Reviewer's report

Title: pRb2/p130 protein expression and RBL2 mutation analysis in Burkitt lymphoma from Uganda

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Reviewer: Miguel Campanero

Reviewer's report:

In this manuscript, Kalungi and co-authors report a pRb2/p130 protein expression and RBL2 mutation analysis in endemic Burkitt’s Lymphoma (eBL) cases from Uganda. This study has been well defined and appropriately described. The data are clearly presented and indicate that p130 subcellular localization in eBL cases from Uganda is mostly nuclear. In addition, their data suggest that p130 nuclear localization signal (NLS) is not mutated in these patients. These findings are of relevance in this particular field.

The authors acknowledge that exon 21 could not be fully covered in their sequencing studies. However, as they also state, the region sequenced by them includes all RBL2 regions whose mutations affected p130 nuclear localization. Because p130 was found in the nucleus in most of their BL cases and RBL2 NLS has been sequenced in all these specimens, the lack of sequence information about some regions of exon 21 should not be considered a major caveat in this manuscript.

Minor Essential Revisions:

1. These results seem to disagree with two previous reports from another group that suggested that p130 NLS is mutated in eBL and that p130 location is cytosolic in biopsy specimens from most of these patients. Notably, these two studies deal only with patients from Kenya. The conflict is addressed in the Discussion section of the manuscript. To support that mutations on RBL2 are less frequent in BL than previously suggested, the authors have used another report describing the absence of RBL2 mutations in BL cases from Brazil. However, the authors should also take into account that the analyzed cases of Brazilian BL correspond to sporadic BL and that endemic and sporadic BL might arise through different lymphomagenesis mechanisms. The authors should also consider the possibility that geographic variations (Uganda versus Kenya) or differences in other factors involved in eBL formation, such as the presence of different arboviruses or differences in other environmental factors between these two countries might account for the discrepancies of their results with those previously published. Thus, it cannot be ruled out that most eBL patients from Kenya, but not those from Uganda, undergo mutations in the RBL2 NLS.

2. The authors refer to the Retinoblastoma family of proteins as “Retinoblastoma proteins” along the manuscript. The term “Retinoblastoma proteins” is not correct
and should be changed in the text for other expressions such as “Retinoblastoma family of proteins” or “pocket proteins”.

**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