NG2 cells in Huntingtons disease

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Research Abstract

PROJECT SUMMARY Huntington’s disease (HD) is a devastating neurodegenerative disorder that manifests in midlife with motor, cognitive, and psychiatric deficits inexorably progressing to death within 15-20 years of onset. The abnormal expansion of CAG repeats in the huntingtin gene is the cause of the disease. Currently, no cure is available. The mechanism of mutant huntingtin (Htt) induced toxicity is still largely unclear. However, the subtle onset of behavioral and psychiatric symptoms long before motor impairment suggests that dysfunction of brain connections controlling emotional and behavioral response may characterize the early phases of the disease, giving a possible explanation to early symptoms and potential early intervention

to defeat this devastating condition. White matter is composed of bundles of myelinated axons, which connect various grey matter areas of the brain to each other, and carry nerve impulses between neurons. Interestingly, white matter abnormality has been revealed as an early indicator in HD brain by neuroimaging. The key question is whether white matter abnormality is necessary for, or consequent to, the neurodegenerative process in HD. NG2 cells are a type of oligodendrocytes precursor cells (OPCs) which are abundant in mammalian brain and differentiated into oligodendrocytes, major component of white matter. Interestingly, NG2 cells also express ion channels and neurotransmitter receptors, and form synapses with neurons, suggesting that these cells have profound functions that we realized so far. Whether mutant Htt alters NG2 cell property and whether NG2 cells expressing mutant Htt contribute to neurodegeneration remain elusive. We will take advantage of accessible PDGF?R-CreER;Z/EG mice from our collaborator, these mice inducibly express GFP in NG2 cells, we will determine the fate of NG2 cells in HD condition. Moreover, we will determine whether elimination of mutant Htt expression in NG2 cells or mature oligodendrocytes will attenuates neuropathology in HD mice. Our Specific Aims are: In Specific Aim 1, we will investigate the effects of mutant Htt on the oligodendrocyte lineage, we will examine proliferation, differentiation, survival of OPCs through in vivo genetic fate tracing. In Specific Aim 2, we will test the hypothesis that elimination of mutant Htt in NG2 cells will attenuate neurodegeneration and improve motor function in HD mice. By completion these two independent and complementary aims, a new role of NG2 cells and oligodendrocytes in HD condition will be revealed and the results will potentially lead to a new target for therapeutic development for HD.

Further information available at:

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