Reviewer's report

Title: Association of loss of epithelial syndecan-1 with grade, stage, and local metastasis of colorectal adenocarcinomas: an immunohistochemical study of clinically annotated tumors

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Reviewer: Luigi M Terracciano

Reviewer's report:

"Association of loss of epithelial syndecan-1 with grade, stage and local metastasis of colorectal adenocarcinomas: an immunohistochemical study of clinically annotated tumors".

The article by Hashimoto and colleagues is a nicely written work on the prognostic relevance of a novel potential biomarker in colorectal cancer, namely syndecan-1. The authors analyze a tissue microarray of 131 adenocarcinoma samples by immunohistochemistry and find significant associations between loss of the marker with more advanced TNM stage and lymph node positivity but no association with survival. In addition they describe a correlation between a second marker, fascin, and syndecan-1.

Major Compulsory Revisions:

It is difficult to discuss colorectal cancer today without mention of mismatch repair (MMR) status. The authors should comment on the MMR status of the tumors included in this study?

Syndecan-1 appears to play a role in epithelial-mesenchymal transition. Are the whole tissue sections for the corresponding tissue microarray punches available? If so the current manuscript could be significantly improved by analyzing the association of syndecan-1 (and fascin) with tumor budding and expression at the tumor border.

Minor Essential Revisions:

The figures clearly show loss of syndecan in more poorly differentiated tumors. Is there an association between syndecan and tumor grade? This parameter should be added to Table 1 particularly because this feature is mentioned in the title of the manuscript but without results supporting this.

Concerning the scoring of syndecan, the authors mention two independent observers. What was the rate of agreement between the scores of the two observers? In cases of disagreement how was the evaluation handled? How many cores were taken from each tumor? Was the punch taken from the center of the tumor? The tumor border?
How many normal tissues and adenomas were evaluated? Perhaps a figure of adenoma staining for syndecan could be included in the panel in Figure 1?

Why combine 0 and 1+ in the table and also 2+ and 3+ in the figures? The numbers appear to be large enough to leave the negatives as one category (although a combination of categories 2 and 3 would make sense due to the few cases in 3+). Also, adding the row % to the tables would facilitate interpretation of the numbers.

It may be beneficial to report the 5-year survival rate and the median survival time (and 95%CI where possible) for each of the 0, 1+, 2+ and 3+ categories, despite the lack of statistical significance. What about a stratification of survival by negative versus positive lymph nodes?

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests