Reviewer’s report

Title: Stat3 is a positive regulator of gap junctional intercellular communication in cultured, human lung carcinoma cells

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Reviewer: Jacqueline Bromberg

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This is an interesting manuscript demonstrating an inverse relationship between src expression and GJIC in nsclc lines and some primary tumors. Furthermore, over-expression of src leads to a loss of GJIC. Knock-down or inhibition of Stat3 does not restore GJIC function. I think that although the findings are interesting, there should be a further examination of the contexts where activated Stat3 can alter GJIC. Also, additional positive controls should be considered.

For example,

1. I think it's important that the authors demonstrate that dasatinib treatment of cell lines expressing high levels of src and pStat3 leads to a restoration of GJIC as well as other inhibitors known to restore src-mediated loss of GJIC. MEK, PI3K? What happens to GJIC and pSTAT3 in the presence of a JAK inhibitor?

2. Does over-expression of a constitutively activated Stat3 in cells, where the levels are low, lead to changes in GJIC and Cx-43 levels. Similarly, what does exogenous stimulation with IL-6 (or family members) do to GJIC expression levels.

3. In the context of a src transformed cell, what are the consequences of inhibiting both src (with dasatinib) and stat3? Maybe in this context you would have restoration of gap junctions?

4. Your data suggest that Stat3 functions differently in different cell types as a potential regulator of GJIC expression. CPA-7 and shRNA does not have a direct effect of pSTAT3 but rather Stat3 binding and total Stat3 levels in cells where pSTAT3 is quite low to begin with. Where is Stat3 in these cells that express low levels? Can you think of a hypothesis which explains its role in GJIC formation? How quickly do GJIC’s form or disappear after treatment with appropriate inhibitors?

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