Reviewer’s report

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

Version: 1 Date: 19 April 2013

Reviewer: Francesco Fabbri

The article “Up-regulation of Wnt5a promotes epithelial-to-mesenchymal transition and metastasis of pancreatic cancer cells” by Haiji Bo et al. deals with the investigation of the role of Wnt5a in EMT regulation. The topic is interesting, but not particularly original, innovative or completely well performed. Although in dissimilar forms, a number of aspects have already been suggested by literature (see for example, Ripka S et al., Carcinogenesis 2007; Kikuchi A et al., Acta Physiol 2012; Yingzi Yang, Cell & Bioscience 2012). Moreover, despite the importance of exploring new pathways and signals driving EMT, the paper describes only a partial event connected to this phenomenon, not deeply reporting (or at least suggesting) the complexity of the regulatory networks that control Wnt5a and therefore EMT. There are a number of genes and networks that control EMT. What would be really interesting is to know those that are most important and why. This paper describes only one of the possibilities and therefore its importance remains severely limited.

Major Compulsory Revisions

• Authors did not show any indication of one essential aspects of EMT, i.e. cell morphological changes; they have to demonstrate this aspect;
• they are not clear in describing how they reach their aims; they should be more clear and concise;
• the clinical significance is not clearly suggested by results (see later)

More specifically:

1 – (Paragraph “Wnt5a expression negatively correlates with histological grade of tumors”) Patients included in the different tumor grade classes are not balanced; although the result is statistically significant, authors cannot be so sure their results are absolutely true and therefore they have to be less categorical in stating their assumptions. Second, from what I can understand, authors assert Wnt5a has a negative role: it promotes EMT and therefore metastatic spread. But at the same time they observed patients with Wnt5a-positive tumors had a slightly higher median cancer-specific survival than those with negative Wnt5a expression although not statistically significant. How they explain this? They should make some suggestions.

2 – In vitro results seem to diverge strongly from in vivo results: from the presented data, in pancreatic CELLS in vitro, Wnt5a seems to be a master
regulator of EMT, BUT from in vivo results presented by authors it seems not particularly important (it is expressed almost in every pancreatic cancer and shows no influence on survival).

In my opinion, the paper needs a complete ‘overhaul’ before being considered for publication in BMC Cancer.

**Level of interest:** An article of limited interest

**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