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EVALUATION OF HIPPOCAMPAL NEUROGENESIS IN YAC128 HUNTINGTON'S DISEASE TRANSGENIC MICE

J. Gil-Mohapel[1], J.M. Simpson[1], M.A. Pouladi[2], M. Hayden[2], B.R. Christie[1]

[1]Division of Medical Sciences, Island Medical Program, University of Victoria, Victoria, [2]Centre for Molecular Medicine and Therapeutics, University of British Columbia, Vancouver, Canada

Given the capacity of the adult brain to generate new neurons (a process called neurogenesis), adult neuronal stem cells have been proposed as an endogenous source of healthy cells for the treatment of certain neurodegenerative diseases. However, it is not completely understood to what extent this process is altered in neurodegenerative conditions such as Huntington's Disease (HD). An increase in neurogenesis in the subventricular zone (SVZ) of HD patients has been previously reported. On the other hand, we and others found a dramatic decrease in neurogenesis in the dentate gyrus (DG) of the hippocampus of the most studied HD transgenic mouse models, the R6/2 and R6/1 lines. We are now examining neurogenesis in a transgenic model that expresses the full-length huntingtin gene with 128 CAG repeats, the YAC128 mice. We are analysing how disease progression in the YAC128 model affects each stage of the neurogenic process (i.e., proliferation, survival, migration, and differentiation) in the two neurogenic regions (SVZ and DG). Proliferation will be evaluated in end-stage, symptomatic, early-symptomatic and pre-symptomatic YAC128 mice by immunohistochemistry for a variety of exogenous and endogenous cell cycle markers. Cell survival, migration and differentiation will be assessed by immuno-labelling of immature and mature neurons. Since hippocampal neurogenesis is thought to be involved in cognitive processes, a reduction in it might contribute to the cognitive deficits and/or depression in HD. Furthermore, these results will ascertain how well the HD brain might sustain neuronal transplant therapies.

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