Reviewer's report

Title: Simultaneous Aurora-A/STK15 overexpression and centrosome amplification are required to induce chromosomal instability in cells with a MIN phenotype

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Reviewer: Jonathan J J Li

Reviewer's report:

This manuscript presents some very interesting new findings and extends previous observations regarding Aurora A over-expression, centrosome amplification, and aneuploidy using HCT16 cells and their isogenic KO-derivatives. It is generally well-written with a few exceptions.

General comments.

1. Characterization of HCT1 cells is needed. As stated MIN and CIN phenotypes are understood to be mutually exclusive events. The data suggest that HCT1 cell line is heterogeneous. A mixed tumor population of diploid cells MIN+ and possibly MIN-. What is the frequency of MIN in this cell line? This may reflect human colon cancer, unlike breast or bladder cancer in which MIN+ is minimal.

2. There is in-vitro evidence in HeLa cells that both active and inactive Aurora A give rise to centrosome amplification and CIN via formation of polyploidy. Has the transfected Aurora A protein been checked for activity in HCT1 cells and their KO-derivatives?

Specific comments.

3. In Fig 6C, the % of cells with 2 or >2 centrosomes in p53 KO-STK15 + siRNA declined markedly less compared to p53 KO-STK15 relative to STK15 and STK15+ siRNA. The authors should comment regarding the difference between these two groups in the data obtained. Also, in Fig 6D, p53KO resulted in much more chromosomal gains relative to losses on STK15 ± siRNA whereas in p53KO-STK15 vs p53 KO-STK15 + siRNA did not have much effect on either of these parameters. A comment is also warranted.

4. Conclusions. It is suggested that “to alterations in genes regulating mitosis progress to trigger” should substitute Aurora A centrosomal protein substrates and mitotic, respectively.

5. References. It is suggested that a more relevant physiological finding in breast cancer related to Aurora A, CIN, and aneuploidy (Proc. Natl. Acad. Sci. USA. 101:18123-128, 2004) should be added in addition to reference 22.

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field
**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

A. The manuscript is important in the field and closely related research interest, particularly for hematopoietic and solid tumors in general.
B. I declare I have no competing interest.