Reviewer’s report

Title: Low expression of hTFPI-2 associated with poor survival outcome in patients with breast cancer

Version: 1 Date: 14 December 2012

Reviewer: Pascale Reverdiau

Reviewer’s report:

In this manuscript, Dr Cheng Xu and his colleagues studied the relationship between Tissue Factor Pathway Inhibitor-2 expression and survival rate in 196 patients with breast cancer or benign tumor. They demonstrated that the expression of TFPI-2 in patients with breast malignant tumor is lower than in patients with breast benign tumor and suggested that a low level in TFPI-2 is associated with a poor prognosis.

The purpose of the study is well defined and this paper brings new information concerning the expression of a proteinase inhibitor, TFPI-2, in breast cancer when compared to the previous data published in this field. Methods are appropriated and clinicopathologic features are well documented. Moreover, statistical analysis strengthens adequately the data. Finally, the paper is well written with only some points that remain to be elucidated.

Discretionary Revisions

Introduction:
- p4 line 8, the authors list one reference (Whitley et al., 2004) about the tumor migration and invasion in the breast and ovarian cancer cell lines that is reduced by active PAI-1. However, in the 6th sentence “active plasminogen” is disturbing and authors should explain this expression.
- The authors should list other references demonstrating that hypermethylation of TFPI-2 gene promoter is a factor for poor prognosis in patients with other cancer (lung cancer, gastric carcinoma, colorectal cancer).

Results:
- Positive staining on stroma areas were observed. However this data is not discussed. Which cells are positive ? (endothelial cells, macrophages)
- In figure 2D : negative staining was obtained in breast cancer, which clinical stage ?
- In table 2 : How was evaluated the vascular invasion ?

Discussion
The authors should add a comment about the direct inhibition of MMP activity by TFPI-2 that is discussed by some authors.
In conclusion, this paper is of importance in its field and could be accepted after minor revision.

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

**Quality of written English:** Acceptable

**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