

ANSWERING REVIEWERS

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5545-review.doc).

Title: Effect of Insulin, IGF-1 and IGFBPs on the Colorectal Cancer

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The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

The investigation is interesting, but I would like to point out some considerations.

1.Abstract. It is mentioned that BMI has a correlation with cancer, which in the results it is not.

The research conclusion is not “ BMI has a correlation with cancer” , but “BMI of colon cancer patients were positively and significantly correlated with the levels of insulin and IGF-1/IGFBP-3,...”.

2.Methods. A. Some sentences such as “The patients should be collected before and after operation” should be corrected.(may be they can ask for helping in the style). B. Details about the time course of the disease (what does it mean ” before and after surgery”) in order the authors can refer to initiation and progression of the cancer.

Thank you for your suggestion.I have rewrited the sentence.

3.Results. Number 2, I think the sentence is wrong or may be expressed in other form, it is confuse. Number 4, also the results are confuse in one sentence said: “The levels of serum IGF-1, IGFBP1 and IGF-1/IGFBP3 ratio were significantly higher in rectal cancer patients than colon” and the next: “ while there were no statistical differences in leptin, insulin and IGFBP-3 levels between the two groups” Number 7 and table 7, it appears as repetitive information,

the table should indicate the significance of T1,T2,T3. Units must be presented in all the tables.

4. Discussion. It is long, the authors refer to the literature in which have been reported relation between cancer and alimentation, but they could focus on their own results. Although they present some evidence of the association of some serum biomarkers I think are not conclusive. They mention in the method section that have information that include age, occupation, education, ethnic group, so they may analyze that with the serum biomarkers

Thank you,I have remended the part you mentioned.

The authors evaluated the relationship of changes in serum insulin, Insulin-like growth factor-1 (IGF-1), Insulin-like growth factor binding proteins (IGFBPs), body mass index (BMI), waist-to-hip ratio (WHR) with the initiation and progression of colorectal cancers. The serum levels of insulin and IGF-1 as well as IGF-1/IGFBP-3

ratio of pre-surgical patients were elevated, but the level of IGFBP-3 was reduced with post-surgical patients. WHR and BMI of colon cancer patients were positively and correlated with the levels of insulin and IGF-1/IGFBP-3, but the correlation of WHR and BMI with IGFBP-3 level was negative. Comments: They have concluded that the elevation of insulin, IGF-1 as well as IGF-1/IGFBP-3 ratio and the reduction of IGFBP-3 may relate to the initiation of colorectal cancer. The findings are novel and interesting. I have several concerns as follows.

1.The reviewer miss a significance of IGF-1, IGFBP-1 and IGFBP-3 IGF-1/IGFBP3 ratio in patients of colorectal cancer. Author should present the significance of IGF-1, IGFBP-1 and IGFBP-3 IGF-1/IGFBP3 ratio in the cancer.

I have rewrited this part and added the significance of these markers.

2.The subjects in the present study may have several medical treatment. Is it possibility that the drugs influenced on the results including insulin and IGFs in the present study? 3.It would be better to add regarding gender differences. Did the levels of circulating IGFs similarly change both in male and female?

Furthermore,we should analy them.Thank you for your suggestion.

4. Did the elevation of insulin, IGF-1 and the reduction of IGFBP-3 relate to only colorectal cancer? Similar changes were not observed

in other cancer such as lung cancer? Some comments would be helpful.

IGF-1 and IGFBP-3 are not only relate to colorectal cancer, but also to breast cancer et al.

5. The manuscript has several strengths including a significant topic of interest that pathophysiological links IGFs and colorectal cancer. Author should discuss the pathophysiological mechanisms between IGFs and colorectal cancer in greater detail.

I have added the mechanisms between IGFs and colorectal cancer.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the World Journal of Gastroenterology.

Sincerely yours

LiLi Du