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# Investigation of the antitumor activity of cisplatin loaded long-circulating and pH-sensitive liposomes in a breast cancer animal model

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Recent experimental data suggest that cisplatin (CDDP) may have an important role on triple negative breast cancer (TNBC) treatment. Besides the great antitumor efficacy of this anticancer agent, severe side effects and the possibility of resistance development limit the therapy. Previous studies of our research group have shown that the encapsulation of CDDP into long-circulating and pH-sensitive liposomes (SpHL-CDDP) was able to overcome cell resistance, reduce acute toxicity and enhance antitumor efficacy on Ehrlich tumor-bearing mice. Therefore, the purpose of this work was to develop a TNBC xenograft animal model, and evaluate the antitumor activity after SpHL-CDDP administration .

Firstly, Balb/c nude mice were inoculated with MDA-MB-231 cell line and the animals were divided into three groups when the tumor reached approximately 50mm$^3$. The animals were treated, intravenously, once a week for three weeks with 0.9% (w/v) saline, free CDDP (cumulative dose equal to 30mg/kg) or SpHL-CDDP (cumulative dose equal to 12mg/kg). Tumor volume was monitored twice a week using a caliper. Body weight of all animals was also monitored at the same time frame.

Control group presented an increase of the tumor volume (573%) during the entire experimental time. This increase was statistically higher from that observed for treated groups. No statistically difference on tumor growth was observed when treated groups (free CDDP or SpHL-CDDP) were compared. However, animals treated with free CDDP were the only ones to present loss of weight (~13%) at the end of the experiment, while animals treated with SpHL-CDDP or 0.9% (w/v) saline presented a slight gain of weight (~2%).

Results indicate that higher concentration of free CDDP is needed to reach the antitumor efficacy attained after SpHL-CDDP treatment. In addition, animals of the free CDDP treated group showed loss of weight indicating the appearance of toxicity. These findings demonstrate that the encapsulation allows administration of lower concentration of the drug leading to the same antitumor efficacy together with lesser side effects. In summary, these results suggest that SpHL-CDDP may be useful on TNBC treatment.