To

Dr. Nicole Rusk

Senior Editor

Nature Methods

January 2017

Dear Dr. Rusk,

Thank you for your reply regarding our manuscript titled “Using pattern recognition of epigenetic signals for supervised enhancer prediction”. [[We would like you to reconsider your decision... and perhaps send our paper out to review....

Since we submitted the paper to Nat. Methods on XXX we have continued to work on it and have now made some substantial improvements that have addressed most of your criticisms...

in particular, you were conerned about sw avail.

in response,

you also asked us to compare our method...

in response

you were concerned about utility for the community . now we have some responses

We are thankful for your comments. We have made revisions to the manuscript according to your critiques. We believe that the new tool we developed will be useful to the community. Our newly developed method is one of the only methods that utilizes supervised machine learning methods of epigenetic signals to predict tissue-specific enhancers. In addition, the conservation of these epigenetic signals across millions of years of evolution implies that the pattern within these signals learnt from fly can be utilized to predict enhancers in humans.

In order to show their utility to the research community, we are already using these methods to predict enhancers in a few publications resulting from the third phase of the ENCODE consortium. Furthermore, we have now added experimental validation of our predictions and show that the enhancers predicted by our methods are capable of regulating gene expression of a target gene in the experimental assay.

These changes have improved the manuscript considerably and we hope that you would reconsider it for publication in your journal.

Sincerely,

Mark Gerstein