Reviewer's report

Title: Large-scale proteomic identification of S100 proteins in breast cancer tissues

Version: 3 Date: 18 April 2010

Reviewer: Serhiy Souchelnytskyi

Reviewer's report:

This manuscript describes analysis of S100A proteins in human breast tumors. Proteomics was used to identify various S100A proteins in tumors from 2 cohorts of patients. The authors showed enhanced expression of S100A proteins in tumors, as compared to non-cancerous tissues, and showed overall high level of S100A proteins in tumors. Correlation analysis showed an association of S100A2, S100A11, S100A8, S100A7, S100A4 with metastatic development of cancer.

The goal of this work is of importance, and conclusions contribute to the efforts for finding markers for management of breast cancer.

The manuscript is generally well written, data presented clear and discussion is relevant.

Comments:

Essential revisions

1. Quantification of S100A proteins expression in tumors vs non-tumors/normal tissue would be of importance to show (Fig 4, page 8; as an option – N%V values). Such quantification would help in evaluation of the correlation of S100A proteins expression and tumorigenesis and metastasis (Figures 5 to 7).

2. The similar comment about quantification – for data shown in Figures 5 and 6 (pages 8 and 9). It is difficult to trace each case from Figure 5, where there is no quantitative information, to the image in Figure 6. This comment is also linked to the analysis of relationship in expression between various S100A proteins (Figure 7; page 9). There description and analysis is virtually absent, i.e. only 2 short sentences (page 9, “Relationship...” section).

This manuscript may benefit from more thorough analysis of quantitative information in relation to clinico-pathological data. It may be that the authors have already done that (page 10; was correlation analysis based on quantitative data?), then it would be good to show this quantitative analysis.

3. Reported correlations with metastasis (pages 9-10, Fig 8) are highly interesting. Why the authors referred to the expression level 1.07 (page 10, top of the page) if it is not significant (p>0.05)?

Mentioned correlations with Ki67 and nodal status would be beneficial to show (page 10, the last sentences of the top paragraph).
4. Reference to documentation related to ethical permits is required (page 5; clinical specimens). To mention that the recommendations were followed is not enough. These recommendations should be referred (number, decision-taking body, legislation followed, etc).

Discretionary Revisions

5. Conditions of MALDI TOF MS have to be described, e.g. notes about digestion of proteins, conditions for generation and collection of spectra, parameters of searches, etc (page 6).

6. Please provide annotation of Figure 7. What mean “No” and “Yes”? If “No” means no correlation, than what is the reason to show it?

Table 1 requires more annotations, as example, it is not obvious to all readers what is the Mowse score, and how you obtained numbers of peptides and coverage.

Figure 3, mass spectra – Spot 10 is annotated twice. Please correct (S100A7a seems to be spot 8).

7. The authors are advised to check the text to avoid misuse or misspellings. As examples: p.2, methods section – “Tissue extraction was ...”; p. 3, background, second paragraph – “S100 proteins are small, acidic proteins of Ca2+ binding proteins...”; p. 6, Protein identification – “Mass spectrometric sequencing...”, while in the text peptide mass fingerprinting was described; p. 8, top of the page – “...focalize.” or “localize”?: what is “...mass-screaning..”? 

8. Page 3. Conclusion should be about specific results reported in this manuscript. Only a general note about importance of this work is not sufficient. Please re-write this section to highlight specific findings.

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

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