Reviewer's report

Title: Matrix-metalloproteinases-1, -2, -3, -9, their inhibitors TIMP-1, -2, and the MMP1/TIMP1-complex in blood plasma as markers for transitional cell carcinoma of the bladder

Version: 3 Date: 9 January 2006

Reviewer: sanaa eissa

Reviewer's report:

General
The study is among the first to quantify MMPs, TIMPs and MMP1/TIMP1 complex in plasma by samples to identify its potential role in diagnosis of bladder cancer. The aim of the study is clear and the experimental design is acceptable after considering some aspects. The manuscript still need major revision considering the following points.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1- Results are very poorly presented due to inadequate presentation and tabulation of results (The authors presented all data in only one table):
- Non parametric analysis of MMPs, TIMPs and MMP1/TIMP1 should be tabulated illustrating: median values, mean ranks, range in two tables: the 1st one comparing normal vs malignant groups. The 2nd comparing the different malignant subgroups (different stages and grades) to each other and to normal group.
- It is not clear at all why did the authors select the Cutoff values for the investigated parameters as 95 percentile value?, Why they did not use cutoff values calculated from ROC curves (receiver operating characteristic curve)?.
- ROC curves should be plotted denoting the calculated cutoff points (the best cutoff value which discriminates between non malignant and malignant groups) and the authors will identify, area under the curves, confidence limits, significance.
- The positivity rates (no of cases >cutoff) of different investigated parameters (MMPs, TIMPs and MMP1/TIMP1), in different gps and in different malignant subgroups were partially mentioned in the text, these data should be completely analyzed (Chi square) and tabulated.
- Why did not the authors calculate a ratio between MMPs/TIMPS and calculate their cutoff values and sensitivities and specificities? They may give better sensitivities and specificities rather than using absolute values.
- The combination between different parameters should be tabulated.

2- Why did not the authors include a group with benign urological diseases as non-malignant control group?

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1- Language and spelling mistakes:
- Abstract: Conclusion, line 1, MMP2 as should be corrected to: MMP2 is
- Page 7: line 15, i.v.pyelography should be corrected to I.V.
Page 7, line 19, G4 is corrected to G3 (there is no G4 in table)

Page 12, line 17 The sentence “Taking into account...................(Table 1), should be deleted.

Page 15, line 10, Plasma concentrations .............control group, the sentence is not clear at all?

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions