CALIFORNIA STATE SCIENCE FAIR
2016 PROJECT SUMMARY

Name(s)

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Project Number

S0535

Project Title

Development of a Novel Microfluidic System to Study Neurodegenerative Disorders

Abstract

Objectives/Goals

Huntington's disease (HD) is a neurodegenerative disease characterized by loss of medium spiny neurons (MSN) in the striatum due to mutation in the Htt gene. The mutant Htt (mHtt) protein leads to decrease in transport of brain derived neurotrophic factor (BDNF). The loss of BDNF along the cortico-striatal axis causes the deterioration of MSN. Introducing BDNF to striatum shows promise in slowing down HD progression, but the exact mechanism is unclear. Furthermore, traditional neuron culture cannot provide an in-vitro neuro-research platform to simulate in-vivo cortical-striatal circuit. We combined microfluidic nano-engineering with molecular tools to create an in-vitro microfluidic system, simulating an in-vivo cortico-striatal axis. Using single molecular labeling of BDNF with quantum dots, we can track BDNF transport along the cortico-striatal circuit.

Methods/Materials

A custom microfluidic chamber was designed using AutoCAD, fabricated by soft lithography. Consisting of cortical and striatal cell body chambers, long axon and short dendritic microgrooves, and a central synapse chamber, microfluidic devices offer greater advantages over traditional neuron cultures. They allow cell bodies to grow in one compartment while axons/dendrites are directed to adjacent compartment through microgrooves, and fluidic isolation can be created between cell body and axonal/dendritic compartments. Using these chambers, we cultured cortical/striatal neurons from Q140 HD and wild-type (WT) mice. We conjugated biotin BDNF with quantum dots, added to axonal chambers. Through live cell imaging, we recorded the transport of BDNF, and analyzed with MetaMorph.

Results

We discovered significant BDNF transport disruption in Q140 HD axons, evidenced by a lower average speed and higher pausing time in comparison to WT axons for both retrograde and anterograde transport ($p<0.01$). HD/WT axons had similar moving speeds, proving that dynein/kinesin motor complex is unaffected.

Conclusions/Discussion

Based on these findings, future studies could utilize this platform to develop therapeutic approaches to restore BDNF expression, to bypass the defective BDNF transport using lentivirus--induced BDNF expression in cotical-striatal axis, or to test anti-sense RNA drugs to silence mHtt mRNA message in our microfluidic system. This platform also holds the potential to develop therapeutic strategies for other neurodegenerative diseases.

Summary Statement

We innovated a microfluidic co-culture system with molecular labeling to examine transport defects of cortical-striatal axis in Huntington's disease, providing a platform to develop therapeutic strategies for neurodegenerative diseases.

Help Received

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