Review of: "Dithiothreitol causes toxicity in C. elegans by modulating the methionine-homocysteine cycle"

Ling Feng Wang

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In this manuscript, the authors demonstrated the toxicity mechanism of dithiothreitol (DTT) on the development of C. elegans. The experiment is well designed and the results are consistent and convincing. I am also interested in the findings, and I have done some reading and learning according to the literature cited in this paper. The following are some minor problems, which I hope to discuss with the author in-depth.

1.N-acetylcysteine (NAC) are employed as antioxidant scavengers for comparison. As mentioned in the introduction part of this paper, NAC could have detrimental effects on the health and lifespan of C. elegans. DTT is similar to NAC to a certain extent. What does the author think of the usage of NAC?

2.Arles Urrutia et al. (Bacterially produced metabolites protect C. elegans neurons from degeneration) find that fed with HT115 showed a higher neuroprotective effect than OP50 because of the metabolic differences of GABA and lactate. Whether the author has considered the link between metabolites such as lactate to methionine-homocysteine cycle and possible function.

3.C. elegans were maintained at different times such as 72h or 84h because different strains have different growth times. Considering the important role of methionine-homocysteine cycle in the development of C. elegans, the development time should be different in the strains like drm-1 (gk231506), metr-1 (ok521), sams-1 (ok2946) and so on. Has it been verified?

4.The results of Fig.S1 seem do not correspond to the fluorescence intensity of strains fed with S. enterica (D) and S. marcescens Db11 (C) at a concentration of 10mM DTT. The S. enterica group should be better.

5.Inhibition of XBP-1/IRE-1 did not reproduce the salvage effect of B12 on the developmental toxicity of high concentrations of DTT but PEK and ATF-6 can be done. This is a very interesting discovery.

The workload of this paper is abundant, but it is a pity that the expression of related proteins is not determined. Otherwise, should it be considered that the affected regulation of SAM on protein translation or degradation pathway (PEK, ATF-6 involved) is the main cause of developmental toxicity caused by DTT?