CDK8 maintains stemness and tumorigenicity of glioma stem cells by controlling the c-MYC pathway

Kazuya Fukasawa, Kazuya Tokumura, Sayuki Iwahashi, Takashi Iezaki, Eiichi Hinoi


Glioblastoma (GBM), the most malignant type of primary brain tumor, has a very poor prognosis. Glioma stem cells (GSCs) play a key role in tumor initiation and progression. Cyclin-dependent kinase 8 (CDK8), which belongs to the transcription-related CDK family, is considered both an oncogene and a tumor suppressor. However, the functional role and underlying mechanisms of CDK8 expressed in GSCs on gliomagenesis is still poorly understood both in vitro and in vivo. Disruption of CDK8 by shRNA resulted in an attenuation of the self-renewal potential and tumorigenicity of patient-derived GSCs, which can be significantly rescued by the overexpression of MYC, a stem cell transcription factor. Moreover, the pharmacological inhibition by CDK8 inhibitor significantly repressed the self-renewal potential and tumorigenicity of GSCs. Bioinformatics analyses have revealed that CDK8 expression was significantly higher in human GBM tissues compared with normal brain tissues, and its expression was positively correlated with stem cell markers including MYC and SOX2 in human GBM specimens. Additionally, CDK8 expression is associated with poor survival in GBM patients. These findings highlight the importance of the CDK8-c-MYC axis in maintaining stemness and tumorigenicity in GSCs, indicating that targeting GSCs through CDK8 inhibition could be a promising strategy against GBM.