

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 5853

Title: Molecular biomarkers for the early detection of metastatic colorectal cancer cells and their clinical significance: current status

Reviewer code: 00112237

Science editor: Gou, Su-Xin

Date sent for review: 2013-09-29 13:51

Date reviewed: 2013-10-07 16:03

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google 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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Add a paragraph about the importance of stem cell markers.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 5853

Title: Molecular biomarkers for the early detection of metastatic colorectal cancer cells and their clinical significance: current status

Reviewer code: 00069881

Science editor: Gou, Su-Xin

Date sent for review: 2013-09-29 13:51

Date reviewed: 2013-11-17 23:13

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The manuscript by Kamiyama H, et al. reviewed the molecular biomarkers that were used for the detection of metastatic colorectal cancer (CRC) cells in different types of clinical samples and their clinical significance. It provides a relatively comprehensive information in this field. However, these molecular biomarkers were not referred to "early detection", and also it is improper to put a method (immunomagnetic separation) into the molecular biomarkers. A major revision should be made before the consideration of this manuscript to be published in the World Journal of Gastroenterology. A few suggestions to improve the manuscript are as follow. 1.The references should be closely related to the early detection of metastatic colorectal cancer (CRC) cells; 2.The manuscript should be re-organized, suggesting that each biomarker is a separate subtitles in which the detection method, samples, clinical significance are described together. 3.More recently published articles related should be referred and their results should be presented in the manuscript. 4.The significance of the biomarkers should be more highlighted because readers are interested in it.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 5853

Title: Molecular biomarkers for the early detection of metastatic colorectal cancer cells and their clinical significance: current status

Reviewer code: 00070803

Science editor: Gou, Su-Xin

Date sent for review: 2013-09-29 13:51

Date reviewed: 2013-12-02 14:34

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google 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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

see editor comments

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 5853

Title: Molecular biomarkers for the early detection of metastatic colorectal cancer cells and their clinical significance: current status

Reviewer code: 00504731

Science editor: Gou, Su-Xin

Date sent for review: 2013-09-29 13:51

Date reviewed: 2013-12-04 22:52

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

This review manuscript (by Kamiyama et al) described types of molecular biomarkers and clinical specimens that might be used for monitoring progression or recurrence of CRC. Although the authors intended to review the biomarkers for early detection of metastatic CRC, none of the biomarkers described are metastatic CRC specific, as those biomarkers also present in local regional tumors and could be detected in body fluids. Presence of those biomarkers in lymph node or bone marrow samples may suggest metastasis, however, such samples are less accessible in clinic. While many biomarkers have been reported by various groups, few of them have been translated to clinic application. It will be helpful to include a discussion on how to translate some promising biomarkers to clinical applications. The authors described the heterogeneous mixture of normal and cancer cell which may affect levels of a biomarker in the samples, however, CRC is a heterogenic disease. Frequencies of each biomarker in CRC will likely determine the sensitivity. Combination of a set of biomarkers will be required to increase the sensitivity. A discussion on recent publications on this topic will be helpful.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 5853

Title: Molecular biomarkers for the early detection of metastatic colorectal cancer cells and their clinical significance: current status

Reviewer code: 00068364

Science editor: Gou, Su-Xin

Date sent for review: 2013-09-29 13:51

Date reviewed: 2013-12-12 00:11

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input checked="" type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Because approximately half of all colorectal cancer (CRC) patients develop local recurrence or distant metastasis, it suggests that conventional pathology may fail to detect occult nodal metastasis. The molecular detection of metastatic cancer cells in various types of clinical samples has been investigated as a potential prognostic marker. Therefore, it is important to identify reliable markers that can be used in clinical practice, indicating the significance of the research contents. With a title of "Molecular biomarkers for the early detection of metastatic colorectal cancer cells and their clinical significance: current status", the authors reviewed the prognostic value of different types of molecular biomarkers of CRC in the detection of metastatic cancer cells. It is important in not only in research, but also in clinic. However, many contents in the review are focus on identify CRC tumor associated markers that may not necessary relevant to tumor metastasis. Even the main conclusion is based on comparison of molecular marker between tumor specimens and normal controls that are far from the goal of this review. My major concern is the covered areas of this review are too broader, including different clinical samples (serum/ plasma, lymph nodes, and bone marrow), different molecular markers (DNA methylation, mRNA, miRNAs, mutation, protein and CellSearch), and different methods used to detect those markers. It makes the overall review lack of innovation in the selection of relevant researches. The authors only listed limited results for those markers from different studies, but no further thinking about the reliability of those results, and the comparisons between different studies and markers. What you want to tell the readers about these studies? No sure the clinical significance if the sensitivity of an assay is so low (22%-44%)? Why select these studies? No any discussion for the limitations or advantages for different markers in different



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samples? The authors mention a crucial issue in biomarker study that “the ratio of neoplastic cells to normal cells varies considerably from one clinical sample to another. clinical samples are frequently a heterogeneous mixture of normal and cancer cell DNA, RNA, and protein.” However, in this review, no any discussion is for this issue. The review is presented in a readable way, and no ethics concerns. Overall, this review only simply presents previous results of CRC biomarkers studies, but no deeply thinking and discussion for important issues involved in biomarker discovery, validation, and clinical application. No future direction is pointed out, especially in investigation of CRC metastatic markers. It is unclear why in the future to conduct “clinical trials is a crucial part of marker development” if no reliable markers have been identified.