Reviewer's report

Title: Deregulation of SnoN expression in alternate pathways of colorectal tumorigenesis.

Version: 1 Date: 26 July 2006

Reviewer: Carla Oliveira

Reviewer's report:

General
In this paper, entitled “Deregulation of SnoN expression in alternate pathways of colorectal tumorigenesis,” the authors study 52 colorectal carcinomas for SnoN expression levels specifically in MSS and MSI cases. The authors propose MSI-H cancers as an excellent model for studying the dual roles of SnoN in both tumour suppression and promotion on the basis of SnoN expression analysis and the dual role of this gene either as a tumour suppressor gene or as an oncogene. Authors show that while MSI cancer display either increased or decreased levels of SnoN expression in comparison to matched normal mucosa, MSS cancers display increased expression in 50% of the cases and never display decreased expression. Based on these results the authors claim that SnoN may be an important tumour suppressor gene, exclusively in CRCs progressing via the MSI pathway of tumorigenesis.

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

1. The data are very interesting but the series analysed in this work is very small to draw conclusions about the role of SnoN as a tumour suppressor gene in MSI carcinogenesis. The number of cases should be enlarged to consolidate these results.
2. Of more concern if the fact that the reverse primer the authors have used to analyse SnoN expression does not match ant sequence in the SnoN cDNA, which may compromise the whole work.
3. Sno gene has at least 4 known isoforms. The sequence of SnoN2 is very similar to the sequence of SnoN, but the difference in their function is still poorly understood, though when analysing the involvement of SnoN expression in colorectal carcinogenesis the authors should be very careful in order to design a strategy that amplifies specifically SnoN isoform. While the forward primer present in this manuscript binds to both SnoN and SnoN2, the sequence of the reverse primer is completely impossible to find in the SnoN cDNA sequence.
4. It is impossible to understand the distribution of TGFbRII mutations MSI cases with decreased or unchanged SnoN expression, as these results are not included in the table.
5. The low number of cases analysed for TGFbRII mutations do not allow conclusions so authors should be more careful when discussing this subject.
6. For clinicopathological features of MSI cases, in the text there are two stage D MSI-H tumours which are not present in the table.
7. All results should be better discussed and put in perspective with the literature.

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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. The number of cases included in this work in miswritten in the methods section (51 instead of 52).
2. In table 1 there is a mistake in the number of MSIH cases with no cchange for sex (six instead of 5).

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Discretionary Revisions (which the author can choose to ignore)

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 limited interest

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests.