Identification of Gliotropic Factors That Induce Human Stem Cell Migration to Malignant Tumor.

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Neural stem cells are mobile, are attracted to regions of brain damage, and can migrate a considerable distance to reach a glioma site. However, the molecular basis of the progression of gliotropism to malignant gliomas remains poorly understood. With the use of clinically and histologically assessed glioma cells, we have assessed their protein and gene profiles via proteomics and microarray approaches, and have identified candidate genes from human glioma tissues. This research is expected to provide clues to the molecular mechanisms underlying the migration of neural stem cells (F3 cell) to glioma sites. The expression of 16 proteins was shown to have increased commonly in human glioma tissues. Among them, the expression of annexin A2, TIMP-1, COL11A1, bax, CD74, TNFSF8, and SPTLC2 were all increased in human glioma cells, as confirmed by Western blotting and immunohistochemical staining. In particular, annexin A2 effects an increase in migration toward F3 and glioblastoma cells (U87 cell) in a Boyden chamber migration assay. An ERK inhibitor (PD98057) and a CDK5 inhibitor (rescovitine) inhibited 50% and 90% of annexin A2-induced migration in F3 cells, respectively. A similar chemotactic migration was noted in F3 and U87 cells. These results demonstrated that 7 candidate proteins may harbor a potential glioma tropism factor relevant to the pathology of malignant glioma. These results reveal that this novel molecular approach to the monitoring of glioma may provide clinically relevant information regarding tumor malignancy, and should also prove appropriate for high-throughput clinical screening applications.

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