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Cancer Cell Biology

Inhibition of telomerase in the endothelial cells disrupts tumor angiogenesis in glioblastoma xenografts

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KEYWORDS

HUVEC • glioblastoma multiforme • telomerase • tumor xenograft

ABSTRACT

Tumor angiogenesis is a complex process that involves a series of interactions between tumor cells and endothelial cells (ECs). *In vitro*, glioblastoma multiforme (GBM) cells are known to induce an increase in proliferation, migration and tube formation by the ECs. We have previously shown that in human GBM specimens the proliferating ECs of the tumor vasculature express the catalytic component of telomerase, hTERT, and that telomerase can be upregulated in human ECs by exposing these cells to GBM *in vitro*. Here, we developed a controlled *in vivo* assay of tumor angiogenesis in which primary human umbilical vascular endothelial cells (HUVECs) were subcutaneously grafted with or without human GBM cells in immunocompromised mice as Matrigel implants. We found that primary HUVECs did not survive in Matrigel implants, and that telomerase upregulation had little effect on HUVEC survival. In the presence of GBM cells, however, the grafted HUVECs not only survived in Matrigel implants but developed tubule structures that integrated with murine microvessels. Telomerase upregulation in HUVECs enhanced such effect. More importantly, inhibition of telomerase in HUVECs completely abolished tubule formation and greatly reduced survival of these cells in the tumor xenografts. Our data demonstrate that telomerase upregulation by the ECs is a key requisite for GBM tumor angiogenesis. © 2007 Wiley-Liss, Inc.

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