

POSTER SESSION 9: Experimental therapies – preclinical

P9.2

Anticancer activity of melatonin analogues

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Introduction: Melatonin plays fundamental roles in diverse physiological functions ranging from the regulation of circadian rhythms to tumor inhibition, owing to its antioxidant, immunomodulatory and anti-aging properties [1-3]. The therapeutic potential of melatonin and its analogues [4,5] prompted us to investigate the in vitro and in vivo antitumor activity of new melatonin derivatives on melanoma and breast cancer cells, and explore the underlying molecular mechanisms.

Materials and methods: New indole melatonin analogues were synthesized and tested for their ability to inhibit proliferation and induce apoptosis in DX3 melanoma cells and in MCF-7 and MDA-MB231 breast cancer cells by viability and apoptosis assays. The oncostatic effect of melatonin analogues was also measured on a human melanoma xenograft mouse model. The changes in the expression levels of different proteins in cancer cell lines during treatment with melatonin analogues were investigated by Western blot analysis.

Results: The experiments revealed that the new melatonin analogues inhibited the growth of DX3 melanoma cells in a dose- and time-dependent manner. In addition, the study demonstrated that low concentrations (0.1 mM) of the melatonin analogue UCM 1037 exhibited antiproliferative and cytotoxic effects also in MCF-7 and MDA-MB231 breast cancer cells. The suppression of DX3 tumor growth by the melatonin analogues was further demonstrated in vivo in a xenograft mice model. Caspase 3 resulted to be involved in the pro-apoptotic mechanism induced by UCM 1037 in DX3 and MDA-MB231 cells. A decrease in the activation of both Akt and MAPK pathways was observed in breast cancer cells following UCM 1037 treatment.

Conclusions: This study describes melatonin derivatives showing promising antiproliferative and cytotoxic activity in melanoma and breast cancer cells.

References and acknowledgements:

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