Reviewer's report

Title: The relation between deoxycytidine kinase activity and the radiosensitising effect of gemcitabine in eight different human tumour cell lines.

Version: 1 Date: 13 March 2006

Reviewer: Ian J Stratford

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General

This is largely a correlative paper, which does not come up with the answers expected. Nevertheless, it adds to the body of information on the interactions between gemcitabine and radiation, and importantly further demonstrates the potentiating activity of gemcitabine at low (clinically relevant) doses of radiation.

Specific comments:

Abstract, Results Section: A comment should be made relating enzyme activity to gemcitabine toxicity clone.

Page 4, para 1, lines 13/14: Question - has dCK activity vs gemcitabine toxicity been done in the NCI 60 cell line panel?

Page 4, para 1, lines 17-19: Why should the relationship between sensitization and drug concentration be dependent on the rate of drug phosphorylation?

Page 8, para 2, lines 5-9: In view of the previous comment, there should also have been measurement of total drug phosphorylation as well as dCK activity.

Page 8, para 3, line 1: Delete "rate" since this refers to change in function in TIME.

Page 8, para 3, line 3: Survival should be surviving fraction.

Page 9, para 3, line 1: This sentence is NOT correct, as you could equally define it as chemosensitization, with radiation enhancing the chemotherapy!! TRUE radiosensitization is observed when the efficacy of radiation is increased with drug concentrations that themselves have no effect.

Page 11, para 2, line 10: What is made DEF? DEF at a given concentrations?

Page 12, para 1, All: By inspection of the survival curves it would be impossible not to disagree with the statement made by the authors that the effect of gemcitabine is to increase sensitivity to radiation at low doses. However, it is a complete over-interpretation of the date to try and extract alpha and beta values. Reasons: Many of the survival curves do not go below a surviving fraction of 0.1 and further those that do are compromised because the accuracy of the SRB assay decreases substantially at surviving fractions below 0.1. Extracting beta values when you have "hockey-stick" survival curves eg for ECV304, HT29 etc is impossible. This analysis can be omitted.

Page 13, para 2, line 4: What was the rationale for giving the gemcitabine before and NOT after radiation?
Page 13, para 3, line 1-4: Lots of different cell lines are mentioned here, yet on page 4, para 2, lines 2-4, you would have thought that work in this area was limited. Some rewording of the text is necessary.

Page 22, Table 1: Concentration units should be given for IC50 and ID50.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable