CALIFORNIA STATE SCIENCE FAIR
2012 PROJECT SUMMARY

Name(s)

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Project Number

S1732

Project Title

Effect of Histone Deacetylase Inhibitors on H3K4 Trimethylation in Mouse in vitro Models of Huntington's Disease

Abstract

Objectives/Goals

The project tested whether treatment of two different Huntington's Disease models with the HDAC inhibitors Trichostatin A and sodium butyrate would increase not only Histone 3 lysine 9 acetylation (H3K9Ac) but also H3K4 trimethylation (H3K4Me3) by causing transcriptional repression of the demethylase Jarid1C.

Methods/Materials

Cells from a mouse striatal cell line and primary cortical neurons were treated with TSA (25 or 100 nm) or NaB (.5 or 2 mM) for 24h or 48h. mRNA was extracted with the Quiagen kit and converted to cDNA. PCR was run using the SYBR Green method, with primers for Jarid1C, Jarid1B, or BDNF. For the western blot, cells were lysed and protein quantitated by the Lowry method. Protein was loaded onto the gel, and proteins were transferred to a nitrocellulose membrane. Primary antibodies were added first to H3K4Me3, and then to H3K9Ac. Secondary antibody conjugated to horse radish peroxidase was added, followed by color development.

Results

Treatment of striatal cells and primary cortical neurons resulted in an increase in both H3K9 acetylation and H3K4 trimethylation. In the primary cortical neurons, downregulation of brain-derived neurotrophic factor (BDNF) in HD-phenotype cells was rescued by 48h treatment with NaB. The demethylase Jarid1C did not show a decrease upon treatment in either model.

Conclusions/Discussion

As hypothesized, treatment with the HDAC inhibitors increased both H3K9 acetylation and H3K4 trimethylation. However, the increase in methylation was not caused by downregulation of the demethylase Jarid1C. Overall, this study supports the idea that HDAC inhibitors restore aberrant transcription in HD by increasing both acetylation and methylation, although more work must be done to fully understand the cross-talk between these two chromatin marks.

Summary Statement

This project is meant to study the effect of two histone deacetylase inhibitors on H3K4 trimethylation in Huntington's Disease.

Help Received

Used lab equipment at Dr. Leslie Thompson's lab at the University of California, Irvine under the supervision of Mrs. Alice Lau