Reviewer’s report

Title: Development of a transgenic mouse model of hepatocellular carcinoma with a liver fibrosis background

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Reviewer: Bruno Christ

Reviewer's report:

The manuscript by Chung et al describes a novel HCC model in the mouse using stable transfection of c-myc and shRNA to silence p53 after hydrodynamic injection. They used this model to show that tumor formation was increased and survival decreased in the background of fibrosis induced by CCl4 treatment. Indeed, it is a short and easy way to generate mice with liver tumors. But at this point, the study suffers from a preliminary characterization of the tumors as compared to other tumor models like DEN-induced liver tumors and confirmation in another fibrosis model avoiding toxic compounds.

The authors show GFP expression in tumors and conclude that therefore the tumors derived from transgenic hepatocytes overexpressing myc and silenced p53. It would be nice to show whether this is really the case by showing RNA or protein data. Otherwise, integration of the plasmid in a random genomic place could also be responsible for tumor induction.

The experiment described in Fig. 2 induces cirrhosis in the background of existing tumors. "In real life" , it is the other way round. What happens after inducing fibrosis first by CCl4 and then injecting the tumorigenic plasmids?

It seems that in this experiment another control should have been run. Control animals should have been injected with the plasmid mycGFP instead of mycP53GFP and then treated with CCl4 or not.

The quality of the pictures is a bit poor, which might result from the conversion into a pdf-file. Nonetheless, differences in GFP and alpha-SMA stains are hardly visible if at all in Fig. 4.

The authors conclude that fibrosis induced by CCl4 treatment decreased survival. Yet, it is not clear whether the decrease in the survival rate is not due to a toxic impact of CCl4 even after long-term treatment. Therefore, similar experiments with another fibrosis model like bile duct ligation or DEN would be necessary to support this conclusion.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
Does the work include the necessary controls?  
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No

Are the conclusions drawn adequately supported by the data shown?  
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No

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