

## PEER-REVIEW REPORT

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

**Manuscript NO:** 34038

**Title:** A novel systemic immune-inflammation index for predicting the prognosis of colorectal cancer

**Reviewer's code:** 02575643

**Reviewer's country:** Italy

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2017-04-16

**Date reviewed:** 2017-04-16

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 checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

This is an interesting study. Obvious conclusions from a well known phenomenon: correlation between inflammation and cancer development and progression. Inflammation per se determines the production of several cytokines and growth factors which can facilitate the occurrence and development of any type of cancer. In the near future, we will assist to the presentation of thousand of papers describing mathematical formulas, written in a laboratory far away from the clinical scenario, trying to quantify the inflammation associated to any type of cancer, giving importance to these new formulas through retrospective non-sense analysis of overall survival and disease-free survival. Despite this basic criticism, I think the paper should be published to address an important point: to cure or prevent inflammation can prevent cancer formation and progression. I spoke about this idea of mine some 25 years ago, making all the audience of the meetings laughing. At least, if I am not a good researcher, I am at least a good comedian. There are several specific points to be made and addressed: 1- The

introduction is too long. It should be shorter and more focused 2-In The Material and Method Section the new index SII should be specified in detail, so that everybody who is interested in the paper can read it and understand immediately, before continuing to read the paper. 3-A colour drawing explaining the different phases which correlate inflammation and cancer progression can be useful-. I recommend to look at the picture of a paper recently published in New England Journal of Medicine about clear cell renal carcinoma from the Sloan Kettering in New York (NEJM 2017;23: 326). The Authors can have made a drawing in which inflammatory cells produce growth factors which stimulate cancer growth. At the same time (this is my old hypothesis) new replicating cancer cells, stimulated in such an analogous situation, could express surface antigens not recognized by the host, recruiting more inflammatory cells, with consequent production of growth factor, determining a cascade effect. 3-They used univariate and multivariate analysis, which currently are the most common used method in medical statistics. I think that the analysed problem is very complex and these two analyses are inevitable superficial. The Author should add a Multidimensional analysis, to analyze the combination of two or more factors. Let me make a simple example related to their paper. In the multivariate analysis they found to have statistical significance age and SII. Is not possible, that the inflammatory reaction is more evident in younger patients. All this brings to the conclusion that in all studies a multidimensional analysis should be applied where several risk factors are analysed determining specific groups with more risk factors. This kind of analysis allows to get closer to the everyday clinical practice, away from the abstract, surreal world of mere statistics. 4-The importance of this SII index should be confirmed in a prospective study. The conclusion of this study, based on a retrospective study presents so many statistical biases that the results can not be accepted until they are confirmed by a prospective study. This should be clearly addressed in the discussion. 5-In the discussion, I would like to advise to introduce a new concept (I expressed in a letter to Annals of Surgery: Sterpetti et al 2012): there is a good and a bad inflammatory reaction. In other words if the inflammation is based on the production of simply growth factors, the inflammatory reaction has a negative effect. But if the inflammatory reaction consists on neutralizing antibodies produced by activated lymph nodes, this reaction can have a positive effect All this brings to a basic concept: cancer development and progression results from an anomalous, inadequate response from the host.

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**Reviewer's code:** 02954661

**Reviewer's country:** Romania

**Science editor:** Ya-Juan Ma

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<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

Dear Editor, Thank you for the opportunity to review the manuscript entitled 'A novel systemic immune-inflammation index for predicting the prognosis of colorectal cancer' by Zhai et al. The article presents 1383 patients with colorectal cancer; the authors investigated the a novel immune inflammation index. The material is interesting and has merits to be accepted, after minor revision. Minor concerns: In methods - data collection: SII calculation is unclear.  $SII = (PxN) \text{ all divided by } L$ . Or only N is divided by L?