Reviewer's report

Title: Prognostic significance of fascin expression in advanced colorectal cancer: an immunohistochemical study of colorectal adenomas and adenocarcinomas

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Studies by Hashimoto Y et al., reported the Fascin immunoreactivity in tissue microarray tissue sections of colorectal adenoma and carcinoma lesions. Other aims of this study were to correlate Fascin expression levels with the Ki67 labeling index and to determine the utility of Fascin expression in predicting patient prognosis. Authors have reported that Fascin expression may be a prognostic biomarker of aggressive colorectal carcinomas. However, some of the concerns that needs to be addressed to improve the quality of the manuscript.

Major Compulsory Revisions:

1. There is no consistency in use of terminology. For example, colorectal tumors, colorectal cancer and colorectal adenocarcinoma. Also, authors have used adenomas as well as polyps as interchangeable terminology which makes it difficult to interpret whether they are using polyps for their small cohort of FAP population.

2. Methods and Patient Selection:
   a. It appears that authors used two sets of tissues, Set I: Adenomas (Sporadic and FAP) and conventional carcinomas; the rational for using these two sets of tissues is not clear. Set II: Normal colonic mucosa, and tissue microarrays of colorectal tumors. Does this set include mesenchymal tumors of colon too? Or was it a pure population of colorectal carcinoma. This confusion needs to be clarified.
   b. It appears from the methods section that authors have used colorectal adenomas that were >2 cms and those that were < 2 cms. It is also not clear whether any of these adenomas had associated high grade dysplasia. Such information would provide a more clear view of the study set.
   c. Since this study is assessing the clinical outcome, i.e. patient survival, they have not described whether these patients received any adjuvant therapies (chemo or radiation), because, this study includes 53 advance stage patients (Stage III and Stage â€” Table 1b). During the study period of tissue collection, 5-fluorouracil alone or in combination with Leucovorin or Levinisol usage was approved by FDA. Thus, some of these advance stage patients might have received adjuvant therapy. The adjuvant chemotherapy or radiation (rectal carcinomas) might have influenced the survival of patients. Therefore, authors need to provide the treatment details.
   d. It was described in the methods section (page 7) that these patients have a mean of 5 years clinical follow-up information, but in the results section of the abstract provided 3-year overall survival data. This inconsistency in the analysis need to be cleared.

3. Interpretation of Results:
   a. Authors suggest that Fascin expression pattern as â€˜patchy and heterogeneousâ€™ in colorectal carcinomas on conventional sections. In this setting it will be difficult to trust the lack of staining in TMA samples, which were categorized as negative, may skew the results and remains difficult to interpret.
   b. Because of the heterogeneous staining pattern of Fascin it would also be difficult to trust the reported significant differences in fascin expression in colorectal carcinomas of the proximal and distal colon origin (Table 1b).
   c. The findings suggest an inverse correlation between fascin expression and Ki67 index. Have they checked the expression of these markers in relation to tumor differentiation?
   d. The authors described the stromal fascin staining and its correlation with different features (page 11 the last sentence of 1st paragraph), but the data was not presented. If they decide not to present the data in this manuscript, they need to describe as â€˜data not shown.â€™

Minor Essential Revisions:
Discretionary Revisions:

Since these findings indicate that the expression of fascin was higher in proximal colonic tumors (though the numbers of 2+ and 3+ positive tumors are small), the tumor location-based analysis may be ideal.