Reviewer's report

Title: Expression of CIAPIN1 in human colorectal cancer and its correlation with prognosis

Version: 2 Date: 16 April 2010

Reviewer: Alessandro Lugli

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The study entitled "Expression of CIAPIN1 in human colorectal cancer and its correlation with prognosis" by Hai Shi et al. is an interesting approach to the carcinogenesis of colorectal cancer. There are some points that should be discussed.

Minor Essential Revisions

1. Background

- 1st paragraph: The text needs some language corrections.

- Last paragraph: The aim should be clearly stated. The last sentence should be removed as it is repetitive compared to the first part of this paragraph. For example a suggestion that the authors could consider: "The aim of this study was 1) to determine the prognostic impact of CIAPIN1 in 273 CRC samples and 2) to investigate the CIAPIN1 expression in CRC cell lines after inducing differentiation".

2. Methods

- Patient characteristics: To facilitate the reading of the paper a table 1 including all the clinicopathological data should be considered. Although the clinical data seem to be complete (age, gender, location, survival) with the exception on the information on local recurrence, the pathological data should be reelaborated. According to the UICC T stage, N Stage, M stage, L and V status are essential prognostic factors and should be included in a biomarker study in colorectal cancer; additionally, the inclusion of tumor grade, tumor budding, tumor border configuration, peritumoral lymphocytes, histologic subtype and mismatch repair status would strengthen the study. My suggestion is to include all the clinicopathological data in table 1 with the "%" numbers for comparison. Tables 2 and 3 could show the univariate and multivariable analysis.

- Scoring system: The use of arbitraty scoring systems in evaluating immunohistochemical biomarkers is according to the literature a well known problem in pathology and often a reason for different results between different study groups; here the authors use "staining intensity x staining (%)"; although this approach could be used, the authors should explain why the final scoring was stratified in negative, weak, moderate and strong using the ranges of 0-1,
2-4, 5-8 and 9-12. Theoretically, another study group could choose different ranges, for example 0, 1-5, 6-10, 11-12.

The authors should use an additional scoring system to validate the present scoring system (i.e. receiver operating characteristic (ROC) curves, often used in oncological studies. The reason is that to underline the reproducibility of a new biomarker in a possible, future daily diagnostic work.

3. Results

- Adjuvant therapy should be included in the multivariable analysis.

4. Table 1

- Histology should be replaced by tumor grade (well, moderate, poor) as histology means actually the histologic subtype.

5. Table 2

- Age: Why was a cut-off of 65 years choosen?
- Why was the location entered twice, once left and once rectum+sigmoid? Did the autors mean "right" vs left (sigmoid+rectum)?

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

**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 that I have no competing interests.