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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 17717

**Title:** Dexamethasone inhibits hypoxia-induced epithelial-mesenchymal transition in colon cancer

**Reviewer's code:** 03094606

**Reviewer's country:** Denmark

**Science editor:** Yuan Qi

**Date sent for review:** 2015-03-21 16:23

**Date reviewed:** 2015-04-07 05:02

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

### COMMENTS TO AUTHORS

The authors address a clinically very interesting issue, considering the fact that most patients undergoing chemotherapeutic treatment for metastatic colorectal cancer also receive anti-emetic treatment with synthetic corticosteroids. There are emerging clinical data pointing in the direction of a unfavourable effect of dexamethason perioperatively on the survival of colorectal cancer patients. The underlying molecular mechanisms are unclear. Kim et al. aim to investigate the effects of dexamethason on hypoxia-dependent EMT in colorectal cancer cell lines. Their introductory remark about increasing incidence of colorectal cancer leads too far away from the topic. The statement that dexamethason is proven to have cytostatic effect in hematologic malignancies lacks references. Apart from that, the introduction is presenting the clinical problem in an effective manner. The method section is clear and concise. The results section guides the reader nicely through the experiments and presents the results in a clear manner. The figures add to the understanding. Would the authors in the discussion please add comments on the following issues: ? Why are two different cell lines used? ? Did the authors study any other markers of hypoxia (CA-IX)? ? What is the effect of



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dexamethasone on colorectal cancer cells under normoxic conditions? All in all, the paper is easily read, addresses an interesting question and adds to the evidence in the field.



**ESPS PEER-REVIEW REPORT**

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

**ESPS manuscript NO:** 17717

**Title:** Dexamethasone inhibits hypoxia-induced epithelial-mesenchymal transition in colon cancer

**Reviewer's code:** 02903408

**Reviewer's country:** China

**Science editor:** Yuan Qi

**Date sent for review:** 2015-03-21 16:23

**Date reviewed:** 2015-04-02 16:59

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"/> 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**

The author proposed to elucidate the effects of dexamethasone on hypoxia-induced EMT in colon cancer. Though the real-time PCR, Western blot, Transwell and Wound healing tests, the authors verify that dexamethasone inhibit HIF-1 $\alpha$  protein level and its downstream gene, VEGF mRNA level in hypoxic condition. In addition, dexamethasone down-regulated not only hypoxia-induced Snail and Slug mRNA levels, but also hypoxia-induced integrin  $\alpha$ V $\beta$ 6 protein level. Furthermore, reduced E-cadherin in hypoxic condition was found to be recoverable by treating with dexamethasone in colon cancer cell lines; dexamethasone blocked the migration and invasion of colon cancer cells in hypoxia. Thus, in all it suggested the potential role of dex in cancer therapy and the mechanism involved in and it is possible to accept this manuscript with minor improvements. Major issues 1. In the paper, they only told that DEX may have some role in EMT of cancer, but they can not tell us if the role is direct, for example, if there is no HIF-1 $\alpha$  signal pathway, what would happen? So, the author may perform some gene over-expression experiments which would testify if the role is only one or direct? 2. If the author can clarify the mechanism of the migration and invasion by DEX in



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colon cancer. Or try to discuss some of them. Minor concerns: 1. "These data suggest that Snail plays a major role as an inducer of tumor invasion andmetastasis[19]." For this sentence, there should be a space between "andmetastasis" and this should be take care in the whole text. 2. Both the cell lines of HCT116 and HT29 have got the same results with DEX, but if there is any other colon cancer cell line with the different characteristic or if it would relate with the colon cancer stem cell?