Abstract
DOE Low Dose Radiation Research Investigators' Workshop
July 30-August 2, 2006

Biphasic Dose-efficacy in Antiangiogenic Therapy.

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Many biological processes can be modeled by linear functions. Examples include blood pH, oxygen tension, and hematocrit. However, it has recently been recognized that the activity of certain biological processes, especially those in vascular biology, can be optimally described by a biphasic function. The antiangiogenic and anti-tumor activities of interferon-alpha are optimal at low doses, but not higher doses, i.e., a U-shaped dose-efficacy curve.[1] The dose-efficacy curve of endostatin for anti-tumor activity is similar, whether the therapy is administered as a protein, [2, 3] or as gene therapy.[4] In fact, when endothelial cells are incubated *in vitro* with endostatin at increasing concentrations, gene expressions also reveal a U-shape dose response.[5] Another angiogenesis inhibitor, rosiglitazone, displays a U-shaped dose-efficacy curve.[6] Anti-cancer cytotoxic chemotherapy, administered at frequent low doses is more effective in tumor-bearing mice than high doses of chemotherapy administered less frequently.[7, 8, 9].

The mechanism of the biphasic response of vascular endothelium to different angiogenesis inhibitors is unclear. However, the function of the biphasic response may be to protect endothelium from surges in plasma concentrations of endothelial regulatory molecules. The principles of hormesis in the physical sciences and in toxicology may provide insights for vascular biology.

References:

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