Reviewer's report

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

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Reviewer: Karin Jirström

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In this paper, Shi et al. have investigated the prognostic role of the anti-apoptotic protein CIAPIN1 as assessed by immunohistochemistry in colorectal cancer. Expression of CIAPIN1 was also compared in cancerous and adjacent normal tissue by western blotting. They also induced differentiation in HT29 and SW480 cells whereby an increased expression of CIAPIN1 was denoted.

The authors conclude that high expression of CIAPIN1 is associated with a prolonged survival.

While these findings may be of interest, several major issues need to be clarified before this manuscript can be considered for publication. Since the pages are not numbered, all my comments are listed consecutively below, the majority of which are major points, and minor points denoted in parentheses:

1. The manuscript needs extensive language editing throughout. Also, there are several sentences that are incomprehensive, with missing words and other inconsistencies, all of which can not be specified in this report. One example: Introduction, second last paragraph; "Immunohistochemical studies have shown that there was low expression of CIAPIN1 in gastric cancer, but the expression in the distal cancerous tissues was high". Please specify what you mean by "distal cancerous tissues", this phrasing is too simplistic.

2. Methods section; "Patients and collections of samples":

2.1. Are the patients prospectively or retrospectively collected? Was this a consecutive cohort? Lease specify the selection criteria.

2.2. How was the information on death due to cancer obtained? Please mention this in the "Patients" paragraph and not only in "Statistical analysis"

(2.3. Please move the sentence on preparation of formalin-fixed tissue etc to the section detailing the immunohistochemical procedure. )

2.4. The mean patient age was 58 years. This is rather young. Please explain the reason for this.

2.5. Why do you group cancers of the rectum and sigmoid together in Table 1? The number of rectal cancers should be specified separately.

2.6. Last sentence: Do you mean that 23(8.4%) of the patients received neoadjuvant chemotherapy and 242 (88.6%) adjuvant chemotherapy? Please clarify. It seems like a rather high proportion of patients that received
chemotherapy, particularly in the light of the distribution of TNM stage. How many patients with Stage II disease received adjuvant chemotherapy? Also, how many patients with rectal cancer received neoadjuvant radiation?

(3. Methods section; "Immunohistochemical staining": Please specify from where the anti-CIAPIN1 antibody was obtained.)

4. Methods section; "Immunohistochemical analysis".

(4.1. Please reference the statement that clear cell renal carcinoma has previously been used to express CIAPIN1. Please also reference how CIAPIN1 has been scored previously.)

4.2. You only mention that CIAPIN1 was expressed in the nucleus and cytoplasm in the abstract. Please describe the staining distribution in this section as well and specify whether the scoring system was applied on each subcellular compartment separately or on the total staining? Did cytoplasmic and nuclear staining correlate throughout or did some cases show only one or the other?

5. Results:

(5.1. Figures should be numbered 1, 2... not 1A, B)

5.2. Description of Figure 1A is totally incomprehensible. For example, please specify which tumours that were classified as being of high and low differentiation grade, respectively.

5.3. You state that there was "no significant difference in the expression level of CIAPIN1 protein between normal and dysplasia colonic epithelial tissues". Which kind of dysplastic lesions do you refer to? Please indicate in Figure 1. Was this an incidental observation or did you also sample adenomas etc separately?

5.4. Second paragraph: What do you mean by "CIAPIN1 protein expression correlated with having a primary tumour...". Didn’t all the patients have a primary tumour?

5.5. Multivariate analysis (Table 2): Why did you use pT1 as a cutoff for a dichotomized T-stage variable? The number of patients with pT1 tumours was rather low. Why not adjust for Stage I-II vs III-IV, i.e. metastatic and non-metastatic disease? Why did you adjust for both left vs right location and sigmoid/rectum? Why 65 years when, as far as I know, 75 years is more commonly used? (I am aware of the rather low mean patient age in this cohort).

6. Discussion:

6.1. The two first paragraphs do not have a place in this section but rather in the introduction, from which the first paragraph is more or less repeated. The second paragraph is superfluous, since you have not looked at CIAPIN1 expression in relation to any kind of genetic aberrations here.

6.2. When the above is removed, the discussion is rather brief, and poor.

(6.3. Your previous work on gastric cancer is not referenced.)

Level of interest: An article of limited interest
Quality of written English: Not suitable for publication unless extensively edited

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 interest