



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36554

Title: Overexpression of CREPT confers colorectal cancer sensitivity to Fluorouracil

Reviewer’s code: 03505493

Reviewer’s country: Italy

Science editor: Ke Chen

Date sent for review: 2017-10-25

Date reviewed: 2017-10-26

Review time: 1 Day

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" 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 checked="" 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

I have read with interest this paper. This is a good manuscript, well designed, with very nice images. I suggest to revise English language, since it is not so fluent. About the overall message of this paper, I think that it is of importance. The most important point of strength is the good number of different approaches used for this investigation (IHC, western blot,). I suggest to address these points (see below), and after this step I think that this paper may merit publication. Major points: 1. Summarize in 1 or max 2 sentences this last part of the introduction, since it is too long and inappropriate in this place: “Here we set out to systematically determine the expression of CREPT in either CRC clinical samples or the established colorectal cell lines. Moreover, the relationship between CREPT expression and tumor progression has been comprehensively analyzed. The indispensable roles of CREPT in CRC was evaluated with manipulation the expression of CREPT. Most importantly, the potential role of CRETP expression in



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modulation of 5-FU sensitivity in CRC cell line was elucidated in our system. Based on all these results, we suggested that fundamental role of CREPT in tumorigenesis of CRC via inducing proliferation and stimulating cell cycle. Contradictorily, the over-expression of CREPT rendered cell sensitivity to chemotherapeutic drug 5-FU as well, which reinforced the apoptotic response. We proposed the prognostic biomarker function of CREPT for clinical application of 5-FU in addition to its conventional view as an oncogene". Please use 1 or 2 sentences, this is not acceptable as part of introduction, it seems a part of results mixed with discussion. 2. Method: "The proportion of positive cancer cell staining was classified on a scale of 3 grades: (-), no positive cells; (1+), <25%; (2+), 25-75%; (3+) >75%.". This scale has 4 grades and not three: first grade: (-) = no positive cells; second grade (1+) <25%; third grade 25-75%, 4th grade >75%. Please correct this point. Also please explain the choice of this peculiar score. Please indicate better the protocol of immunohistochemical analysis, the Source (manufacturer) and the method in a specific way (antigen retrieval, incubation,...) 3. 5-FU is used also in other cancer types. Please discuss this point and write a comment indicating if your data may be translated for other cancer types or may address future research. 4. In the text you have used the terms of "benign adenoma": please remove benign, since adenoma are precancerous lesions, benign may indicate that they are not invasive but this word is formally incorrect in this context. Minor points: 1. Introduction: "Colorectal cancer (CRC) is a malignance disease with apparent signs or symptoms such as blood in the stool, aberrance in bowel movement and weight loss [1]." Malignance or malignant? Please use correct words. 2. Introduction: "Globally, colorectal cancer is the third most common malignance". Please use malignancy or tumor, malignance is not a good word in a scientific paper. 3. I see a part of Fig.4 overlapped on figure 4 legend, please correct overlapping if it is due to your error, if not it will be corrected by the journal.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36554

Title: Overexpression of CREPT confers colorectal cancer sensitivity to Fluorouracil

Reviewer's code: 03478911

Reviewer's country: South Korea

Science editor: Ke Chen

Date sent for review: 2017-10-25

Date reviewed: 2017-10-31

Review time: 6 Days

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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The authors investigated the relationship between the expression of CREOT and 5-FU efficacy in the colorectal cancer, and they concluded that increased CREPT expression would be a potential prognostic biomarker to treat 5-FU for colorectal cancer therapy. It showed that the research has been carried out through appropriate methods combining clinical data, and the results are clear. However, there are major concerns that need to be addressed before article publication. [Major] 1. There are a lot of reports about the relationship between CREPT expression and colorectal cancer progression (eg. Zheng G., et., al. 2016), however the authors did not describe what is different point with the previous reports. 2. Please consider this point. Increased CREPT is a sign of poor prognosis, and it is contradictory that 5-FU will be treated to such patients. If not, please describe the authors' opinion in the discussion part. 3. Is the purpose of this paper to simply exploring the CREPT for diagnostic purposes to enhance 5-FU efficacy? If not so,



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this reviewer though that it would be appropriate to treat 5-FU in patients with increased CREPT and concomitant therapy to reduce CREPT will be processed. [Minor]
1. It will need to abide by the rules for using abbreviations. 2. There are a lot of grammatical errors.



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36554

Title: Overexpression of CREPT confers colorectal cancer sensitivity to Fluorouracil

Reviewer’s code: 01207047

Reviewer’s country: Turkey

Science editor: Ke Chen

Date sent for review: 2017-10-25

Date reviewed: 2017-11-10

Review time: 16 Days

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
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Dear Editor, thank you for your kind invitation to review this interesting manuscript. Comments: 1-The pathologic terms, “high differentiation, medium and low differentiation are not suitable. Instead it will be better to use, “well differentiated, moderately differentiated and poorly differentiated”. 2-It will be nice to add a pathologist to their author list. 3-Results part: what does they mean with margin? Is it tumor margin or benign stromal tissue at the tumor periphery? 4-Results part: which pathologic type did show positive association with high CREPT expression? Please explain in the text. 5-Figure 1 A: The tissue seems like normal colonic mucosa not an adenoma. 6-Figure 2B: In Kaplan-Meier graphics please indicate which lines do belong to patients with high Level of CREPT and patients with low level of CREPT. And in the results part please mention about The Kaplan-Meier graphic results. 7-Figure 2A: I think there is an error about differentiation. In pathology highly differentiated tumor means



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well differentiated. So CREPT level should be low. Low differentiation means poorly differentiated tumor and CREPT level should be high.