Peer Review File

Reviewer A
Major comments

Comment 1: It is important to show images of representative ovarian cancers case of Fibulin-3 positive and negative
Reply: We thank the reviewer for the comment, we added figure 2 to show images.
Changes in the text: In figure 2.

Comment 2: The survival analysis needs to be improved:
 a. Details about the treatment should be included;
 b. The survival curve should be presented together with the at risk table;
 c. a Cox regression including major prognostic factors (histologic subtype, stage, grade, age, treatment should be presented).
Reply a: Your advice has been very helpful, and I know that including treatment options in survival analysis can help us improve our article, but our main subject is pathology, and there is a lack of research on clinical treatment options, but now we're doing it, and we're going to keep doing it. And in the design of the experiment before, reference to some literature, did not design to the treatment, so led to a little negligence in the design of the experiment(eg:1. Yu Lan, Zhou Lei,(Expressions of CD133, E-cadherin, and Snail in epithelial ovarian cancer and their clinicopathologic and prognostic implications) Chen J, Wei D, Z et al(Overexpression of EFEMP1 correlates with tumor progression and poor prognosis in human ovarian carcinoma) Song En-lin, et al (The expression of EFEMP1 in cervical carcinoma and its relationship with prognosis)

Reply b, c: We add Table3 (Univariate and Multivariate analysis of patients with

ovarian cancer) and add some date (see Page 10, line 134-144)

Minor comments
Comment 1: The English language needs some improvement; there are some grammatical and spelling issues.
Reply: We have modified these mistakes in the text

Comment 2: In the abstract, present numerical values for age and stage, not only p values.
Reply: We have modified our text as advised (see Page 3, line 15-17).
Changes in the text: The expression of Fibulin-3 was found to be correlated with the

FIGO stage of EOC, high stage tumors (FIGO III + IV) expressed high.

Comment 3: Please remove Graph Pad Prism 7.0 from abstract and from Figure 1 legend
Reply: We have modified in Figure 4 and abstract.

Reviewer B

Major comments
Comment 1: "However, studies on the relationship between Fibulin-3 and ovarian cancer have been limited." The available references have not even been described e.g. Chen et al (Overexpression of EFEMP1 correlates with tumor progression and poor prognosis in human ovarian carcinoma. PLoS One 2013). That paper demonstrated the association between high expression of fibulin-3 expression and poor survival in ovarian cancer. Furthermore, it described the increased expression in moving from normal to benign to cancer in a larger series of samples. There is value in publishing confirmatory studies, but it is highly inappropriate to not acknowledge the previous studies in the field especially when they have the same findings. All previous relevant papers should be described.
Reply: We have modified our text as advised and add some date (see Page 11-12, line 164-169).

Comment 2: I have concerns about the data shown in Table 2, especially if this is the only novel data within the manuscript. The total number of cancers mentioned throughout the manuscript is 84. This is backed up by the data in Table 1. In Table 2, the numbers add up to 85 used in the 3 comparisons. This extra sample should be removed and the data re-analysed. I would have particular concerns if this sample made the difference for the first comparison (Fibulin-3 vs E-cadherin) where $p = 0.049$.
Reply: We thank the reviewer for the careful analysis of our data. We have removed the extra sample and re-analysed the date (see Table 2).

Comment 3: "The ovarian cancer patients belonging to the age group of >45 years showed high expression of Fibulin-3, and the difference was statistically significant (P< 0.05):" All 102 patients are included here rather than just the 84 ovarian cancer patients and only these 84 should be considered. The data should be checked to confirm that $p<0.05$ for this group.
Reply: We have modified in Table 1.

Minor comments

Comment 1: "diagnosis frequently at an advanced stage." rather than "diagnosis at an advanced stage."

Reply: We have modified our text as advised (see Page 3, line 3).

Comment 2: "most patients are diagnosed" rather than "most patients are almost diagnosed

Reply: We have modified our text as advised (see Page 5, line 33).

Comment 3: It is unclear what Type I and Type II classification refers to. I presume that this is referring to the Shih and Kurman dualistic model but if so this should be made clear and referenced.

Reply: We have modified our text as advised (see Page 7, line 72).

Comment 4: "Known positive sections were used as positive control" - which tissues were used as positive controls (please supply references also). Representative images should be shown.

Reply: We have modified our text as advised (see Page 8, line 88), and have shown representative images (see figure 2)

Changes in the text: Cervical cancer tissue sections (Fibulin-3 positive) were applied as positive control.

Comment 5: IHC. Representative images for sections stained with all the antibodies used should be provided to allow reader assessment of the quality of the IHC staining.

Reply: We have shown representative images (see figure 3)

Comment 6: "The expression rate of Fibulin-3 protein in ovarian cancer was 45.24%..." – Just to confirm what this means. So 45.24% had any level of expression ie any positive cells and 54.76% were completely negative? I think the authors mean that 45.24% were high expressors rather than just positive.

Reply: We have modified our text as advised (see Page 9, line119-120).

Comment 7: Title of Table 1. "Serum levels of Fibulin-3 in patients with ovarian cancer" – do the authors mean "Tissue levels of Fibulin-3 in patients with ovarian tumors"? Firstly, serum levels don't appear to have been studied and benign tumors are not cancers.

Reply: We have modified in Table 1.

Comment 8: In Table 1 the high expression percentage for fibulin-3 in carcinoma should be 45.24% not 54.24%.

Reply: We have modified in Table 1.