Targeting Tumors with Nanoparticles
review of presentation given by Dr. K. Dane Wittrup of Massachusetts Institute of Technology

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According to Dr. Wittrup of MIT, the usage of the term targeting is a misnomer. This is due in large part to the cultural expectation that a target is visible and exclusive of other interference. When it comes to medical applications where therapies seek out tumors or infections to eliminate them, they also injure a broader, general region. So often, the success of such therapies is in their ability to limit this collateral damage. The promise of novel therapies, often attending the breakthrough research of nanotechnology, are the renewed assurances that specific cells will be selectively eliminated.

Even here, the tumor presents difficulties through its sheer bulk. Any drug delivery system that relies on the transport of antibodies or nanoparticles to the site of infection, such as a tumor finds issues of barriers and diffusion. The first barrier is with the capillary wall. With antibodies or nanoparticles being delivered in the blood stream, the tumor presents both the opportunity of being richly supplied with them, but being separated from them by the capillary wall. This barrier alone can force a diminution of drug concentration by one thousandth. On one hand, drug concentration might follow a proportionality such that increasing the concentration by a thousand-fold could solve this; but it could present a significant issue of toxicity to the patient that it is flowing through. When the dose is administered it circulates in the blood plasma where it runs the risk of being absorbed by tissue, or being flushed out before sufficient amounts find their way to the tumor site.

This dilution of a thousandth is substantially a matter of the capillary wall, but there is also a component of transporting the drug into the bulk of the tumor mass, beyond that wall. This is diffusion limited. The diffusion has many mechanisms that limit the transporting of the drug. The first requirement for diffusion is that there is a gradient of concentration of the drug. In other words, there is a richer concentration behind the flow that is pressing the border of low concentration deeper into the tumor mass. This is like a sponge absorbing a pool of spilled ink. At the outer edge of the sponge, the stain is very pronounced, but if the sponge were split open, it would reveal that through its radius toward the center, the stain was progressively lighter in shade, and possibly exhibiting voids where no stain was evident.

For the tumor, the same situation exists with a progressively lower concentration of drug. Unfortunately, if the delivery is slow, the concentration at the source, the drug in the serum within the capillary, will fall over time as well. This is called clearance. This means that without a renewal of drug (more shots from the physician), that the center of the tumor may never experience any drug in any form. Here it can be seen that the speed of diffusion is a critical parameter and that speed needs to be in terms of seconds or minutes instead of hours or days. To show the scale of the problem, drugs that should diffuse 100 μm in 10 minutes according to models, instead take nearly three hours as measured.

Another issue arrives in the form of drug consumption by the tumor. The diffusion may be limited by the tumor's capacity to use the drug at the outer radius before it can be delivered to the deep interior of the tumor.