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Future Oncol. 2011 Jul;7(7):841-3.**When tumor cells make blood vessels: implications for glioblastoma therapy.**

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Abstract

Evaluation of: Soda Y, Marumoto T, Friedmann-Morvinski D et al. Transdifferentiation of glioblastoma cells into vascular endothelial cells. *Proc. Natl Acad. Sci. USA* 108, 4274-4280 (2011). The paper by Soda et al. provides experimental evidence for the plasticity of glioblastoma multiforme (GBM) cells, specifically their ability to form vascular endothelial cells (ECs). The study demonstrates the existence of tumor-derived ECs (TDECs) in GBM blood vessels of transgenic mice and humans. Blood vessels with TDECs were functional and were more frequently found in hypoxic tumor regions. In vitro hypoxic conditions enhanced the transition of tumor-initiating cells to an endothelial-like morphology and the formation of tube-like structures. Contrary to normal ECs, TDECs did not express VEGF receptors, and treatment of experimental GBM tumors with anti-VEGF/VEGF receptor agents led to an increase in the proportion of TDECs relative to normal ECs. These findings identify a new potential mechanism of resistance of GBM tumors to anti-VEGF therapies. Future strategies for GBM therapy will likely require the combined targeting of normal ECs and TDECs, as well as the development of strategies that prevent the conversion of tumor cells into vascular ECs.

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