Reviewer's report

Title: Fibulin-1 is Epigenetically Down-regulated and Associated with Bladder Cancer Recurrence

Version: 2 Date: 6 July 2014

Reviewer: Marcus Horstmann

Reviewer's report:

This paper evaluates fibulin in bladder cancer using different methods in tissue of NMIBC and BC cell lines.

Major drawbacks are:

1. In the introduction: If the search for molecular markers in BC is motivated by its high recurrence rate, how do the authors think a molecular marker might help the clinicians to improve recurrence rates or progression? This links to molecular markers and remains completely unclear and should be explained more substantially.

1. The clinical data of this paper only support that fibulin is associated with tumour recurrence in NMIBC. The association between fibulin and tumour progression is not supported by clinical data but only cell cultures and the association between tumour grade and fibulin expression. The end points „recurrence“ and „progression“ need to be more clearly differentiated and critically discussed though out the paper.

2. Even though the methods are well described it is a major draw back of this paper that it is only stated in the discussion that the cell lines „J82 or T24“ are from MIBC and not from NBIC. This is especially important as otherwise the paper only deals with NMIBC. This needs to be put more clear.

Minor revisions:

p3 „as the prognosis of patients' remains poor, with a high recurrence rate, it is also one of the most expensive cancers to treat“

Please specify what you mean by „the prognosis remains poor“? The reader would probably think in this situation that you talk about survival rates. But this is probabl not the cas as your paper is rather about recurrence rates of NMIBC. It should be more clearly stated prognosis for what: PFS, RFS or overall survival.

P3-4:

The question for this paper is generally well defined however it should be more clearly stated in the introduction that the aim of the study is to evaluate fibulin 1 in NMIBC and not in BC in general. Here the endpoints should also be cearly stated (see above PFS or RFS?)
P5: "Beside that, telephone follow up was taken every month"

We all know that a complete follow up in patients with BC is difficult to obtain. In this paper an ideal follow up seems to be obtained, even thouhg in China to my knowledge patients often only come for interventions to the hospital.

Please comment on this problem and explain what you asked for in the „telephone follow – up“ every month. This seems for the PFS or RFS a little bit overdone.

The following sentences in the discussion need rewording:

1. We conjectured that in the progression progress of bladder cancer, the methylation degree of FBLN1 promoter follow increased, which resulted the progression loss of fibulin-1 expression, so that enhanced the bladder tumor growth and ability of metastasis and angiogenesis.

2. In conclusion, our study provides evidences that FBLN-1 functions as a novel candidate tumor-suppressor gene in bladder cancers and its down-regulation may (be??) due to the promoter hypermethylation

P5 There was no case of death in the study.
This contradicts to your initial statement of BC having a poor prognosis. Please change your introduction accordingly as stated before.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests: 'I declare that I have no competing interests'