

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Immunology

**ESPS manuscript NO:** 15758

**Title:** GRP78 expression beyond cellular stress; a biomarker for tumor manipulation.

**Reviewer's code:** 00608272

**Reviewer's country:** Japan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2014-12-09 09:38

**Date reviewed:** 2014-12-14 10:56

| CLASSIFICATION   | LANGUAGE EVALUATION   | SCIENTIFIC MISCONDUCT                          | CONCLUSION   |
|--|---|--|--|
| <input checked="" type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing                 | PubMed Search:                                 | <input checked="" type="checkbox"/> Accept             |
| <input type="checkbox"/> Grade B: Very good            | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title        | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good                 |   | <input type="checkbox"/> Duplicate publication |  |
| <input type="checkbox"/> Grade D: Fair                 | <input type="checkbox"/> Grade C: A great deal of language polishing  | <input type="checkbox"/> Plagiarism            | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade E: Poor                 | <input type="checkbox"/> Grade D: Rejected                            | <input checked="" type="checkbox"/> No         | <input type="checkbox"/> Minor revision                |
|  |   | BPG Search:                                    | <input type="checkbox"/> Major revision                |
|  |   | <input type="checkbox"/> The same title        |  |
|  |   | <input type="checkbox"/> Duplicate publication |  |
|  |   | <input type="checkbox"/> Plagiarism            |  |
|  |   | <input checked="" type="checkbox"/> No         |  |

## COMMENTS TO AUTHORS

Manuscript Review Comments ESPS Manuscript NO: 15758 Title: GRP78 expression beyond cellular stress; a biomarker for tumor manipulation] Authors: Drs. Britta Hardy and Annat Raiter General comments Authors reviewed and focused on some recent published literatures for studying the 78 KDa glucose-regulated proteins. It is interesting that GRP78 have two different roles on the apoptosis. One is hypoxia-induced intercellular GRP78 pathways to affect intracellular ATF PERK and P38, p-Akt and caspase pathway for inhibiting apoptosis. This pathway is effective for inhibition of some ischemia diseases such as cardiac or brain ischemia diseases. Another is Cellular surface GRP78 regulated survival and apoptotic pathways. This new pathway may provide a new theoretical concept for treatment of some cancers' diseases. As conclusion by the authors, "the significance of cell surface GRP78 expression, beyond cellular stress, might be the focus of new therapeutic strategies for ischemic diseases. Pharmacological manipulation of cell surface GRP78 in tumor cells may serve as a new modality for tumor therapy". Therefore, it has very important significance for treatment the cancer diseases if the biomarkers are really successful be remedied. Specific Comments: 1. Even though the title wrote: GRP78, a biomarker for tumor: However, there are no any sentences to show



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author how to thinking or how to do it to use GRP78 as a biomarker for diagnose or treatment tools. Please add some sentences for this. 2. Page 5, line 2, "Ischemic Vascular Diseases (IVD)", there are no necessary use uppercase for first capital letters for first alphabet; 3. Sentence "that can might effect the legs" maybe "that can might affect the legs". 4. Also in the same page, the 4th paragraph, line 4, the word "reveresed" maybe "reversed". 5. Page 7, authors may need to consider for adding a figure to summarize some possibilities for how GRP78 escapes to the cell surface in tumor cells that may be very important and interesting.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Immunology

**ESPS manuscript NO:** 15758

**Title:** GRP78 expression beyond cellular stress; a biomarker for tumor manipulation.

**Reviewer's code:** 00033009

**Reviewer's country:** Afghanistan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2014-12-09 09:38

**Date reviewed:** 2014-12-09 21:57

| CLASSIFICATION                                    | LANGUAGE EVALUATION   | SCIENTIFIC MISCONDUCT                          | CONCLUSION   |
|---|---|--|--|
| <input type="checkbox"/> Grade A: Excellent       | <input type="checkbox"/> Grade A: Priority publishing                 | PubMed Search:                                 | <input type="checkbox"/> Accept                        |
| <input type="checkbox"/> Grade B: Very good       | <input checked="" type="checkbox"/> Grade B: Minor language polishing | <input type="checkbox"/> The same title        | <input type="checkbox"/> High priority for publication |
| <input checked="" type="checkbox"/> Grade C: Good | <input type="checkbox"/> Grade C: A great deal of language polishing  | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D: Fair            | <input type="checkbox"/> Grade D: Rejected                            | <input checked="" type="checkbox"/> Plagiarism | <input checked="" type="checkbox"/> Minor revision     |
| <input type="checkbox"/> Grade E: Poor            |   | [Y] No   | <input type="checkbox"/> Major revision                |
|   |   | BPG Search:                                    |  |
|   |   | <input type="checkbox"/> The same title        |  |
|   |   | <input type="checkbox"/> Duplicate publication |  |
|   |   | <input type="checkbox"/> Plagiarism            |  |
|   |   | [Y] No   |  |

## COMMENTS TO AUTHORS

The review entitled "GRP78 expression beyond cellular stress; a biomarker of tumor manipulation" by Hardy and Raiter is an interesting manuscript showing the potential role of GRP78 as modulator of cell survival/death in different malignancies. However, more than 100 papers have been recently published showing induction of GRP78-related cell death signaling. The authors should include a paragraph in the last section of the manuscript suggesting the role (if any) of GRP78 on the intrinsic or extrinsic cell death pathways.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Immunology

**ESPS manuscript NO:** 15758

**Title:** GRP78 expression beyond cellular stress; a biomarker for tumor manipulation.

**Reviewer's code:** 02445717

**Reviewer's country:** Spain

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2014-12-09 09:38

**Date reviewed:** 2014-12-24 04:16

| CLASSIFICATION   | LANGUAGE EVALUATION  | SCIENTIFIC MISCONDUCT                          | CONCLUSION   |
|--|--|--|--|
| <input type="checkbox"/> Grade A: Excellent            | <input checked="" type="checkbox"/> Grade A: Priority publishing     | PubMed Search:                                 | <input checked="" type="checkbox"/> Accept             |
| <input checked="" type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language polishing           | <input type="checkbox"/> The same title        | <input type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good                 | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection                     |
| <input type="checkbox"/> Grade D: Fair                 | <input type="checkbox"/> Grade D: Rejected                           | <input checked="" type="checkbox"/> Plagiarism | <input type="checkbox"/> Minor revision                |
| <input type="checkbox"/> Grade E: Poor                 |  | [Y] No   | <input type="checkbox"/> Major revision                |
|  |  | BPG Search:                                    |  |
|  |  | <input type="checkbox"/> The same title        |  |
|  |  | <input type="checkbox"/> Duplicate publication |  |
|  |  | <input type="checkbox"/> Plagiarism            |  |
|  |  | [Y] No   |  |

## COMMENTS TO AUTHORS

This is a very good review paper about the role of the heat shock GRP78 protein expression in normal and tumor cells in cellular stress, as well as a possible biomarker for tumor manipulation for a new modality of cancer therapeutic intervention. The authors have broad experience in this field and have published several papers about the heat shock GRP78 protein. In summary, it is a competent review addressing a subject of interest and potential value for the scientific community, and it should be useful for interdisciplinary correlative studies.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Immunology

**ESPS manuscript NO:** 15758

**Title:** GRP78 expression beyond cellular stress; a biomarker for tumor manipulation.

**Reviewer's code:** 01560498

**Reviewer's country:** Japan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2014-12-09 09:38

**Date reviewed:** 2014-12-24 19:26

| CLASSIFICATION   | LANGUAGE EVALUATION  | SCIENTIFIC MISCONDUCT                          | CONCLUSION  |
|--|--|--|---|
| <input checked="" type="checkbox"/> Grade A: Excellent | <input checked="" type="checkbox"/> Grade A: Priority publishing     | PubMed Search:                                 | <input type="checkbox"/> Accept                                   |
| <input type="checkbox"/> Grade B: Very good            | <input type="checkbox"/> Grade B: Minor language polishing           | <input type="checkbox"/> The same title        | <input checked="" type="checkbox"/> High priority for publication |
| <input type="checkbox"/> Grade C: Good                 | <input type="checkbox"/> Grade C: A great deal of language polishing | <input type="checkbox"/> Duplicate publication | <input type="checkbox"/> Rejection                                |
| <input type="checkbox"/> Grade D: Fair                 | <input type="checkbox"/> Grade D: Rejected                           | <input checked="" type="checkbox"/> No         | <input type="checkbox"/> Minor revision                           |
| <input type="checkbox"/> Grade E: Poor                 |  | BPG Search:                                    | <input type="checkbox"/> Major revision                           |
|  |  | <input type="checkbox"/> The same title        |   |
|  |  | <input type="checkbox"/> Duplicate publication |   |
|  |  | <input type="checkbox"/> Plagiarism            |   |
|  |  | <input checked="" type="checkbox"/> No         |   |

## COMMENTS TO AUTHORS

This paper is well written. If possible, please add important articles of cell-surface biomarkers, involving GRP 78.