Reviewer's report

Title: Expression of endosialin is associated with the progression and with the more aggressive biological characters of rectal cancers with a clinical trial of preoperative radiotherapy

Version: 2 Date: 29 March 2010

Reviewer: Carolyn Staton

Reviewer's report:

The authors present an interesting study on the effects of radiotherapy on the expression of endosialin in both the normal mucosa and in rectal tumours. This is a follow up study from others previously published by this group with the same cohort of patients and data presented are correlated with those from previous studies. In general the paper presents some interesting findings and is much improved from the previous version although there are still a few issues with it.

Major essential revision:

1. The discussion is still the weakest part of the manuscript with a lot of facts strung together and lacking a cohesive argument or understanding. It is very 'hand wavy' and unclear in many places. For example:
   a. TEM1 was considered an important vascular target and then you go onto say that it was not selectively expressed in tumour epithelia - this surely should be endothelia. There seems to be a fairly consistent muddle throughout the discussion as to what endosialin is doing and in which compartment it is doing it.
   b. On page 12 you start to relate endosialin in the stroma to Cox-2, p73 & PRL, but it is not clear from your discussion whether these were in the stroma as well or in the tumours.
   c. On page 13, having listed your previous data with Cox-2, p73 and PRL the data needs to be tied in clearly with your data on endosialin together with an explanation as to what this might mean. What do you think endosialin is actually doing in the stroma and what might the correlation between endosialin and Cox-2 etc after surgery actually mean. The final two sentences of that paragraph are very weak and it is not entirely clear what you mean by this.
   d. An important and interesting observation that the endosialin expression is reduced in the most advanced tumours has not been discussed. There are some interesting possible explanations for this observation which should be considered.
   e. On page 14 you state 'The endosialin was positively related to p73 in the non-RT group and the expression of Cox-2 and PRL in the RT group'. Why might this be and what might it mean?
f. On page 14 (near the bottom of the page) you state that 'therefore endosialin might have a therapeutic value in the treatment of tumours'.

What do you mean by this? You haven't 'treated' your tumours with endosialin so this sentence does not fit with the rest of your study. Do you mean as a marker?

g. Finally the conclusion is not strong enough, especially as you don't show an increase (Figure 2) or real change in expression of endosialin after RT (Tables 1-4). What you show is a change in correlations/relationships with other factors after RT.

Minor essential revisions
1. In the abstract expand PRL at first use 2. On page 9 in the results section, how do you get the number 74% for the II+III=IV group? If you average the numbers given in the previous II+sentence (70%, 87% and 57%) it should be 71.33%
3. On page 13 please give a reference for the statement 'p73 over-expression was correlated with a poor prognosis in colorectal cancer patients.'

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare I have no conflicting interest.