Reviewer's report

**Title:** Upregulation of Wnt5a promotes epithelial-to-mesenchymal transition and metastasis of pancreatic cancer cells

**Version:** 2  **Date:** 11 June 2013

**Reviewer:** Francesco Fabbri

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Response 1:
Although authors affirmed their data validate and extend in vitro studies, and make known that Wnt5a expression facilitates cancer invasion and metastasis in an orthotopic mouse model of pancreatic cancer, I still don’t see their point: they must not state “Up-regulation of Wnt5a promotes EMT and metastasis in pancreatic cancer”, generalizing a preclinical concept, because they saw it only in preclinical models and not in the clinical setting. They cannot extend the meaning of their preclinical results to the general situation because their “data indicate that the median cancer-specific survival was comparable between patients with positive versus negative expression of Wnt5a [and] this result suggests that tumor Wnt5a expression alone may NOT be suitable for predicting survival in patients with operable pancreatic cancer.”. So, at present, Wnt5a will retain only a base research value without a clear clinical meaning. In other words, if a preclinical result, even outstanding, is not confirmed by the clinical setting, its meaning is severely limited.

Therefore their research is important, but still clinically quite irrelevant.

Response 2:
Authors did not upload the complete / final version of this answer. I can read only “As you suggested, morphological changes of pancreatic cancer cells transfected with Wnt5a-expressing plasmid were examined. The results demonstrate that …” … What? I know that the final text has been changed in agreement to my previous suggestion, ok, but, please, be accurate when responding directly to the reviewer also.

Responses 4/5:
Again on the subject of the inconsistency between the biological and clinical findings, I think that the authors did not furnish sufficient evidences / hypothesis on this matter. They affirmed only that, in patients, β-catenin signaling can be regulated by “multiple factors other than Wnt5a”, strengthening in my mind the idea that in the clinical setting Wnt5a may not be a relevant marker. If “multiple factors other than Wnt5a” is the answer, why should I investigate Wnt5a?

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In conclusion, authors have to be very careful when extending the meaning of their preclinical results to the general situation and they must clearly stress it. For example, when the state “Up-regulation of Wnt5a promotes EMT and metastasis in pancreatic cancer”, in the last sentence of the abstract, and they must change it at least adding the word/s “model/cells” (“Up-regulation of Wnt5a promotes EMT and metastasis in pancreatic cancer models”). Notwithstanding the significant pre-clinical data showed by authors, they have to state strongly that further studies are certainly needed to clarify the real clinical value of Wnt5a.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable
**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests