

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 83260

Title: The potential of damage associated molecular patterns (DAMPs) in synergising radiation and the immune response in oesophageal cancer.

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03806663

Position: Editorial Board

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: Ireland

Manuscript submission date: 2023-01-14

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-02-19 14:58

Reviewer performed review: 2023-02-19 17:41

Review time: 2 Hours

Scientific quality	☐ Grade A: Excellent ☒ Grade B: Very good ☐ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Novelty of this manuscript	☐ Grade A: Excellent ☒ Grade B: Good ☐ Grade C: Fair ☐ Grade D: No novelty
Creativity or innovation of this manuscript	☐ Grade A: Excellent ☒ Grade B: Good ☐ Grade C: Fair ☐ Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	☐ Grade A: Excellent ☒ Grade B: Good ☐ Grade C: Fair ☐ Grade D: No scientific significance
Language quality	☐ Grade A: Priority publishing ☒ Grade B: Minor language polishing ☐ Grade C: A great deal of language polishing ☐ Grade D: Rejection
Conclusion	☐ Accept (High priority) ☒ Accept (General priority) ☐ Minor revision ☐ Major revision ☐ Rejection
Re-review	☐ Yes ☒ No
Peer-reviewer statements	Peer-Review: ☒ Anonymous ☐ Onymous
	Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

This article discusses a hot topic in the field of GI malignancy. The sample size is small, and randomized controlled studies and meta-analyses are needed to prove the results of this article. The level of these tumor markers needs to be checked in advanced esophageal adenocarcinomas. The level of these markers varies between well-differentiated and poorly differentiated adenocarcinoma.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00291404

Position: Peer Reviewer

Academic degree: PhD

Professional title: Associate Professor, Professor

Reviewer's Country/Territory: United States

Author's Country/Territory: Ireland

Manuscript submission date: 2023-01-14

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-03-06 14:35

Reviewer performed review: 2023-03-06 19:18

Review time: 4 Hours

Scientific quality	☐ Grade A: Excellent ☒ Grade B: Very good ☐ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Novelty of this manuscript	☒ Grade A: Excellent ☐ Grade B: Good ☐ Grade C: Fair ☐ Grade D: No novelty
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	Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

The authors have examined the expression of two DAMPs (ecto-calreticulin and HMGB1) on the cell surface of oesophageal cancer cells in vitro. They have used two cancer cell lines, one radiosensitive (OE33P) and another radioresistant (OE33R), with radiation regimens of either Bolus dosing or hypofractionated dosing, then with various oxygen concentrations [normoxia (21% O₂), physoxia (5% O₂) and hypoxia (0.5% O₂) conditions, and finally under nutrient depletion conditions (glutamine and glucose. The authors reached some interesting conclusions. In the second portion of the study, they took advantage of blood samples and tumor biopsies from OAC patients before and after therapy, and looked for DAMP expression on T cells, CD45- and CD45+ cells. The authors observed that significantly higher levels of DAMPs are expressed in the tumor tissue compared to blood and this holds true for calreticulin in the post-treatment samples. Overall, this is an interesting study. 1. The authors have made some interesting observations even though the significance of the findings is not clear at this time. 2. There are three key markers of ICD: the cell surface expression of CRT (ecto-CRT) and extracellular release of HMGB1 and ATP. The released HMGB1 and ATP are



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“get-me” signal while cell surface CRT is an “eat-me” signal. In the current study, the authors chose to examine the expression of cell surface HMGB1, instead of released HMGB1, probably for its convenience of analysis. It is not clear to me how much of the HMGB1 would retain on the cell surface and if the cell surface-retained HMGB1 is also a good DAMP indicator? As the authors cannot go back to analyze the released HMGB1 for this study, the authors need to discuss the issue with some previous studies (papers) to support their assumptions. One minor point: The following existing references need correct or additional information: Ref #4. Article number (AN)? Ref #18. AN? Ref #27. AN?