Reviewer's report

Title: Abnormal expression and processing of the proprotein convertases PC1 and PC2 in human colorectal liver metastases.

Version: 1 Date: 20 April 2005

Reviewer: Jean Rosenbaum

Reviewer's report:

General
This manuscript shows that there is an abnormal expression and processing of proprotein convertases 1 and 2 in liver metastases from colorectal cancer, as compared to the normal or surrounding unaffected liver. Given the biological role of these proteins, these findings could be of importance in order to understand the progression of liver metastasis.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
My major remark deals with the comparison that is made between liver and liver metastasis, that are 2 different tissues (liver and colon). It would be very important to know whether the pattern of PC expression and activation in liver metastases is similar or different from that observed in the primary colon tumor. This would be especially interesting since I could not find published data on that matter and since studies on colon cancer cell lines failed to detect PC1 and PC2 expression (Biochem Biophys Res Commun. 1998 246 :155-9). Could PC1 and PC2 be specifically expressed in liver metastasis?

A minimum of details should be given for the RT-PCR analysis. What was the control gene used for normalization?

The statistical methods should be described.

Figs 4B and 5A are not convincing. In addition, negative controls should be presented (at least for reviewing purposes).

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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)

The vertical axis of Fig. 2D, right panel, is mislabeled: it should read ratio of p66/p75

The discussion on the neuroendocrine pathway of colon carcinogenesis is highly speculative and should be removed, or better substantiated. Note also that ref 13 does not deal with colon but with anal canal.

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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 importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests