Reviewer's report

Title: Inhibition of IGF1-R overcomes IGFBP7-induced chemotherapy resistance in T-ALL

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Reviewer: Akira Yoshida

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Major Compulsory Revisions.

Authors investigated the functional role of IGFBP7 in Jurkat and Molt-4 cells as in vitro models for T-ALL. WST-1 assays showed a reduced proliferation of IGFBP7-transfected cells in the TALL cell line Jurkat, leading to a longer survival in a nutrient–limited environment. Furthermore, Jurkat IGFBP7-transfected cells were resistant to vincristine and asparaginase treatment. Surface expression and whole protein measurement of IGF1-R protein expression showed a reduced abundance of the receptor after IGFBP7 transfection in Jurkat cells. Interestingly, combination of the IGF1-R inhibitor NPV-AEW541 restored sensitivity to vincristine in IGFBP7-transfected cells. Additionally, IGF1-R associated gene expression profiles of 86 T-ALL patients revealed an up-regulation of important drivers of T-ALL pathogenesis and regulators of chemo-resistance and apoptosis such as NOTCH1, BCL-2, PRKCI, and TP53.

Authors concluded that these results provide a model for the previously observed association between high IGFBP7 expression and chemotherapy failure in T-ALL patients.

However, reviewer would like to suggest additional important experiments.

1. Regarding resistance to vincristine and asparaginase in IGFBP7-transfected cells, authors performed WST-1 assay at only single drug concentration. It is not convincing. Author should perform WST-1 assay at least 5 different concentrations, and show the change of IC50 value between IGFBP7-transfected and parental cells.

2. Authors used the pharmacological inhibitors in order to inhibit the signaling of IGF1-R. However, reviewer would like to suggest that authors should employ the siRNA method in order to inhibit the IGF1-R.

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:

No competing interests