Reviewer's report

Title: Cytotoxic effects of Gemcitabine-loaded liposomes in human poorly differentiated thyroid carcinoma cells.

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Reviewer: Ferruccio Santini

Reviewer's report:

General
This is an interesting study describing the cytotoxic effect of gemcitabine-loaded liposomes on a cell-line derived from a thyroid cancer. Based on their results the Authors conclude that incorporation within liposomes greatly enhances the anti-tumoral activity of the drug.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1) The terms poorly differentiated thyroid cancer and anaplastic carcinoma are used as synonymous while they are not, the former maintaining several properties of the original cell, having a slower progression rate and exhibiting a different response to chemotherapy. The Authors should specify the characteristics of their cell-line to indicate the tumor type that they would eventually treat.
2) As far as I understand only one concentration of gemcitabine was used for liposome preparation. Thus, cells were not incubated with “liposomes containing the drug at different doses” (as stated in the manuscript, Cell cultures and cell viability, sentence nº 4) but with different concentrations of liposomes containing the same amount of gemcitabine. In this case, equal amounts of liposomes without gemcitabine should be used in parallel experiments as a control.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1) Liposome preparation. Last sentence: The freeze-dried liposomes were resuspended just before the experiment with 2 ml of the culture medium. Does this mean that free gemcitabine (about 10% of the total amount added) was not removed? If so this should be specified.
2) Figure 3: What does “relation of mortality” means? Is it mortality ratio over control like in Figure 1?
3) Micromolar is mistyped throughout the manuscript.

Discretionary Revisions (which the author can choose to ignore)
1) After liposome incorporation, increased delivery of gemcitabine within cells is somehow expected. Therefore, rather then testing a new hypothesis, this study confirms the well known effect of liposomal formulations on drug transport across cell-membranes. However, the main concern regarding selective cytotoxicity against neoplastic cells remains unsolved. As correctly pointed out by the Authors, in vivo studies using cancer models are required before proposing this system for clinical use. Significance of this study would be greatly improved if a panel of antineoplastic substances is tested. This would allow to indicate the drugs that are most effective after liposome incorporation and could then be used for subsequent in vivo testing.
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None