Reviewer's report

Title: DNA methylation and histone modifications regulate SOX11 expression in lymphoid and solid cancer cells

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Reviewer: Samir Parekh

Reviewer's report:

Ek et al describe methylation and histone modifications of the SOX11 promoter region and reversible induction of SOX11 with HDAC inhibitor treatment in hematological and non-hematological malignancies.

Major comments:

1. H3K27me3 is mediated by Polycomb Repressive Complex 2 (PRC2). EZH2, a PRC2 member is overexpressed in MCL - knockdown experiments of EZH2 (or treatment of cells with EZH2 specific small molecule inhibitors such as GSK343) to demonstrate whether epigenetic de-repression of SOX11 is possible by reversal of H3K27me3 would critically support the mechanism proposed by the authors in this manuscript (in contrast to HDAC inhibitors)

2. The link between SOX11 and ER status in breast cancer is intriguing. Does SOX11 directly or indirectly regulate ER expression? ChIP or under/overexpression studies may be useful to understand this link.

Minor comments:

1. Please include the rationale for choosing the various cell lines and doses of inhibitors used. The DNMT inhibitor Azacytidine has previously been used by Wasik et al to induce SOX11 in MCL cell lines, so the cytotoxicity mentioned in this study may be due to use of higher doses than required for demethylation and warrants revisiting.

2. Please include the map of CpGs studied in Supplement 1 in the main figure 1

3. Please reference and include in discussion the recent publication by Tiwari et al (Cancer Cell 2014) showing that SOX4 directly regulates the expression of EZH2 and EMT in breast cancer.

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