Abstract View

DIFFUSELY TRANSFORMED ASTROCYTES BY SV40 EXPRESSION AS A MODEL FOR BRAIN CANCER: ALTERATIONS IN FILAMENTOUS-ACTIN LEVELS

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Astrocytoma is the most common primary brain tumor in humans. Among the known pathways, mutations inactivating pRb tumor suppressor function are the most prevalent in these tumors (70-80%). We inactivated this pathway in mouse astrocytes by transgenic expression of T121, a truncated SV40 T antigen that binds and inactivates pRb and related proteins, p107 and p130. In resulting GdZT121 mice, astrocytes undergo aberrant proliferation and apoptosis and progress over time to fully penetrant high-grade astrocytomas. Increased motility of cancer cells lead us to hypothesize that structural proteins might be altered in transformed astrocytes of the transgenic animals. Tissue sections from wild type and GdZT121 animals were stained with phalloidin, which labels the filamentous form of actin (f-actin), and imaged using a multi-photon microscope. Comparison of staining revealed increased f-actin levels in the transgenic cerebellar and hippocampal regions compared to wild type. All cerebellar layers and deep cerebellar nuclei showed this difference. The molecular layer and processes surrounding granule cells in the dentate gyrus of the hippocampus also showed a similar increase. In some regions, the pattern of increased labeling suggests synaptogenesis, consistent with the concentration of f-actin in dendritic spines. Studies underway in the cerebellum and hippocampal regions of GdZT121 transgenic animals will examine synaptic marker and other structural protein levels. These observations will guide studies of structural proteins in another transgenic animal model that develops focal tumors.

Support Contributed By: NIH-NCI 5UO1CA084314, RR-P4104050

Citation:E.M. Rodrigues, D.L. Price, N.A.B. MacLean, M.E. Martone, R. Bash, T. Van Dyke, M.H. Ellisman. DIFFUSELY TRANSFORMED ASTROCYTES BY SV40 EXPRESSION AS A MODEL FOR BRAIN CANCER: ALTERATIONS IN FILAMENTOUS-ACTIN LEVELS Program No. 462.12. *2004 Abstract Viewer/Itinerary Planner.* Washington, DC: Society for Neuroscience, 2004. Online.