Author's response to reviews

Title: Correlation of microRNA levels during hypoxia with predicted target mRNAs through genome-wide microarray analysis

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Author's response to reviews: see over
Dear Mr. Dunckley:

We would like to again express thanks to the Editorial Board and reviewers for their comments regarding our manuscript entitled “Correlation of microRNA levels during hypoxia with predicted target mRNAs through genome-wide microarray analysis.” All suggestions provided by the reviewers have been incorporated into a revised version of our paper. Specific responses are described below.

**Reviewer #1: Dr. Edwin Wang**

Dr. Wang noted our effort to correlate the expression of miRNAs and their targets using stringent criteria. He also suggested proceeding with publication. We are grateful to Dr. Wang for his earlier and very helpful recommendations regarding presentation and interpretation of our work.

**Reviewer #3: Dr. Bruce Aronow**

Dr. Aronow felt that the paper was improved from the previous revision. He noted that the hypoxia dependent miRNA signature described by our studies is a solid contribution, as was the finding that a large scale direct targeting mechanism for microRNAs is not likely. Dr. Aronow requested we might speculate regarding ways miRNAs are regulated, including the impact on expression of different transcripts. He suggested an explicit statement indicating that differential translation of miRNA targets may lead to secondary transcriptional and post-transcriptional regulation that could help account for mRNA profile changes observed in our study.

In response: We appreciate these thoughtful and important comments. In the revised paper, we make an explicit statement that not only miRNAs, but their secondary transcriptional effects and post-transcriptional changes all contribute to an experimentally observed mRNA profile. In addition, while we do not know with certainty the mechanism(s) by which miRNAs are regulated, a number of complex inputs (including transcriptional control, post-transcriptional modification, miRNA interactions with protein binding partners, degradative pathways, etc.) are likely to influence this process. We believe our study provides valuable methods for monitoring the transcriptome-wide influence of an miRNA profile, and that our findings will allow these complex pathways to be better understood in the future (Discussion section, pages 17-18).

On behalf of all the authors, I would like to thank the Editorial Board and Reviewers for many valuable suggestions that have strengthened the presentation of our work. All of these changes
have been incorporated into a revised version of the paper. We hope you find these responses suitable, and look forward to receiving your reply.

Very Sincerely Yours,

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