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Flat C, 23/F., Lucky Plaza,  
315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

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

**ESPS Manuscript NO:** 2864

**Title:** Skp2-RNAi Suppresses the Proliferation and Metastasis of Gallbladder Carcinoma by Enhancing p27 Expression

**Reviewer code:** 00503125

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-03-20 13:03

**Date reviewed:** 2013-03-21 10:17

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"/> [ ] 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

In this paper an attempt was made to determine whether RNAi technology applied to the inhibition of S-phase kinase-associated protein-2 (Skp2) would be effective in inhibiting the proliferation of a gallbladder carcinoma cell line both in vitro and when grown subcutaneously in a mouse model. The results demonstrate that silence of the Skp2 gene inhibited the proliferation of the tumor cells both when grown in vitro and when the tumor cells were injected subcutaneously into a nude mouse. The mechanism of action appears to be in part due to enhanced expression of the p27 suppressor gene. The conclusion is that Skp2 inhibitors and/or Skp2 regulatory sequences could provide a useful therapeutic protocol for the treatment of gallbladder carcinoma, although the results obtained from preclinical mouse models often do not translate into clinical efficacy. Nevertheless this is an interesting study. The photographs of the tumor growth in nude mouse models provided in Figure 5A are of poor quality.



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**ESPS Manuscript NO:** 2864

**Title:** Skp2-RNAi Suppresses the Proliferation and Metastasis of Gallbladder Carcinoma by Enhancing p27 Expression

**Reviewer code:** 00188649

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-03-20 13:03

**Date reviewed:** 2013-03-24 17:32

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"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input checked="" type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The manuscript by Zhang et al reported the antitumor effect of Skp2-RNAi in gallbladder carcinoma by enhancing p27 expression. But there are many issues need to be addressed. 1. Only one gallbladder carcinoma cell line was detected, so the title should give a detailed statement such as "Gallbladder Carcinoma cell line GBC-SD". 2. The authors concluded that silence of the Skp2 gene inhibited both proliferation and metastasis of gallbladder carcinoma cells, but the experiments did not contain the metastatic experiment. The methods, such as Cell proliferation assay, Colony formation assay, Wound healing assay, Cell cycle assay, cannot reflect the cell metastatic ability. Wound healing assay only presents the cell migration ability. 3. In the two experiment groups (L and H), cells were transfected with Skp2- lentiviruses at MOIs of 10 and 20, respectively. But How is MOI in the Scr-RNAi group? When the appropriate amounts of lentiviruses were added to the cells according to the different MOI values, the efficiency of transduction was assessed by fluorescence microscopy, But all text has not give the exact data of transduction efficiency. 4. In section of Materials and Methods, the first paragraph was stated that cells were transduced with lentivirus vectors, suggesting that authors have already had viruses, but the following paragraph described the construction and identification of the RNAi lentivirus vectors, it is difficult to understand. 5. In Fig. 1, are the numbers "1,2,3,4" presents "C1,C2,L and H"? Labeling columns with "1,2,3,4" does not simplify compared with "C1,C2,L and H". 6. In Fig. 3 and 4, the images of clone formation as well as wound healing in every cell group should be exhibited. 7. The manuscript in current form contains much more writing mistakes and poor grammar, resulting in difficulty to understand.



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

**ESPS Manuscript NO:** 2864

**Title:** Skp2-RNAi Suppresses the Proliferation and Metastasis of Gallbladder Carcinoma by Enhancing p27 Expression

**Reviewer code:** 00051382

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-03-20 13:03

**Date reviewed:** 2013-03-25 20:40

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

## COMMENTS TO AUTHORS

This is a well-designed study. The authors used several assays to explore the role of S-phase kinase-associated protein-2 (Skp2) in gallbladder carcinoma. The results indicate that Skp2 inhibitors and/or Skp2 regulatory sequences may be a useful therapeutic protocol for the treatment of gallbladder carcinoma. Minor points: 1.real-time PCR is not RT-PCR. 2.Fig 1 is too small and hard to understand.