Reviewer’s report

Title: Immunotherapy of hepatocellular carcinoma with 22-nt dsRNA

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Reviewer: Steve Pascolo

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The manuscript by Kabilova et al. reports the in vivo immunostimulating and anti-cancer activity of short dsRNA (19bp with 3 bases overhang at 3’ end of both strands). The dsRNA was chosen according to previously published results indicating that this sequence is most efficacious. It is formulated in Lipofectamine. Intra-venous injections in mice induce interferon-alpha; intra-peritoneal injections are not efficacious in controlling tumor growth (treatment versus control) or increasing survival but may reduce metastasis (treatment group versus control or Mock).

Major compulsory revisions:
- Interferon-alpha is detectable in serum after intra-venous injections (Figure 1). Is it also detectable after intra-peritoneal injection? Intra-peritoneal injections are used in the anti-cancer experiments (Figure 2)....
- Figure 2: Mock treatment (Lipofectamine) increases tumor volume compared to untreated controls. Thus although isRNA treatment is significantly effective when compared to Mock, it is not when compared to control. Any explanation why Lipofectamine would increase tumor growth?
- Figure 2: Poly (I:C) that is efficacious in triggering interferon-alpha (Figure 1) is not providing control of tumor growth and is even boosting lung and liver metastasis (Figure 6). Any explanation for this unexpected result?
- Is interferon-alpha necessary for the anti-metastasis effect (repeat experiments using neutralisation of interferon-alpha or interferon-alpha receptor by antibodies or using KO mice)

Minor revisions:
"For" is missing page 4 "been demonstrated several tumor types"

Page 5, paragraph isRNA line 7: Is siRNA correct? Or it is meant isRNA?

Page 12: Inhibition of primary tumor growth: p<0.01? In Figure 2, p<0.05

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

Quality of written English: Acceptable

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