**CHEMOTHERAPY
KILLING VESSELS
IMPROVES DELIVERY**

Drugs that target the tumor vasculature have an important treatment role but many tumors fail to respond to such drugs, and alternative tumor vasculature-targeting strategies are needed. Alpha-emitting particles conjugated to the E4G10 monoclonal antibody, represent a new approach. The ^{225}Ac -E4G10 labeled antibody recognizes and targets vascular endothelial cadherin, and when bound to the tumor neovasculature depletes endothelial cells within tumors. Using a human colon cancer xenograft model and the ^{225}Ac -E4G10 alpha-emitting particle, David Scheinberg and his team decided to take “a three-pronged approach that correlated clinical antitumor effects with both the pharmacological changes measured in live animals in real time with the changes measured in tumors examined *ex vivo*.”

Treatment with ^{225}Ac -E4G10 was shown to significantly reduce tumor growth. “We show for the first time a mechanism by which antivessel therapy can lead to improved drug uptake in the tumor by remodeling vessels. This finding is counter-intuitive as the therapeutic destruction of vessels might have been expected to reduce drug delivery”.

Next, the authors asked whether the sequence of administration of the antiangiogenic drug and standard chemotherapy impacted outcome. The researchers showed that the drug sequence was important; tumor inhibition was only observed when the antivasculature agent was followed by chemotherapy. Thus, antivasculature therapy specifically affects the efficacy of subsequent chemotherapy. Scheinberg explains, “the order of administration of the two types of agents, antivasculature and antitumor, is critical to successful outcomes and may have an important impact on the design of combination therapies for clinical trials”.

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Original article Escorcía, F. E. *et al.* Selective killing of tumor neovasculature paradoxically improves chemotherapy delivery to tumors. *Cancer Res.* **70**, 9277–9286 (2010)