Reviewer’s report

Title: S100A4-neutralizing antibody suppresses spontaneous tumor progression, pre-metastatic niche formation and alters the T-cell polarization balance

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Reviewer: Eugene Tulchinsky

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Grum-Schwensen et al report on the role of S100A4 protein in the development of pro-tumorigenic population of tumour-associated lymphocytes. They show that S100A4 shifts the Th1/Th2 balance towards Th2 and attracts Th2 cells to sites of primary tumours and pre-metastatic niches. Importantly, a blocking anti-S100A4 mab, 6B12, rescues the effect of S100A4 on Th1/Th2 equilibrium. The therapeutic application of this antibody is discussed.

The paper is presented by a group of researchers with long-standing interest in the role of S100A4 in human cancer. Previously, the authors published important studies elucidating the extracellular function of S100A4 and in particular its role in tumour-stroma interactions. Current work links S100A4 with Th1/Th2 balance, and, therefore, contains an important element of novelty. The application of anti-S100A4 blocking ab might have clinical perspective.

There are several minor essential revisions to be made.

Page 9, line 259. “...S100A4 slightly suppress the transcription of GATA3 and TGF-beta,...” In Fig. 1A, the effect of S100A4 on these genes seems to be insignificant

Fig. 1B. Mutant S100A4 brings pJAK3 and pSTAT3 to a level lower than the control. This needs to be explained. An increase in p-STAT3 in S100A4-treated cells is not obvious.

STAT1 is upregulated by S100A4 (page 9), but STAT3 is analysed instead.

What is the origin of T-cells used in the analysis (page 10)?

Level of interest: An article of outstanding merit and interest 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:

'I declare that I have no competing interests'