

**ANTICANCER SONODYNAMIC TREATMENT WITH PORPHYRIN COMPOUNDS: INSIGHTS ON *IN VIVO* EFFICACY IN A SYNGENEIC RAT MODEL OF CANCER**

**Capucchio MT., Biasibetti E., Biasato I., Barbero P., Bruni I., Spuria L., Mioletti S., Foglietta F\*, Querio G.\*, Durando G.#, Canaparo R.\*, Serpe L.\***

*Department of Veterinary Sciences, University of Torino; \*Department of Drug Science and Technology, University of Turin; #National Institute of Metrological Research (INRIM), Torino, Italy*

**Introduction:** Sonodynamic therapy is an innovative anticancer approach based on the synergistic effect of ultrasound and chemical compound referred to as “sonosensitizer”. Aim of the study was to investigate the *in vivo* response of the sonodynamic treatment with ultrasound (US) and the natural porphyrin precursor, 5-aminolevulinic acid (ALA) in a syngeneic rat model of solid mammary tumor.

**Materials and Methods:** The effects were evaluated in 36 Fisher 344 rats subcutaneously implanted with  $1 \times 10^6$  MAT B III cells. 8 days post-inoculum, 24 rats were treated with: ALA (IV, 375 mg/kg) - 5 rats; ALA and US ( $1.5 \text{ Wcm}^{-2}$  at 1.8 MHz for 5 min) - 12 rats, and US only - 7 rats. 12 rats were used as controls. At day 11, all rats were sacrificed and the tumor masses removed and submitted for histological, immunohistochemical (Ki67 and caspase 3) and biomolecular (cleavage of PARP and LC3A/B expression by western blot analysis) investigations.

**Results:** All the tumors were characterized by a high mitotic index and a variable degree of apoptosis. Voluminous scattered necrotic areas were present. Immunohistochemical investigations showed a decrease of apoptotic cells in all treated tumors. Ki67 expression revealed a severe decrease of mitosis in treated tumors, but particularly in the masses treated by ALA and US. Moreover, a significant expression of the LC3A/B protein was observed in the sonodynamic treated tumors.

**Conclusions:** Preliminary data suggest a potential therapeutic effect of ALA and US, even if additional investigations are in progress to confirm this hypothesis.

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