Reviewer's report

Title: Immune targeting of autocrine IGF2 hampers rhabdomyosarcoma growth and metastasis

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Reviewer: Dedong Cao

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In this manuscript, the authors tried to inhibit rhabdomyosarcoma growth by immune approaches targeting IGF2. They used passive and active immune methods to treat transgene mice model, and found that both passive and passive administration of anti-IGF2 antibodies hampered the growth of IGF-2 addicted rhabdomyosarcoma. This sounds interesting. However, few concerns should be addressed before publication.

1. What is responsible for the overexpression of IGF2 in rhabdomyosarcoma. Is there any reference?

2. The authors mentioned "Immune targeting of IGFs has been reported in a few non-rhabdomyosarcoma experimental models, both in preventive and in therapeutic approaches" in lines 34-39. Please provide detailed key outcomes of these studies.

3. In the methods and materials section, "Two groups of vaccinated and control mice (n=5-6)" was presented. Please provide accurate number of mice for each group.

4. In the "Monoclonal antibodies against IGFs" section, it is mentioned "BALB-p53Neu male mice at a pre-neoplastic stage (5-6 weeks of age) were randomized to three experimental groups". Is there any imaging evidence supporting this stage, such as CT. Please also provide method of randomization.

5. Is CT or MRI applied to measure tumor diameters or detect metastasis number?

6. It is better to present pathological tissue section of rhabdomyosarcoma and salivary gland carcinomas, and typical colony images in addition to the charts in results. It is essential to provide evidence demonstrating transgene model. In "Autocrine IGF2 circuit in the BALB-p53Neu murine model of rhabdomyosarcoma" result section, was the expression of IGF2 measured after treatment of inhibitor and siRNAs? Was there any changes before and after treatment?
7. In "Prevention of rhabdomyosarcoma by passive administration of anti-IGFs antibodies" result section, there is lack of enough data supporting "neutralizing the autocrine IGF loop".

8. The numbers of mice used in the survival assay is small. It is better to test the immune effects on more mice.

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?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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