Advancing cancer research

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New computer model designs a drug delivery strategy to fight cancer

Researchers from Michigan State University and Stanford University have created a computer simulation, validated by experimental results, to help design drug-delivery nanoparticles that carry cancer-fighting medicines directly to tumors, while minimizing the potential side-effects on healthy cells.

Bryan Smith, MSU associate professor in the College of Engineering who conducted the research at Stanford University, and Eric Shaqfeh, professor at Stanford University, describe their work in a recent issue of Biophysical Journal.

The study builds on previous research, which showed drugs embedded in nanoparticles are generally better able to evade biological barriers than free-roaming drug molecules. Nanoparticles have shown limited success in reaching their targets. The critical roadblock has been getting the drug from the bloodstream into the tumor.

In their study, the researchers sought to identify the optimal shape for nanoparticles to act as a molecular carrier to get small-molecule drugs out of the blood vessels and into the interstitial fluids that bathe the tumor where the drugs can enter cancerous cells. Once inside, the nanoparticles dissolve, allowing the drug molecules to kill the tumor cells.

The nanoparticle delivery strategy exploits one of cancer’s great weaknesses: the haphazard way in which tumors grow.

Cancers are hastily assembled patchworks of cells riddled with porous, leaky blood vessels. These pores are like open doors through which researchers want to deliver cancer-killing drugs.
Through simulations and experiments the researchers showed how nanoparticles of different shapes flow through blood vessels, tumble through these pores in the tumor blood vessels and reach malignant cells.

The researchers said that because cancers can be very different, the shapes and sizes of nanoparticle delivery systems may have to be tailored to the specific tumor. Unlike previous models, which oversimplified nanoparticle shapes, the researchers say their model is expected to help drug designers accurately predict the optimal particle shape and size to most effectively treat the tumor.

The team also validated their theoretical assumptions with real-world experiments. Combining simulations with experiments helped them reveal that long, thin, so-called one-dimensional particles typically traverse the pores best.

The researchers also learned the process of diffusion, through which particles move from areas of higher to lesser concentration, can play an unexpectedly large role in governing whether nanoparticles slip through pores.

In future research, Smith and Shaqfeh hope to explore how the polymers that make the nanoparticles more biocompatible control their delivery properties. They also plan to broaden their models to include electrical forces that might cause pores to attract or repel nanoparticles.

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