

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 24629

**Title:** Longitudinal molecular characterization of endoscopic specimens from colorectal lesions based on CIMP/MSI/BRAF/KRAS classification: prospective comparison of large adenomas to early and late carcinomas

**Reviewer's code:** 00069634

**Reviewer's country:** Mexico

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-02-29 08:46

**Date reviewed:** 2016-03-10 01:52

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 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input 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 type="checkbox"/> No	

## COMMENTS TO AUTHORS

The 4 molecular subtypes of Colorectal Cancer, as defined by combinations of their CIMP and MSI statuses, differ with respect to demographics, clinical features, prognosis, response to therapy, repertoires of activated or inactivated genes, and histomorphologic features that can be readily recognized by pathologists in endoscopic biopsies. The fact that each molecular subtype of Colorectal cancer has its own precursor lesion indicates that the molecular pathways are determined at an early evolutionary stage and are already fully established within precursor lesions. The role of pathologists now extends beyond furnishing an accurate tissue diagnosis obtained during colonoscopy procedures to provide prognostic information and additional findings relevant to patient management. This approach to the molecular classification of Colorectal cancer should accelerate understanding of causation, have an impact on clinical management, and facilitate the development of new ways to prevent and treat Colorectal Cancer.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 24629

**Title:** Longitudinal molecular characterization of endoscopic specimens from colorectal lesions based on CIMP/MSI/BRAF/KRAS classification: prospective comparison of large adenomas to early and late carcinomas

**Reviewer's code:** 00004699

**Reviewer's country:** Japan

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-02-29 08:46

**Date reviewed:** 2016-03-19 17:31

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 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input 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 type="checkbox"/> No	

## COMMENTS TO AUTHORS

Dr. Manarikova et al studied molecular profiles of proximal and distal colon and rectum in colorectal adenomas and carcinomas (CRC) that were obtained by routine endoscopic biopsy. They analyzed CIMP, MSI and mutations of KRAS and BRAF, and then classified into molecular subtypes in colorectal tumors. Most importantly, longitudinal molecular characterization was clearly shown in colorectal tumors based on CIMP/MSI/BRAF/KRAS classification. This manuscript is well organized, and further provides the good understandings that prospective molecular classification is feasible in routine endoscopy samples. Several comments are listed below: 1) This study was focused on tumor location and molecular subtypes of colorectal tumors. Were there any correlations between molecular subtypes and other clinic-pathological parameters, such as gender and age? 2) Although there are no data on prognosis of CRC patients in this manuscript, Figure 2 showed them. For example, types 1 and 5 were good prognosis, but type 2 and 3 were poor. Were there any significant relations between them? 3) MSI is generally caused by defective mismatch repair pathway.



## BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

<http://www.wjgnet.com>

---

If CIMP status is related to MSI, was methylation of MLH1 detected in the cases with MSI? 4) No discussion of p53 and APC alterations was shown in this manuscript. However, p53 was known to be detected in CIMP(-) CRCs (Toyota M, PNAS, 2000). Recently, the CIMP-High CRC without MLH1 methylation was significantly associated with high frequencies of KRAS and APC mutations (Kim JH, Oncotarget, 2016). The authors should re-check the possibility of APC and p53 alterations for molecular subtypes in this study.