McMaster's Bacchetti and Cold Spring Harbor's Greider, decided to see whether telomerase activation might allow cultured cells to escape the normal limits on their growth and become "immortalized." And it did.

When the researchers tried to mimic the tumor-forming process by introducing oncogenes from simian virus 40 or an adenovirus into cultured cells, they found that telomerase activation was a good predictor of immortality. The oncogenes stimulated cell growth, as expected, and most cells' telomeres continued to shorten with each division until the cells died. But some survived and continued to divide—and those cells, Harley says, had an active telomerase, which presumably stabilized their telomeres. Exactly what allowed the cells to make telomerase is unclear, although the Harley-Bacchetti group detected numerous abnormal chromosomes in cells that had extremely short telomeres. These chromosomal abnormalities, which are similar to those commonly seen in cancer cells, may have led to mutations in the telomerase gene and in other genes that contribute to tumor malignancy. "When cells lose telomeric DNA, it may open the window for all kinds of horrible things to happen," says Zakian, who has noted similar chromosome abnormalities in her yeast experiments.

More recently, Harley, Bacchetti, and their colleagues have turned their attention to cells taken directly from cancerous tumors. They reported in the 14 April *Proceedings of the National Academy of Sciences* that telomerase is active in ovarian cancer cells, although not in normal ovarian tissue. The researchers have since gone on to survey telomerase activity in a variety of additional human cancers, and the preliminary results look promising.

Those findings, together with the signs that the enzyme is not active in normal cells, make it an important new target for cancer drugs. "We think [telomerase] will be a specific and probably universal target in tumorigenesis," says Harley, who last year moved to the biotech firm Geron Inc., in Menlo Park, California, to work on developing inhibitors of the enzyme. The hope is that if telomerase activity can be blocked, cancer cells won't be able to maintain adequate telomere length and will die. This may be easier said than done, however.

For one thing, researchers still have much to learn about telomerase. So far, they have not been able to isolate the protein portion from any organism, and they have obtained the RNA part only from ciliates. That may soon change, however. Both Blackburn and Gottschling have described candidates for yeast telomerase RNAs at meetings. And a yeast gene identified by Szostak and Victoria Lundblad, who's now at Baylor College of Medicine in Houston, may encode the protein component of yeast telomerase. Greider's group also has a candidate telomerase protein, although in this case from a ciliate.

Having the complete enzyme may aid researchers in designing inhibitors, but whether they will actually kill cancer cells remains to be established. Blackburn finds, for example, that some yeast cells are able to survive without telomerase. "There is life without telomerase," as she puts it. That may be true for cells, but for many researchers, the enzyme—along with the telomeres it synthesizes—is now an essential part of their scientific lives.

–Jean Marx

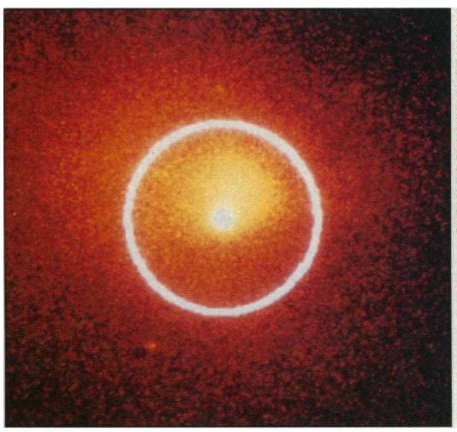
ASTRONOMY

How Comets Stay Frisky in the Cold

Most comets spend nearly all their lives as inert lumps of ice and dust, enjoying brief bursts of activity only when they enter the inner solar system. Like animals emerging from hibernation, they are energized by the sun's heat, which turns their water ice to vapor in a process called sublimation. The vapor in turn blows dust and other gases outward to form a halolike coma and, often, a magnificent tail. When a comet swings back out among the outer planets, it usually goes back into hibernation.

Not always, though. In the far reaches of the solar system, where the temperatures are too low for ice to sublimate, some comets, including Halley's, experience brief flare-ups of activity, while others, such as Schwassmann-Wachmann 1 (SW1), sport persistent comae. Now, Matthew Senay and David Jewitt of the University of Hawaii in Manoa think they know one reason why. In yesterday's issue of *Nature*, the pair reports detecting radio emission from carbon monoxide (CO) molecules in SW1, which orbits well beyond Jupiter. Because solid CO sublimates at a much lower temperature than ice, they say, it could be what keeps some comets lively in the cold.

Astronomers had already guessed that the puzzling activity of distant comets is driven by the sublimation of molecules more volatile than water. "But up to now, we had no direct evidence as to what these molecules could be," says comet expert Jacques Crovisier of the Observatoire de Paris-Meudon in France. And there seemed to be little hope of finding out: In the cold, dim environment of the outer solar system, the radio emissions characteristic of the gas molecules would probably be so faint as to be undetectable.



SUSAN RIDGWAY/UNIV. OF HAWAII

Gas-powered. Dust envelops comet SW1, driven by the CO detected by radio observations *(circle indicates the telescope's view).*

But the quantity of gas ejected by SW1 made up for the feeble signal. Using the 15-meter James Clerk Maxwell Telescope on Mauna Kea in Hawaii, Senay and Jewitt were able to pick up submillimeter radio emissions from SW1 at a frequency characteristic of CO. Based on the strength of this spectral line, Senay and Jewitt estimate that the comet is emitting CO at a rate of about 2 tons per second. "This is remarkable," says Jewitt, "because it is comparable to the outgassing rates of comets [in the inner solar system]." The style of outgassing is comparable, too. A slight Doppler shift in the line, the researchers believe, implies that the gas is spewing out of SW1 in a jet like those produced by water vapor in comets closer to the sun.

To pin down the link between CO and the comet's visible activity, Senay and Jewitt measured the width of the CO line with the 10-meter submillimeter telescope at the California Institute of Technology. The line width indicates how fast molecules are darting around within the gas cloud surrounding the comet—and therefore how fast the cloud is expanding. The result agreed well with the observed expansion of SW1's dust coma. With all these pieces falling into place, says Crovisier, "we know that CO is at least one" of the gases driving distant activity.

The two researchers stress that their findings don't rule out a role for other highly volatile molecules such as nitrogen. But Crovisier notes that "we have no way to detect nitrogen at the present time," because its spectral fingerprint would be masked by those of other gases. For now, Senay and Jewitt are planning to study several other distant comets to see whether they, too, are gassed up by CO.

–Ray Jayawardhana

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