Author's response to reviews

Title: Hepatic stellate cells: central modulators of hepatic carcinogenesis

Authors:

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Version: 3 Date: 11 May 2015

Author's response to reviews:

Dear Dr Morawska,

Please find enclosed our revised manuscript ‘Hepatic stellate cells: central modulators of hepatic carcinogenesis’. We thank the reviewers for their very helpful comments, and we feel the changes we have made in response to their comments has enhanced our manuscript.

With best wishes,
Neil Henderson

Reviewer's report
Title: Hepatic stellate cells: central modulators of hepatic carcinogenesis
Version: 2 Date: 6 April 2015
Reviewer: Shannon Glaser
Reviewer's report:
Minor Essential Revisions:
1. The review “Hepatic stellate cells: central modulators of hepatic carcinogenesis” by Thompson, et. al. does cover an area of importance in the field covered by the journal.
2. The review presents a comprehensive, authoritative review of existing work on the role that HSCs play in the progression of hepatocellular carcinoma (HCC), specifically the key components produced by HSCs that modulate HCC tumor formation and how these pathways may be targeted as new therapeutic options for the treatment of HCC.
Other comments:
In Lines 54-57 the authors mention that chronic Hepatitis B infection is one of the major risk factors for HCC. Then, in the next sentence in Lines 57 and 58 they mention that “In most countries, the mortality rate approximates the incidence,
which is increasing”. It is not clear whether the authors are referring to the mortality rate of HCC or the mortality rate of Hepatitis B in this sentence, so that should be clarified.

We thank the reviewer for highlighting this, and have amended the text accordingly (new text highlighted in blue).

In line 415 the references in the brackets should be combined [119-121] instead of [119] [120] [121].

We thank the reviewer for highlighting this, and have amended the text accordingly (new text highlighted in blue).

Reviewer's report
Title:Hepatic stellate cells: central modulators of hepatic carcinogenesis
Version:2Date:11 April 2015
Reviewer:Diego F Calvisi

Reviewer’s report:
In the present review article, Thompson et al. summarized the current knowledge on the link between hepatic stellate cells (HSC), the major source of extracellular proteins during fibrogenesis, and hepatocarcinogenesis. In particular, the authors focused on the molecular mechanisms whereby HSC modulate hepatocellular carcinoma (HCC) growth, immune cell evasion and angiogenesis. In addition, the authors describe the mechanistic crosstalk between HSC and HCC, and the novel strategies developed to target HSC for the treatment of human HCC.

The work by Thompson et al. is an excellent, well-written review article on this important topic. The review presents a comprehensive, authoritative review of the existing work in this area. The appropriate references are cited, and all statements of fact accompanied by a reference. Besides a comprehensive summary, the authors elegantly discussed the most recent strategies and therapeutic possibility of targeting HSC in human liver cancer.

I would kindly suggest the authors few, minor modifications.

Discretionary Revisions:
1. The authors should include a table in which the major molecular targets of the HSC-HCC crosstalk (and the presumable role of these targets) are summarized.
2. The authors should add a scheme where the innovative therapeutic approaches targeting HSC and the related challenges are summarized.

We thank the reviewer for this excellent suggestion, and to this end we have added a new figure (Figure 3) summarising therapeutic approaches to targeting HSC, and we feel this new figure has enhanced our manuscript.