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Localization of Radiolabeled Streptavidin in Tumor

TO THE EDITOR: In a January 1998 article Zhang et al. (*1*) compared the biodistribution of radiolabeled biotin administered to mice bearing a human colon xenograft with that of radiolabeled streptavidin injected either intravenously or intraperitoneally to mice bearing the same tumor model but pretargeted with unlabeled biotinylated monoclonal antibody directed against the colon cancer. As with virtually all experiments performed with radiolabeled streptavidin and pretargeting with antibody, a very important control was left out; that is, the distribution of radiolabeled streptavidin in nonpretargeted tumor-bearing mice. Zhang et al. state that such data is available. It would be most helpful to publish it in concert with the rest of the data. Of particular importance is the determination of the ratio of tumor to normal tissues after administration of streptavidin alone. Our experiments suggest that radiolabeled streptavidin demonstrates high localization in breast tumors not pretargeted with monoclonal antibody (*2,3*), and it would be most interesting to determine whether this is unique for breast tumors or also true for other tumors such as colon cancer.

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REPLY: We thank Drs. Fawwaz and Wang for their interest in our article (*1*). The main purpose of our article was to investigate the effect of the distribution pattern of binding sites on the intratumoral penetration of radiolabels, not to confirm the effectiveness of biotinylated antibody pretargeting in tumor uptake of radiolabeled streptavidin. We agree that biodistribution data of streptavidin without pretargeting is important, and we have already examined the biodistribution in mice bearing subcutaneous or intraperitoneal human colon cancer xenografts with radiolabeled streptavidin injected intravenously or intraperitoneally, respectively (*2–5*). In all cases, both the tumor uptake and tumor-to-nontumor ratios of radioactivity were significantly higher with pretargeting than without pretargeting (*2–4*). In the experiments performed in the article under discussion (*1*), tumor uptake and tumor-to-nontumor ratios at 6 hr postinjection of 5 μg of radiolabeled streptavidin (Table 1) were significantly lower than those with pretargeting, which is similar to results from our other studies (*2–4*). Although radiolabeled streptavidin may accumulate in some tumors, our experiments demonstrate that pretargeting techniques using biotinylated antibody provided higher tumor localization of radiolabeled streptavidin.

TABLE 1
Biodistribution of Radioiodinated Streptavidin in Tumor-Bearing Mice

	Biotinylated antibody pretargeting	
	+ (n = 5)	− (n = 4)
Tumor uptake (% of injected dose per gram)	32.13 ± 4.00	6.27 ± 1.15
Tumor-to-blood ratio	1.53 ± 0.38	0.77 ± 0.09

Mean ± s.d.
+ = pretargeted; − = nonpretargeted.

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