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Incorporation of Bone Marrow-derived Flk-1-expressing CD34+ Cells in the Endothelium of Tumor Vessels in the Mouse Brain.

Experimental Studies

Neurosurgery. 59(2):374-382, August 2006.

Santarelli, Justin G. B.S.; Udani, Vikram M.D.; Yung, Yun C. M.D.; Cheshier, Sam M.D., Ph.D.; Wagers, Amy Ph.D.; Brekken, Rolf A. Ph.D.; Weissman, Irving M.D.; Tse, Victor M.D., Ph.D.

Abstract:

OBJECTIVE: Neoangiogenesis is a prerequisite for the full phenotypic expression and growth of a malignant tumor mass. It is believed to be triggered by tissue hypoxia and involves proliferation and sprouting of the preexisting vessels and the recruitment of endothelial progenitor cells from bone marrow.

METHODS: A chimeric mouse model was used to examine the contribution of these progenitor cells to the neovasculature of brain tumor. T-cell knockout (RAG/KO5.2) mice were irradiated lethally, and their bone marrow was repopulated with T-cell depleted green fluorescent protein (GFP)-expressing bone marrow cells. RAG/RT-2 glioma cells were implanted into the striatum of the animals. Neovascular formation at various times of tumor growth was monitored together with the extent of incorporation of GFP+ bone marrow-derived cells within the vascular tree, in particular, cells carrying the endothelial progenitor markers CD34 and Flk-1.

RESULTS: The recruitment of GFP+ cells to the growing tumor and their incorporation into the vascular network occurred during the period of increasing vascular density and preceded the expansion of the tumor. The number of marrow-derived cells with endothelial morphology and phenotype was small but significant (4% of all endothelial cells at Day 12); 54% of all tumor vessels contained at least one GFP+ cell.

CONCLUSION: Our results suggest that bone marrow cells are recruited to newly formed and remodeled tumor vessels. Their recruitment may occur in response to signals from a highly proliferating milieu, and their role is to support the neovascular complex and to promote tumor growth.

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