CD47 prevents the RBC destruction.

Other experiments pointed to macrophages as the purveyors of the destruction. For example, the CD47-deficient RBCs were quickly destroyed when they were transfused into mice that lacked functional B and T cells, indicating that those cells were not involved. In contrast, removing the spleen, the organ where old and faulty RBCs are usually disposed of by macrophages, prevented RBCs from being eliminated. Evidence confirming that macrophages use SIRPα to recognize CD47 came when the researchers added an antibody against SIRPα to a mixture of macrophages and RBCs. Now, the "blindfolded" immune cells eliminated even normal CD47-bearing RBCs.

Taken together, Lindberg says, these results suggest that "CD47 is a safeguard against macrophages going off too easily. If CD47 is present [on a target cell], the macrophage leaves it alone, but if it's absent the macrophage goes: 'Let's get cracking!'"

To Colonna, CD47's new job makes perfect sense. "RBCs don't express MHC molecules, so they need something else to mark them as self," he says. Lindberg adds that his findings might also explain the anemia seen in individuals who fail to express Rh blood markers on their RBCs. These patients also have a drastically reduced CD47 density on their RBC surfaces, and this may make them more prone to elimination by macrophages, speculates Lindberg.

Still to be determined, however, is whether changes in CD47 concentrations on cells play a role in other pathological conditions. There are hints that they might. For example, ovarian cancer cells express CD47 at a much higher than normal level. "This may signal 'I'm self, don't kill me,'" Lindberg says.

Another open question centers on the role of SIRPα in other tissues. Unlike other inhibitory immune receptors, SIRPα is found on brain cells, for instance. "I'm very intrigued by that," says UCSF's Lanier. "There may be an even broader context in which we need to think about these inhibitory receptors. I guess now the neuroscience people need to get busy." **–MICHAEL HAGMANN**

ALTERNATIVE MEDICINE

Herbal Product Linked to Cancer

A Chinese herb that damaged the kidneys of dozens of Belgian dieters in the 1990s appears to pack a vicious second punch—cancer and precancerous lesions, according to a report in the 8 June issue of *The New England Journal of Medicine*. These findings draw one of the strongest links yet between use of a herbal product and cancer and, critics argue, serve as a grim warning that dietary supplements need more regulation.

The unfortunate subjects of this study are a subset of some 10,000 Belgian dieters, who between 1990 and 1992 took a mixture of Chinese herbs and Western drugs prescribed by weight-loss clinics. After dozens of dieters developed symptoms of kidney failure, investigators discovered that Belgian pharmacists had been using mislabeled Chinese herbs to concoct the diet pills. Instead of *Stephania tetrandra*, pharmacists had packed the pills with derivatives of the herb *Aristolochia fangchi*, known to damage kidneys and to cause cancer in animals. At least 70 people experienced complete kidney failure, and some 50 more suffered kidney damage severe enough to require treatment.

The first urinary tract cancers were found among these patients in 1994. To deter onset of the disease in others, doctors at Erasme Hospital in Brussels counseled patients whose kidneys and ureters had stopped functioning to consider surgical removal of the organs. Thirty-nine people opted for the operation over the past several years. When a team of researchers—coordinated by kidney specialist Joélle Nortier—inspected the excised tissues, they were startled to discover that cancer had already developed in 18 patients, and precancerous lesions (dysplasia) were present in 19 others. Prescription records confirmed that patients who had taken the highest cumulative doses of *Aristolochia* were most likely to have cancer. As further evidence that *Aristolochia* was to blame, the team found in all 39 patients evidence that *Aristolochia* had bound to DNA, a process that could trigger mutations.

Beautiful but deadly. Plants in the *Aristolochia* genus, used in Chinese herbal preparations, can cause kidney damage and perhaps cancer.

Belgium banned the import of *Aristolochia* in 1992. But there's little to prevent a similar herbal disaster in the United States, asserts David Kessler, dean of Yale University School of Medicine and former commissioner of the Food and Drug Administration (FDA)—especially because he was just able to purchase *Aristolochia* in capsule form, he writes in an accompanying editorial. Unlike food additives and drugs, which are subjected to strict premarket tests for safety and effectiveness, products labeled "dietary supplement" may enter the market untested, thanks to the 1994 Dietary Supplement Act. In effect, FDA cannot restrict the use of supplements unless substantial harm has been proven, Kessler says. "You shouldn't have to wait for harm to occur before you do a systematic safety review," Kessler told *Science*. "It's time to have a premarket safety system."

Others argue that FDA's hands are not tied as tightly as Kessler implies. Varro Tyler, a retired dean of the School of Pharmacy at Purdue University in West Lafayette, Indiana, considers company-sponsored premarket testing impractical—the manufacturers simply can't afford it. Instead, he backs a recommendation by a 1997 presidential commission that called for FDA to convene an expert committee to review the wealth of information that already exists on botanicals and then inform consumers and manufacturers about unsafe preparations. "No company in its right mind" would market preparations deemed unsafe, he says. "That would be signing their own death warrant in terms of legal actions."

Last month, the FDA distributed warnings to health professionals and the supplements industry about the dangers of *Aristolochia*. In a few weeks, the agency plans to block the herb's entry into the United States. The action is long overdue, says Norman Farnsworth, director of the Center for Dietary Supplements Research on Botanicals at the University of Illinois, Chicago. The dangers of *Aristolochia* are so well known, he says, that Germany banned it in 1981 and the World Health Organization issued a warning on the herb in 1982. If the FDA "had been doing its job," he says, "they would have banned this stuff 10 to 15 years ago."

–LIESE GREENSFELDER

Liese Greensfelder is a writer in Nevada County, California.

ASTROPHYSICS

Galaxies, Black Holes Shared Their Youths

ROCHESTER, NEW YORK—The origin of massive black holes and the galaxies that surround them is a chicken-and-egg conundrum. In one model of galaxy formation, whopping black holes arose early in the history of the universe. Then, gas spiraling into

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each hole powered quasars, while great whorls of more distant gas gradually collapsed inward to form the galaxy's stars. An opposing hypothesis holds that galaxies coalesced first, and then black holes slowly grew at their hearts. A popular third model, which astronomer Virginia Trimble of the University of California (UC), Irvine, calls the "potato-salad model," maintains that galaxies and their black holes matured simultaneously. "Of the three possibilities, this one always seemed the most intuitively obvious," says Trimble.

The best census to date of massive black holes justifies that intuition: Researchers reported here last week at a meeting of the American Astronomical Society that giant black holes and their host galaxies appear to be cosmic siblings that grew up at the same time. That conclusion rests on a newly unveiled relationship between the masses of black holes and how tightly gravity binds together the billions of stars around them.

A team of 15 astronomers used a spectrograph aboard the Hubble Space Telescope to peer at the centers of galaxies within 120 million light-years of the Milky Way. The team found eight new black holes and included six more new ones recently discovered by other scientists in its study, bringing the number of well-identified massive black holes to 33. That's enough for a good statistical analysis, says team member Richard Green, director of Kitt Peak National Observatory in Tucson, Arizona. "Our knowledge about black holes has moved beyond individual detections to a real look at the population," he says.

The spectrograph revealed the rapid orbital motions of stars in the core of each galaxy, providing a firm estimate of the mass of the hidden black hole. Those masses ranged from 3 million to 2 billion times the mass of our sun. Then the team went beyond previous analyses by examining how stars move throughout each galaxy's central "bulge," a spherical cloud containing billions of suns. Those stars are too distant to feel the gravitational pull of the black hole, says astronomer Karl Gebhardt of UC Santa Cruz. Instead, their orbits through space reveal the mass and compactness of the overall bulge. That's a measure of how tightly the galaxy's parent gas cloud collapsed in on itself in the young universe.

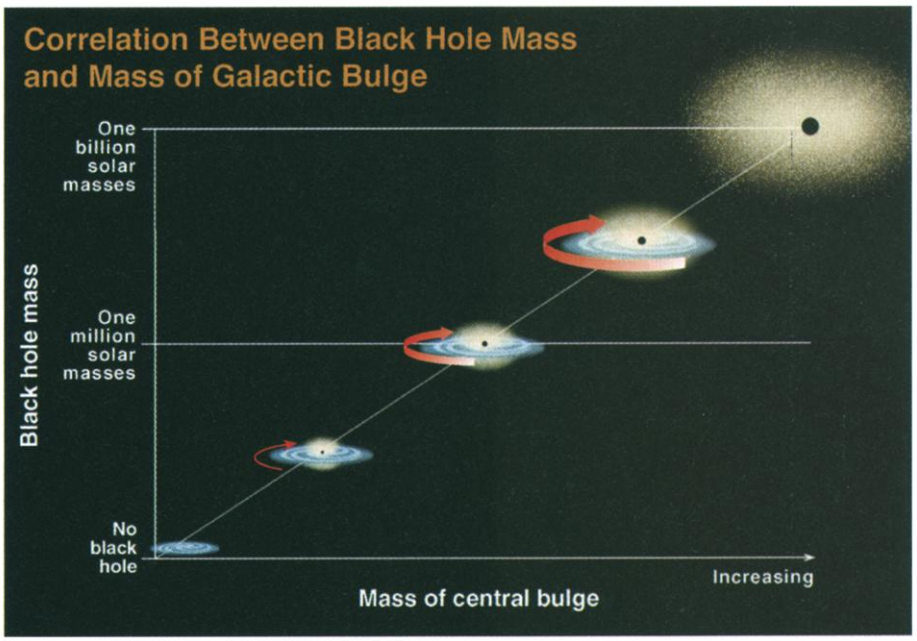
The team was surprised to find a near-perfect correlation between the orbital speeds of these far-flung stars in the galactic bulges and the masses of the black holes in the middle. The more massive the hole, the faster the stars throughout the bulge moved. "Normally, we don't see such a tight relationship," Gebhardt says. "It's a slap in the face that something fundamental is going on."

That something, says astronomer John Kormendy of the University of Texas, Austin, almost certainly is an evolutionary partnership between galactic bulges and massive black holes. "If black holes are unusually massive whenever galaxies are unusually collapsed, then the black hole masses must be determined by the collapse process," Kormendy says. "The major events that made the bulges and the black holes were the same events." An alternative explanation for the partnership between bulges and black holes—that massive black holes arose first and then attracted massive bulges around them—is much less palatable, he notes. Baby black holes of such size would ignite powerful quasars, and their intense radiation pressures would drive apart the cocoons of gas around them rather than drawing them in tightly.

Other astronomers aren't quite ready to discard alternative scenarios. "The new correlation is impressive," says Andrew Wilson of the University of Maryland, College Park. "But I think we have a long way to go before we understand the symbiosis between black holes and galactic bulges." Trimble sounds another caution: "It's difficult to know whether they have studied a really representative sample of galaxies." If Hubble takes a broader census of black holes in galaxies chosen at random and finds a similar pattern, she says, more astronomers will find the case convincing.

The study raises another puzzle: Each black hole is about 1/500th as massive as the bulge of stars it inhabits. No one knows why that figure is so consistent from one galaxy to the next, although Kormendy views it as another indication that the growths of galaxies and black holes are intimately linked. Outpourings of energy from quasars may stall torrents of gas from feeding black holes when they reach a particular size in relation to their host galaxies, says astrophysicist David Merritt of Rutgers University in Piscataway, New Jersey. However, no models or computer simulations have yet shown how nature arrives at that magical ratio.

–ROBERT IRION



In tandem. Orbital speeds of stars (curved arrows) suggest that black holes and galaxies grow up together.

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OCEANOGRAPHY

Missing Mixing Found In the Deep Sea

Climate modelers thought they could get away with a simple-minded ocean. In their simulations of how the sea's ponderous flows of water and heat affect climate, including future greenhouse warming, they assumed that something—they were vague as to what—evenly stirred the world ocean from top to bottom around the globe. But oceanographers gauging the tides of the world's seas from a satellite perch have found intense patches of tidally driven mixing deep within the open ocean. Once modelers include these patches, they should see some changes in model predictions of global warming. Climate prediction models "have a long way to go," says oceanographer Raymond Schmitt of the Woods Hole Oceanographic Institution in Massachusetts, before they match the tidal mixing of the real ocean.

The study of tides has already come a ways. "Tides are considered an old subject, a 'solved problem,' of no interest to most oceanographers," laments physical oceanographer Carl Wunsch of the Massachusetts Institute of Technology. Beginning early in the 18th century, it became obvious that the moon raises sea level by meters along the