Reviewer's report

Title: Norcantharidin inhibits tumor growth and vasculogenic mimicry of human gallbladder carcinomas by suppression of the PI3-K/MMPs/Ln-5gamma2 signaling pathway

Version: 1 Date: 11 December 2013

Reviewer: Orit Itzhaki

Reviewer's report:

Peer review for the manuscript entitled: "inhibits tumor growth and vasculogenic mimicry of human gallbladder carcinomas by suppression of the PI3-K/MMPs/Ln-5#2 signaling pathway"

Vasculogenic mimicry (VM) is a process by which tumors cells directly form blood-conducting tubes and sinusoids, by angiogenesis independent mechanisms. These structures can be found in a variety of malignancies, and their presence is usually associated with poor prognosis. Gallbladder carcinomas commonly presents in a late stage and has limited therapeutic options thus the development of targeted therapies directed against key signaling pathways including anti-VM is crucial.

The authors suggest Norcantharidin (NCTD) as a novel anti-VM agent. They further characterized this effect and studied the underlying molecular mechanisms. VM-targeting strategies may have profound implications in the development of future novel anti-cancer lines of therapy.

Comments:

Abstract:
1. Please add short statements on the main subjects (VM, gallbladder carcinoma and NCTD) before the recently found facts and the article objectives.
2. Note: need to add the full name before abbreviations (VM, NCTD).
3. The methods section in the abstract: consider shortening and clarifying.

Background:
1. Please add current citation reviewing gallbladder carcinoma (for example: McNamara MG et al., Curr Opin Oncol 25: 425-31, 2013).
2. Please add a several sentences describing the rationale behind choosing NCTD.

Methods:
1. First sentence of the first paragraph: please add "Establishment of GBC-SD cell line..."
2. Add reference for "acute toxicity test".
3. Invasion assay: please include correction for proliferation (is the invasion capacity influenced by low proliferation rate?).

4. Please check the wording throughout the methods section.

Results:
1. Question: is VM inhibition sustained after NCTD withdrawal? This will strengthen the results.

Discussion:
1. Please consider shortening of the introduction in the discussion section, it may be more suitable for the background section.

2. Please clarifies the last sentence in the first paragraph ("an anti-VM therapy for VM when in … tumors").

3. In general consider discussion shortening and rephrasing (note: detailed methods include in discussion, several repeats for the same conclusion etc…).

Question/Answers
1. Is the question posed by the authors well defined?
   Yes.

2. Are the methods appropriate and well described?
   Yes.

3. Are the data sound?
   Yes.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   Yes.

6. Are limitations of the work clearly stated?
   Need to be discussed.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
   Yes.

8. Do the title and abstract accurately convey what has been found?
   Yes.

9. Is the writing acceptable?
English revising required.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests