Dear Editors,

We would like to submit for publication in Oxford Academic Bioinformatics (Section: Application Notes) the enclosed manuscript, “MetaMutationalSigs: Comparison of mutational signature refitting results made easy”. Mutational signature analysis has become very common in cancer genetics and many tools have been developed that use different methods and produce different results. In this manuscript, we describe our tool MetaMutationalSigs which makes mutational signature analysis and comparison across different mutation signature analysis tools user friendly. Our major contributions and insights are as follows:

\* We created a user-friendly wrapper for frequently used signature refitting packages using Docker <https://hub.docker.com/r/pp535/metamutationalsigs>

\* We create visualizations using all tools that can be used for effective comparison.

\* We further show that our model can provide biological insights by providing sequence level embedding ordination and attention weights visualization. We show that our model can learn sequence similarity and identify subgenera groups and are associated with different phenotype labels. The attention weights can highlight informative regions with nucleotide variations across different phenotype classes.

\* We have made our code on GitHub (https://github.com/PalashPandey/MetaMutationalSigs).

We sincerely believe that our interpretable deep learning model will be of great interest to your readers.

Please address all correspondence to Zhengqiao Zhao ([zz374@drexel.edu](mailto:zz374@drexel.edu)) and Gail Rosen ([glr26@drexel.edu](mailto:glr26@drexel.edu)).

We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal. All authors have approved the manuscript and agree with its submission to PLoS Computational Biology. And the authors declare that they have no competing interests.

We suggest the following individuals as qualified reviewers:

\* George E. Dahl ([gdahl@google.com](mailto:gdahl@google.com)); Google Inc., Mountain View, CA

\* Yang Dai ([yangdai@uic.edu](mailto:yangdai@uic.edu)), University of Illinois at Chicago, Chicago, Illinois United States 60612

\* Maude David ([maude.david@oregonstate.edu](mailto:maude.david@oregonstate.edu)); Department of Microbiology, Oregon State University, Corvallis, OR

\* Radu Marculescu ([radum@ece.cmu.edu](mailto:radum@ece.cmu.edu)); Department of Electrical and Computer Engineering, Carnegie Mellon University, 5000 Forbes Ave., Pittsburgh, PA, USA

\* Ryan Poplin ([rpoplin@google.com](mailto:rpoplin@google.com)); Google Inc., Mountain View, CA

We thank you very much for your time and consideration in reviewing our manuscript.

Sincerely,

Zhengqiao Zhao

[zz374@drexel.edu](mailto:zz374@drexel.edu)

PhD Candidate

Drexel University

Department of Electrical and Computer Engineering