A patient tumor-derived orthotopic xenograft mouse model replicating the group 3 supratentorial primitive neuroectodermal tumor in children.


Abstract

Background Supratentorial primitive neuroectodermal tumor (sPNET) is a malignant brain tumor with poor prognosis. New model systems that replicate sPNET's molecular subtype(s) and maintain cancer stem cell (CSC) pool are needed.

Methods A fresh surgical specimen of a pediatric sPNET was directly injected into the right cerebrum of Rag2/SCID mice. The xenograft tumors were serially sub-transplanted in mouse brains, characterized histopathologically, and subclassified into molecular subtype through qRT-PCR and immunohistochemical analysis. CSCs were identified through flow cytometric profiling of putative CSC markers (CD133, CD15, CD24, CD44, and CD117), functional examination of neurosphere forming efficiency in vitro, and tumor formation capacity in vivo. To establish a neurosphere line, neurospheres were propagated in serum-free medium.

Results Formation of intracerebral xenograft tumors was confirmed in 4 of the 5 mice injected with the patient tumor. These xenograft tumors were sub-transplanted in vivo 5 times. They replicated the histopathological features of the original patient tumor and expressed the molecular markers (TWIST1 and FOXJ1) of group 3 sPNET. CD133⁺ and CD15⁺ cells were found to have strong neurosphere-forming efficiency in vitro and potent tumor-forming capacity (with as few as 100 cells) in vivo. A neurosphere line BXD-2664PNET-NS was established that preserved stem cell features and expressed group 3 markers.

Conclusion We have established a group 3 sPNET xenograft mouse model (IC-2664PNET) with matching neurosphere line (BXD-2664PNET-NS) and identified CD133⁺ and CD15⁺ cells as the major CSC subpopulations. This novel model system should facilitate biological studies and preclinical drug screenings for childhood sPNET.

KEYWORDS: cancer stem cell, orthotopic xenograft model, supratentorial primitive neuroectodermal tumor
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