Acknowledge editing support

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Scientific Editing Report

Dear Author,

It was a pleasure working on your document. This study on the value of galectin-1, -3, and -7 expression patterns in predicting overall survival in ovarian cancer presented findings that are likely to be of substantial interest to cancer researchers and clinicians.

This document contains an assessment of the manuscript in terms of its language and presentation, content, and submission readiness. Where relevant, I have also provided recommendations for improving the manuscript. Should you have any questions on the report, do let me know.

Best regards,
Shane Rydquist

Managing Editor

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LANGUAGE AND PRESENTATION

Notes from the Language Editor

Overview

Scientific Reports does not have a required format in terms of section order; however, it is usually best to have the Conclusions section immediately follow the Discussion section, and I have therefore moved the Conclusions section to improve the flow of the manuscript. In addition, the Abstract was heavily edited to remove irrelevant information, increase the conciseness of the text and reduce word count, and provide a concluding sentence.

The significance of the study findings, their implications in the field at large, and their multidisciplinary relevance are important criteria for publication. In particular, *Scientific Reports* caters to a broad scientific audience; therefore, it would be beneficial to highlight any implications in other fields of research.

Please see my recommendations below.

Organization and flow

Abstract. A good abstract generally concludes with 1–2 sentences describing the broader implications of the results. I have added a sentence to the end of the Abstract stating the major implication of the results.

Discussion and Conclusion. The implications of the results in the context of ovarian cancer were appropriately described in the Discussion section. However, as *Scientific Reports* caters to a broad audience, I recommend including in the manuscript any additional implications of your findings for other fields of research. For example, it appears that galectins have been implicated in a broad range of pathological conditions, including important roles in inflammation and fibrosis. A brief mention of these in the Discussion or Conclusions sections would therefore improve the multidisciplinary appeal of your manuscript.

Formatting

The manuscript has largely been formatted for submission to your target journal.

Recommendation 1. Please ensure that a reference list is provided and formatted per the requirements of the target journal. These are the following formats that you should be aware of for different types of references:

Published papers:

Printed journals

Schott, D. H., Collins, R. N. & Bretscher, A. Secretory vesicle transport velocity in living cells depends on the myosin V lever arm length. *J. Cell Biol*. **156**, 35-39 (2002).

Online only

Bellin, D. L. *et al*. Electrochemical camera chip for simultaneous imaging of multiple metabolites in biofilms. *Nat. Commun*. **7**, 10535; 10.1038/ncomms10535 (2016).

For papers with more than five authors include only the first author's name followed by '*et al.*'.

Books:

Smith, J. Syntax of referencing in *How to reference books* (ed. Smith, S.) 180-181 (Macmillan, 2013).

Online material:

Manaster, J. Sloth squeak. *Scientific American Blog Network* http://blogs.scientificamerican.com/psi-vid/2014/04/09/sloth-squeak (2014).

Hao, Z., AghaKouchak, A., Nakhjiri, N. & Farahmand, A. Global integrated drought monitoring and prediction system (GIDMaPS) data sets. *figshare* http://dx.doi.org/10.6084/m9.figshare.853801 (2014).

CONTENT REVIEW

Notes from the Scientific Reviewer

Title, Abstract, and Keywords

Overall, the title, abstract, and keywords give the readers a good idea of the paper. However, the abstract does not clearly present the novelty of the study. It indicates that galectins serve as prognostic factors for various cancers, but does not clarify whether they have ever been used as such for ovarian cancer.

Recommendation 1. The title should be revised. Consider: "**Expression Patterns of Galectins-1, -3, and -7 Predict Overall Survival in Ovarian Cancer**".

Recommendation 2. The Abstract should clearly present the originality of the study by identifying the gaps in the knowledge about galectins as indicators of the outcome in ovarian cancer.

Literature Review and Research Rationale

The Introduction does not provide a sufficient background of the problem studied. Thus, the biological functions of galectins related to tumorigenesis, including malignant transformation, invasion, and metastasis, are not described, and it is unclear how galectins are involved in all these processes. As the study was specifically focused on the correlation of galectin expression in different compartments (extracellular, cytoplasmic, and nuclear) with ovarian cancer, the authors should outline localization-dependent functional activity of galectins. Thus, it should be indicated that extracellular galectins mediate cell–cell and cell–ECM contacts via binding to mucins, including cancer antigen 125, which promotes tumor cell adhesion, migration, and invasion. Through interaction with glycosylated cell surface receptors, galectins induce the expression of oncogens, promoting cell proliferation.

On the other hand, intracellular galectins regulate signaling pathways and gene transcription by interacting with cytoplasmic and nuclear

proteins (Funasaka et al. Nuclear transport of galectin-3 and its therapeutic implications. Semin Cancer Biol. 2014 Aug; 0: 30–38; Proc Natl Acad Sci U S A. 2016 Aug 16; 113(33): E4820–E4827. Bhat, et al. Nuclear repartitioning of galectin-1 by an extracellular glycan switch regulates mammary morphogenesis; Understanding the biochemical activities of galectin-1 and galectin-3 in the nucleus. Patterson et al. Glycoconj J. 2002;19(7-9):499-506).

The second aim of the study was to investigate wh*ether* "expressions of different galectins are correlated in ovarian cancer" because "*there is a critical need for a comprehensive study of various galectins in a representative ovarian cancer panel*". The purpose of such analysis is unclear, as the authors did not evaluate the correlation between combinations of different galectins and the outcome (survival).

Recommendation 1. Mechanisms underlying the oncogenic effects of galectins should be outlined in view of their localization. Distinct functional activities of galectins in intracellular compartments should also be presented and appropriate references cited. Such information would justify the rationale of studying the effect of galectins on survival in ovarian cancer depending on their cellular localization.

Recommendation 2. At the same time, the information not relevant to the study, such as Gal oligomerization or the number of CRD domains (lines 40-45) should be removed.

Recommendation 3. The aspect of the study regarding to correlation between the expression of Gal-1, -3, and 7 should be clarified.

Study Design or Methodology

Overall, the methodology applied in the study is adequate to answer the research question. However, there seems to be some flaws in method reporting.

First, the number of patients was not justified by power analysis, and it is unclear whether the sample size was sufficient to achieve statistical significance.

Second, there were no control samples, i.e., those from cancer-free individuals.

Recommendation 1. The correlation between different combinations of galectins and survival should be analyzed.

Recommendation 2. Power analysis should be performed and it should be indicated whether it confirmed that the results of the study were statistically conclusive.

Recommendation 3. Control tissue staining for all galectins should be presented in Fig. 1 and in Table 5.

Recommendation 4. Histological groups (serous, endometrioid, clear cell, mucinous) should be briefly characterized, especially in regard to their comparative malignancy.

Results and Statistical Analyses

Reporting of the results has several weaknesses regarding the structure of the section and description of the findings. There is also certain ambiguity in data presentation in the figures and tables. In addition, analysis related to paired expression of the studied galectins is incomplete.

Recommendation 1. The Results section was not appropriately organized, and presentation of the data did not correspond to their structure in the illustrations. As a rule, the data shown in a single illustration should be described in the same paragraph. However, the Results were structured according to individual galectins, whereas certain illustrations present the data related to all studied galectins (Fig. 1 – IF results; Fig. 2 – Survival; Table 2 - Multivariate analysis of prognostic factors), which complicates comparative analysis of the data and decreases the coherence and readability of the text.

Therefore, the Results should be restructured. First, IF data should be presented and interpreted for all galectins (Fig. 1). Then, each galectin should be described for its correlations with clinical and pathological factors (Tables 1, 3, and 4), and compared. Then, overall survival depending on galectin expression (Fig. 2) should be presented. After that, multivariate analysis of prognostic factors for overall survival in ovarian cancer (Table 2) should be analyzed. Finally, correlations among galectin expression patterns (Table 5) should be described.

Recommendation 2. In Fig. 1, nuclear and cytoplasmic staining for Gal-3 and -7 could be hardly seen and should be indicated by arrows or asterisks.

Recommendation 3. In Table 1, the last line (≤ 60) should be changed to > 60.

Recommendation 4. It is unclear what statistical significance (*p*-value) is related to in Histology (Tables 1, 3, and 4). There are four histological tumor types in these tables and three levels of expression (negative, low, and high) in Table 4, but only one p-value is shown and it is unclear what groups were compared. It should be clearly indicated in the column (*p* versus …) or a footnote to each table.

Furthermore, ovarian cancer subtypes should be presented in terms of their malignant potential, and correlation of galectin expression with the cancer subtype interpreted.

Recommendation 5. The purpose of performing analysis presented in Table 5 is totally unclear, as correlations between galectin expression patterns and their significance in ovarian cancer were not interpreted. Thus, nuclear Gal-3 correlated with cytoplasmic Gal-1 and -7; however, nuclear Gal-3 indicated good prognosis, whereas cytoplasmic Gal-1 and -7 – poor prognosis. How can the authors explain this contradiction? Did any of galectin combinations presented in Table 5 correlate with patient survival? What were such combinations in normal control samples? These issues must be addressed.

Discussion and Conclusion

Typically, the Discussion should start by presenting the main findings of the study, and then interpret them in view of directly relevant previous results, whereas general information regarding galectin role in cancer should be presented in the Introduction. The Discussion should serve to emphasize the contribution of the study to the knowledge of prognostic potential of galectins in ovarian cancer, which is missing.

Recommendation 1. Biochemical mechanisms underlying galectin activity in cancer should be presented in the Introduction rather than in the Discussion.

Recommendation 2. The result that "*Gal-1 stromal staining serves as an independent prognostic factor for overall survival*" has already been obtained in a previous study (**Kim et al. Eur J Cancer. 2012 Aug;48(12):1914-21. High galectin-1 expression correlates with poor prognosis and is involved in epithelial ovarian cancer proliferation and invasion**). This fact should be indicated and the previous study appropriately cited.

Recommendation 3. The statement that "*it is apparently nuclear and not cytoplasmic Gal-3 expression that has a major influence on patients' outcomes*" (lines 260, 261) is premature and does not correspond to the facts. Other studies (17, 27) obtained the opposite results both in terms of Gal-3 localization and cancer prognosis, as they showed that cytoplasmic Gal-3 had negative correlation with cancer prognosis. This statement should be deleted as the authors do not present enough evidence for total dismissal of the previous findings. Instead, the reason for such controversy between the present and earlier studies should be discussed.

Recommendation 4. Correlations between expression patterns of Gal-1, -3, and -7 should be interpreted in view of your own findings regarding distinct influence of these galectins on survival of ovarian cancer patients mentioned above, i.e., the fact that nuclear Gal-3 indicates good prognosis and cytoplasmic Gal-1 and -7 – poor prognosis, whereas their expression showed positive correlation. Given these data, the statement that "*This observation … suggests that galectins might also share common functions in ovarian cancer molecular biology*" (lines 286-288) is not supported by the results, as obviously high expression of Gal-3 inhibits cancer progression, while those of Gal-1 and -7 promote it, indicating that their functions are far from common in ovarian cancer according to your data.

Recommendation 5. The novelty of the study should be highlighted in the Discussion by stating how it furthered understanding of prognostic value of the investigated galectins in ovarian cancer.

Recommendation 6. The limitations of the study must be mentioned.

SUBMISSION CHECKLIST

Journal Scope

Section	Assessment	Comments
The paper can be submitted to the target journal.	Yes	*Scientific Reports* has a fairly broad scope and publishes original research in all areas of the natural and clinical sciences. In this regard, the manuscript meets the scope of the target journal.
The study conforms to all relevant ethical standards.	No	Please note that *Scientific Reports* requires a Data Availability Statement to be included in the Methods section of submitted manuscripts (see 'Availability of materials and data' section for more information).

Journal Requirements

Section	Assessment	Comments
The title page contains the title and all author information, including the complete contact details of the corresponding author.	No	*Scientific Reports* has a specific format for the presentation of author names. I have provided a template for you.
The paper is in the format preferred by the journal (MS Word, PDF, TeX).	Yes	*Scientific Reports* allows for the submission of manuscripts in the MS Word format.
All figures and tables have been prepared in the correct format and in keeping with the journal's	No	The tables have to be provided in an editable format.

requirements.		
In-text citations and references correspond to each other and are accurate.	NA	The references were not provided in this paper. Please make sure this is done prior to submission.
Citations have been provided where necessary.	Yes	-
A cover letter has been included with the manuscript.	Yes	A cover letter has been provided for you to submit to the target journal. This letter summarizes the key findings in your work and highlights the manuscript's relevance to the target journal.