Correlation of Nucleophosmin, CRMP2 and RKIP with Tumor Progression in Astrocytomas

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Astrocytomas comprise a wide range of neoplasms those differences reflect genetic alterations acquired during the malignant transformation. Low-grade astrocytomas (grade II) display an intrinsic tendency to progress to a more malignant phenotypes, that is, anaplastic astrocytomas (grade III) and eventually glioblastomas (grade IV). We developed a proteomic study based on 2D gel electrophoresis and mass spectrometry to identify differentially expressed proteins according to increasing levels of malignancy in astrocytoma. Five samples of each grade were compared with non-neoplastic brain tissue. Thirteen proteins were differentially abundant in tumor progression ($p < 0.005$). Nucleophosmin (NPM1) showed increased levels of expression correlating with progression of low to high grade astrocytoma and it was confirmed by western blot and real time PCR in 160 patient samples (grades II, III and IV) using BCRP and HPRT as housekeeping genes. Collapsin response mediator proteins 2 (CRMP2) and Raf kinase inhibitor protein (RKIP) were decreased in abundance and also showed a direct correlation to tumor progression ($p<0.005$). NPM1 and RKIP are downstream of two survival signaling pathways, Akt/mTOR and RAS-RAF-MEK-ERK. CRMP2 interacts with NF1, a tumor suppressor which is inhibitor of RAS. These proteins have been playing several crucial functions into the cell as genomic integrity, biogenesis of ribosome and dynamics of cytoskeleton and their alteration at expression level are involved in cancer.

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