds treatment of the A375 melanoma cells, lead the activation of caspase-8 and caspase-9 leading to caspase-3 activation. Furthermore, we found that both the TPPS derivatives, induce the cleavage of Bid and the release in the cytosol of the cytocrome c, suggesting that these compounds activate both the mitochondrial and the death-receptor apoptotic pathways that, working together, induce the apoptosis of melanoma cells.