Author's response to reviews

Title: Multilocus loss of DNA methylation in individuals with mutations in the histone H3 Lysine 4 Demethylase KDM5C

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Author's response to reviews: see over
Dear Dr. Ghosh,

Please find attached the paper entitled: “Multilocus loss of DNA methylation in individuals with mutations in the histone H3 Lysine 4 Demethylase KDM5C” for your consideration.

There are a substantial number of neurodevelopmental syndromes caused by mutations in genes involved in epigenetic regulation, suggesting that epigenetic dysregulation is an important component in the etiology of these disorders. We propose that the identification of dysregulated epigenomic targets due to loss of function of these proteins could advance our understanding of the molecular pathophysiology of these disorders. In this paper we have for the first time identified such dysregulated targets in patients with an X-linked intellectual disability and mutations in KDM5C gene. The data presented in this paper represent the first demonstration that locus-specific loss of DNA methylation occurs in association with functional loss of a histone modifying enzyme in a human disorder. We also present, for the first time, data demonstrating for non-imprinted genes, that epigenetic biomarkers in blood can reflect DNA methylation alterations occurring in brain.

The success of our study creates new opportunities to elucidate the epigenetic basis of other disorders caused by loss of function of genes involved in epigenetic regulation, as well as non-genetic forms of neurodevelopmental disorders.

We have previously submitted this paper to Genome Biology where the paper was positively peer-reviewed but not accepted for publication. It was suggested by Dr. Naomi Attar that we submit the manuscript to BMC Medical Genomics as she felt this was a more suitable journal for the publication of our paper. Dr. Attar has kindly offered to forward to you the reviews that were received by Genome Biology.

Please let me know if you require any further information.

Sincerely yours,

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