Reviewer's report

Title: Validation of a VEGFR2 antagonist peptoid in vivo

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Reviewer: Nikki Cheng

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Lynn et al presents a report on the effects of a GU81 on mammary tumor progression using a mouse model of spontaneous tumor formation, specifically, the MMTV-PyVmT mouse model. GU81 is a derivative of GU40C4, a peptoid, previously shown to be effective in a different mouse model of tumor progression. These current studies are well designed and articulated. In addition, peptoids represent a new approach to towards molecular targeting in cancer rendering the findings interesting and relevant to the field of angiogenesis and cancer therapeutics.

Concerns are as follows:

Minor Essential Revisions

1. Although the authors state that the development strategy of GU81 will be published in another paper, the rationale for obtaining a derivative of GU40C4 is unclear. Why was GU81 designed?
2. Genetic background can significantly affect latency of tumor formation and aggressiveness of tumor progression. The PyVmT model is available in different backgrounds. Please specify which genetic background is used.
3. The mechanism of action for peptoids, especially for GU40C or GU81 are unclear for those who are unfamiliar with the subject. More background in the intro is needed for GU40C and GU81. For example, does GU81 specifically bind to VEGFR2 or does it affect VEGFR1 also? What previous studies were done on GU40C to describe the mechanism of action?
4. It is interesting that GU81 does not significantly affect angiogenesis in vivo but does affect VEGFR phosphorylation in vitro. Does GU81 inhibit VEGF induced sprouting or proliferation in vitro?
5. Given that the in vitro dosages in Figure 1 differ from the in vivo dosages given and the in vitro results differ from in vivo results, does the in vivo dosage correlate with the in vitro dosage?
6. For clarity, a separate description in the methods section of how the statistics were performed is advised.
7. How was microvessel density measured?

Discretionary decisions

1. While is it mentioned that no differences in vivo angiogenesis were observed
between GU81 treatment and controls, showing the results anyway may help the reader to further understand the effects of GU81 in vivo.

2. Given that increased VEGF expression is increased in tumors with GU81 treatment, could GU81 enhance VEGF expression in cultured tumor cells?

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

Quality of written English: Acceptable

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