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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 8918
Title: IGF2 DMR hypomethylation in relation to pathological and molecular features of serrated lesions
Reviewer code: 00040631
Science editor: Gou, Su-Xin
Date sent for review: 2014-01-11 16:34
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

WJG JAPANESE ARTICLE This is an interesting multicentric study which provides an important contribution to the literature. There are some criticisms to meet prior to accept it for publication. The authors should better specify the different categories of serrated polyps, namely the SSAs sessile serrated adenomas, as the literature report a architectural dysplasia in such polyps, not a cytological dysplasia as reported for TSAs traditional serrated adenomas. Abstract: "More then 100" please state exact numbers Abstract: P ≤ 0.038 does it refer to DMR0 or LINE1? Introduction: "SSAs are hypothesized to develop to some populations of MSI-high CRCs with BRAF mutation in the proximal colon" please change the word populations In the introduction I would spend a sentence on the mechanism of carcinogenesis of DMR0/IGF2 While the rationale for Kras, BRAF and MSI testing is implicit in the introduction the rationale of examining IGF and PIK3 is not explained Results: in table 2 I is unclear if the 120 SSA include dysplasia. I would put all the dysplasia cases in table 3 In table 3 SSA are missing because they are reported in table 2 There is a large amount of data that is difficult to digest, the authors should use multivariate analysis where possible It is unclear how DMR0 hypometilation correlates with MSI, Kras, BRAF and PIK3, specifically was DMR0 hypometylation correlated with Kras mutations? Discussion: "Therefore, our data challenge the common conception of discrete molecular features of SSAs versus other serrated lesions (TSAs and HPs) and may have a substantial impact on clinical and translational research, which has typically been performed with the dichotomous classification of SSAs"= I do not understand, since the SSA had different levels of methylation compared to TSA and HP, why the

authors say that their findings challenge the concept of different molecular features among serrated lesions As the authors state, the conclusions on TSA high grade dysplasia (and SSA HGD) are based on few samples, TSA per se was not correlated with hypometylation so the results are very preliminary. Finally, given the high percentage of CRC cases with DMR0 hypometylation how do the authors reconcile this with the rarity of TSA? DISCUSSION The authors write: "IGF2 DMRO hypomethylation was less frequently detected in SSAs compared with HPs TSAs and non serrated adenoma" .

The interaction between hyperplastic HPs microvescicular and SSAs should be better clarified. Passages and non return point of IGF2 DMRO between HPs and SSAs should be better detailed.

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ESPS Peer-review Report
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[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
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[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
This is an original article which is based on a huge analyzed data, indicating the role of IGF2 DM0 hypomethylation in the progression of serrated tumors related to malignant transformation. It should be determined that it is worthy to be published in this journal.