Reviewer’s report

Title: Gm40600 suppressed SP 2/0 isograft tumor by reducing Blimp1 and Xbp1 proteins

Version: 1 Date: 04 Feb 2019

Reviewer: John D Shaughnessy

Reviewer’s report:

This manuscript, entitled "Gm40600 suppressed SP 2/0 xenograft tumor by reducing Blimp1 and Xbp1 Proteins, is a revision of a previously submitted version. The authors suggest that Gm40600 is a master regulator of Blimp1 and Xbp1, two transcription factors known to regulate plasma cell differentiation. They also claim that Blimp1 and Xbp-1 regulate Bcl2 expression and that in so doing, Gm40600 is a potential therapeutic target for human myeloma. Mouse plasmacytomas, like SP2/0 are mineral oil induced tumors arising in the peritoneum of the inbred mouse strain BALB/c. These tumors do not grow in bone and have very few similarities with human multiple myeloma. They are universally associated with IGH-mediated translocations that activate the c-myc oncogene, an event that is rare in myeloma and represents a secondary event in this plasma cell malignancy. Thus the suggestion that the results described here are sufficient to be extrapolated to human myeloma is not warranted.

The authors describe an "SP2/0 xenograft model". If SP2/0 is of mouse origin and the tumor is transplanted into a mouse, how can this be considered a xenograft model?

To make this work more relevant and impactful, the authors are encouraged to:

1) Show that Gm40600 is relevant to other mouse plasmacytoma cell lines and that the same effects are observed when manipulated.

2) Manipulate Gm40600 in BALB/c mice and show that the induction of plasmacytomas in such transgenic mice is altered

3) Show that Gm40600 is relevant to human multiple myeloma by showing that the phenomena described here, for the mouse plasmacytoma cell line SP2/0, hold in the case of readily available human cell lines.

4) That Blimp1 and Xbp1 are targets of Gm40600 in such cell lines.

5) There is an enormous amount of gene expression profiling data on primary multiple myeloma, myeloma cell lines, and normal plasma cells and plasmablasts. The authors should access these data and provide a figure showing the expression of Gm40600 and its target genes in these samples and determine if there is a correlation between the expression of Gm40600 and Blimp1 and XBP1
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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

No

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

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

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