YAP1 is widely expressed in human brain tumors and promotes glioblastoma growth

Brent A. Orr M.D., Ph.D.1, Haibo Bai Ph.D.1, Yazmin Odia M.D.2, Deepali Jain M.D.1, Robert A. Anders M.D., Ph.D.1,4, Charles G. Eberhart M.D., Ph.D.1,3,4

1Department of Pathology, The Johns Hopkins University School of Medicine,  
2Department of Neurology, The Johns Hopkins University School of Medicine,  
3Department of Ophthalmology, The Johns Hopkins University School of Medicine,  
4Department of Oncology, The Johns Hopkins University School of Medicine

The hippo pathway and its downstream mediator yes-associated protein 1 (YAP1) regulate mammalian organ size in part through modulating progenitor cell numbers. YAP1 has also been implicated as an oncogene in multiple human cancers. Currently, little is known about the expression of YAP1 either in normal human brain tissue or in central nervous system neoplasms. We used immunohistochemistry to evaluate nuclear YAP1 expression in the normal adult brain, the developing human brain, and in 264 brain tumors. We found that YAP1 is expressed in fetal and adult brain regions known to harbor neural progenitor cells, but identified little YAP1 immunoreactivity in the adult cerebral cortex. YAP1 protein was also readily detected in the nuclei of human brain tumors. In medulloblastoma, expression varied between histologic subtypes and was most prominent in nodular/desmoplastic tumors. In gliomas, YAP1 was frequently expressed in infiltrating astrocytomas and oligodendrogliomas, but rarely in pilocytic astrocytomas. Using a loss of function approaches we show that YAP1 promotes growth of glioblastoma in vitro. Furthermore, high levels of YAP1 mRNA expression associates with reduced survival in human glioma patients. Our findings suggest that YAP1 may play an important role in normal neural development and promote an aggressive phenotype in human gliomas.