August 25, 2017

Dear Dr. Noor,

I have finished editing your *Cell Reports* manuscript, and I hope that you can help me with the questions below.

Please type your answers directly below my queries rather than sending a revised version of your manuscript. I have already copyedited your paper, so if you need to send a revised manuscript, you must use Word’s Track Changes feature to indicate changes.

It would be helpful if you could respond by the end of the day Monday (8/28), but please let me know if you won’t be able to reply by then.

1. Final Check of Author List, Affiliations, Author Contributions, and Acknowledgments
2. At this time, please carefully check your author list, affiliations, author contributions, and acknowledgments. We will not be able to make any changes to these sections after publication. In the author list, different colored highlighting indicates a **last name** versus a **first or middle name**. First and middle names are abbreviated in the table of contents and on PubMed, whereas last names are not (e.g., X.Y. Zhang). In the Acknowledgments, **funding organizations** and **grant numbers** relevant to your research have been highlighted pink and green, respectively. Please review this tagging carefully and confirm that these sections (author list, affiliations, author contributions, and acknowledgments) are complete and accurate or indicate any changes that need to be made.

Ed Reznik,1,2,7,\* Dimitris Christodoulou,3,4,7 Joshua E. Goldford,5 Emma Briars,5 Uwe Sauer,3 Daniel Segrè,2,5,6 and Elad Noor3,7,8,\*\*

1Center for Molecular Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, USA

2Department of Biomedical Engineering, Boston University, Boston, MA, USA

3Institute of Molecular Systems Biology, ETH Zurich, Zurich, Switzerland

4Systems Biology Graduate School, Zurich 8057, Switzerland

5Bioinformatics Programs, Boston University, Boston, MA, USA

6Department of Biology, Boston University, Boston, MA, USA

7These authors contributed equally

8Lead Contact

\*Correspondence: reznike@mskcc.org

\*\*Correspondence: noor@imsb.biol.ethz.ch

Author Contributions

E.R., D.C., and E.N. designed the analysis, performed the analysis, and wrote the paper. J.E.G. and E.B. performed and contributed to the analysis. U.S. and D.S. supervised the study. All authors read and approved the final manuscript.

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Please add one more affiliation for Ed Reznik:

Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Other than that, we confirm the author list, affiliations, acknowledgments and contributions are correct.

1. Request for Keywords

We are able to include up to ten keywords with your manuscript to improve searchability online. If you wish to include keywords, please send them to me at this time. These keywords will appear with the article online, as well as with the PubMed entry.

Small molecule regulation, metabolism, trade-offs, enzyme kinetics, elasticity, regulatory network

1. Nomenclature Check

We require gene nomenclature to conform to the standards set by HUGO, MGI, FlyBase, WormBase, SGI, and other oversight organizations. Could you please confirm that the capitalization, italicization, and style of the gene names within your paper are consistent with the rules set by one or more of these databases?

We confirm

1. Database Linking

Does your paper mention any database accession numbers? If so, our preferred format is “**Database: xxxx**,” which allows us to hyperlink the accession number to the online database. For more information, see <https://www.elsevier.com/authors/author-services/research-data/data-base-linking/supported-data-repositories>. Please let me know if any modifications to your text are needed to meet this guideline.

Does not apply

1. Institutional Review Board Approval

All papers dealing with human or animal subjects should include mention of oversight by an institutional review board (or the equivalent) within the methods. Can you please confirm that your paper includes this mention if applicable?

Does not apply

1. Error Bar Definitions

Although it is possible that this does not pertain to this paper, as a matter of policy we would ask you to confirm that, for any figures that contain error bars, these bars have been defined in the corresponding figure legends (not simply in the Experimental Procedures). If any have not been defined, please indicate how and where to add definitions.

Does not apply

1. Accession Numbers
2. Did you deposit any **new** data in an online database in conjunction with the research reported in this paper? If so, did you provide an Accession Number statement? Our recommended format is as follows:
   * **“The accession number for the \_\_\_\_\_ [sequence or data] reported in this paper is [Database]: [xxxx].”**
3. Also, please confirm that the **new** accession number(s) will be accessible to readers upon publication of your manuscript. Your paper’s publication date will be available in the proofs of your paper, which you will receive in the coming weeks.

Does not apply

1. Abbreviations
2. Will you please define the following abbreviations, unless (a) they are gene or protein names (which do not require expansion) or (b) they do not have an expanded form?
   * TCA

TCA cycle = Tricarboxylic acid cycle

Should we add it to the text during the proofing stage?

1. The following abbreviations are used inconsistently in the text. Will you please indicate which version of the term you would like to use (the abbreviation or the spelled-out form) after the first mention of the abbreviation for consistency?
   * CCM or central carbon metabolism

We think that it would be better to always use the expanded form (central carbon metabolism) throughout the manuscript.

1. Figure Legends
2. Figure 5 does not contain panels, but the legend refers to panels A and B. Will you please revise the legend so these panels are not mentioned or provide a new image that includes these panels?

We have added the letters (a) and (b) to the figure. How can we send you the new version?

That concludes my questions. At the proof stage, we can accommodate only essential changes (for example, to correct scientific error). Therefore, if you have any additional changes you would like to make to your manuscript, please send them now.

Thank you for your help,

**Alicia Wallace**

**Senior Account Team Leader | Sheridan**

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