Partial Withdrawal

TRANSPARENT PROCESS

EMBO reports

Mitofusin gain and loss of function drive pathogenesis in *Drosophila* models of CMT2A neuropathy

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The authors have requested to withdraw Figure 3B–F and Figure EV4D of the above article noting:

"We, the authors, have requested to withdraw panels B–F of Figure 3 and panel D of Figure EV4 and the corresponding text because the mouse embryonic fibroblasts (MEFs) analysed in these experiments did not express the human *MFN2-R364W* allele. Instead, the MEFs expressed a human *MFN2-R364T* mutant allele never reported in CMT2A patients. This mistake in the mutagenesis process was discovered while pursuing the characterization of the human *MFN2* mutations described in the paper and was immediately brought to the attention of *EMBO Reports*.

All other genetic constructs used in this study were verified, and we confirm that the error is restricted to human *MFN2-R364W* expressed in MEFs. Consequently, the results obtained in MEFs with the other human *MFN2* mutants, including the fusion competency of *hMFN2-L76P,* and all the findings made on the different *marf* alleles in the *Drosophila* model system remain valid.

Following the discovery of this mistake, we generated the correct human *MFN2-R364W* allele, expressed this construct in *MFN1/MFN2* double-knockout MEFs and analysed mitochondrial morphology. The results revealed that, in contrast to the erroneous R364T allele, the correct R364W substitution does not efficiently restore mitochondrial filamentation and, therefore, cannot be considered as a fusion competent allele in MEFs.

The reason for the discrepancy between human *MFN2-R364W* expressed in MEFs and *marf-R404W* expressed in fly neurons remains unknown. It could be due to differences between these cell types as discussed in the manuscript, to specific characteristics of mouse and *Drosophila* model organisms, or to non-conserved molecular properties between *Drosophila* Marf and human MFN2 proteins. Further work will be needed to resolve these questions.

Since this affects the relevance of our findings to human CMT2A pathogenesis, we have decided to withdraw the proposals we made regarding the pathogenicity of the *MFN2-R364W* allele in CMT2A patients:

- '…[we] propose for the first time that excessive mitochondrial fusion drives CMT2A pathogenesis in a large number of patients' (abstract)
- 'Our data also indicate that anti-fission or pro-fusion drugs, envisioned as treatments for CMT2A or neurodegenerative disease, could be detrimental for patients with *R364W* and *L76P* alleles that would rather benefit from the development of pro-fission or anti-fusion molecules' (discussion).

We deeply regret this mistake and apologize for any inconvenience it may have caused".