Reviewer's report

Title: FTY720 Inhibits Proliferation and Epithelial-Mesenchymal Transition (EMT) in Cholangiocarcinoma through Inactivation of STAT3 Signaling

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Reviewer: Huey-Jen Lin

Reviewer's report:

Dr. Liu and authors have demonstrated an immunosuppressive anti-cancer agent namely TY720 that could potentially combat Cholangiocarcinoma (CC) through inactivation of STAT3 signaling. The inhibitory effect is involved with induction of apoptosis, inhibition of cell cycle progression and EMT as well as impeding tumor growth and metastasis. Though this report presented logical experiment design and accompanied with solid data for supporting conclusions, the following concern shall be brought to authors’ attention for improving the quality of the article.

Major Compulsory Revisions

The issue of activated STAT3 signaling in CC shall be better addressed. Authors shall somehow demonstrate human CC tumors harbor elevated STAT3 signaling by providing immunohistochemical stained tumor slides or by citing published articles revealing the phenomena.

Only one cell line for respective animal study seemed to be short. HuCCT1 was for in vivo invasion/metastasis assay while QBC939 was for tumor growth study in xenograft mice.

If any published reports have reported Stat3 inhibitors could render similar tumor suppressive effect on CC as FTY720 did, these pertinent articles shall be discussed.

The statement of “without notable “Side Effect” shown in line 23 of page 10 needs some experimental data. Are there any evidence to support the statement? Shall control mice lacking tumor be treated similarly and then followed by close assessment for evaluating the drug’s side-effect on healthy mice?

Minor Essential Revisions

1. Discussion section virtually reiterated what have been described in the result section which made the article reads redundantly. Citing additional publications in the discussion section for comparing data generated from various groups would improve the quality of the manuscript.

2. English writing could be better improved. For example, line 29 of page 8 stated:

And, FTY720 treatment also strongly decreased.
It is an uncommon writing grammatically.

3. Some statements could be added with clarity. For example: The IHC analysis showed the changes of Ki-67, cleaved-caspase-3 and CD31 in different group (Fig. 6C), can be added with a few extra words “respectively assess tumors’ ability of proliferation, apoptosis, and forming microvessels”.

**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.