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Dear Dr. Nguyen,

We are happy to submit our revised manuscript (JoVE52246R2) 'Enhanced Reduced Representation Bisulfite Sequencing for assessment of DNA methylation at base pair resolution', for your consideration. This paper serves to offer readers a detailed protocol for the preparation of next generation sequencing libraries to interrogate base pair resolution DNA cytosine methylation data at GC-rich genomic loci, inclusive of code for computational analysis downstream.

We have included a full response to the first set of reviews for our paper. Dr. Doron Betel has joined the authorship list, offering critical input (editorial comments and revisions) to the revised submission. The paper has been enhanced by the addition of information on multiplexing approaches for the protocol, manual size selection procedure, and a figure to address several reviewers' comments about data yields. Our manuscript is written per our current protocol. While many protocol enhancements recommended by the reviewers are reasonable, we do not routinely utilize them and have included suggestions in the manuscript text for the readers' consideration of such protocol developments.

We thank Dr. Nandita Singh for the invitation to submit to your journal and for assisting us in the submission process. We welcome any further comments or questions about this manuscript from the reviewers or the editors and we look forward to hearing from you.

Thank you for your time and consideration.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Francine Garrett-Bakelman', written over a horizontal line.

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