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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 13962
Title: Combined detection of plasma GATA5 and SFRP2 methylation is a valid noninvasive biomarker for colorectal cancer and adenomas
Reviewer code: 02908153
Science editor: Yuan Qi
Date sent for review: 2014-09-11 20:03
Date reviewed: 2014-09-14 17:31

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	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

The authors describe the Hypermethylated GATA5 was identified as a novel plasma gene in CRC and adenomas. In this study, a combination of GATA5 and SFRP2 methylation could be used as a promising marker for the detection, diagnosis, and prognosis of CRC and adenomas. 1. The details of the TNM stage should be mentioned in the materials and methods section because the reader will not be able to interpret the data. 2. How did you combined ROC analyses using the two genes, and please show us the predicted values of logistic regression equation, and provide AUC. 3. In Figure 2, (A), (B), and (C) may refer to GATA5, SFRP2, and ITGA4.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 13962
Title: Combined detection of plasma GATA5 and SFRP2 methylation is a valid noninvasive biomarker for colorectal cancer and adenomas
Reviewer code: 02451547
Science editor: Yuan Qi
Date sent for review: 2014-09-11 20:03
Date reviewed: 2014-09-24 08:44

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	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

This paper aimed to investigate the feasibility of detecting aberrant hypermethylated GATA binding protein 5 (GATA5), secreted frizzled-related protein gene 2 (SFRP2), and integrin, alpha 4 (ITGA4) in plasma DNA as noninvasive biomarkers for colorectal cancer (CRC) or adenomas, and to evaluate the clinical utility of these markers. The results showed that hypermethylated GATA5 was identified as a novel plasma gene in CRC and adenomas, and it showed high potential as a biomarker in plasma-based DNA testing. However, there are some issues: 1. In this paper, the mean age of the patients in the CRC, adenoma, and control groups was 56.64 ± 8.27, 57.00 ± 11.27, and 61.40 ± 12.41 years, respectively. Why the authors selected 60 years old as cut-off point when stratified by age. 2. GATA5 methylation in CRC tissues and in normal colon tissue samples from controls has been explored in other ethnic population. Why the authors did not detect it in CRC tissues when they detected it in plasma. If the data were obtained, the paper might provide more meaning information. The authors could compare the sensitivity and specificity between in plasma and in tissues and compare them with previous studies. 3. In this paper, the authors declared that most of these studies only analyzed a small number of plasma samples. Do the authors think the sample size is enough large to detect the difference among different groups, would you please give the power of statistical test. 4. In this paper, the authors found the methylation frequency of GATA5 gene was significantly higher in CRC plasma samples and in adenomas than in normal plasma samples and GATA5

methylation in the plasma significantly correlated with larger tumor size ($p = 0.019$), differentiation status ($p = 0.038$), TNM stage ($p = 0.008$), and lymph node metastasis ($p = 0.008$), but there was no statistical difference in the incidence of GATA5 gene in the plasma of CRC and adenoma patients. Would you please give the reasonable guess and possible clinical meanings.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 13962
Title: Combined detection of plasma GATA5 and SFRP2 methylation is a valid noninvasive biomarker for colorectal cancer and adenomas
Reviewer code: 02906811
Science editor: Yuan Qi
Date sent for review: 2014-09-11 20:03
Date reviewed: 2014-09-26 21:01

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	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

In this paper, the authors investigated the feasibility of detecting aberrant methylation of GATA5, SFRP2, and ITGA4 promoters in plasma DNA as noninvasive biomarkers for colorectal cancer (CRC) or adenomas, and to evaluate the clinical utility of these markers. Rationale and aim are clear. However, I have several concerns as follow: Abstract: I think "prognosis" should be removed from the conclusion based on the results of this study . Methods: 1 How did the authors estimate the sample size? 2 The methylation status of GATA5, SFRP2 and ITGA4 genes should be detected both in solid tissue from CRC, adenomas and normal colorectal tissue and their corresponding plasma, especially in the early stage of research on this issue. Results： 1 The title "Plasma GATA5 methylation as a coordinate marker for CRC and adenomas with SFRP2 methylation" can not reflect the content of this paragraph. 2 What is "OR analysis"? 3 The results of sensitivity and specificity for GATA5, SFRP2 and ITGA4 methylation and their combination testing should be shown in a table. 4 With which method did the authors calculate the sensitivity and specificity? 5 How did the authors determine the cutoff values ? Figure 2: There are several mistakes and the quality of the images should be improved.