Tamoxifen Puts Cancer on Starvation Diet

Since it was first marketed in the United States 16 years ago, tamoxifen has become the world's top-selling cancer medication. Ironically, it achieved its success despite pharmacologists' uncertainty about how this synthetic hormone prevents the growth of new cancers in women who have undergone surgery for a first breast malignancy.

A team of Israeli scientists now reports animal data indicating that one of the drug's primary functions is to shut down the natural infusions of blood that budding cancers need in order to thrive.

In the Nov. 1 CANCER RESEARCH, Hadassa Degani of the Weizmann Institute of Science in Rehovot and her coworkers demonstrate that tamoxifen can starve to death cells deep within a tumor by shutting down the internal network of microscopic blood vessels that nourishes them. However, the drug did not affect the thin rim of surviving cancer cells, which continued to be fed by external blood vessels.

In roughly half of all breast tumors, the hormone estrogen stimulates cancer cells to issue regular chemical reveilles that signal nearby cells to grow. But by binding to estrogen receptors on these cells, tamoxifen appears to block or mute these wake-up calls, permitting cancer cells to sleep right through their growth cycle.

Indeed, in 1 week, tumor growth ground to a halt in 17 of the new study's 21 tamoxifen-treated mice.

By the end of 2 weeks, their tumors had shrunk an average 26 percent. That shrinkage, argues Degani, probably traces to tamoxifen's muting of growth cues to endothelial cells — noncancerous cells that form the basis of the body's vascular system.

Small colonies of cancer cells can grow as long as they're fed from an external blood supply. But once such a developing tumor reaches some critical size, it will stop growing — unless a new network of infiltrating vessels supplies it with blood. Degani's team found evidence that tamoxifen not only could stop tumor-penetrating vessels from forming, it could also help eliminate existing ones.

She says that areas of dead tissue within the center of the tumor expanded in most drug-treated mice. Using magnetic resonance imaging, her group mapped an average growth of 464 percent in the tumor's dead zone in 10 of the 17 mice whose tumors shrank during treatment. Even in the four tamoxifen-treated mice whose cancers continued to grow, the amount of dead tissue tripled during 2 weeks on the drug.

No similar increases in tumor necrosis, or tissue death, appeared in animals treated with estrogen or given no hormone supplement.

Two previous studies had suggested that tamoxifen can inhibit angiogenesis — the formation of new blood vessels. But the Israeli study appears the strongest and "very dramatic," observes Judah Folkman of Harvard Medical School in Boston.

Delwood C. Collins of the University of Kentucky in Lexington, an author of one of those earlier studies, notes that even newer data gathered by his group and reported at a meeting last month in Washington, D.C., indicate that tamoxifen is but one of several estrogen-blocking drugs capable of inhibiting angiogenesis. In fact, it probably does so through pathways independent of either estrogen or its receptor, he adds. Folkman's data also support the idea that tamoxifen's antiangiogenesis activity may not require estrogen receptors.

The new findings hint that tamoxifen might be used differently in the future, Folkman says — perhaps as an adjunct to therapies that kill cancer cells directly or as a means of strengthening the angiogenesis inhibition of one or more other drugs. It's even possible, he speculates, that if chemists can isolate a more purely antiangiogenic tamoxifen derivative, it might provide a less toxic alternative to the current multiaction drug, which has a number of undesirable side effects.

— J. Raloff

Behind the Milky Way: Unveiling a galaxy

The fuzzy arc of the Milky Way has fascinated skywatchers for millennia. But this patchy collection of gas and dust — the disk of our galaxy — takes up some 20 percent of the sky, blocking from view a sizable chunk of the universe.

What lurks behind the disk of the Milky Way?

A new study supports the notion that the hidden region teems with galaxies, some of them in our own cosmic backyard.

An international team of astronomers began its work by using a radio telescope to search for emissions from atomic hydrogen gas located outside — but in the same part of the sky as — our galaxy. Such radio emissions can penetrate the Milky Way's veil of gas and dust — if the extragalactic gas moves at a different speed than gas in the galaxy.

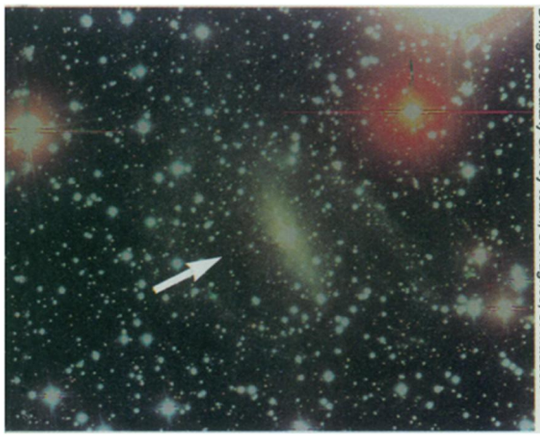
The team now reports that it has found a previously unknown galaxy, a spiral neighbor only 10 million light-years from the Milky Way. Astronomers dubbed the galaxy Dwingeloo 1 in honor of the 25-meter radio telescope at Dwingeloo, the Netherlands, through which it was first viewed. The galaxy probably belongs to a nearby group of galaxies that includes IC342, Maffei 1, and Maffei 2.

Unlike another nearby galaxy recently discovered behind our own (SN: 4/9/94, p.228), Dwingeloo 1 lies too far away for the Milky Way to devour it. But it does seem to reside close enough to affect the motion of the Milky Way and its family of galaxies, known as the Local Group.

Ofer Lahav of the University of Cambridge in England and his colleagues, including Harry C. Ferguson of the Space Telescope Science Institute in Baltimore, detail their work in the Nov. 3 NATURE.

The group found that the location of the newfound galaxy coincides with a dim, unidentified feature on photographic plates taken as part of the Palomar Sky Survey. Lahav and his coworkers then confirmed their finding with the Westerbork radio telescope in Hooghalen, the Netherlands. They also imaged the galaxy in visible light with the William Herschel Telescope in the Canary Islands, Spain.

In a commentary accompanying the NATURE report, David Burstein of Arizona State University in Tempe notes that the new discovery may rank among the first of many galaxies found behind the murk of the Milky Way. "It is encouraging to see the veil of the Milky Way slowly lifted, and we await with anticipation the full unveiling," he writes. *— R. Cowen*



Dwingeloo Galaxy Survey team, S. Hughes, S. Maddox

False-color, composite image of Dwingeloo 1 (arrow), a newly discovered spiral galaxy hidden by the Milky Way. This large galaxy lies about five times as far away as Andromeda, our nearest spiral neighbor.