Selenomethionine Protects Mutant Tau N27A Cell from Oxidative Stress and Decreases Phosphorylation of Tau

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Background

- Alzheimer's Disease (AD) is neurodegenerative disease characterized by loss of cells and aggregated tau in the hippocampus (3,4)
  - Hyperphosphorylated tau causes misfolding proteins and forms neurofibrillary tangles (3)
- Previous research has found that Set-Met decreases the amount of phosphorylated tau at pS404 site within mutant and wild type 3xTg-AD mice (4)
  - Selenium can be toxic dependent on type of cells, and concentration of the selenium (2)

Cellular Model

- N27A cells
  - WT and P301L mutant tau mutation (AD linked gene)
  - YFP tau cell line

Objectives

Determine the effect selenium methionine has on:

a. Decreasing hyperphosphorylation of tau
b. Protecting cells from oxidative stress
c. Reducing aggregated tau

Results

MTT Assay

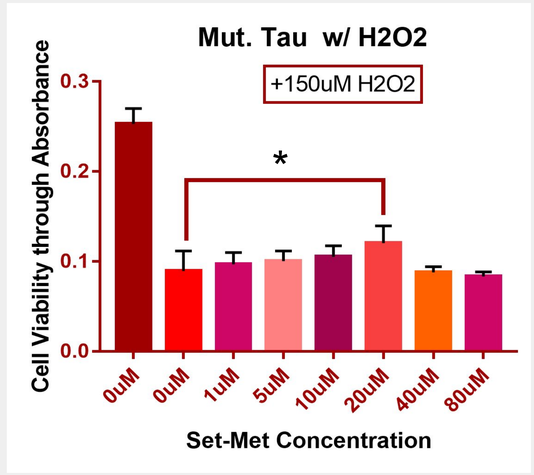

Figure 1a. MTT Assay of N27A (n=6) after H2O2 treatment. Error bars represent standard error of mean. * =p<0.01. Comparing 0uM Set-Met w/ H2O2 and the 20uM Set-Met w/ H2O2, there was a significant increase of cell viability.

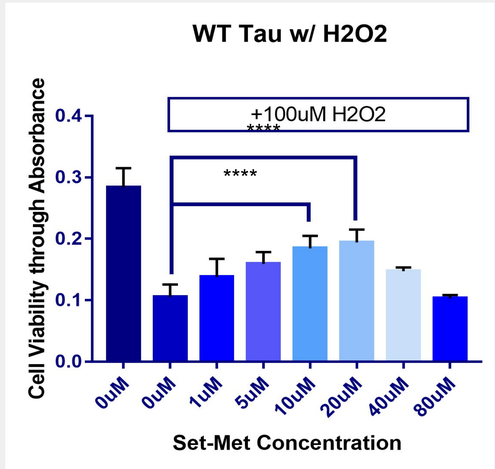

Figure 1b. MTT Assay of N27A (n=6) after H2O2 treatment. Error bars represent standard error of mean. **** =p<0.0001.Comparing 0uM Set-Met w/ H2O2 with the 10uM and 20uM Set-Met w/ H2O2, there was a significant increase of cell viability.

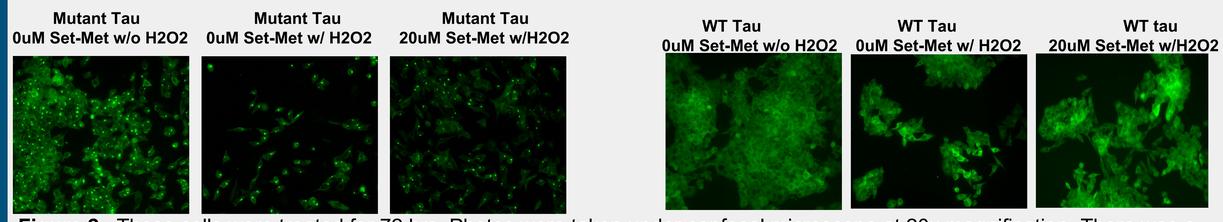

Figure 2. These cells were treated for 72 hrs. Photos were taken under confocal microscope at 20x magnification. There was a significant change between the 0uM Set-Met w/o H2O2 treatment and 0uM Set-Met and 20uM Set-Met w/ H2O2 treatment. There was no significant difference between the amount of aggregated tau (green signal) between any of the treatment groups.

Western Blot

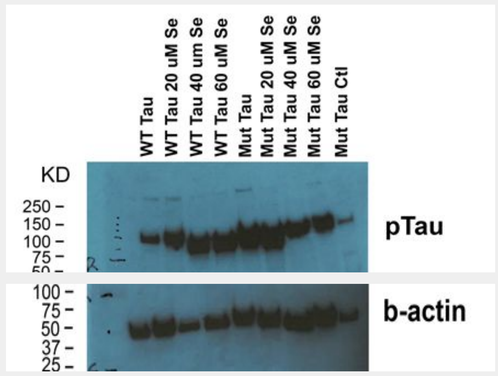

Figure 3a. Western Blot of WT and mutant tau cell treated with Set-Met after 72 hrs.There was a significant difference between the p-tau and the amount of b-actin in the cells for the mutant tau cells at 20uM.

Results for Western Blot

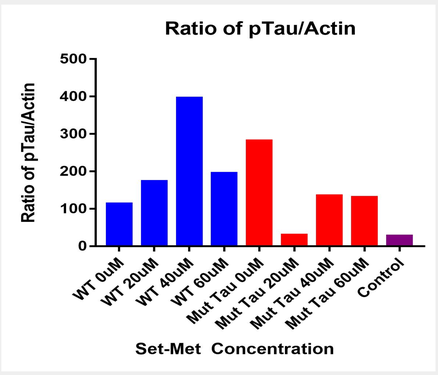

Figure 3b. Comparison between the amount of B-actin protein vs. p-tau for the western blot treated with Set-Met. The mutant tau 20uM Set-Met had the same amount of p-tau as the control group, suggesting that it is the ideal dosage of Set-Met to reduce p-tau.

Conclusion

- Decrease amount of p-tau for mutant tau cell at 20uM
- Protect mutant tau cells at 20uM and WT tau cells at 10uM and 20uM from oxidative stress
- Set-Met is toxic to cells at 80uM concentration.
- Overall,Set-Met could be preventing further phosphorylation to continue and protecting cells from oxidative stress, but are not destroying aggregated tau

Future Work

- Testing other drugs to see it effect it has on phosphorylation of tau
  - CHIR-99021
    - Found to inhibit GSK-3A/B (1)

Acknowledgement

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Reference

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