

Experimental Therapeutics

Intravital Microscopy Reveals Novel Antivascular and Antitumor Effects of Endostatin Delivered Locally by Alginate-encapsulated Cells¹

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The current study describes new, antivascular, and antitumor effects of human endostatin. A novel system for continuous, localized delivery of antiangiogenic compounds to brain tumors was used. The delivery system was composed of endostatin-producing 293 cells encapsulated into immuno-isolating sodium alginate. Intravital multifluorescence microscopy was used to assess vascular and antitumor effects of endostatin in C6 glioma spheroids implanted into an ectopic as well as an orthotopic setting. Analysis of total and functional vascular density, microvascular diameters, vessel perfusion, tumor growth, and tumor cell migration were performed repetitively.

Tumor growth was reduced by 35% in treated animals. It was of interest that tumor cell invasion into the surrounding tissue was also inhibited. The total vascular density was reduced by 67.6%, perfusion by 67%, and vessel diameters by 37%. This resulted in a significant reduction in tumor perfusion, although the vessel permeability was not influenced.

We have demonstrated that human endostatin not only reduces total vascular density, as shown previously, but also greatly reduces the functionality and the diameters of the vessels. Furthermore, we show that this therapeutic approach also inhibits tumor cell invasion, thus supporting the hypothesis that tumor angiogenesis and invasion represent two interrelated processes. Finally, this work further confirms the new therapeutic concept using alginate cell-encapsulation technology for the localized delivery of therapeutic compounds to central nervous system malignancies.