Neural stem cells preferentially migrate to glioma stem cells and reduce their stemness phenotypes.

Zhang S, Xie R, Zhao T, Yang X, Han L, Ye F, Lei T, Wan F.

Abstract

Glioma stem cells (GSCs), characterized by self-renewal, multi-potentiality and tumorigenicity, are responsible for the tumor propagation, recurrence and resistance to traditional treatments, representing a critical therapeutic target. Neural stem cells (NSCs) possess inherent tropism to brain tumor cells and inhibit their growth. However, there is a limited understanding of the mechanism underlying NSC tropism and the effect of NSC migration on GSC stemness phenotypes. In the present study, we showed that GSCs exhibited enhanced chemotaxis for NSC tropism compared with their differentiated cells. Chemokines secreted by GSCs contributed to the targeted migration of NSCs. Hypoxia enhanced NSC tropism via the upregulated chemokine expression of GSCs, such as VEGF, EGF and bFGF. In vitro migration of NSCs induced GSC differentiation and reduced stem-like phenotypes. Moreover, in vivo data provided direct evidence that transplanted NSCs could migrate to GSCs from either the homolateral or contralateral brain injection site, which prolonged the survival of grafted mice. Taken together, these findings show that NSCs preferentially migrate to GSCs and reduce their stemness phenotypes, raising the intriguing possibility that the targeted migration of NSCs can be applied as a novel therapeutic strategy to target these intractable brain tumors.