Reviewer's report

Title: Modulation of SOCS Protein Expression Influences the Interferon Responsiveness of Human Melanoma Cells.

Version: 1 Date: 19 November 2009

Reviewer: Howard M Johnson

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In this study, authors show basal levels of SOCS1 and SOCS3 in 10 melanoma cell lines and that IFN treatment can result in increased levels in some of these cells. Overexpression of SOCS1 and SOCS3 in these cells had an inhibitory effect on IFN alpha and IFN gamma activation of STAT1 and siRNA treatment cancelled some increase in STAT1 activation. The study does not show a causal relationship between SOCS expression and the virulence of tumor cells. Thus, the last sentence of the DISCUSSION that suggests that inhibition of SOCS proteins is a therapeutic strategy is really not addressed in this study. Further, the authors state that others have not shown such a strategy. There is a study, however, that shows that SOCS1 siRNA treatment of dendritic cells results in potent anti-melanoma vaccine efficacy in the mouse melanoma model (Shen L et al. 2004, Nature Biotech 22: 1546).

Specific Comments:
1. siRNA transfections are suggested to affect greater than 90% of cells (p. 10). It would seem that the knockdown in Figure 5 would be more effective if this were so.
2. No data are presented on non-melanoma cell lines for comparison.
3. At the beginning of the RESULTS (p. 8), the authors indicate that “SOCS-specific peptide competitors eliminated SOCS3 specific immunoreactivity (Data not shown)”. If the authors have a SOCS peptide inhibitor, it would seem that this has an important observation. It warrants more than “data not shown”. More importantly, what do they mean by this statement?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests.