THE EMBO JOURNAL

Manuscript EMBO-2012-84125

TET2 and TET3 regulate GlcNAcylation and H3K4 methylation through OGT and SET1/COMPASS

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Review timeline:

Submission date:	05 December 2012
Editorial Decision:	17 December 2012
Revision received:	18 December 2012

Transaction Report:

(Note: With the exception of the correction of typographical or spelling errors that could be a source of ambiguity, letters and reports are not edited. The original formatting of letters and referee reports may not be reflected in this compilation.)

Editor: Thomas Schwarz-Romond

Transfer Note 05 December 2012

PLEASE NOTE that this manuscript was transferred from a different journal and the two referees assessing suitability for The EMBO Journal had access to both the original anonymous comments as well as the point by point response from the authors.

Editorial Staff
The EMBO Journal

1st Editorial Decision 17 December 2012

Thank you very much for transferring your study, including all relevant information from peer-review at another title for consideration to The EMBO Journal editorial office. Two recognized experts on the subject formally reviewed the paper and all related correspondence. Based on their assessment, I am happy to communicate that we will publish your study in The EMBO Journal.

As the manuscript was presented in a short-letter format, I kindly ask you to adapt style and outline at this stage to our guidelines. I am convinced that this longer, article format will benefit the presentation of your impressive results in a concise manner to ease comprehension for a broad and general audience.

I am very much looking forward to receiving such a revised manuscript.

Please do not hesitate to get in touch in case of further questions (preferably via E-mail).

REFEREE REPORTS:

Referee #1:

In this manuscript the authors describe an exciting new connection between the human ten-eleven translocation proteins (TETs) and the N-acetylglucosamine transferase OGT, the enzyme that catalyze the addition of the GlcNAc group to Ser/Thr. Indeed, purification of the TET-associated proteins by mass-spectrometry led to the identification of OGT as a major interactor. Genome-wide analysis suggested that OGT and TET2/3 overlap at TTS and within CpG islands.
Furthermore, the authors demonstrated that TET2/3 are required for the activation of OGT enzyme, which in turn facilitates O-GlcNAcylation of HCF-1 transcription factor. HCF-1 is then directly involved in modulating the occupancy of the SET1/COMPASS complexes, which activity is required for deposition of H3K4me3 mark at TTS.
Overall the data presented clearly support the identification of a novel transcriptional network that link TET, OGT, HCF1 or the SET1/COMPASS complex.

In terms of its scope and impact the manuscript appears very well suited for The EMBO Journal.

Moreover, the comments of earlier reviewers and the responses of the authors related to submission at another journal (and made available to me to govern a rapid peer-review process), I am of the opinion that this study represents a novel and interesting set of experiments, which in my opinion will be of interest to a broad readership.
Based on this, I deem the presented data suitable for publication in The EMBO Journal without further amendments.

Referee #2:

The present manuscript by Deplus et al., entitled "TET2 and TET3 regulate GIcNAcylation and H3K4 methylation through OGT and SET1/COMPASS" describes a novel interaction between OGT and the DNA modifying enzymes Tet2 and Tet3. This interaction proves necessary for OGT activity suggesting that these Tet enzymes regulate OGT activity. The genome wide mapping provided indicate that OGT and Tet2/3 show common binding sites on 50% of the ChIPed material. The next integration of OGT and Tet2/3 in a larger complex involving SET1/COMPASS opens up exciting avenues for a role in gene activation.
The significant contribution made in this manuscript warrant publication in the EMBO J. This work should stimulate many more investigations in an area that is just developing.

1st Revision - authors' response 18 December 2012

Please find attached our manuscript in the adapted EMBO style. I am also sending along the model as discussed.

Please let me know if you need additional information.