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Identification of cancer stem cells from human Glioblastomas: growth and differentiation capabilities and CD133/Prominin-1 expression.

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Abstract

CD133 has been proposed as a marker of tumorigenic cancer stem cells (CSCs) in human Glioblastoma multiforme (GBM), although tumorigenic CD133-negative CSCs have been also isolated. Additional evidence also indicates that CSCs from GBM could exhibit different phenotypes, rising interest into the potential significance of these different CSCs with respect to diagnosis and prognosis, and for development of novel targets for future treatment. We analyzed the expression of CD133 in freshly isolated cells from 15 human GBM specimens. Interestingly, only 4 out of 15 GBMs contained cells positive for AC133 by FACS analysis. Of note, all 4 AC133-positive tumors yielded distinct CSC lines, while only 6 CSC lines were obtained from the 11 GBM that did not contain AC133-positive cells. Of these 10 CSCs lines, we further characterized 6 CSC lines. Three CSCs grew as fast-growing neurospheres with better clonogenic ability, while the remaining 3 grew as slow-growing semi-adherent spheres with lower clonogenic ability. In addition, the former CSC lines displayed better differentiative capacities than the latter ones. Surprisingly, PCR and Western Blot analysis revealed that all 6 GBM CSC lines expressed CD133/Prominin1, suggesting that cells negative by FACS analysis may actually represent cells expressing low levels of CD133 undetected by FACS. Nevertheless, all the 6 CSC lines were tumorigenic in nude mice. In conclusion, CSCs from human primary GBMs show different phenotypes and express CD133, though at varying levels. However none of these parameters is directly correlated with the tumorigenic potentials of the cells.

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