

## LIPOSOMAL DISULFIRAM: A NEW STRATEGY AGAINST PANCREATIC DUCTAL ADENOCARCINOMA?

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### **Purpose**

Disulfiram (DS) is a commercially available antialcoholism drug that has shown anticancer activity *in vitro* and *in vivo*. This activity is the result of several mechanisms such as inhibition of NFκB, inhibition of aldehyde dehydrogenase activity and ROS production. DS also potentiates the cytotoxicity of cyclophosphamide, cisplatin, 5-fluorouracil, paclitaxel and gemcitabine. Recent study shows that DS is a specific breast cancer stem cells targeting agent [1]. The aim of the present work is to prepare and to characterize new liposomal formulations able to encapsulate DS and change its pharmacokinetic behaviour to obtain high and specific release on pancreatic adenocarcinoma cells.

### **Methods**

We prepared two liposomal formulations composed of 1,2 dipalmitoyl-phosphatidyl-choline (DPPC) and cholesterol (CHOL). These formulations have different amounts of CHOL, (30 and 10%).

Liposomes were prepared by reverse-phase evaporation technique [2] and then characterized in terms of size, drug encapsulation efficiency and stability in storage (4°C) and physiological conditions (37°C).

### **Results**

Both formulations showed a mean diameter of 200 nm and were stable for 28 days in storage conditions. During storage, no appreciable liposome size change was detected and no drug precipitation or liposome aggregation was observed. The formulation with 10% of CHOL showed an higher drug encapsulation efficiency and released 50% of encapsulated DS after 48h in serum.

### **Conclusions**

Preliminary *in vitro* studies with PSN1 pancreatic cancer cell lines showed an higher cytotoxic activity of liposomal formulation in comparison to free DS. On the basis of these preliminary results the encapsulation of DS into liposomes can be a novel approach to extend its half life and translate it into cancer indication.

1 NC Yip, IS Fombon, P Liu, S Brown, V Kannappan, AL Armesilla, B Xu, J Cassidy, JL Darling and W Wang. Disulfiram modulated ROS–MAPK and NFκB pathways and targeted breast cancer cells with cancer stem cell-like properties. *British Journal of Cancer* (2011) 104, 1564 – 1574.

2 F Szoka F Jr, Papahadjopoulos D. Procedure for preparation of liposomes with large internal aqueous space and high capture by reverse-phase evaporation. *Proc Natl Acad Sci U S A.*(1978) 75, 4194-4198.