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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 45788

Title: Predictive and prognostic implications of the autophagy-related proteins 4E-binding protein 1, Beclin-1 and microtubule-associated protein 1A/B-light chain 3 for cetuximab treatment combined with chemotherapy in advanced colorectal cancer with

wild-type KRAS: Analysis from real-world data

Reviewer's code: 03724953

Reviewer's country: Taiwan

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-01-24 11:44

Reviewer performed review: 2019-01-30 01:54

Review time: 5 Days and 14 Hours

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

SPECIFIC COMMENTS TO AUTHORS

In this article, Guo GF and colleagues evidenced the autophagy-related proteins 4E-BP1,



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Beclin-1 and LC3 for cetuximab treatment combined with chemotherapy in advanced colorectal cancer with wild-type KRAS. The study is technically sound but need further clarify. 1. Please define the abbreviation while firstly use, including the official symbol or official full name of genes. 2. In figure 1C, the quality of western blot is poor. Over exposure and poor transfer quality is noted. 3. In figure 2, the authors provide the IHC staining of LC3. Would it possible to provide staining results of BP1 and Beclin-1? 4. The prognostic results is confusing. Please define the reference in the table 3. For example, the HR of Beclin-1 is 0.209 which suggest favorable outcome in the gene. However, the true result is opposite.

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wild-type KRAS: Analysis from real-world data

Reviewer's code: 03002093

Reviewer's country: Hungary

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-01-29 09:56

Reviewer performed review: 2019-02-04 07:23

Review time: 5 Days and 21 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[] Grade A: Excellent	[] Grade A: Priority publishing	[] Accept	Peer-Review:
[] Grade B: Very good	[Y] Grade B: Minor language	(High priority)	[Y] Anonymous
[Y] Grade C: Good	polishing	[] Accept	[] Onymous
[] Grade D: Fair	[] Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
[] Grade E: Do not	language polishing	[] Minor revision	topic of the manuscript:
publish	[] Grade D: Rejection	[Y] Major revision	[] Advanced
		[] Rejection	[Y] General
			[] No expertise
			Conflicts-of-Interest:
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SPECIFIC COMMENTS TO AUTHORS

Please provide a numbered reference list!



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wild-type KRAS: Analysis from real-world data

Reviewer's code: 03806663

Reviewer's country: Egypt

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-02-15 18:39

Reviewer performed review: 2019-02-18 13:31

Review time: 2 Days and 18 Hours

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

SPECIFIC COMMENTS TO AUTHORS

it is a great work, some comments are presented here: 1- in the discussion section, you



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did not discuss your work with other studies, it means that your work is pioneer in this issue is that true, or other investigators also work on this issue, so you need to mention that. 2-some grammar comments are present in the uploaded file.

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wild-type KRAS: Analysis from real-world data

Reviewer's code: 00073640

Reviewer's country: Slovenia

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-02-15 06:30

Reviewer performed review: 2019-02-19 16:30

Review time: 4 Days and 10 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS	
[] Grade A: Excellent	[] Grade A: Priority publishing [] Accept		Peer-Review:	
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publish	[] Grade D: Rejection	[] Major revision	[Y] Advanced	
		[] Rejection	[] General	
			[] No expertise	
			Conflicts-of-Interest:	
			[] Yes	
			[Y] No	

SPECIFIC COMMENTS TO AUTHORS

The main focus of the manuscript was to evaluate the potential predictive value of three



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autophagy related proteins (4E-BP1, Beclin-1, LC3) for patients with metastatic colorectal cancer and wild-type KRAS treated with cetuximab and chemotherapy. Authors conducted in vitro test on CACO-2 cells and immunohistochemical analyses on tissue samples (paraffin-embedded surgical or biopsy samples) from patients with metastatic colorectal cancer treated with cetuximab and chemotherapy. The title/subject is interesting and topical, the manuscript is well structured and well written. However, to improve the manuscript I suggest the following: - I have difficulties with understanding the wording -patients with advanced colorectal cancer - what does this mean? Are these patients with metastatic colorectal cancer? - Page 7, line226: Please explain more exactly what are the tissue samples - biopsy specimens taken from colon or from other organs as well? What was the pathological diagnosis of samples - In World Health Organization (WHO) classification, a number of histologic variants of colorectal carcinomas are listed, such as mucinous, signet ring cell, medullary, micropapillary, serrated, cribriform comedo-type, adenosquamous, spindle cell, undifferentiated. It is known that some histological types of carcinomas have tipical molecular pathology, therefore it is important to state the histological type of the samples - Page 9, line 279: COCA-2 cells correct into CACO-2 - Page 11, line346: the authors write about the degree of pathological differentiation but in the results section they do not mention anything about the degree of differentiation or histological type of tumors - Table 1: what was meant by the word "pathological level"? Please correct. - Table 3: the term pathological differentiation is not correct - what does it means? Please use correct terminology or explain what does it mean.

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