



**ESPS PEER REVIEW REPORT**

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

**ESPS manuscript NO:** 12123

**Title:** Impact of high glucose on the metastasis of colon cancer cells

**Reviewer code:** 02551692

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-06-23 11:22

**Date reviewed:** 2014-07-13 21:36

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [ Y] Accept
<input type="checkbox"/> [ Y] Grade B: Very good	<input type="checkbox"/> [ Y] Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> [ ] Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> [ ] Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> [ ] Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

The work is very interesting and well done. The laboratory results may have important clinical implications. For this reason in the discussion the authors could give more space to explain their work and to provide food for thought for clinical applications. In the text some corrections must be made: -In the third line of introduction it must be written "according to" -In materials and methods: in the reagents section it is necessary to write what is "stattic and siRNA" in Western blotting section the term PBS must be explained at the first appearance in the text The following sentences must be corrected to improve English language: In the section entitled "the effect of Stattic on the migration of CT-26 cells" of Results ,the sentence: "the higher the concentration of Stattic was, the fewer cells that migrated" In the second line of Discussion: "Adding STAT3 inhibitors, Stattic and siRNA, to a high-glucose environment, inhibited CT-26 cell migration and invasion. This indicated that the STAT3 signaling pathway is associated with regulating the effect of glucose on CT-26 cell migration and invasion". Figure Legends must be reviewed to use a correct and concise language. It is also important to report in the figure the technique used such as fluorescence or inverse microscope or western blotting. In the fig 9 it is not explained the effect of "stattic" on MMP9 and STAT3 expression



### ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12123

**Title:** Impact of high glucose on the metastasis of colon cancer cells

**Reviewer code:** 02454257

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-06-23 11:22

**Date reviewed:** 2014-07-20 19:43

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

Introduction: The introduction part is insufficiently focused, since too much is written about general problems of invasion and metastasis which is not primary focus of the here presented manuscript. The Introduction should be focused on the consequences of higher glucose level for invasion and metastasis. 26 literature citations are way too much for an introduction; not every argumentations requires 2-3 references support. Some citations are chosen not too well. For example: regarding the question of ECM degradation and angiogenesis especially in tumor patients are more targeted references available than ref. 7. Materials and Methods: The methods part is comprehensible and clear. Here or in the discussion section the authors should provide a statement why they decided to apply a rat colon cancer cell line. There are multiple well examined human colon cancer cell lines available which would more suitable for this project. Results: Wound healing assay is a pretty rough assay for the evaluation of cell migration. Has been made sure that this phenomenon is not due to a different cell proliferation under the condition of a higher glucose concentration but a "true" migration? Was the cell count at the time of observation the same under every condition? Same question arises regarding the migration assay. It is well known from many cancer cell lines they show an increased proliferation under conditions of higher glucose levels (Beckner ME, J Natl Cancer Inst, 1990). So the results of the migration assay should correlate to the final cell count. This must be clarified to exclude the higher migration rate as a result of a higher proliferation rate. In figure 1 the authors should explain why with 10mM glucose the wound strip became wider instead of smaller. In



## BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

<http://www.wjgnet.com>

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general the data regarding cell staining (with what) and which magnification has been applied for the recordings (see figure 2). The Material and Methods part or the legends to the figures should mention the number of independent measurements from which the results originated. Discussion: Discussion should be more focused. The situation remains that regarding the questions of diabetes and cancer, especially colorectal cancer many open questions remain. As an example: is there a direct connection or a secondary connection caused by obesity and/or changed life style - see Giovannucci et al Diabetes Care, 2010. This unclear situation should be shown in the discussion. The same applies for MMP-9 whose position should be evaluated in a more critical fashion. There are evaluations available (Koskensalo S BMC Clinical Pathology 2012) that not only the overexpress of MMP-9 may be a negative prognosis factor but the missing expression of MMP-9 may be a negative prognosis factor as well. Furthermore should it be pointed out that MMP-9 in colorectal cancer more often come from tumor surrounding connective tissue cells than from primary colorectal cancer cells and may have an inverse influence on the angiogenesis (see Taguchi et al PLOS one ,2014). Taken together the manuscript shows good approaches but the deficits mentioned above should be improved.



# BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

http://www.wjgnet.com

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 12123

**Title:** Impact of high glucose on the metastasis of colon cancer cells

**Reviewer code:** 02537353

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-06-23 11:22

**Date reviewed:** 2014-07-31 23:06

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

The obtained result are very interesting but I have some suggestions: 1) It's very important to introduce in the several experiments another monosaccharide as control 2) There are several english mistakes, I suggest the revision of the text by native speaker