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

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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

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

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.

Western Blot
- 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.

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

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Reference

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