**Reviewer’s report**

**Title:** Bortezomib prevents cytarabine resistance in MCL, which is characterized by downregulation of dCK and up-regulation of SPIB resulting in high NF-κB activity

**Version: 2 Date:** 03 Jan 2018

**Reviewer:** Samir Parekh

**Reviewer's report:**

Freiburghaus et al describe DCK downregulation in a mantle cell lymphoma cell line (Z138) cultured in sub-lethal concentrations of cytarabine.

Gene expression analysis identifies upregulation of SPIB, a regulator of NFKB signaling in Cytarabine resistant cells.

Their findings suggest that DCK downregulation is prevented by co-culture with bortezomib, which may be of therapeutic significance.

**Major comments**

1. Recommend assessment of cell viability with an orthogonal technique eg MTT or Annexin/PI instead of solely relying on trypan blue exclusion.
2. The control group for the resistant cells for the GEP comparison groups should be CYT-ES-21. Please justify using alternate controls used in this experiment.

**Minor comments:**

1. Is the acquired resistance to Cytarabine in Z138-R reversible if the cells are cultured without ARA-C?
2. Please show a histograms of (a) DCK expression over primary samples (range) as well as (b) mean+-SD in the groups described
3. Please describe study limitations including use of a single cell line and lack of in-vivo modeling of bortezomib to prevent cytarabine resistance in the discussion.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes

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None

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