Reviewer's report

Title: Transforming growth factor-beta suppresses metastasis in human colon carcinoma.

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Reviewer: Sam Thiagalingam

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This manuscript describes the findings from a study that could potentially extend the observations previously made by authors' laboratory to explain why intact TGF-beta signaling could render suppression of colon cancer metastasis. These observations question the general consensus that in majority of the cases, the opposite phenomenon is true and hence TGF-beta signaling is targeted for therapy. While the data presented here is not robust which decreases the enthusiasm, it highlights the potential importance of this phenomenon for a subset of patients.

The major concerns are as follows:

(1) The title of the manuscript need revision to highlight the fact that this phenomenon is likely to be true for only a small “subset” of colon cancers.

(2) While there has been an attempt to emphasize that defective TGF-beta signaling is only involved in suppressing metastasis and not invasion, these conclusions are primarily based on selected IHC data rather than from overall analysis of the properties of the model cells. Since this is an important point, more data will be necessary in terms of in vitro and in vivo assays and the analysis of invasion specific markers to make this conclusion.

(3) This study is entirely based on two model cell lines originally developed in the senior author’s laboratory. It is not clear how prevalent this would be to metastatic colon cancer in general and for therapeutic applications. It would be preferred to extend these studies to metastatic colon cancer in general by including other models. Furthermore, while this study has potential implications to cancer therapy, without clinical studies it is premature make these conclusions correlating to the patient populations. A discussion about identifying cancers with and w/o intact TGF-beta signaling in the clinical setting and the preliminary nature of these conclusions in the absence of clinical studies should be emphasized.

In summary, despite there are potentially interesting observations reported in this study using two model cell lines previously used in other studies by the authors, inclusion of other models, a thorough investigation of invasive versus metastatic potential, acknowledging the fact that this phenomenon may be true for only a small “subset” of cases and emphasizing the need for future clinical studies, would make this manuscript acceptable for publication.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
No conflicts