

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 26996

Title: Carbonic anhydrase enzymes II, VII, IX, and XII in colorectal carcinomas

Reviewer's code: 00008736

Reviewer's country: Germany

Science editor: Yuan Qi

Date sent for review: 2016-05-04 14:26

Date reviewed: 2016-05-06 13:12

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" 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 checked="" 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 checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Biomarkers for colorectal Cancer are still under intense Investigation and novel predictive and prognostic markers are urgently needed. The authors investigate the Protein Expression Levels of several carboanhydrases (CA) in a large series of colorectal Cancer and conclude that CA II and CA XII could be useful prognostic markers. While the study is technical of good Quality, some issues Need to be discussed: 1. Why was the Expression only rated by either intensity or extensity and not via h-score (intensity x extensity) ? This would be a more Standard Approach and should be shown. 2. Were the statistical results corrected for multiple testing? 3. While the number of cases is adequate, it is unclear if also colorectal adenomas were included. 4. The Collection period of the samples was very long! What is the influence of changed Treatment regimens (e.g. radiation on rectal Cancer) on the observed survival times? This could be a strong confounder. 5. Does the Protein Expression of CA also correlate with its enzymatic activity? 6. The authors Need to be careful when using the term "prognostic" related to Treatment Outcome (ll. 290 ff). This is rather a predictive marker in this context. 7. The term "gender" should be replaced by "sex" in table 1. There also seems to be a bias towards rectal Cancer in the study Population which Needs to be discussed! Does the term



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"differentiation" relate to grading? 8. IN Table 2 the values for extent do not seem to fit the examples shown in Fig 1 9. A scale bar is missing in Figure 1.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 26996

Title: Carbonic anhydrase enzymes II, VII, IX, and XII in colorectal carcinomas

Reviewer's code: 00033010

Reviewer's country: Italy

Science editor: Yuan Qi

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" 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 checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In the present paper, entitled "Carbonic anhydrase enzymes II, VII, IX, and XII in colorectal carcinomas", Viikila et al analyzed the expression of four different carbonic anhydrase (CA) isoforms in 539 cases of colorectal cancer by immunohistochemistry. They demonstrated that CA II and CA XII are related to worse prognosis and shorter survival. The very impressive number of enrolled patients make the paper of high quality and let the results be reliable. The statistical analysis is proper. Some criticisms may be addressed. Page 3 line 70: please define "extent". Were all cases of colorectal cancer sporadic, or have other subsets (IBD-related, familial adenomatous polyposis or other inherited CRC) been included? Despite immunohistochemistry for CA in normal colon tissue has been performed, Authors did not report the intensity of the staining in this control group. It is important to compare the expression of CA in CRC vs normal colon. A table may be useful. Page 10 line 230: cancers arising in the transverse colon were considered as left- or right-sided in the statistical analysis? It is strange that, despite CA IX is overexpressed in CRC (as shown in figure 1I), no correlation with survival was found. This detail needs to be discussed. Table1: please define "differentiation" (histological?). Finally, Authors should underline in the discussion that, although statistically significant, the value



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of HR is very close to 1, therefore CA expression may contribute only marginally to the prognosis of CRC.

ESPS PEER-REVIEW REPORT

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ESPS manuscript NO: 26996

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<input checked="" 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
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		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The paper was well-written with favorable quality.