Reviewer’s report

Title: Concomitant heterochromatinisation and down-regulation of gene expression unveils epigenetic silencing of RELB in an aggressive subset of chronic lymphocytic leukemia in males

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Reviewer: Michael Chan

Reviewer’s report:

The manuscript by Marteau et al demonstrated the down-regulation of RELB gene in male CLL patients is due to histone modification but not DNA mechanism. This is an interesting findings however several additional experiments need to be performed before it can be accepted for publication:

Major revision

1. By immunofluorescence labeling, the authors conclude in figure 1 that healthy donor and CLL patients has different level of DNA methylation. However, the author did not mention how many cells did they count.

2. In figure 4, the authors demonstrated that resistant male patients has higher tri-methylated H3K9 and lower acetylated H3K9/K14 level in RELB promoter. The author should treat the cells with TSA to further demonstrate the relationship between histone modification and down-regulation of the gene.

3. By computational analysis, the authors identified that STAT1 and PAX5 binding site are located in the promoter region of RELB gene. Knock-down experiment has to be performed to demonstrate if these 2 TF play any roles in the transcriptional regulation of RELB gene.

Minor revision:

1. RF and SH in figure 4A and B should be RM and SM

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