

vators of the Cdks and the proteins, such as p16, which inhibit them. As Beach puts it for Cdk4, "The D cyclins are in competition with p16, courting the affection of Cdk4." And anything that leads to overactivity of the Cdks, whether excessive cyclin production or loss of inhibition by proteins such as p16 and p21, can tip cells into the abnormal growth of cancer.

All this evidence led researchers to expect that p16 might be a tumor suppressor. But Kamb says he and his colleagues never expected that it would rival the current champion, p53, as a cancer contributor. The first indications that it might came when the Utah group looked for p16 deletions in the melanoma cell lines, and later in a wide variety of other kinds of cancer cell lines, a total of 290 in all. Deletions of the gene would indicate that the loss or inactivation of p16 might help cause the cancers.

The results were startling: The researchers found that 50% of the cancer cells displayed deletions in the p16 gene, as did some primary tumors, an indication that the mutations weren't just lab artifacts. "If you go after a melanoma susceptibility gene, at the end of the day you're surprised if it turns up

in 50% of all cancers," Kamb says. In fact, so far, the group has failed to detect p16 deletions in only two types of cancer: colon cancer and the nerve cell tumor called neuroblastoma. And these findings may well be an underestimate. "The initial screen was very crude," Kamb points out, detecting only large deletions and not subtler changes such as deletions of only a few bases or substitutions of one base for another. When the researchers looked more carefully at their melanoma cell lines, for example, they found that another 25% have such small p16 mutations—bringing the grand total of mutations in the gene to 75%.

What is more, the Utah group is not alone in seeing p16 mutations in a wide variety of tumors. Curtis Harris of the National Cancer Institute and Beach confirm that they, too, have similar results, although they are not yet willing to discuss their work in detail because it is still unpublished.

Despite the growing evidence that p16 is a tumor suppressor, the Utah workers do not yet know for sure that they have attained their original goal of identifying the melanoma susceptibility gene. To make sure p16 is the melanoma gene, they are conducting

studies of families in which the skin cancer is hereditary to see whether the members who get the cancer have the expected mutations in p16. Also needed is a direct demonstration that introducing a normal p16 gene into cancer cells in which the gene is mutated can restore normal growth, as would be expected for a tumor suppressor.

Other researchers won't wait for the results of those studies before extending the Kamb group's work, predicts Stanbridge: "Once this is out, a lot of people will be looking at their favorite tumors to see if [p16] is involved." The task will be made only more urgent by the possibility of using the information about p16 to develop new cancer therapies. "Because the gene is small," says Kamb, "it will be technically easier to work with for gene therapy" than, for example, p53, which is four times as large. Also, since p16 currently seems to inhibit only Cdk4, cancer drug developers have a very specific target to shoot at. The prospect of finding such drugs will no doubt help keep attention firmly focused on cellular braking mechanisms as researchers attempt to keep the cell cycle from careering out of control.

—Jean Marx

## ASTRONOMY

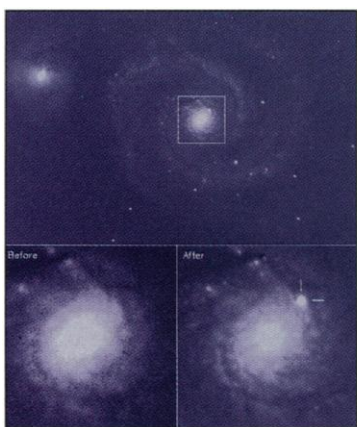
### A Supergiant Dies in the Whirlpool

For supernova researchers, the last few years have brought one treat after another. First, in 1987, the nearest and brightest stellar explosion in more than 300 years flared in the southern sky. Last year came supernova 1993J, which evened the score by giving Northern Hemisphere astronomers their best view of a supernova in decades. And last week, 1994 brought a supernova that, although not quite as bright as last year's, appears to belong to a rare type never before seen in close-up.

The news came, as it did last year, from the amateur supernova hunters who regularly scan the sky for stellar catastrophes. On the night of 1 April, several groups of amateurs in the United States and Japan alerted the rest of the astronomy community to a spot of brightness in the Whirlpool galaxy, M51, an elegant spiral 15 million light-years away. Within days, as the new supernova brightened to its peak and then started to fade, radio and optical telescopes had turned toward the spot and made a preliminary diagnosis.

What the amateurs had spotted was the

explosion of a massive star, the same kind of cataclysm responsible for the other bright supernovas. But this year's, designated 1994I, seems to have taken place in a very different kind of star—one so massive and turbulent that it had already blown off its tenuous outer layers and was little more than a naked star core. In coming weeks, astronomers will be



**Out with a bang.** Before (7 January) and after (3 April) views of the blast.

watching intently to see how the unusual structure of the progenitor star affects the course of the explosion. "This is the first supernova [of this kind] that is close enough and bright enough...to study in detail," says Kurt Weiler of the Naval Research Laboratory in Washington, D.C.

Initially, some astronomers guessed they were seeing an ordinary type II supernova—the explosion of a massive star within its vast hydrogen envelope, like SN 1987A—or a type Ib, in a massive star that has lost its hydrogen but retains deeper helium layers. But by last Tuesday, Robert Kirshner of Harvard University had taken spectra of the supernova at the Whipple Observatory on Mount Hopkins, Arizona, and found that they showed

no sign of hydrogen or helium. "It is pretty clear," says Kirshner, "that it resembles what we call a Type Ic object"—the collapse of a star with perhaps 40 times the mass of the sun. Such supergiant stars are so active, astronomers believe, they can shed their hydrogen and helium in a powerful stellar wind.

The turbulent past of the progenitor star could explain another early observation: the detection of radio signals from the explosion. This finding was made by Weiler and his colleagues, using the Very Large Array in New Mexico, just two days after the discovery—"the earliest anyone has ever detected radio waves from a supernova," says Weiler. He thinks the signals may have been generated as the supernova's fast-moving shock wave slammed into the dense wind expelled from the star just before its explosion.

By Friday, a group led by George Sonneborn of the NASA Goddard Space Flight Center had reported what may be another sign of the progenitor star's history: a burst of ultraviolet emission, detected by the International Ultraviolet Explorer (IUE) satellite. The burst may have been generated, says Kirshner, when energy from the explosion stimulated the surrounding gases. If so, observations he is planning with the Hubble Space Telescope should reveal still more clues to this latest blast's past.

—Ray Jayawardhana

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