Reviewer's report

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

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Reviewer: James W Freeman

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This interesting and mechanistically driven study uses two interesting colon cancer cell line models to show that TGFβ signaling acts as a suppressor of metastases. The study is carefully controlled and combines both in vitro and in vivo orthotopic models to address critical questions related to the role of TGFβ in these two weakly metastatic cell line models. The study provides compelling evidence that blockade of TGFβ signaling in the non- or weakly metastatic colon cancer cell line FET causes an increase in metastasis; the increase in metastases is linked to an increase in XIAP and decrease in apoptosis without a significant overall change in proliferative potential. Conversely, restoring TGFβ signaling in the TGFβ receptor deficient CBS cell line caused the opposite effect. The results also indicated that the repression of metastasis by TGFβ did not prevent the invasion step of the primary carcinoma.

The study raises the important conundrum of whether or when is it advisable to use TGFβ inhibitors for cancer therapy. The study suggests that in some cases blockade of TGFβ pathways might promote metastases. The paper further separates the processes of invasion and metastases in context with the cell line models used.

There are only minor discretionary revisions:

1. Figure 2 is not paired appropriately for easy interpretations. Fig 2.B and 2C are linked and 2A and 2D. It would be easier to read if the graphs are placed adjacent to the corresponding IHC image.

2. Also in relation to the legends for 2C and 2D implies a 100 % of cells are positive for staining; actual percentages would be more meaningful.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

No competing interest