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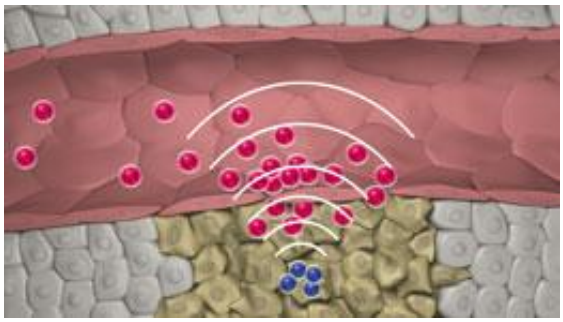
News

Nanoparticles hit tumours with one-two punch

Using scout particles to pave the way makes drug delivery more effective.

Corie Lok

By harnessing the body's blood-clotting system, researchers have designed nanoparticles that scout out tumours and then call in a second type of nanoparticle to deliver cancer-killing drugs.



'Signalling' particles enter the tumour and trigger a blood clot that attracts drug-delivering 'receiver' particles.

G. Carlson

Sangeeta Bhatia, a bioengineer at the Massachusetts Institute of Technology in Cambridge, and her colleagues found that using the two nanoparticles in tandem in mice increased the amount of drug delivered to a tumour by 40-fold relative to controls. Tumours in these mice stopped growing, whereas those in mice that received only one type of nanoparticle did not.

Bhatia's team was inspired by the ability of the body's clotting system to mount a huge response at an injured site. A clot forms thanks to a cascade of reactions that leads to the cross-linking of a large amount of a protein called fibrin.

The researchers designed their nanoparticles to piggyback on this cascade. "We use the body's natural amplification processes to get more drug to the target," says Bhatia. The study is published in *Nature Materials*[1].

Division of labour

Several targeted, drug-delivering nanoparticles are already in use, and more are in clinical trials. Some of these particles have molecules on their surface that bind to receptors on the target tissue.

Bhatia's team decided to allocate each job — finding the tumour and delivering the drug — to a different particle.

The 'scout' nanoparticle, a gold nanorod, is designed to fit through the abnormally large pores of the tumour's blood vessels. When near-infrared light is shone on the nanorods, they heat up just enough to damage the tumour and trigger the clotting cascade.

At the end of the cascade, an enzyme called Factor XIII cross-links fibrin to grow the clot. The drug-bearing nanoparticle, called the receiver, has a protein fragment on its surface that is a substrate for Factor XIII. The particles are attracted as the clotting process occurs at the tumour.

Factor XIII then cross-links the receivers' protein coating to the fibrin in the clot, where the receivers unload their drug cargo. The Factor XIII and fibrin generated during the clotting process produce additional binding sites at the tumour for the receiver nanoparticle, which leads to the 40-fold increase in the amount of drug delivered.

This is a big improvement on other nanoparticles, which typically deliver 2–7 times the dose of conventional drug delivery methods, says Omid Farokhzad at the Brigham and Women's Hospital in Boston, Massachusetts. "What's new here is that the system triggers the body to create an environment that favours the accumulation of nanoparticles," he says.

Clotting complexity

"This is on the right path," says Farokhzad. "But given the level of innovation, a lot of work will be needed to translate this to the clinic."

One challenge will be to ensure that the particles trigger and target blood clots only in tumours, as cancer patients are susceptible to blood clots elsewhere in the body, says Anil Sood, an oncologist at the MD Anderson Cancer Center in Houston, Texas. "If you're going to trigger coagulation, you want to be very selective, so that you don't cause damage in other parts of the body."

Bhatia admits that her system is complex; her group is working on ways to simplify it. But cancer is a complex disease, says Dan Peer, a nanotechnologist at Tel Aviv University in Israel. "Maybe the solutions won't be so simple."

References

1. von Maltzahn, G. *et al. Nature Materials* advance online publication doi:10.1038/nmat3049 (2011).

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Very interesting. Good work so far

#24485

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