Reviewer's report

Title: MicroRNA signatures associated with diagnosis and prognosis of patients with intrahepatic cholangiocarcinoma

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Reviewer: Laura Gramantieri

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The aim of the study is to identify miRNAs signatures associated either with diagnosis and prognosis of ICC. Indeed, a 30 miRNAs signature is identified as a diagnostic tool, while a 3-miRNAs signature is associated with prognosis in patients undergoing surgery for ICC.

The study design is not original and no mechanistic insights are provided. In addition previous studies performed by using the same approach and on the same malignancy were published, reporting miRNA signatures different from those reported here. My major compulsory revisions are the following:

1. The choice of normal intrahepatic bile ducts as a control tissue when trying to identify a signature with a diagnostic purpose should be argumented. I suppose that a diagnostic aid might be sought in the case of nodular liver lesions difficult to be characterised with the traditional histopathological tools. Thus I think of poorly differentiated HCCs or metastatic liver tumors, etc. Conversely, we don’t need to know which miRNAs differentiate ICC from normal bile ducts, because the differential diagnosis between these two entities does not represent a clinical need in which molecular tools are likely to be helpful. Different is the case of signatures identified with the aim of unraveling the transcriptomic aberrations and molecular mechanisms associated with the development of ICC.

2. The study was performed in patients resected for ICC and a miRNA signature associated with prognosis is identified. I wonder whether patients received any treatment following surgery. Also, I wonder if cirrhotic patients were treated in the same way and with the same schedules as non cirrhotic patients. It would be surprising to know that either patients did not receive any adjuvant treatment or they received the same treatments irrespective of the presence or absence of cirrhosis. Were all the death cancer-related? In cirrhotic patients also? This last question derives from the observation that in table 1 AFP increase is one factor associated with overall survival.

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

Quality of written English: Needs some language corrections before being published
Declaration of competing interests:

I declare that I have no competing interests.