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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology
Manuscript NO: 38475
Title: Emerging evidence of the molecular landscape specific for hematogenous metastasis from gastric cancer
Reviewer's code: 00112071
Reviewer's country: Australia
Science editor: Ya-Juan Ma
Date sent for review: 2018-02-23
Date reviewed: 2018-02-25
Review time: 2 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[Y] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This manuscript in present form does not have much clinical relevance. It's value for patient benefit would be raised by addressing below comments. Specific comments: 1. Reference 12 is not a good reference to support ascertion. This is a phase II trial of intraperiotoneal therapy which treats transcoelomic spread and not relevant in this situation. Contrary to this there is level 1 evidence for the benefit of adjuvant therapy in both Western and Asian populations with gastric cancer.There are large well conducted phase III trials to support this: MAGIC, CLASSIC, ACTG-GC, The GASTRIC metanalysis further supports the benefit of adjuvant systemic therapy in gastric cancer as a standard of care. 2. INT0116 demonstrates benefit of chemoradiotherapy as a adjuvant strategy. 3.The focus of this review should be to evaluate potential targets that can be drugable to improve on the present treatments which are considered to be best

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practice and standard of care. 4. Matrix metalloproteinases have already been targeted in clinical trials. Marimastat trialed in the 1990's. Gilead GS5745 in present clinical testing in advanced gastric cancer 5. Exosomes to deliver miRNA 214 to reverse cisplatin in tumour resistance 6. NFKB as target. Justification: Chemotherapy can elicit cellular stress that confers chemoresistance through NFKB 7. VEGF as target. Bevacizumab (AVAGAST study) and ramucirumab (RAINBOW and REGARD trials) proven in clinical management. 8. IL6 antibodies available 9. Her2 targeting used routinely in metastatic gastric cancer with Her2 overexpression. ToGA trial of trastuzumab. Trial of lapatinib 10. Listing HIF targeting drugs available and where they are in clinical testing.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology
Manuscript NO: 38475
Title: Emerging evidence of the molecular landscape specific for hematogenous metastasis from gastric cancer
Reviewer's code: 00573611
Reviewer's country: Taiwan
Science editor: Ya-Juan Ma
Date sent for review: 2018-02-23
Date reviewed: 2018-03-01
Review time: 6 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Shimizu et al. reviewed the molecules reportedly contributing to hematogenous metastasis from gastric cancer and to become the groundwork for the further development of novel biomarkers and molecular targets. Comments This is an interesting review article. This manuscript is well-written. The authors provided the novel information for the molecular landscape specific for hematogenous metastasis from gastric cancer. The reviewer has no further comments and this review article can be accepted to publish.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology
Manuscript NO: 38475
Title: Emerging evidence of the molecular landscape specific for hematogenous metastasis from gastric cancer
Reviewer's code: 03008931
Reviewer's country: China
Science editor: Ya-Juan Ma
Date sent for review: 2018-02-23
Date reviewed: 2018-03-10
Review time: 15 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This work by Drs. Shimizu et al., have summarized molecules reportedly contributing to hematogenous metastasis from gastric cancer (GC), the authors intend to establish the landscape of molecules that specifically participate in metastasis in distinct secondary organs in GC, and hope this will lead to the development of novel biomarkers for patient stratification. Numerous published works have indicated various molecules that are involved in the processes of metastasis, this work focus on hematogeneous metastasis markers as potential marker in this process. The work is therefore interesting, novel with merit. The manuscript appears well organized and written, but also appears missing in-depth analysis of the selected molecules and inner link between the metastasis and mechanisms, of which important aspects are roles of epigenetics, stem cell, E-cadherin etc. The work may require more in-depth revision with supporting

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data to strengthen the claim and point out directions for future investigation to guide readers. Authors are encouraged to revise and add more input to make the manuscript more attractive theoretically.