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: David Stenoien

Reviewer's report:

General
Since genomic instability is prevalent in many types of cancer, understanding the molecular mechanisms by which this phenomenon arises is critical to our understanding of the oncogenic process. This manuscript highlights an important role of Aurora-A overexpression in the development and maintenance of centrosome amplification and aneuploidy. While this role has been previously reported by other laboratories, the authors here demonstrate by parallel experiments with hydroxyurea treatment that centrosome amplification alone is insufficient to produce sustained populations of aneuploid cells and this requires altered protein expression of critical regulatory proteins such as Aurora-A and p53. While it is not too surprising to the reviewer (although the authors do find this result surprising on page 6) that the centrosome amplification is rapidly lost without the continued selective pressure of hydroxyurea, the authors results indicate that the development of aneuploidy in the presence of amplified centrosomes requires alterations in the Aurora-A which plays an important role in centrosome maturation and dynamics.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1) there are numerous grammatical and spelling errors that should be fixed prior to final publication either by the authors or the editorial staff. These are too numerous to point out each occurrence.

2) The title is misleading. The work shows that centrosome amplification alone is insufficient to induce chromosomal instability and maintain this in future cell generations. The results do not prove that both Aurora-A overexpression and centrosome amplification are required for aneuploidy but that their is a correlation between the two. It remains a possibility that the development of aneuploidy and centrosome amplification are two separate effects of Aurora-A overexpression.
Discretionary Revisions (which the author can choose to ignore)

1) The increased expression of Aurora-A in the p53-/- cell line may be due to these cells dividing more rapidly leading to a higher percentage of cells in mitosis rather than by altered control of Aurora-A expression as implied on page 7 and in figure 3. A comparison of the levels of Aurora-A protein in cells from comparable cell cycle stages (derived from flow cytometry or cell synchronization) could resolve this issue.

**What next?:** Accept after minor essential revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**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:**

I declare that I have no competing interests' below