



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23358

Title: Serrated colorectal cancer: molecular classification, prognosis, and response to chemotherapy

Reviewer's code: 03442051

Reviewer's country: United Kingdom

Science editor: Yuan Qi

Date sent for review: 2015-11-12 11:55

Date reviewed: 2015-11-14 20:53

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input 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 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"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Comments and Suggestions: 1) Text Highlighted in yellow colour Although only a minority of HPs will progress to CRC, mainly when they are right-sided, there can be progression to other serrated lesions that can evolve into CRC. ----- Please reference it. TSAs account for about 1%-2% of serrated polyps and are more frequent on the left colon. Finally, MPs constitute around 1%-4% of serrated polyps. Mixed tumors usually comprise a dysplastic lesion (TSA or conventional adenoma) plus a non-dysplastic one, usually an HP or SSA. ----- Please provide evidence and reference it. CIMP-H is present in around 41%-73.3% of MVHPs but only in about 8%-18.2% of GCHPs. The proportion of CIMP-H in evolved serrated lesions is similar: the proportion is about 44%-76.8% in TSAs and about 80% in SSAs ----- Please provide evidence and reference it. , there seems to be a strong relationship between the CIMP status and BRAF mutations, with the prognostic value of CIMP status being related to the presence of BRAF mutations and, less frequently, to the presence of KRAS mutations ----- Please reference it. It seems likely that when a CIMP serrated tumor shows MSI, the MSI acts to confer a good prognosis. ----- Please reference this sentence. MLH1 and



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MGMT methylation have been suggested to be predictors of good prognosis ----- Is this related to serrated polyp pathway at all? Please explain in detail. 2) Text highlighted in green colour Notably, the combination of KRAS mutation plus low grade CIMP - Are there any phenotypical differences ? p16INK4a and IGFBP7 ----- Please provide their exact role in CRC microRNA-31 ----- Please provide little introduction about their role in CRC Moreover, combined MSS and CIMP CRC with mutant BRAF or KRAS frequently correlates with liver metastasis at diagnosis and has the worst prognosis of all CRCs ----- Metastatic disease is a different concept altogether, so please add a paragraph explaining the role of CIMP in metastasis. 3) Text highlighted in red colour - Needs either alteration or more further explanation Upregulation ---- up regulation it appeared to counter the adverse prognostic effect of BRAF mutation in serrated cancers ---- How does BRAF and CIMP interacts at molecular level? This is very bold statement. Please explain. In addition, patients with CIMP tumors seemed to benefit more after the tumors were stratified according to MSI status. Moreover, in this study, CIMP status was more strongly associated with the response to irinotecan than was MMR status. --- MSI status is a independent predictor. CIMP status could be mere association. Can you pool the data published in literature on both MSI and CIMP status and conduct a subgroup analysis to assess the differences.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23358

Title: Serrated colorectal cancer: molecular classification, prognosis, and response to chemotherapy

Reviewer's code: 00227403

Reviewer's country: Italy

Science editor: Yuan Qi

Date sent for review: 2015-11-12 11:55

Date reviewed: 2015-11-16 02:53

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> 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"/> 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

In the section introduction the authors should clarify the term "CpG islands" Pag 6 the authors should clarify the term "MAPK pathway" Pag 12 In the sentence "In the QUASAR study, KRAS was not a negative predictive factor for the response to standard CT", the authors should detail the drugs included in the standard CT. This review need of a conclusion like "key messages for clinicians" where the authors conclude about the main points of this field.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23358

Title: Serrated colorectal cancer: molecular classification, prognosis, and response to chemotherapy

Reviewer's code: 00068574

Reviewer's country: France

Science editor: Yuan Qi

Date sent for review: 2015-11-12 11:55

Date reviewed: 2015-11-19 19:31

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" 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 type="checkbox"/> High priority for publication
<input checked="" 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

This manuscript is a detailed and well-documented review about serrated CRC and the associated molecular mechanisms. There are different recent reviews dealing with this topic but the originality of the present manuscript is to focus on the prognosis and response to chemotherapy according to the characteristics of the serrated CRC. The authors should include in their references the interesting review by Haque et al (Current Gastroenterol rep, 2014).



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23358

Title: Serrated colorectal cancer: molecular classification, prognosis, and response to chemotherapy

Reviewer's code: 03270739

Reviewer's country: China

Science editor: Yuan Qi

Date sent for review: 2015-11-12 11:55

Date reviewed: 2015-11-23 09:42

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" 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 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"/> 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

It is a very good and helpful review for the prognosis and chemotherapy on CRC. Detailed information and discussion were involved, which was very suggestive. One suggestion is that authors should make a conclusion in the final part of the review to summarize the total content and progress. It should be easier for readers to grasp the main points of their review.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23358

Title: Serrated colorectal cancer: molecular classification, prognosis, and response to chemotherapy

Reviewer's code: 03270735

Reviewer's country: Turkey

Science editor: Yuan Qi

Date sent for review: 2015-11-12 11:55

Date reviewed: 2015-11-23 17:11

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
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<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		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

should not be regarded



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23358

Title: Serrated colorectal cancer: molecular classification, prognosis, and response to chemotherapy

Reviewer's code: 00001114

Reviewer's country: Japan

Science editor: Yuan Qi

Date sent for review: 2015-11-12 11:55

Date reviewed: 2015-11-24 20:06

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This review entitles "Serrated colorectal cancer: molecular classification, prognosis, and response to chemotherapy" is well-written and comprehensive review about this subject. I have one comment – I feel a sense of a little discomfort about the title. I was wondering if all advanced colorectal cancer with the genetic profiles that show BRAF gene mutations, KRAS gene mutations, MSI, or hypermethylation of CpG islands is derived from serrated polyps via serrated pathway. Because, there are few data regarding their natural course from serrated polyps to advanced cancer despite the increased recognition of the importance of SSA/Ps and serrated pathway. It seems that this review is premised on above because of including the prognosis or response to chemotherapy. Therefore, please describe the natural course from serrated polyps to advanced cancers based on recent knowledge or reconsider the title. Minor 1. Please show the reference in Page 4, Line 10, TSA account about 1-2%, and MPs constitute around 1-4% of serrated polyps.