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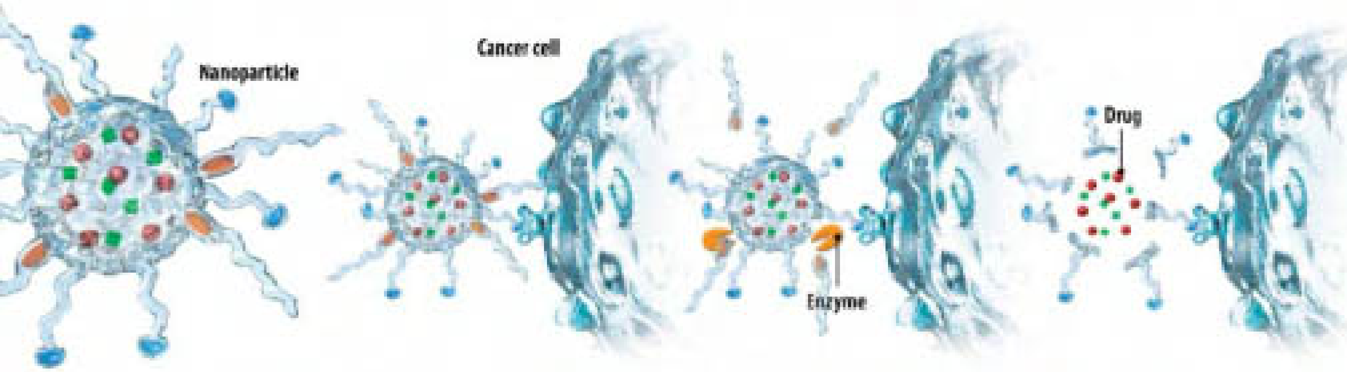
Ultrasmall spheres loaded with anticancer drugs target tumors while leaving healthy cells unscathed.

Better Medicine through Nanotechnology

How Cancer-Seeking Nanoparticles Work

Nanoparticles can be used to deliver drugs directly to cancer cells. Here's one way scientists are targeting tumors:



1. Some nanoparticles loaded with drugs are designed to detonate when they reach their target.

2. One of these particles makes its way through the bloodstream to the cancerous tumor.

3. Certain enzymes found in cancer cells cause the drug-laden nanoparticle to fall apart.

4. The drug, a chemotherapy agent traditionally administered intravenously, is now released.

CANCER

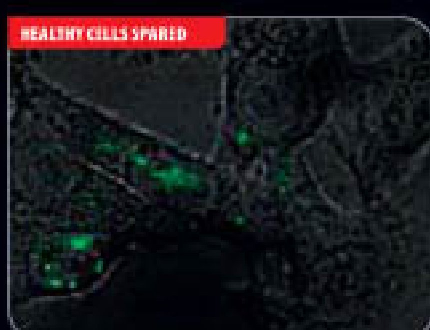
Targeted Compounds Fight Cancer without Side Effects

Cancer patients and their loved ones know the terrible toll that chemotherapy can take on the body. The drugs are indiscriminant killers, wiping out healthy cells as well as cancerous ones. As a result, patients end up with severe side effects, including nausea and hair loss. Nanomedicine promises a new generation of treatments that spare patients collateral damage by homing in on tumors and could also result in better recovery rates.

Unlike objects you can see with the naked eye or beneath a conventional microscope, nanoparticles are especially suited to the task of killing tumors. Their size means that they can travel through even the smallest blood vessels and permeate the vessel walls to reach their final destination. And because these particles are about the size of a virus, they can easily get inside cells and deliver their therapeutic payload without disrupting surrounding tissue.

Carbon Nanotubes Kill Cancer Cells

Nanotubes marked with a fluorescent green dye and tagged with the vitamin folic acid accumulate in human cancer cells.

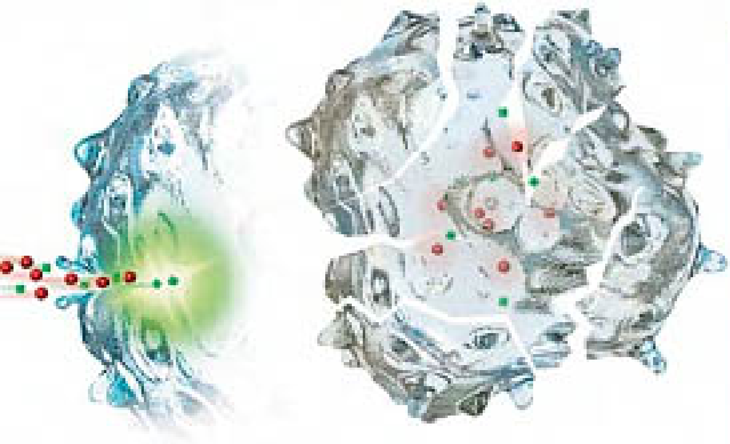


Healthy cells [black] have very few receptors for folic acid, and therefore nanotubes are not attracted to them.

So how do you make a drug-loaded nanoparticle? Scientists at the University of Michigan begin by coating a tiny sphere (about 0.000002-inch diameter) with proteins that seek out and bind to the blood vessels that feed tumor cells. They load the sphere with an anticancer drug called Photofrin and a tracer compound that makes it easy to see the drug using standard scanning techniques such as magnetic-resonance imaging (MRI).

In tests, particles injected into rodents with cancer hunt down tumors with remarkable precision. But the real magic happens when the researchers expose the particles to laser light. This activates the Photofrin and breaks it down to a molecule called porphyrin that disrupts DNA inside the tumor cell. On average, rats treated with these nanoparticles lived for 33 days—and some survived up to seven months—while untreated rats died within nine days.

The results in the rat study were impressive, but will nanoparticles work in humans? Researchers at Erasmus University Medical Center and Leiden University Medical Center in the Netherlands are conducting one



5. Once released from the particle, the chemotherapy agent can be absorbed into the cancer cell.

6. The chemotherapy disrupts normal cellular function, causing the cell to break down and die.

BLINDNESS

Nanofibers Could Restore Sight to the Blind

One common cause of blindness is the destruction of the par of the brain that processes visual input. Tumors or injury can kill nerve cells in this region and sometimes even sever the optic nerve that connects the eye to the brain.

Researchers at the Massachusetts Institute of Technology are developing nanofibers that may be able to help the body heal itself. These mixtures of peptides spontaneously form a scaffold on which nerve cells can easily grow. Remarkably, thi technique has restored vision in hamsters with injured optic tracts. The question now is whether it will work in humans an if so, to what extent it can heal severe damage.

of the first clinical trials to find out. Patients are injected with liposomes, little hollow spheres made of fat cells that deliver the anticancer compound cisplatin to tumor cells. Developed by the Danish pharmaceutical company LiPlasome, these orbs break open only when exposed to tumor-related enzymes. It's still too early to report results, but if prior tests in mice are any indication, the liposomes should kill cancer faster than non-targeted chemotherapy does and with fewer side effects.

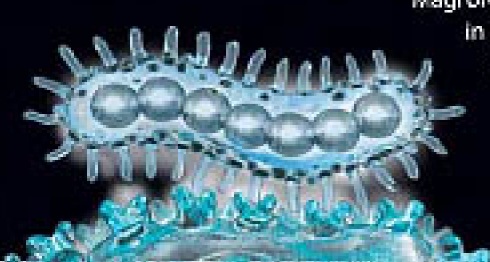
Killing Cells with Heat

Nanoparticles can be more than just vehicles for drugs. Certain types of nanoparticles can make even the tiniest tumors visible to doctors—early detection of tumors makes them easier to treat—using MRI scans. And under the right conditions, these same nanoparticles can kill cancer without additional drugs. To aid in a cancer diagnosis, researchers at the University of California at San Diego have created a chain of iron-oxide particles, coated with proteins that bind tightly to cancerous cells, and highlight them in MRI scans. Using individual iron-oxide nanoparticles, MagForce Nanotechnologies in Germany is attempting to destroy brain, prostate and pancreatic cancers. The trick to killing cancer with the iron oxide is exposing the nanoparticle-injected tumors to a rapi oscillating magnetic field, which gener temperatures up to 158°F that cook th cancerous cells.

Researchers at Stanford Universit have replaced the iron oxide with car nanotubes, which absorb infrared lig and heat up to 158°. This technique i fective for treating malignancies just neath the skin's surface. To treat deep cancers, doctors must insert infrared fiber-optic lasers into the body.

Iron-oxide nanoparticles are especially susceptible to external magnetic fields like those produced in an MRI scanner.

Injecting iron-oxide particles into a tur and exposing it to an oscillating magn field heats it up and destroys the cance



Chains of iron-oxide particles make small tumors visible in an MRI scan.

BROKEN BONES

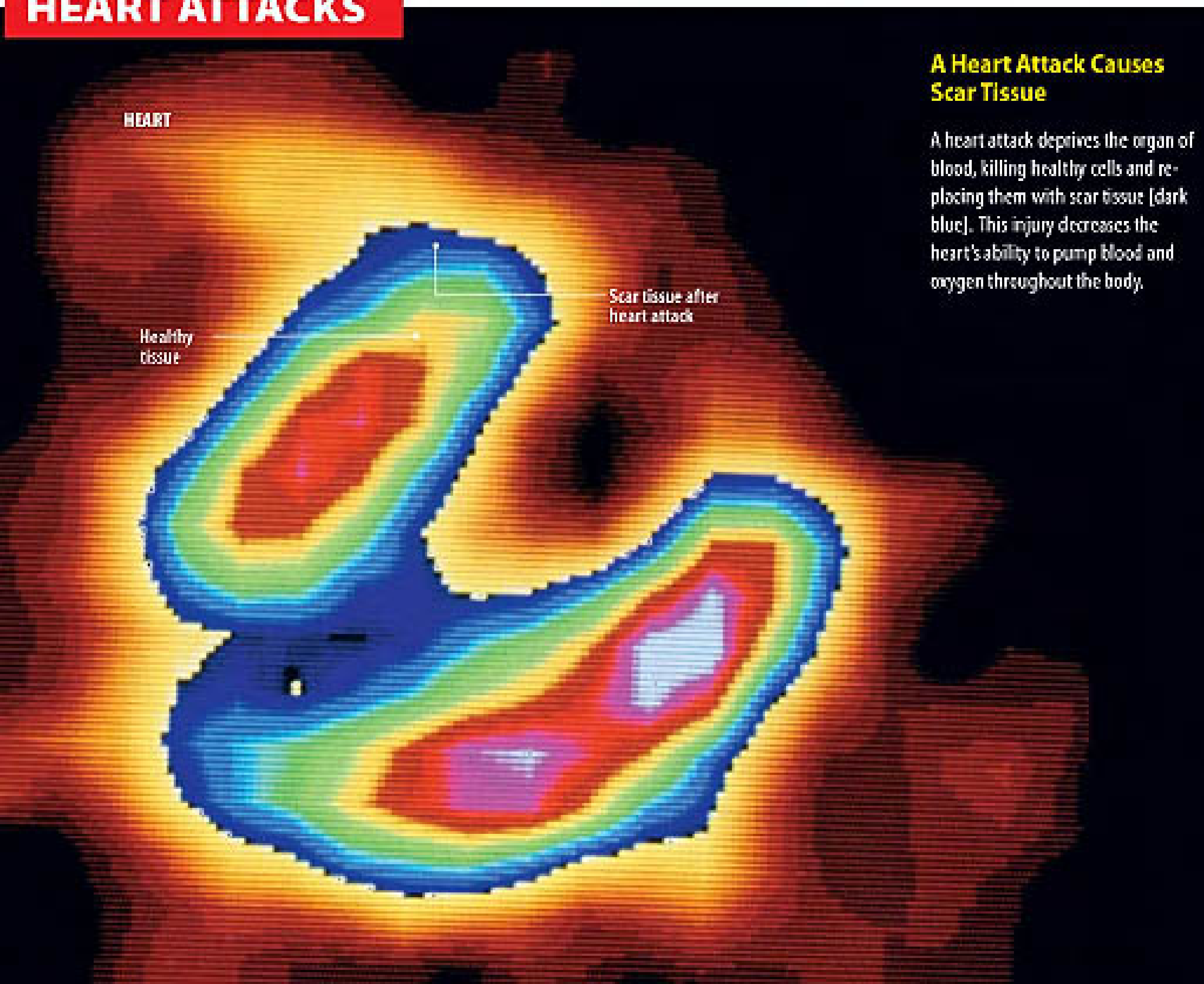
Nanoscaffolding Heals Bones

In their quest for new ways to treat severely fractured bones, a research team at the Institute of Bioengineering and Nanotechnology in Singapore has developed a foamlike scaffolding material. Made of the protein collagen and nanoparticles of the mineral apatite—two main components of bone—the nanofoam promotes the growth of cells, which bind to the artificial scaffold and eventually form new bone. The foam proved successful in studies with rats, and researchers are now testing it in pigs, whose healing time for broken bones is similar to that of humans. The foam is sculpted so that it fits perfectly into the fracture area and is then anchored in place, allowing the patient's own stem cells to begin making new bone.

More than 80 percent of the fractures in the pigs healed completely within three to six months, and the newly generated bone was just as dense and strong as the bone before it was damaged. Human trials are up next.

Broken Rat Bones Grow Together
In preliminary tests, scientists in Singapore implanted a nanoscaffold made of collagen and apatite into the bones of rats. These serious fractures healed completely in five months.

HEART ATTACKS



A Heart Attack Causes Scar Tissue

A heart attack deprives the organ of blood, killing healthy cells and replacing them with scar tissue [dark blue]. This injury decreases the heart's ability to pump blood and oxygen throughout the body.

The artificial scaffold has both apatite nanocrystals and pores within the collagen network that are the same size as those found in natural bone, producing a strong foundation for new bone growth.

DIABETES

Nanodrugs Could Replace Insulin Injections

Patients with insulin-dependent diabetes (Type 1 and cases of Type 2 that can't be controlled with medication) must check the level of their blood sugar several times a day and administer frequent injections of insulin, the hormone that absorbs excess sugar in the bloodstream. Researchers at Smart-Cells, a biotechnology company in Massachusetts, are creating nanoparticles that could one day automatically detect a spike in blood sugar and dispense the exact dose of insulin needed to keep the sugar level in balance.

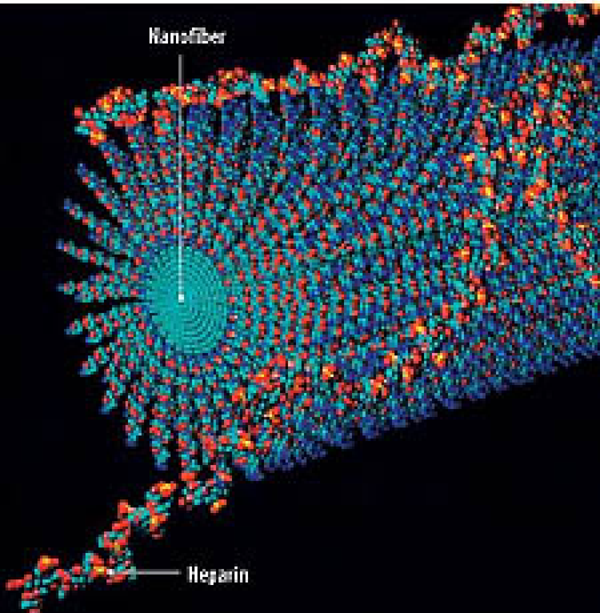
This nanodrug will be made up of an insulin molecule and a second molecule that binds to sugar. As the blood-sugar level rises, the sugars attach to the sugar-binding molecule. This dislodges the insulin, leaving it free to react with glucose, thus decreasing the blood-sugar level. Unlike injectable insulin that can bring the level down too far, the nanodrug process stops when blood-sugar level reaches a normal range.

Nanomedicine Creates New Blood Vessels in Diseased Hearts

Another promising area in nanomedicine is the creation of new blood vessels to help heal damaged tissue. Here's how it works: One of the major biological components to wound healing is a class of molecules called growth factors. These molecules encourage the creation of blood vessels, which support new tissue. The problem is, you need a high concentration of growth factors in the wound to speed healing, but controlling where those compounds gather is difficult. Enter heparin, a protein that attracts growth factors.

Scientists have found a way to capture heparin with self-assembling nanofibers. Once the nanofibers are in place, they bind with heparin. This in turn lures growth factors to the area to speed healing. Researchers at Northwestern University think that they can jump-start healing if they can increase the number of growth factors at the wound site.

In a clinical trial, the Northwestern researchers induced heart attacks in mice and then gave half of the wounded rodents an injection of the heparin-binding nanofibers. A control group comprising the remaining animals received only growth factors. The doctors suspect that in the latter group, the growth factors rapidly disappeared from the heart and diffused throughout the body. They believe that in the heparin group, the nanofibers quickly assembled in the damaged area. One month later, the diseased mouse hearts were pumping blood almost as well as those of healthy mice. Meanwhile, the hearts of the control group were working at only half the power because the heart muscle hadn't regenerated.



Nanofibers Help Rebuild Hearts

To help rebuild the injured tissue, scientists injected engineered molecules into mouse hearts that were damaged by heart attacks. The molecules spontaneously formed fibers and bound to heparin, attracting the growth factors in the blood that stimulate new blood-vessel growth.