Cancer-killers from macrophages

Many cancer deaths occur not from the primary tumor, but from the secondary growths, called metastases, spawned by that primary cancer. Although oncologists try to hunt down and eliminate metastases, even with today's sophisticated diagnostic tools, "it is not likely that we will diagnose metastases or tumors in internal organs that are smaller than a centimeter cubed" (clusters of roughly 1 billion cells), says Isaiah Fidler of the M.D. Anderson Hospital and Tumor Institute in Houston. But he and others are pioneering a strategy to seek and destroy those unseen metastases – one that employs the body's own defense system.

Potentially less toxic than existing chemotherapies, this treatment may also prove more effective, Fidler's studies indicate. The cancer researcher recently described preliminary animal studies suggesting its promise at the Second International Conference on Anticarcinogenesis and Radiation Protection last month in Gaithersburg, Md.

The strategy uses liposomes, microscopic lipid-based, laboratory-made containers, to carry drugs that "activate" macrophages – scavenging cells that ordinarily hunt down, swallow up and degrade foreign particles such as viruses. Though, in the 1970s, researchers demonstrated that these cells could also be activated to attack tumor cells, a problem developed over how to deliver the activators so that they wouldn't cause undue toxicity or degrade too quickly. Fidler's work now suggests that liposomes provide an ideal controlled-release system for delivering activators.

He fashions his liposomes from the same lipoproteins found in all cell membranes, including those of red blood cells. A thin ribbon of the lipoproteins is wound into a microscopic, onion-like roll. Then he chemically sandwiches macrophage-activating chemicals between layers of the "onion." As they encounter liposomes, macrophages gobble them up – just as they would aging red cells. Digesting the liposomes releases the activators.

In studies where malignant melanoma had been surgically removed from mouse footpads, metastases to the lymph nodes and lungs killed animals within 80 days. But eight to 12 intravenous injections of liposomes, containing the macrophage activators gamma-interferon, muramyl tripeptide or both, saved 75 percent of Fidler's treated animals.

Similar results were recently observed in a study at the University of Wisconsin in Madison with 18 dogs following their surgery for osteogenic sarcomas. By the time this canine disease is initially diagnosed, metastases have almost always implanted in the lungs, leading to death – despite surgery – within three months. But six of the nine dogs treated with liposomes carrying muramyl tripeptide are still alive more than 200 days after surgery, notes E. Gregory MacEwen, head of the study. As for the three treated animals that died, MacEwen believes their tumor burden was already too high for the activated macrophages to counter.

Since macrophages naturally home in on inflammation, Fidler notes, he tried pretreating the site of fibrosarcoma metastases in mice with low-dose irradiation to induce inflammation. The result: three-fold better mouse survival than with radiation or liposomes only.

And in the April JOURNAL OF THE NATIONAL CANCER INSTITUTE, researchers at the Roswell Park Memorial Institute in Buffalo report better survival and less toxicity in mice whose metastases of colon cancer were treated with liposome-trapped doxorubicin, rather than just the cancer drug alone. Though macrophage activation was not examined here, Eric G. Mayhew says other work by his group suggests "liposomal doxorubicin can potentiate the host defense – similar to what the people at M.D. Anderson have shown with other drugs." *– J. Raloff*

Another launch failure

Weather has long been a concern during orbit-bound launchings from Florida's Cape Canaveral, where low January temperatures have been one possible factor cited in the explosion of the space shuttle. This week, NASA investigators were looking to see whether another meteorological hazard – lightning – was connected with the March 26 loss of an $83 million military communications satellite when its $78 million Atlas-Centaur rocket went out of control and had to be destroyed.

Lightning was in the skies that morning, and officials later announced that four lightning bolts were detected about 48 seconds after liftoff. In addition, there were "large current and electrical transients" as well as "major changes" recorded by accelerometers in both rocket stages and the satellite's housing.

NASA safety regulations say that launches need be scrubbed only if lightning is detected within 5 miles of the launchpad, and the nearest prelaunch bolt initially announced by the investigators was about 16 miles away, 16 minutes before launch. The bolts during the ascent, however, were said to have been recorded as little as 1.9 miles from the site. Officials expressed hope that debris being dredged from the Atlantic would include an on-board control unit that possibly mis-aimed the rocket's engines and sent the flight off course.

– J. Eberhart

Superconductivity: A hard frost

As superconductivity appears at higher and higher temperatures, the prospect of a resistanceless electrical technology glimmers more brightly. As of last week the limit has risen to 240 kelvins, claimed by a group at Wayne State University in Detroit.

At this rate there may be an advantage to living in the frost belt: This temperature is the equivalent of -33°C or -27°F. Indications of superconductivity at temperatures near this had previously been seen by the group working with Paul Chu at the University of Houston and the group working with Marvin Cohen at the University of California at Berkeley. At the recent meeting of the American Physical Society, Cohen had spoken of sudden drops in resistance. This could be a precursor of superconductivity, but as Lowell E. Wegner of Wayne State points out, it could also be what happens when an insulator becomes an ordinary conductor – a normal phenomenon that does not lead to superconductivity.

To verify superconductivity, physicists want either a demonstration of zero resistance in a sample of the material or a showing of some other phenomenon that requires the presence of a superconductor. The Detroit group, which includes Wegner, J.T. Chen, Eleftherios M. Logothetis, Charles J. McEwan and Winston Win, used a kind of inverse-Josephson effect.

In the Josephson effect, a direct voltage in a particular kind of superconducting junction will cause a stepwise *alternating* current to flow, and under certain conditions this current can generate a radio wave. In the inverse, the experimenters bathe the sample in radio waves and look for the alternating current and the direct voltage. The Josephson effect requires a superconductor, Wegner says.

What the Wayne State researchers think they have is a material in which a part becomes superconducting at 240 K, and another part at 90 K. Cohen told SCIENCE NEWS that this is what his group thought they had, too: a "filament" inside the sample that went superconducting at 234 K, but then broke so that the indication disappeared. "We always had the 90 K phase," Cohen says, "and we see indications at 150 K and 180 K also."

These materials are compounds of copper, oxygen and rare-earth elements. They are granular, and the exact proportion of the different elements can vary from place to place. Chemists refer to these variations as different "phases." Wegner says his group is now trying to find the exact composition of the phase that goes superconducting at 240 K, in the hope of being able to prepare a pure sample of it. *– D. E. Thomsen*