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315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 5597

**Title:** Inhibition of Girdin enhances chemosensitivity of colorectal cancer cells to oxaliplatin

**Reviewer code:** 02369386

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-09-16 17:50

**Date reviewed:** 2013-10-04 01:24

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"/> Existed	<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)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

To investigate the mechanisms of Girdin knockdown on the chemosensitivity of colorectal cell to oxaliplatin. Authors constructed a lentivirus mediated shRNA targeting Girdin and infected DLD1 cells. They examined the expression levels of Girdin mRNA and protein, the chemosensitivity to oxaliplatin, the downstream gene expression profiles after Girdin suppression and the cytotoxic effect of combination treatment of oxaliplatin with TOP2B inhibitor. Their results show that Girdin known enhances chemosensitivity of colorectal cancer cells to oxaliplatin via reduction of TOP2B expression. This report is extremely interesting as the effects observed are really clear-cut. However, several points are not properly addressed and some lack of detail in some experimental procedures need more precise description to make the report fully convincing. 1. Materials and methods, Protein extraction and Western blot analysis For Girdin protein quantification, the description of the quantification method should be more specific. 2. Materials and methods, Evaluation of chemosensitivity to oxaliplatin Why and how the treatment dose was chosen is not clear. Do these doses comparable to the clinical treatment dose? a corresponding reference should be given. 3. In Results section. Again, the reasons why 10 $\mu$ M and 3 $\mu$ M oxaliplatin were chosen to investigate how Girdin and TOP2B influence the chemosensitivity of DLD1 cells is not clearly defined. Please add a sentence to explain why these dosages were chosen. 4. Due to the heterogeneity of tumor cell, author should screen more drug resistant colorectal cancer cell lines to verify their conclusions. 5. Fig 3B. showed that DLD1 cell viability decreased to 50~60% and 10~20% when treating with 9 $\mu$ M and 24 $\mu$ M adriamycin only, respectively. One point that should be addressed in this regard is : If adriamycin could be a useful colorectal cancer drug candidate? What's the effect on normal cells treated with this molecular? 6. Another issue is the effects of Girdin knockdown and inhibition of



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TOP2B on normal cells? This should be discussed in discussion section.



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### ESPS Peer-review Report

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

**ESPS Manuscript NO:** 5597

**Title:** Inhibition of Girdin enhances chemosensitivity of colorectal cancer cells to oxaliplatin

**Reviewer code:** 00570794

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-09-16 17:50

**Date reviewed:** 2013-11-23 17:21

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

### COMMENTS TO AUTHORS

This article is of interest as resistance to oxaliplatin is a major problem in the treatment of colorectal cancer. The study is well designed and properly developed. I have no major/minor suggestion to make. In its current form it can be published



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### ESPS Peer-review Report

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

**ESPS Manuscript NO:** 5597

**Title:** Inhibition of Girdin enhances chemosensitivity of colorectal cancer cells to oxaliplatin

**Reviewer code:** 00077481

**Science editor:** Zhai, Huan-Huan

**Date sent for review:** 2013-09-16 17:50

**Date reviewed:** 2013-11-29 00:31

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 checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

### COMMENTS TO AUTHORS

The manuscript by Zhang et al investigated drug resistance in colorectal cancer by examining the role of Girdin expression in DLD1 cells, the cell line most sensitive among several to oxaliplatin. They found that downregulation of Girdin by siRNA and shRNA increased inhibition of cell proliferation and suppressed the expression of, among many others, Top2B gene. They also found that oxaliplatin enhanced the inhibition induced by Adriamycin, an TOP2B inhibitor, suggesting that the Girdin-TOP2B axis is involved in resistance to oxaliplatin. The study addresses an important issue in cancer therapy and the findings are novel. The experiments are well designed overall and data consistent. Figure 2D needs a statistical analysis to check the difference between scramble shRNA and girdin shRNA. Near the end of the Discussion, the authors stated that Girdin suppression and oxaliplatin had synergistic effect. This needs more rigorous tests such as isobologram by Chou and Talalay. However, the authors may want to simply state that oxaliplatin effect is enhanced by Girdin inhibition if data for such tests are not available. In the Result section, there needs to be an introduction of TOP2B and its function before introducing its otherwise abrupt downregulation, though it was explained somehow in the Discussion. The graphs need more professional editing to be consistent, e.g. the grid line and its absence in figure 3. Also the y axis lacks consistency in labeling. The first two paragraphs of Discussion may be more appropriately moved to Introduction with a more condensed form. The mid part of the 2nd paragraph, "... Subsequent PI3K/AKT activation..." has a grammar problem. There are a few places that require polishing of language. For example, in the last paragraph of Introduction, "we firstly reported" could be better expressed as "we reported for the first time."