number of phalanges—four—and the overall shape of a ring finger. "That really told us it's the interdigital regions that lay down digit identity," says Dahn. It also suggested that interdigital signals are transmitted "downstream" toward the thumb: That's why the digit became a ring finger and not a pinkie.

The next step was to probe how the webbing gives these marching orders. For years scientists have known that interdigital cells churn out bone morphogenetic proteins (BMPs), a family of signaling molecules crucial to the proper development of many tissues in organisms from fruit flies to humans. BMPs are also known to influence structural identity: A team led by Paul Sharpe at Guy's Hospital in London recently demonstrated that altering BMP levels in the lower jawbone of mice results in molars sprouting where incisors should be. Following this lead, when Dahn and Fallon implanted tiny beads in chick feet that slowly released a BMP inhibitor into the webbing, downstream digits always developed fewer segments than expected. Conversely, a BMP-boosting protein increased the segment number downstream. "The stronger the BMP signal, the more phalanges," Dahn says.

He and Fallon suggest that the BMP signal from the chick interdigital regions rises stepwise in strength from thumb to pinkie, programming an increasing number of digit segments along the way. Although "there's no evidence yet for a gradient of BMP signaling," says developmental biologist Gail Martin of the University of California, San Francisco, she says the duo has proposed an extremely promising model that may well explain how digit identity is assigned.

–MICHAEL HAGMANN

ASTRONOMY

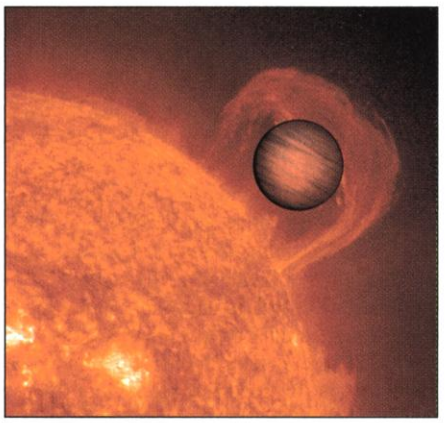
Brown Dwarf's Flare Opens X-ray Eyes

When the Chandra X-ray Observatory pointed its snout at a failed star 16 light-years away, astronomers expected it to see little sign of activity. Instead, the orbiting telescope got smacked in the eye by an x-ray flare—and astrophysicists are still trying to explain why.

The source of the flare, a brown dwarf called LP 944-20, is a stellar underachiever. When it formed, about 500 million years ago, there wasn't enough hydrogen in the area to start nuclear fusion at its core. As it collapsed under its own gravity, it warmed up slightly, but since then it has been cooling and fading.

So when Gibor Basri, an astrophysicist at the University of California, Berkeley, and colleagues pointed Chandra at the dwarf, they expected little in the way of high-energy light. "We wanted to put a new upper limit on the x-ray flux from brown dwarfs," says Basri. "According to what happens at low temperatures to stellar activity, we expected to see nothing."

For the first 9 hours of Chandra's 13-hour run, they saw exactly that. Then the observatory's x-ray counter started ticking: The brown dwarf was flaring. "It was quite exciting," says Thomas Fleming, an astronomer at the University of Arizona's Lowell Observatory in Flagstaff. "It's a fly in the ointment."



Sunstroke. Though not active stars, brown dwarfs can emit bursts resembling solar flares.

The problem posed by LP 944-20's sudden outburst is that in general, x-ray flares go hand in hand with other powerful x-ray activity. Both arise because stars are huge dynamos that create magnetic fields. A rapidly spinning star stretches and twists the field lines. The greater the kneading, the fiercer the blast of x-rays from the star's corona, its halo of wispy, million-degree plasma. Sometimes the magnetic field lines get so tangled that they snap and reconnect, causing an explosion, or flare.

Our sun, which spins on its axis roughly once a month, is constantly belching flares and glowing with x-rays. Brown dwarfs, however, can spin much faster; LP 944-20, for example, rotates once every 5 hours. If brown dwarfs had sizable magnetic fields, astronomers concluded, then they would have hot coronas and powerful x-ray emissions, too. But nobody had seen much x-ray activity; therefore, brown dwarfs had to have weak magnetic fields.

The first 9 hours of the Chandra observations backed this theory up, as Chandra detected almost no x-ray activity from the dwarf. But the flare threw a wrench in the works. "The flare tells us that magnetic fields are still there," says Basri. So why no sign of a corona? "It's quite curious that there are only flares and no hot plasma at all," Fleming says. "We have to find a reason or an explanation."

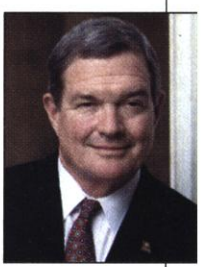
One possibility is that the outer atmosphere of the brown dwarf consists of electrically neutral atoms; deeper inside, the atmosphere contains many charged ions. The neutral atoms wouldn't knead the magnetic

CREDIT: (TOP) SOHO/NASA (SUN), CXC/K. KOWAL (BROWN DWARF)

ScienceScope

Czech Rebound After enduring a decade of bleak postcommunist science budgets, Czech scientists are celebrating a bigger budget and a new program. The government this year gave science a 20% boost to $300 million, fulfilling an earlier promise to raise R&D's piece of the budget pie from 0.5% of GDP in 1999 to 0.6% in 2000 toward a goal of 0.7% by 2002. Besides fulfilling the country's contributions to the European Framework 5 research program, the extra money will endow a new 5-year program to strengthen research groups within top institutes. Starting this month, 33 competitively chosen centers studying everything from humanities to genetics will get grants for equipment, overhead, and salaries for postdocs and young scientists. Each center will receive, on average, $3 million for 5 years. And to bolster university-based science, each must recruit an academic partner. "We're trying to improve the quality of research," says Josef Syka, vice chair of the government's Research and Development Council.

Double Trouble Thirteen senators have so far thrown their weight behind an effort to double the National Science Foundation's (NSF's) budget to $8 billion by 2006. In a 12 July letter to Senate leaders Trent Lott (R–LA) and Tom Daschle (D–SD), the lawmakers touted investments in R&D and education as "the building blocks of the new economy" and noted that Congress has already put the budget of the National Institutes of Health on a doubling path. "It is now time to launch a parallel effort" for NSF, concluded Senators Kit Bond (R–MO, above) and Barbara Mikulski (D–MD), the letter's lead authors and senior members of the appropriations subcommittee that funds NSF.



Science lobbyists say the letter should revive a bid to double the NSF budget, currently bogged down in politics (*Science*, 7 July, p. 31). "It signals that the idea is being taken seriously," adds a Senate appropriations aide. But he notes that House lawmakers have already severely trimmed the Administration's $675 million requested increase for 2001, a major step toward doubling. The question now, he says, is whether the Senate "can muster the votes to turn things around."

Contributors: David Malakoff, Richard Stone, Jocelyn Kaiser

field lines very strongly. "The atmosphere is still roiling, but the field lines don't feel that any more. That explains the lack of activity," Basri says. Deeper inside the star, however, the whirling ions might give rise to buried flares. "You wouldn't normally see that, but if you make a big enough flare down there, it can ionize material up to the surface" so that the flare breaks free, Basri explains.

"This is a really interesting observation," says Fleming, noting that understanding the coronas of small protostars might help scientists understand how solar systems are born. "One of the biggest questions in how planets form is the coronal activity of stars," he says. "How active stars like this are determines what kind of planets form."

–CHARLES SEIFE

MOLECULAR BIOLOGY

Targeting Intron Insertion Into DNA

With imagination, even junk can be put to good use. Take introns, bits of genetic debris that litter the DNA and interrupt the coding sequences of many genes. Introns must be removed from the RNA copies of the genes before the RNAs can be translated into proteins. Some introns, however, can insert themselves into nucleic acid. In work reported on page 452, a team led by molecular biologist Alan Lambowitz of the University of Texas, Austin, has now found a way to coax these introns to hop into the exact sequences where the researchers want them.

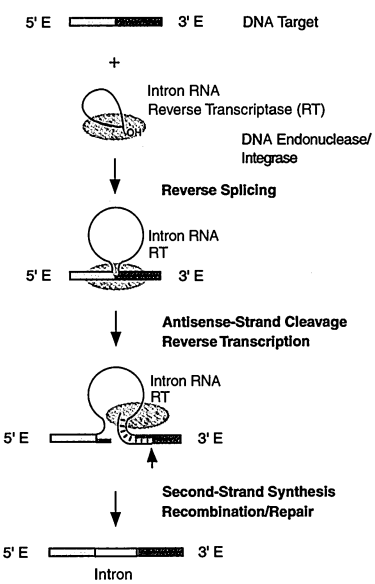
The method could enhance all sorts of genetic manipulations, from studying basic gene function to combating viral infections to delivering genes for gene therapy. "It holds promise for making permanent modifications to the genome," says Anna Marie Pyle, a biochemist at Columbia University in New York City.

The current experiments stem from earlier ones in which Lambowitz and colleagues found that so-called group II introns—which occur in bacteria and in organelles of plants, yeast, and fungi—have a surprising talent. These introns excise themselves as usual from the RNAs in which they initially reside. But then they incorporate themselves into double-stranded DNA and, with the help of a protein they encode plus host cell machinery, they generate a double-stranded DNA version of themselves in their new home. The Lambowitz team showed that the intron uses a stretch of about 14 nucleotides to recognize the appropriate insertion site.

That observation suggested that the researchers could redirect the intron by changing the recognition sequence so that it is complementary to—and will thus bind—a sequence in the target gene. "When we worked out the mechanism, we realized that we could control the site at which the introns were inserting," Lambowitz says. Early efforts to do this worked inefficiently, however, presumably because the researchers didn't fully understand the targeting rules. So in the current work, they devised a way to let cells identify those introns that insert where the researchers choose.

As DNA targets, Lambowitz and his colleagues picked genes from the AIDS virus HIV and also a cellular gene called *CCR5*, which encodes a protein that HIV uses to infect cells. To tell when an intron had inserted, the researchers attached the target genes to a tetracycline-resistance gene missing its activation sequence and then put these constructs separately into *Escherichia coli* bacteria.

Graduate student Huatao Guo, meanwhile, engineered a collection of introns with randomized sequences in the region known to be important for target site recognition. These introns also contained a sequence that would trigger the expression of the tetracycline-resistance gene if they inserted next to it. Thus, the researchers could put the collection of introns into a population of bacterial cells containing the target genes and identify those in which the intron hit the target by adding tetracycline to the culture media. Only those cells with the proper insertions would grow. The strategy worked. Lambowitz and his colleagues isolated 13 introns that inserted at different positions in the HIV and *CCR5* genes. "The general scheme should apply to any gene" in any organism, Lambowitz says.



Splicing in. A group II intron enters DNA by reversing the process that cut it out of messenger RNA.

Group II introns have never been found in mammals, however, so the researchers wanted to test whether their engineered introns could function in human cells. To deliver the modified introns and their target genes to mammalian cells in culture, collaborator Bruce Sullenger, a molecular biologist at Duke University Medical Center in Durham, North Carolina, and his colleagues first packaged them separately in tiny membranous sacs called liposomes, which merge with the cells. The researchers then mixed mammalian cells with liposomes containing the target genes, either *CCR5* or an HIV gene, and with liposomes containing the matching intron. Subsequent polymerase chain reaction analysis of DNA isolated from the cells revealed that the introns had successfully integrated into the HIV and *CCR5* genes.

Although this result suggests that the reaction can occur in mammalian cells, "the evidence isn't quite bulletproof," says Jef Boeke, a molecular biologist at Johns Hopkins University School of Medicine in Baltimore. He notes that the initial step in intron integration, the insertion of the RNA intron into the gene, could have occurred outside the cell in liposomes that fused with each other before they fused with the cell. Consequently, he notes, the researchers still have to prove that this key step can occur with genes inside cells, especially those in the chromosomes.

Sullenger responds that the conditions under which the experiments were performed make it unlikely that the liposomes fused before entering the cells. He and Lambowitz are eager to resolve the issue by targeting introns directly to one of the cell's own genes in its natural chromosomal location. If that works efficiently and specifically, the method could boost laboratory studies of gene function tremendously.

Currently, precise gene targeting can be done in only one mammal, the mouse, and even there, says Andy McMahon, a developmental geneticist at Harvard University, "it's quite inefficient. Any approach that facilitated the process would be beneficial." Lambowitz and Sullenger are also testing whether the intron insertion method might combat HIV. For example, it might be possible to disable the latent virus in the human genome and prevent it from reactivating and spreading.

In other work, Lambowitz and others have shown that group II introns can carry foreign genes to new locations. This capability raises the possibility of using them to deliver therapeutic genes to particular sites in the genome, thereby avoiding the creation of deleterious mutations, say by inactivating tumor suppressor genes. "The gene-delivery vectors we have now either go everywhere randomly or they stay out of the genome altogether," says Haig Kazazian, a human geneticist at the University of Pennsylvania School of Medicine in Philadelphia. "Here we've got the possibility of targeting specific DNA sites." Indeed, it looks as though introns may turn out to be anything but junk.

–EVELYN STRAUSS

CREDIT: H. GUO