Biomedicine

Capillaries identify spreadable cancers

Not all cancerous growths have the same propensity to spawn deadly new "satellite" tumors, or metastases. If physicians could identify which cancers have spread or will soon do so, it would help them determine which patients need costly and toxic postoperative radiation or chemotherapy to survive. Researchers at Harvard Medical School in Boston have now identified one marker of metastatic potential in patients with invasive breast cancer: rapid and widespread capillary development, or angiogenesis, mainly at the edges of the primary tumor.

Without angiogenesis, a tumor essentially becomes blood starved and will stop growing once it reaches a few millimeters in diameter (SN: 5/19/90, p.308). But if new microvessels begin sprouting, the cancer can resume rapid growth and will also have an increased chance of initiating new tumors by seeding the bloodstream with malignant cells.

Using 200-power magnification, the Harvard team counted microvessels in tumor tissues extracted from 49 Boston-area women with invasive breast carcinomas. During the count, the researchers did not know whether the women had signs of metastases in nearby lymph nodes or elsewhere. The investigators then followed the women's cases over the next 10 years.

Of the seven patients with microvessel counts under 34, only one developed metastases during that time, they report in the Jan. 3 New England Journal of Medicine. For every 10 additional microvessels counted, metastatic risk increased another 1.6 times. For example, tumors spawned new cancers in nine of 20 women (45 percent) with microvessel counts between 34 and 67, and in five of seven women (71 percent) with counts between 68 and 100. Metastases eventually appeared in all 15 patients whose excised tumors had contained at least one region with more than 100 microvessels.

At present, physicians who treat breast cancer patients commonly base the decision to forgo aggressive postsurgical therapy on a finding that the nearby lymph nodes remain free of cancer. Yet one-third of breast cancer patients with cancer-free lymph nodes ultimately develop metastases, notes study coauthor Judah Folkman. Angiogenic activity may help predict which of these seemingly cancer-free women are at greatest risk, he says. Of the 17 "node-negative" women in the Harvard study, the four who eventually developed fatal metastases had microvessel counts between 80 and 140, Folkman says.

Though "not an unexpected discovery," this correlation between angiogenic activity and metastatic disease "is quite significant," particularly for the insight it offers into cancer development, says pathologist Lance A. Liotta of the National Cancer Institute in Bethesda, Md.

Folkman agrees. Despite animal studies suggesting that cancers might at some point mysteriously "switch on" their angiogenesis, he says, some researchers remained unconvinced that human tumors behaved identically, and instead suggested that human tumors were either angiogenic or not from their inception. The new study appears to lay that doubt to rest with "the first demonstration in a human cancer of the actual switch," Folkman asserts. "In a single breast, you can see the tumor just *before* it has turned on angiogenesis and [in another spot] just *after* it has turned on."

The Harvard findings fuel expectations that drugs to block angiogenesis "might be useful to prevent cancer from spreading," Liotta says. Indeed, researchers at Hokkaido University in Sapporo, Japan, report in the Jan. 1 Cancer Research that one such agent – a modified form of chitin, a polymer found in insect skeletons and crustacean shells – suppressed metastases of lung cancer in mice. And one mechanism responsible, the Japanese investigators say, appears to be the sulfated chitin derivative's inhibition of angiogenesis.

Chemistry

How to date a rock artist

Where the Pecos and Devils rivers meet the Rio Grande, ancient peoples with a penchant for painting took refuge in shelters dug into limestone cliffs. Pictographs of panthers, spear-throwing shamans and other figures cover some of these places from stem to stern and from floor to ceiling.

Determining the dates of pictographs helps scientists reconstruct vanished cultures. To obtain their date data, archaeologists and anthropologists traditionally have relied on indirect evidence, including radiocarbon dates of deposits on and near the art, as well as imagery in the paintings.

Direct radiocarbon dating of cave paintings has been mostly out of the question because of scientists' inability to distinguish the inorganic carbon in the limestone "canvas" from the paint's organic carbon, says chemist Marvin W. Rowe of Texas A&M University in College Station. The organic carbon in ancient paints derives from blood, plant resin, juice or other "binders," which, like modern oil- or water-based binders, carried pigments and adhered to surfaces.

Several years ago, Texas A&M anthropologist Harry J. Shafer met Rowe on campus and posed the question: Is there any way to separate a sample's inorganic and organic carbon components to allow direct dating? In the Dec. 20/27, 1990 Nature, Shafer and Rowe, along with chemists Marian Hyman and Jon Russ, describe a technique that seems up to the task.

The researchers tested their method on a thin, limestone-backed fragment of a pictograph that Shafer had found on the ground of a prehistoric shelter in southwest Texas. They scraped paint powder from the limestone and placed the powder in a partial vacuum for a week to let atmospheric carbon dioxide evaporate away. Next, they swamped the sample with an oxygen plasma. The reactive oxygen, although too cool to affect inorganic carbon in the limestone (calcium carbonate), converted the sample's organic carbon into carbon dioxide. The chemists collected this date-bearing gas, now free of contamination by inorganic carbon, by condensing it as dry ice onto a cold surface.

Others entered the picture at this point. A commercial lab purified the carbon dioxide and converted it into all-carbon graphite – a form well suited for sensitive dating techniques. Next, the graphite took a trip to a Swiss research facility where scientists analyzed it by accelerator mass spectrometry, which precisely compared the relative amounts of radioactive and stable carbon isotopes.

The resulting ratio suggests the ancient artists prepared their paint 3,865 years ago, give or take a century. That's far more precise than the "2000 to 6000 years ago" range indicated by indirect methods, Rowe says.

"As organic carbon is a ubiquitous component of pictograph paints, this technique should be applicable to rock paintings throughout the world," the Texas researchers conclude.

Droplets with reproductive drive

Self-replicating chemical structures serve as poor, though recognizable, impostors of living reproduction (SN: 2/3/90, p.69). But scientists in France and Switzerland say they have come up with a chemical process that mimics cell multiplication better than any such system yet reported.

In the Oct. 24, 1990 Journal of the American Chemical Society, they describe their preparation of "self-replicating reverse micelles" – tiny water droplets surrounded by a surfactant layer and suspended in an organic solvent. When precursor molecules dissolved in the solvent stick to the surfactant layer, lithium hydroxide in the droplets splits these molecules into the very components making up the surfactant layer. The reverse micelles divide into a growing population of ever-smaller, cell-like spheres.