Reviewer's report

Title: Prognostic significance of human Mammaglobin B expression in epithelial ovarian cancer

Version: 1 Date: 25 March 2009

Reviewer: Menelaos Zafrakas

Reviewer's report:

General Comments
1. Is the question posed by the authors well defined? Yes
2. Are the methods appropriate and well described? Yes
3. Are the data sound? Yes
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Yes
5. Are the discussion and conclusions well balanced and adequately supported by the data? Yes
6. Are limitations of the work clearly stated? No (see comment 8 under Major Compulsory Revisions)
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Generally speaking, yes (see comment 2 under Major Compulsory Revisions).
8. Do the title and abstract accurately convey what has been found? No the title does not convey the principal finding; the abstract is OK (see comment 1 under Major Compulsory Revisions).
9. Is the writing acceptable? Yes

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)
1. Pages 14-15: There is only one paragraph under the subheading “Expression patterns of Mammaglobin B protein in normal ovary and in epithelial ovarian cancer by immunohistochemistry”. This section could be divided in at least two paragraphs (e.g. the 2nd paragraph could start from “Finally…” in page 15, line 15).

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. Page 3-line 19, page 16-lines 3 and 22, and page 17-line 23: “mRNA level” is more accurate for most readers than “gene level”.
2. Page 6-line 20: “FIGO” stands for “International Federation of Obstetrics and Gynaecology” (in French) – the word “International” is missing from the text.
3. Page 7-line 2: Please change “did not received” to “did not receive”.
4. Page 7-line 7: “expired” could be changed to a more formal verb (e.g. died or succumbed).

5. The authors should provide all details concerning manufacturers of reagents and equipment used, i.e. city and country of origin (e.g. page 9, line 8 etc.)

6. The Discussion section should be divided in paragraphs.

7. Page 21-last line: Please change “design” to “designed”.

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

1. Although this is a well-written, original study with very interesting findings, the title does not convey these new findings.

2. The authors state that “this study was performed on 106 consecutive cases of epithelial ovarian cancer” (page 6). Did the authors include any of the cases included in their previous publication in Gynecol Oncol (Tassi RA, Bignotti E, Rossi E, Falchetti M, Donzelli C, Calza S, Ravaggi A, Bandiera E, Pecorelli S, Santin AD. Overexpression of mammaglobin B in epithelial ovarian carcinomas. Gynecol Oncol 2007;105: 578-585)? In this previous paper, the authors analysed Mammaglobin B expression in ovarian cancer and concluded that evaluation of the clinical utility of Mammaglobin B in future studies is warranted. This has been done now, as described in the present paper. However, the authors should clearly state whether previously published data were in part used in order to generate new results for the present study or not.

3. Pages 9-10: The authors should provide the primer sequences for Mammaglobin B and GAPDH.

4. Page 11-lines 20-23: Why did the authors divide immunohistochemical results in two groups, i.e. negative and positive (with positive including weak, moderate and strong immunoreactivity)? One could argue that negative and weak staining should be grouped together, while moderate and strong immunostaining should comprise a second group or that the four distinct categories of immunoreactivity should be used individually for statistical analysis. Would the results and conclusions be the same?

5. Page 19-lines 12-15: The authors argue that MGB-2 “…could be an attractive diagnostic candidate and prognostic biomarker for ovarian malignancy [18], similarly to its homologous Mammaglobin A (MGB-1) for breast cancer [30]”. In the next two sentences, the authors go on discussing the possible clinical utility of MGB-1, based on previously published studies [citations 29, and 31-40].” However, in another paper [Zafrakas et al. BMC Cancer 2006; 6:88], published later than those cited by the authors, MGB-1 was not found to be as breast-specific as previously thought, and thus its utility as a diagnostic marker in breast cancer appears to have certain limitations. Moreover, in the same paper MGB-1 was found to be expressed in gynaecological malignancies, including ovarian cancer. Since the authors chose to discuss the role of MGB-1 in this extent, these findings should have been also included.

6. Page 20-lines 17-21: The authors mention “… a new intra-operative molecular
assay that qualitatively detects the gene expression of two breast cancer markers (Mammaglobin A and Cytokeratin-19)…”. This development (concerning another type of cancer, other molecular markers, and sentinel node biopsy, a technique not used in ovarian cancer) is not relevant to the findings of the present study, and it should be omitted.

7. Page 20-lines 21-22: The authors state that they “…don’t have any explanation for the biological mechanism linking MGB-2 expression with reduced risk of recurrence…” Which could be the possible biological explanations? Are there any hypotheses on this issue? What should be done in the future in order to clarify these biological mechanisms?

8. The authors should clearly discuss the limitations of this study.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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