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**Editorial Note:** This manuscript has been previously reviewed at another journal that is not operating a transparent peer review scheme. This document only contains reviewer comments and rebuttal letters for versions considered at *Nature Communications*.

Reviewers' Comments:

Reviewer #1:

Remarks to the Author:

In this revised manuscript Zerbib et al have done a very good job revising the work making it suitable for a resource paper as well as a manuscript that highlights important biological findings related to aneuploidy-specific vulnerabilities. I was asked to comment on the adequacy of the authors' response to reviewer 2. In summary, I believe the authors have adequately addressed reviewer 2's comments. I would like to specifically raise the following points:

- While no model is perfect, some are useful. In this respect RPE1 is used by the field as the gold standard for diploid, chromosomally stable cell line. As such generating and sharing data from these clones will be a very valuable resource for the CIN and aneuploidy community.

- The additional validation made by the authors beyond RPE1 enhance the generalizability of these findings.

- While this paper would make a great resource for the community, the biological findings reported are of intrinsic interest and are novel.

- I am satisfied with the authors' response regarding p53 and the CRAF effect

- The authors should qualify that RPe1 lack an important component of the inflammatory responses to CIN but I agree with them that this should not diminish the importance and relevance of the study which is primarily related to aneuploidy.

- I agree with the authors that in large screens like the DEPMap, single gene effects cannot be fully relied on. Like in any screen, the proof is in the pudding. The authors did a great job validating their dependency hits and therefore this should supersede large screens which have known limitations.