



**PEER-REVIEW REPORT**

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

**Manuscript NO:** 42583

**Title:** Relationship between KRAS mutation status, expression of RAS pathway signaling molecules, and the clinicopathological features and prognosis of patients with colorectal cancer

**Reviewer’s code:** 03017753

**Reviewer’s country:** Netherlands

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-11-14

**Date reviewed:** 2018-12-03

**Review time:** 15 Hours, 18 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

This study is very interesting. As we know, the RAS/RAF/MEK/ERK signaling pathway plays a crucial role in the proliferation, differentiation, survival, invasiveness,



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and metastasis of tumor cells. This pathway is frequently abnormally activated in CRC, often due to mutations of upstream genes, such as KRAS and BRAF, that result in aberrant transcription or translation, leading to altered protein expression, activity, and/or signaling. In this study, the authors examined the relationship between the KRAS gene mutation status and the clinicopathological features and prognosis of CRC patients. KRAS can be activated by many tumor-related proteins and is involved in their function as a network master. And also, the effect of the KRAS genotype on the expression of BRAF, MEK, and ERK proteins was investigated, as the CRC tissue specimens from 196 patients were analyzed for KRAS mutations using qPCR and for KRAS, BRAF, MEK, and ERK protein expression levels using immunohistochemistry of tumor microarrays. 1. The title summarizes and reflects the work described in the manuscript, but too long. The authors should shorten the title. 2. The methods are in detail, and the results are very informative, and well discussed. 3. Data in the tables and figures are good. 4. Some minor language polishing should be corrected.

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

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

**Manuscript NO:** 42583

**Title:** Relationship between KRAS mutation status, expression of RAS pathway signaling molecules, and the clinicopathological features and prognosis of patients with colorectal cancer

**Reviewer's code:** 03017782

**Reviewer's country:** Italy

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-11-14

**Date reviewed:** 2018-12-03

**Review time:** 16 Hours, 18 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The study is an excellent study about the the relationship between the KRAS gene mutation status and KRAS, BRAF, MEK, and ERK protein levels in CRC tissue, the



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relationship to clinicopathological features and patient prognosis was also been analyzed. The authors found that the positive expression of KRAS and ERK was associated with poor tumor differentiation, and KRAS expression was also associated with age < 56 years. MEK expression was significantly associated with distant metastasis. And multivariate analysis showed that only the expression of KRAS protein was a risk factor for tumor recurrence. The results indicated that the KRAS protein is associated with poor tumor differentiation, older age, and a risk of tumor recurrence. Only some minor language polishing should be corrected. I have no other specific comments.

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**PEER-REVIEW REPORT**

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

**Manuscript NO:** 42583

**Title:** Relationship between KRAS mutation status, expression of RAS pathway signaling molecules, and the clinicopathological features and prognosis of patients with colorectal cancer

**Reviewer’s code:** 03017793

**Reviewer’s country:** South Korea

**Science editor:** Ruo-Yu Ma

**Date sent for review:** 2018-11-14

**Date reviewed:** 2018-12-03

**Review time:** 16 Hours, 18 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Interesting study. The relationship between the KRAS gene mutation status and KRAS, BRAF, MEK, and ERK protein levels in CRC tissue was well investigated. The study is



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well designed and the results are interesting. No specific comments.

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