The huge burst of star formation first caught astronomers' attention last year, when the Very Large Array radio telescope in New Mexico detected a glowing bubble in a dwarf galaxy known as NGC 5253 in the constellation Centaurus. "Back then, I was nervous about calling this a young globular cluster," Turner says. But infrared observations and spectra obtained with the 10-meter Keck telescopes at Mauna Kea, Hawaii, confirmed her original suspicion. By measuring Doppler changes in infrared light from hydrogen in the bubble, Turner and colleagues calculated that the bubble was being blown by stellar winds moving at 5000 kilometers per hour—far stronger than winds astronomers had seen in other bubbles. Massive, powerful young stars, they concluded, must be churning out light and gases vigorously enough to produce 25% of the energy output of the dwarf galaxy. The infrared data also enabled the team to estimate the size of the star-forming region.

The 12-million-year-old newborn could help resolve enigmas in our own galaxy. The 150-odd globular clusters in the Milky Way are billions of years old, so little is known about their origins. According to Turner, similar clusters-in-the-making probably exist in other galaxies, but most are much farther away and harder to study than the one her team found. "I won't call this a Rosetta Stone," she says, "but if astronomers are to understand the birth of these clusters, they will keep getting back to this one."

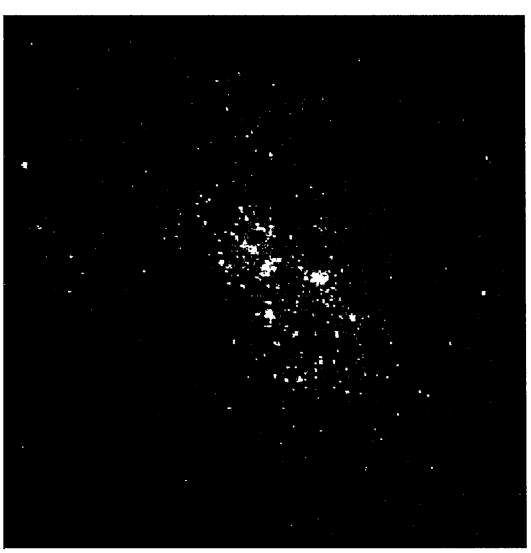
Small galaxies like NGC 5253 are proving fertile breeding grounds for new stars. At the same meeting, Armando Gil de Paz of the Infrared Processing and Analysis Center in Pasadena, California, reported evidence of another huge (though nonglobular) starburst in a dwarf galaxy known as Markarian 86. According to Gil de Paz, the 30-million-year-old burst has triggered the formation of new stars across the galaxy.

Why do dwarf galaxies undergo superstarbursts? Turner says no one knows yet, but in the case of NGC 5253, interaction with a neighboring spiral galaxy may be pumping star-forming material into the dwarf system. "[The luminous bubble] is a short-lived phase in the life of the cluster," she says. "We are lucky that NGC 5253 is at the right place and the right time for us to detect this extraordinary windblown bubble."

–GOVERT SCHILLING

Govert Schilling is an astronomy writer in Utrecht, the Netherlands.

CREDITS: (LEFT TO RIGHT) J. TURNER, RADIO/IR IMAGE; D. CALZETTI AND THE SPACE TELESCOPE SCIENCE INSTITUTE, OPTICAL IMAGE; NOAA



Fireball. One star-filled bubble (false-color red blip) in NGC 5253 radiates 25% of the dwarf galaxy's energy.

CANCER RESEARCH

Why Some Leukemia Cells Resist STI-571

The antileukemia drug known as Gleevec or STI-571 has been heralded as the vanguard of a new generation of cancer chemotherapy agents. Most current cancer drugs were discovered by randomly screening thousands of chemicals to see if any kill cancer cells. But STI-571—which is remarkably effective in treating chronic myeloid leukemia (CML)—was deliberately designed to counteract a specific biochemical change that makes cells cancerous. Yet STI-571 shares an unfortunate characteristic with conventional cancer drugs: Patients with advanced disease often relapse; their tumor cells become resistant and eventually grow out of control. Results published online by *Science* on 21 June (www.sciencexpress.org) now explain why, and perhaps point the way to improved therapies.

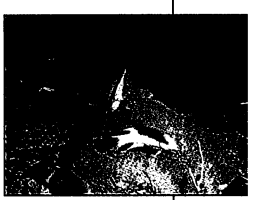
STI-571 works by inhibiting an enzyme that fuels cancer cell growth in CML—a kinase enzyme produced by the *BCR-ABL* oncogene. Almost all patients treated in the early stages of CML respond, and some have been in remission for more than 2 years. But the drug has been less effective in patients who are in an advanced phase of the disease called "blast crisis." These individuals sometimes go into remission on the drug—which almost never happens with older treatments—but 80% relapse in less than a year. "As soon as we saw that, it was obvious that the mechanism of relapse would be interesting," recalls Charles Sawyers of the University of California School of Medicine in Los Angeles, a member of the team that performed the clinical trials of STI-571 in CML patients.

To pin down that mechanism, Sawyers and his colleagues first assayed the level of Bcr-Abl kinase activity in tumor cells from 11 patients who had relapsed. They found that it came back in every patient. This was

ScienceScope

Going to Sea A prominent undersea explorer, a retired admiral, and a former top fisheries regulator are among the 16 people that President George W. Bush named last week to a new blue-ribbon Commission on Ocean Policy.

Congress established the government commission last year after lawmakers concluded that U.S. marine policy—on issues ranging from fisheries conservation to sea-lane security—needed a fresh look. They hope the new commission, whose members were chosen by Bush and the leaders of the House and Senate, will follow in the footsteps of a similar 1960s panel that catalyzed a host of marine research and legislative initiatives.



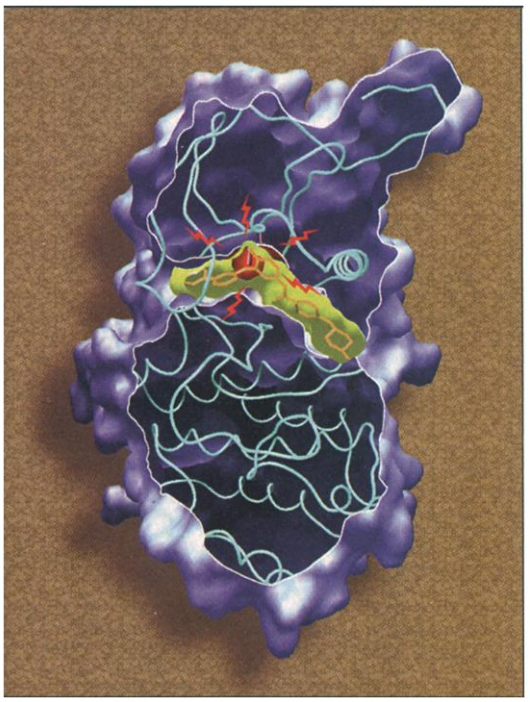
Among those chosen to serve are Robert Ballard, the undersea search wizard who has tracked down the *Titanic* and other sunken treasures; retired Admiral James Watkins, a longtime advocate of marine research; and fisheries scientist Andrew Rosenberg, a University of New Hampshire dean who until recently led the National Marine Fisheries Service. They and the other panel members are expected to meet for the first time within a couple of months, but a final report is at least 18 months away.

Swiss Stem Cells Frozen Switzerland's main researcher funder, the Schweizerische Nationalfonds (SNF), has indefinitely delayed a bid to import human embryonic stem (ES) cells for research. The SNF last week told two Geneva University researchers that—despite a favorable scientific evaluation and positive recommendations from a legal expert and two ethics panels—it will not act on their 15-month-old request until a national bioethics panel debates the issue.

The two researchers—Marisa Jaconi and Karl-Heinz Krause of the university's Louis Jeantet Laboratory for the Biology of Aging—told *Science* that they were pleased that their grant application, the nation's first to request the import of ES cells, had sparked public debate. But they worried that SNF's decision to ignore the positive reviews would "nurture irrational fears" and "unnecessarily" delay research.

SNF officials, however, said they did not want to preempt "the political discussion about this project's ethical and legal aspects." The bioethics panel is expected to take up the issue later this year.

Contributors: Robert F. Service, Charles Whipple, David Malakoff, Robert Koenig



Distorted. Replacement of threonine with isoleucine (red) in the Bcr-Abl kinase active site binding of STI-571 (orange).

a surprise, says Brian Druker of Oregon Health Sciences University in Portland, who's also involved in the clinical trials but is not a co-author on the resistance paper. Because cells in blast crisis are supposed to be highly genetically unstable, Druker says he expected that a mutation in some other gene might cause the relapse, but "[Sawyers] has shown that it's reactivation of *BCR-ABL*." This is encouraging, Druker adds, because it means that targeting the Bcr-Abl kinase or the proteins it interacts with is still a promising strategy for combating the cancer.

Other work by the Sawyers team revealed the causes of the kinase reactivation. The researchers did not have enough DNA from two of the patients to analyze, but they found that in three of the remaining nine, the *BCR-ABL* gene was amplified: The extra copies of the gene overwhelmed the drug by producing more enzyme than it could handle. In the other six, the cause was a point mutation that changed a single amino acid in the enzyme's active site: A threonine was replaced by an isoleucine. "To me what's amazing is that it's exactly the same mutation in everybody," Sawyers says.

An x-ray crystallography analysis of an STI-571 variant bound to the Bcr-Abl active site, which was performed last year by John Kuriyan's group at Rockefeller University in New York City, shows that the threonine that was replaced in these patients is important for binding the drug (*Science*, 15 September 2000, pp. 1857 and 1938). Apparently, the mutation hinders STI-571 binding to Bcr-Abl, but it doesn't knock out the kinase activity. In fact, Sawyers suggests, that may be why they found only one point mutation; the enzyme may not be able to tolerate other changes without losing the kinase activity that drives tumor cell growth.

Now that the cause of STI-571 resistance is known in at least some patients, the next step is to try to get around it—a step that might also turn out to be necessary for patients with early CML. It's too early to tell whether the drug will eventually lose its effectiveness for them as well, but Druker worries that the fate of the advanced patients "could be a harbinger of relapse in our other patients."

Possibilities for future treatments include designing additional kinase inhibitors that would be given along with STI-571, because the enzyme should be less able to become resistant to all the drugs at once. Another is to look for alternative targets for drugs that could also be given in combination with STI-571. Like most successful designs, STI-571 is likely to spark a host of refinements.

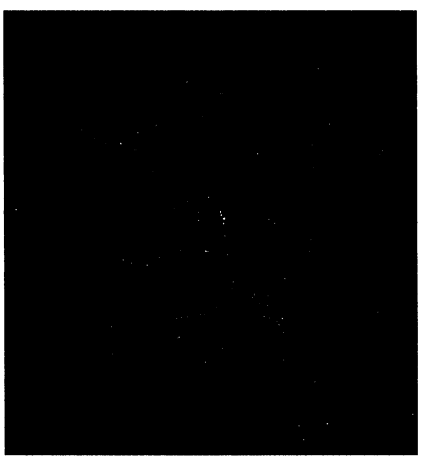
–JEAN MARX

CREDITS: (TOP TO BOTTOM) LORE LEIGHTON/ROCKEFELLER UNIVERSITY; M. GALARRETA AND S. HESTRIN/STANFORD UNIVERSITY

NEUROSCIENCE

Synchronizing the Brain's Signals

Sometimes neurons get so excited that they fire in harmony. This synchronized firing has long excited neuroscientists, but they aren't sure what it means. Some have suggested that it allows the brain to perform sophisticated computations, such as tying together various aspects of an experience that are distributed in many different areas of the brain. But "there are still a lot of holes" in such theories, says Barry Connors of Brown University in Providence. For starters: How do neurons pick up on the synchrony and pass along the precisely timed message?



Feel the beat. Interconnected FS cells (in red and green) favor synchronized signals.

Now, Mario Galarreta and Shaul Hestrin of Stanford University may have provided a partial answer to these questions. On page 2295, they report results suggesting that networks of fast-spiking (FS) cells, a type of inhibitory neuron, could play a central role in detecting and fostering synchrony in the cortex, the large outer region of the brain that processes everything from complicated images to math problems. The study demonstrates that "if you are a neuron," says Daniel Barth of the University of Colorado, Boulder, "it is not just what you have to say that counts, it is exactly when you say it."

Galarreta and Hestrin set out to test just how precisely FS cells can register an incoming signal. They first teased pairs of cells, each consisting of one FS cell and one pyramidal cell, an excitatory neuron that commonly connects with FS cells, from slices of rat cortex. When they then stimulated the pyramidal cell and measured how long it took for the FS cell to respond, they found that it fired within 1 to 2 milliseconds—even faster than they expected.

Because the FS cells fire so quickly, the researchers suspected they might be capable of noticing—and responding to—precisely timed signals from several other neurons at once. Evidence that that might happen came when the researchers tested two interconnected FS cells and found that the cells fired best if stimulated by two signals, one to each cell, that were separated by less than 1 millisecond. But if the two inputs were 5 milliseconds apart, the cells were even less likely to fire than if only one signal had arrived.

In addition to their speedy response times, FS cells have other properties that might allow them to maintain and pass along a synchronized message. Not only do they exchange messages via the chemical neurotransmitter GABA, they're also more directly connected by what's called an electrical synapse, formed by the close juxtaposition of segments of the FS cell membranes. Thus, when one FS cell fires, a shadow of that burst quickly passes through the electrical synapse. This functionally immediate echo might allow a network of FS cells to pick up on a wide spatial distribution of synchronized signals.

The new study "offers a system that's exquisitely sensitive to timing," says Connors, and therefore it's "plausible" that networks of FS cells could detect and pass along synchronized signals. But, he cautions, many tantalizing questions remain. He'd like to know, for instance, whether the electrical synapses or the GABA-mediated connections make the network of two FS cells sensitive to the timing of incoming signals. And even more importantly, no one yet knows if the rest of the brain is paying attention to the precisely orchestrated performance.

–LAURA HELMUTH