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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12238

Title: ARID1A expression in gastric adenocarcinoma: clinicopathological significance and correlation with DNA mismatch repair status

Reviewer code: 02954962

Science editor: Yuan Qi

Date sent for review: 2014-07-02 10:37

Date reviewed: 2014-07-07 15:17

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 type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This article is suitable for world Journal of gastroenterology



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12238

Title: ARID1A expression in gastric adenocarcinoma: clinicopathological significance and correlation with DNA mismatch repair status

Reviewer code: 02965551

Science editor: Yuan Qi

Date sent for review: 2014-07-02 10:37

Date reviewed: 2014-07-08 02:55

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"/> Existing	<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 checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Stratify the age according to sex and then reanalyze the data. This might change the conclusions.



ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12238

Title: ARID1A expression in gastric adenocarcinoma: clinicopathological significance and correlation with DNA mismatch repair status

Reviewer code: 00503536

Science editor: Yuan Qi

Date sent for review: 2014-07-02 10:37

Date reviewed: 2014-07-14 21:02

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"/> Existing	<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	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The manuscript written by Inada et al. analyzed ARID1A expression and its correlation with DNA mismatch repair status in a large series of primary gastric adenocarcinoma. They found that ARID1A inactivation is associated with lymphatic invasion, lymph node metastasis and MMR deficiency. The data are important and provide novel information in the management of patients with gastric adenocarcinoma. However, there are some concerns that need to be addressed. Major points

1. Although multivariate analysis in Cox’s proportional hazard model show weak association between abnormal ARID1A expression and a poor prognosis, abnormal ARID1 expression does not affect disease specific survival as shown in Fig.3. The interpretation of the data are confusing, and the authors should discuss more on that point.
2. There are four different patterns of abnormal ARID1A expression as shown in Fig. 2, its association with lymphatic invasion, lymph node metastasis, prognosis or MMR deficiency is not demonstrated.

Minor point 1. Figures 1 and 2 are not shown in the Results section.

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12238

Title: ARID1A expression in gastric adenocarcinoma: clinicopathological significance and correlation with DNA mismatch repair status

Reviewer code: 00068090

Science editor: Yuan Qi

Date sent for review: 2014-07-02 10:37

Date reviewed: 2014-07-15 00:58

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"/> Existing	<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
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<input checked="" type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Gastric cancer is a heterogeneous disease with diverse molecular and histological subtypes. Has long been known that gastric cancer results from a combination of environmental factors and the accumulation of generalized and specific genetic alterations. Many of the genetic or epigenetic alterations associated with gastric cancer, including loss of heterozygosity, microsatellite and chromosomal instability and hypermethylation, have been reported. Understanding these alterations and the molecular mechanisms involved in gastric carcinogenesis will be critical for the improvement of diagnosis, therapy and prognosis prediction of this disease. It is known that ARID1A (BAF250a), one of the accessory subunits of the SWI/SNF chromatin remodeling involved in the regulation of gene expression, has been reported to be mutated or lost in between 8% and 27% of gastric cancer. Recent studies have identified ARID1A as a tumor suppressor. 1) To investigate the role of ARID1A gene in primary gastric cancer pathogenesis, real-time quantitative PCR and western blotting should be used to examine the ARID1A expression in paired cancerous and noncancerous tissues. To further investigate the clinicopathological and prognostic roles of ARID1A expression, the authors performed immunohistochemical analyses of the paraffin-embedded gastric cancer tissue blocks 2) The authors must show that the loss of ARID1A expression correlated with depth of tumor infiltration and tumor grade, but not only with age, gender, tumor size, distant metastasis and tumor locus or local lymph node metastasis. 3) The authors should demonstrate if ARID1A was



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expressed at different mRNA and protein level in gastric cancer tissues than corresponding non-cancerous mucosa. 4) In methods, the authors indicate that sections were deparaffinized and autoclaved at 121°C for 15 min in Target retrieval solution with a high pH of 9 (Dako, Glostrup, Denmark) and then allowed to cool at room temperature. Normally, in immunohistochemistry the slides were boiled in antigen retrieval buffer containing 0.01 M sodium citrate-hydrochloric acid (pH = 6.0) for 15 min in a microwave oven. What it is the explication to use a solution with high pH? 5) The authors should present data about immunohistochemistry quantification. In this sense, the total ARID1A immunostaining score should be calculated as the sum of the percent of positively stained tumor cells and the staining intensity. So, based on the ARID1A expression levels, the gastric cancer patients can be divided into groups. 6) The authors in discussion chapter should include that loss of ARID1A expression in cancers may vary depending on tissue types and with microsatellite instability (MSI) status.



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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 12238

Title: ARID1A expression in gastric adenocarcinoma: clinicopathological significance and correlation with DNA mismatch repair status

Reviewer code: 00503442

Science editor: Yuan Qi

Date sent for review: 2014-07-02 10:37

Date reviewed: 2014-07-20 17:24

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"/> Existing	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

I read with great interest the revised version of the manuscript entitled "ARID1A expression in gastric adenocarcinoma: clinicopathological significance and correlation with DNA mismatch repair status" by Ryo Inada et al. The manuscript is interesting and well conducted. In order to improve the scientific value of the manuscript several orthographical and grammatical errors found throughout the manuscript should be rectified. Reference no.26 should be updated.