December 12, 2016

Ruth Nussinov, Ph.D.

Jason Papin, Ph.D.

Philip E. Bourne, Ph.D.

Editors-in-Chief

PLOS Computational Biology

Re: Submission of Manuscript Entitled, "Discovering new targets and drugs for neglected diseases by paralog matching"

Dear Drs. Nussinov, Papin, and Bourne:

I am pleased to submit the manuscript entitled "Discovering new targets and drugs for neglected diseases by paralog matching" for your consideration for publication in *PLOS Computational Biology*.

The manuscript describes a novel pipeline to discover disease targets for neglected disease pathogens by computing similarity between existing target sequences and comparing them to all the genes of an organism of interest. Analysis of the data using R determines which targets may be repurposed by establishing statistical criteria that identify a similarity scoring threshold that distinguishes between functionally related genes and all other genes in the data set.

This paper validates a method for discovering cross species targets by identifying 29 distinct drugs for malaria (53, counting different formulations). This list of drugs includes many already known to be effective, as well as identifying new candidate drugs. 592 new targets are identified for further study.

The methods described in the paper use free, open source software as well as *Extract Transform and Load* (ETL) methods written by the author to computationally discover new information using publicly available data. It is this *computational*  content which makes it suitable for inclusion in this journal.

I hope this will inspire others by showing that one can discover new and valuable knowledge with a very small budget and some ingenuity. Repurposing drugs and targets can derive new value from old data.

The results presented in this manuscript have not been published previously nor are they being considered by any other journal. The author has declared no conflicts of interest.

Please let me know if you have any questions or need any additional information. Thank you very much for your consideration.

Sincerely yours,

Jeremy Singer

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