university officials, who he suggests are trying to assuage Eli Lilly and Co., the maker of Prozac, which in recent years has given $1.5 million to CAMH.

CAMH officials have denied that their actions have any financial motive. In an April letter to Healy (available on his Web site), Goldbloom wrote that Healy's comments about "thousands of people killing themselves … because of fluoxetine [Prozac] … were incompatible with published scientific evidence and hence incompatible with … responsibility of leadership of a clinical and academic program." Jack Barchas, chair of the psychiatry department of Cornell University Medical School in New York City, says that Healy has done "superb" work on the history of psychopharmacology but that his claims about SSRIs are "not convincing."

Healy says that results from a small study of SSRIs on healthy volunteers support his arguments but that "confidentiality orders" prevent him from revealing additional data. But Barchas says publication is the only way for Healy to make a convincing case. "There's not a major journal in the field that wouldn't be delighted to receive a careful evaluation of this data," Barchas says.

–CONSTANCE HOLDEN

GENETICS

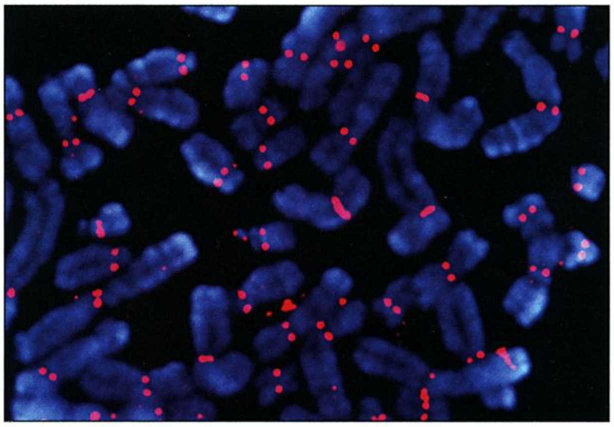
Closing In on the Centromere

The centromere is one of the genome's greatest enigmas. First noticed 120 years ago under a microscope as the cinched waists of the chromosomes, these sections of DNA have until now defied the best efforts of cell biologists and geneticists to understand them. Yet the centromere is critical for the proper sorting of chromosomes during cell division; if it doesn't work correctly, the result can be cancer, defects in development, or similar misfortunes.

Now, on page 109, geneticists from Case Western Reserve University and University Hospitals of Cleveland Research Institute in Ohio provide the clearest look yet at a human centromere. Huntington Willard and his colleagues have demonstrated that a 3-million-base stretch of DNA embedded in what many have called the centromere is really all it takes to make a functional centromere. To their surprise, the nature of this core DNA indicates that, rather than being highly conserved, the centromere has changed significantly during primate evolution. "It's a fundamental study using an elegant genomics and genetics approach," comments Peter Warburton, a molecular biologist at Mount Sinai School of Medicine in New York City.

For decades, researchers have known that centromeres and their associated proteins are anchor points for the spindle of fibers that separates paired chromosomes, causing the two to move to opposite sides of the cell as it divides. They have observed under the microscope that when each chromosome replicates in mitosis, the two resulting chromatids are linked at the centromere until the spindle pulls them apart.

Twenty years ago, Willard suggested that repetitive DNA—short patterns of bases repeated over and over that are characteristic of the centromere in most higher organisms—could be important to the centromere's function. "I caught a fair bit of flak for suggesting that repetitive DNA had a role," he recalls.



Centromere revealed. The "waist" of paired chromosomes, the centromeres can be located by the yellow stain revealing centromeric proteins in both native chromosomes (blue) and artificial ones (red). The X chromosomes' centromeres are red dots.

About that same time, biologists sequencing budding yeast determined that its centromere was a small stretch of nonrepetitive DNA, just 125 bases long. This new finding suggested that the repetitive DNA, called heterochromatin, was not the actual centromere but rather flanked it.

But when researchers later tried to determine the structure of the centromere in a range of organisms, from humans to flies, they hit a brick wall. Their high-powered sequencing machines stopped dead when they reached the heterochromatin. And in those rare instances when parts of that DNA could be sequenced, researchers were stymied in attempts to reassemble those parts into a whole centromere.

Willard persisted, however, urging grad student Mary Schueler to take a close look at the centromeric regions in human X chromosomes. She and her colleagues also focused on centromeres from patients with Turner syndrome, who often have truncated sex chromosomes. In some of these patients, the X chromosome was chopped off right where one of the chromosome's two "arms," the P arm, meets the heterochromatin flanking the centromere. Using these as a starting point, Schueler began working toward the center of the centromere, mapping the repetitive sequences along the way in anticipation of someday sequencing them.

Called alpha satellite repeats, each "repeat" in this 450,000-base region was about 171 bases long and was almost—but not exactly—identical to the other repeats. As Schueler approached the center of the centromeric region, she found that the DNA sequence changed to what is known as a higher order array. Not only did this stretch contain recurring sets of 171-base repeats—the hallmark of alpha satellite DNA—but each set had a dozen repeats and then the entire set was repeated again.

When Willard and his colleagues deleted the flanking DNA, they found that the higher order array, some 3 million bases long, could still function in cell division, suggesting that it made up the true functional centromere. The researchers put that suggestion to the test by inserting the higher order array into artificial chromosomes; it acted like a normal centromere during cell division, vindicating Willard's earlier hunch. "They showed that the sequence they were looking at was competent to be a centromere," says Steve Henikoff, a geneticist at the Fred Hutchinson Cancer Research Center in Seattle.

Because the centromeres have been so difficult to tackle, they remain as gaps in most completed sequences, including that of the human genome. But this work "is a major boost for convincing people to attack difficult [chromosome] regions," says Daphne Preuss, another persistent geneticist at the University of Chicago who has been unraveling the centromere of the plant *Arabidopsis* (*Science*, 15 December 2000, p. 2057). To date, Schueler and her colleagues have sequenced just a bit of the centromeric region closest to the P arm of the X chromosome, but they plan to forge ahead. "It's been assumed that these regions are too difficult," Schueler explains. "But that is not the case. You can map and sequence them."

Already the data hint at the history of the centromere on the human X chromosome. Based on the sequencing of the centromere completed to date, Willard's team concludes that the higher order array contains far fewer sequence variations—with the sets of repeats being more than 98% identical—than the flanking sequences. This suggests that the core is much younger than the flanking re-

CREDIT: M. K. RUDD/CASE WESTERN RESERVE UNIVERSITY

gions and has had less time to accumulate random variations. Another piece of evidence is that the core also harbors just one type of transposon, a rogue piece of DNA that inserts itself into the genome, and this transposon is relatively young: It exists only in humans and not other primates. Because the flanking regions share additional transposons with other primates, Willard suspects that those flanking regions are the "ancestral centromere," with the modern centromere in the middle evolving after the ancestors of apes and humans diverged from lower primates.

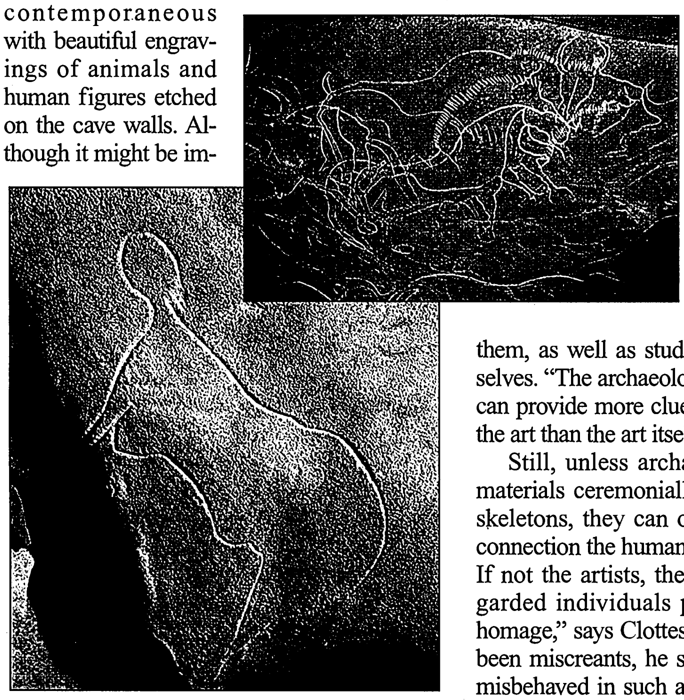
In this scenario, the higher order array replaced the ancestral sequence, leaving behind those "dead" centromeres as heterochromatin. And that, says Willard, suggests that although the centromere is functionally a highly conserved element, playing a key role in a range of organisms, its structure is a "highly fluid DNA sequence." That, in turn, suggests more surprises to come when centromeres of other organisms are unraveled.

–ELIZABETH PENNISI

CAVE ART

Stone Age Artists—or Art Lovers—Unmasked?

PARIS—Archaeologists may be on the way to solving two pivotal mysteries of prehistoric art: Who were the artists, and what was the meaning of their work? Radiocarbon dating of human remains found in the recently discovered Cussac Cave in the Dordogne Valley of southern France indicates that the bones are contemporaneous with beautiful engravings of animals and human figures etched on the cave walls. Although it might be impossible to prove that the remains were of the artists themselves, the skeletons may hold clues to who frequented the cave and why it had special significance.



Whodunit? Human remains found near these engravings in Cussac Cave may hold clues to the art's meaning.

CREDITS: CENTRE NATIONAL DE LA PRÉHISTOIRE, MINISTÈRE DE LA CULTURE ET DE LA COMMUNICATION

Fragmentary human remains have been found near cave art a few times in the past, but there has been no way of knowing that these were not art lovers, accidental visitors, or squatters from some other period. But Cussac is something special. "For the first time ever, we have … human skeletons deep in an uninhabited [decorated] cave," says French cave art expert Jean Clottes. Archaeologist Randall White of New York University agrees: No other cave "even comes close" to Cussac and its complete burials.

Cussac was discovered by a caver in September 2000, but the French government kept it secret until this July (*Science*, 20 July, p. 423). The engravings—which include fantasy animals with deformed heads and gaping mouths, and a voluptuous female profile—were provisionally dated to the Gravettian period, based on their stylistic similarity to other cave art. This would make them between 22,000 and 28,000 years old.

Ever since Cussac was found, archaeologists have been holding their breath, waiting to learn the dating results from the skeletons—four or five adults and one adolescent—found in hollows on the cave floor. Preliminary results from three bone samples analyzed by Beta Analytic, a radiocarbon lab in Miami, Florida, found that one of the samples gave a precise date of 25,120 years, plus or minus 120 years—clearly within the Gravettian period. (The other two samples did not give conclusive results.)

Archaeologists led by Norbert Aujoulat of the National Center for Prehistory in Périgueux will now begin a 3-year program to excavate the burials, including the stone tools and other artifacts found with them, as well as study the engravings themselves. "The archaeological context of cave art can provide more clues about the meaning of the art than the art itself," says Clottes.

Still, unless archaeologists find artists' materials ceremonially buried alongside the skeletons, they can only speculate on what connection the humans had to the engravings. If not the artists, they could be "highly regarded individuals put there as a kind of homage," says Clottes. They even might have been miscreants, he speculates, "people who misbehaved in such a dreadful way that they had to be put away as close to the spirits as possible, so they could not come back."

–MICHAEL BALTER

ScienceScope

A Measure of Quality Scientific groups are welcoming White House efforts to narrow new guidelines that allow the public to weigh in on whether information disbursed by agencies is up to snuff.

The "data quality" rules, which were tucked into a bill last year after lobbying by an antiregulatory group, are meant to assure that agencies disseminate accurate information (*Science*, 13 July, p. 189). But a requirement that scientific information be "substantially reproducible upon independent analysis of the underlying data" drew scores of concerned comments from the National Academy of Sciences and other academic organizations. They argued that peer review—the accepted process for identifying good science—doesn't require reproducing original results.

Last week, the protesting paid off: The Office of Management and Budget's (OMB's) revised guidance "is much improved," says George Levanthal of the Association of American Universities in Washington, D.C. OMB now says that publication in a peer-reviewed journal is "presumptively objective."

Further Fakes The Japanese amateur archaeologist who was caught planting artifacts at a site last year (*Science*, 10 November 2000, p. 1083) has admitted to more deceptions in his efforts to move back the date of the earliest human habitation of the archipelago. But archaeologists say that they will need several more months to complete their investigation of Shinichi Fujimura's work because of his questionable mental health.

Fujimura has been in a mental institution since the scandal broke and has spoken several times with a panel from the Japanese Archaeological Association. But Kunio Yajima, an archaeologist at Meiji University in Tokyo who serves on the committee, says it could only get limited details from Fujimura: "He is, in a word, sick, and our meetings were severely brief." Although the committee will release an interim report this week at a meeting in Morioka, Iwate Prefecture, its final report is not expected until next spring.

Meanwhile, other archaeologists aren't waiting. Charles Keally, an American archaeologist based at Sophia University in Tokyo, says that "the community has largely concluded that material [connected to Fujimura] will always be suspect."

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