—at least in the roundworm. On page 686, neuroscientists Oliver Hobert, Oscar Aurelio, and David Hall describe a new family of proteins that help keep the wiring of the worm's nervous system tangle free.

Scientists have spent decades teasing apart the complex signals that guide axons—the long extensions that allow neurons to communicate with distant cells—to their correct destinations and help them make the right connections. But the discovery of a separate, later-acting maintenance mechanism is "really quite surprising," says neuroscientist Joseph Culotti of the Samuel Lunenfeld Research Institute at Mount Sinai Hospital in Toronto. Developmental neuroscientist Barry Dickson of the Institute of Molecular Pathology in Vienna says the find makes sense. "You don't just have to make sure you wire up the nervous system properly in the first place, but you also have to make sure that the wires don't get tangled up as the animal grows and moves about," he notes.

Hobert and Aurelio of Columbia University and Hall of the Albert Einstein College of Medicine, both in New York City, did not set out to look for the worm's maintenance molecules. Rather, they were examining the expression patterns of unknown genes in the so-called immunoglobulin superfamily, several members of which are known for their roles in neural development. Six genes stood out in the screen. They appeared on the scene later than others—in the larvae and the adult, after the upheaval of embryonic development is complete. "They're expressed after all the excitement is over," Hobert says.

The genes, which the team dubbed the *zig* genes, are expressed in a neuron called PVT in the larval worm's ventral nerve cord. This neuron plays a central role in the nervous system's development. It has an axon that is among the first to blaze a trail through the developing worm. The axon extends the entire length of the worm's body and secretes proteins that help guide other axons to the correct place in the growing nervous system. But most developmental biologists assumed that the neuron's guidance tasks were complete once the worm reached the larval stage.

The timing of the appearance of these newfound guidance-like molecules prompted the team to question that assumption. Aurelio used a laser to kill PVT neurons in early-larval-stage worms. When he examined the animals' nervous systems 2 days after surgery, he found that in nearly a third of the treated worms, axons had wandered across the worm's midline to the wrong side of the nerve cord.

To check whether the *zig* genes keep axons in place, the team examined a strain of worms that lacks *zig-4*. In those worms, the team found, development is normal during the embryonic stage, but once the worm develops into a larva, a subset of axons wanders across the midline—resembling the aberrant axons in the surgically treated worms.

It seems the molecular restraints of the ZIG proteins might be crucial during the early larval stage, when the worms' movements might jostle the still-fragile alignment of axons: When the scientists placed larval worms lacking PVT on a substance that paralyzes them, they observed no wayward axons. Hobert isn't sure what *zig* genes do in the adult worm, but he suspects that they keep axons in place in other parts of the body.

Dickson predicts that similar maintenance molecules will turn up in other animals—perhaps even in humans. "It could be that this only applies to a few axons in the worm nerve cord that are in particular danger of being jostled about as the worm writhes along," he says. "But you can bet it is going to be a lot more general than that. If keeping the wires neat and tidy matters for a worm, it's going to matter for higher animals, too."

–GRETCHEN VOGEL

CREDIT: (TO TO BOTTOM) LESLIE E. KOSSOFF/AP; RICK KOZAK

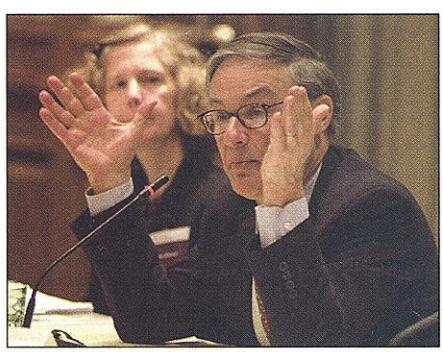
HUMAN CLONING

Report Backs Ban; Ethics Panel Debuts

Cloning and stem cells are once again on the nation's front burner after a 4-month hiatus in the aftermath of 11 September. Last week the National Academy of Sciences (NAS) released a report* calling for a legal ban on human reproductive cloning, and the president's new Council on Bioethics held its first meeting.

The academy panel, led by adult stem cell researcher Irving Weissman of Stanford University, confined itself to scientific and medical issues raised by reproductive cloning. It concluded that the high rate of abnormalities and other problems with animals cloned since Dolly the sheep was in 1997 indicate that such an effort in humans

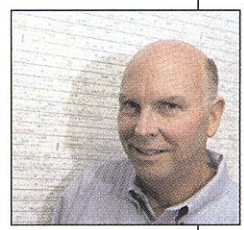
* *Scientific and Medical Aspects of Human Reproductive Cloning*, National Academies (www.nap.edu/catalog/10285.html)



Ethical choices. Chair Leon Kass holds forth at the council's first meeting.

ScienceScope

Overboard Scientist-entrepreneur J. Craig Venter (below) made another big splash this week: He abruptly quit Celera Genomics in Rockville, Maryland, the company he created less than 4 years ago with a goal of sequencing the human genome. The parent firm, Applera Corp. of Norwalk, Connecticut, issued a terse note on 22 January saying that Venter had "stepped down as president" but would "continue his affiliation" as chair of Celera's scientific advisory board. He will have no management authority, however. One visitor to Celera's corporate suite reports that Venter's photos and memorabilia have already been removed. Celera's stock dropped about 6% on the day of the announcement.



Venter could not be reached for comment. But an Applera release says that Venter intends "to spend more time fulfilling my role as Chairman of the Board of the Institute for Genomic Research (TIGR)," a nonprofit research center in Rockville founded by Venter in 1992. TIGR's president, Claire Fraser, is Venter's wife.

Applera chief executive Tony White explained in a telephone interview that Venter and other company officials concluded "just within the last week" that it was time for Venter to leave. "For several months," White explained, "we've been wrestling with the problem" of how Celera could become a "really serious drug discovery and development company." There was no falling-out with Venter, White adds: "I'm not saying I couldn't work with Craig. We made a strategic decision to pursue a business strategy, and implicit in that decision is that you've got to have the right kind of people in charge."

White says that heated discussions within Celera about the release of the company's mouse genome data had "nothing to do with" Venter's departure. There was "a discussion between Craig and a few members of our board of directors," White said, and the board approved the release.

Venter's departure marks the end of a contentious and highly competitive era in human genome sequencing, in which Venter confounded his critics by producing a draft in record time. But his departure may be a sign that the sun is setting on the reign of the gene kings.

"is dangerous and likely to fail." Weissman also said that testimony presented this summer from individuals with plans to clone humans raised serious questions about safety and monitoring (*Science*, 17 August 2001, p. 1237). Even so, the panel concluded that any ban should be revisited in 5 years because of probable research advances in related fields.

Funded by the National Academies themselves, the panel seconded an NAS study issued last fall that strongly endorsed so-called therapeutic cloning—making an embryo that can supply genetically tailored stem cells by inserting the DNA of a person's body cell into an enucleated egg. But it suggested that the procedure be labeled "nuclear transplantation to produce stem cells," rather than cloning, if the blastocyst is not to be implanted in a uterus.

One day before the panel issued its call for a "broad national dialogue" on ethical and societal aspects of a reproductive cloning ban, the president's bioethics council began a 2-day discussion on the larger issues surrounding human cloning, including therapeutic cloning. The newly appointed 18-member group includes three biologists and a clutch of doctors, lawyers, and public thinkers (www.whitehouse.gov/news/releases/2002/01/20020116-9.html).

Its chair, University of Chicago bioethicist Leon Kass, said that the group hopes to go beyond influencing public policy and stimulate a national debate about bioethics. "One feels a palpable increase in America's moral seriousness" since the terrorism attacks, Kass said in welcoming the group to Washington, D.C. He signaled a scholarly approach to the subject by leading a discussion of "The Birthmark," a story by Nathaniel Hawthorne in which a husband kills his wife while trying to make her perfect.

Calling cloning "the hot topic in bioethics circles today," Kass said that the panel "would be remiss not to try to clarify the subject and place it on the most solid moral ground. Public concern stems from the intuition that what's at stake here is what it means to be a human being."

Although council members all seemed to take a dim view of cloning for reproduction, they are clearly divided on the virtues of therapeutic cloning. For example, Michael Gazzaniga, a neuroscientist at Dartmouth College, thought harvesting cells from a blastocyst was no more problematic than harvesting an organ from a brain-dead patient. Others, including Kass himself, believe that a complete ban on all related work is needed even if the goal is only to prohibit the implantation of cloned embryos.

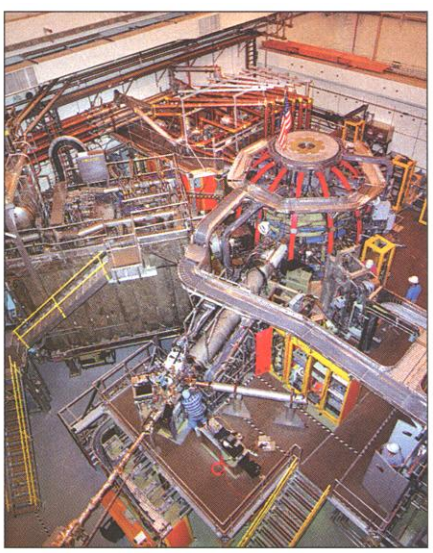
Kass warned reporters that the group plans to move with deliberate speed. The council will meet every couple of months and will convene next month to talk more about cloning. He said to look for a report, with policy guidance, by the summer.

–CONSTANCE HOLDEN AND JOCELYN KAISER

FUSION POWER

Spherical Tokamaks Are on a Roll

Results from two fusion experiments, one in the United States and one in the United Kingdom, suggest that making a reactor, or tokamak, spherical with a hole through the middle—like a cored apple—may be more efficient than the traditional doughnut shape. The two machines both managed to confine a hot plasma of hydrogen ions in the dense, calm state used by traditional machines—an important first step toward fusion. Spherical reactors "may in the end be a better bet for a fusion reactor than the conventional ... tokamak," says Geoff Cordey, a plasma physicist at the Joint European Torus (JET) in Culham, near Oxford, the world's largest conventional tokamak. Still, he cautions, it's not yet a new ball game: "It's very, very early days."



Smooth operator. Princeton's National Spherical Torus Experiment.

CREDIT: PRINCETON PLASMA PHYSICS LABORATORY

Nuclear fusion—the process that powers the stars—promises almost limitless energy with little nuclear waste. But researchers must first find a way to squeeze atomic nuclei together against their electromagnetic repulsion, close enough that pairs of them fuse into a new species of nucleus the mass of which is less than the combined starting masses. The missing mass emerges as energy. In tokamaks, heat does the squeezing: A whirling gas of hydrogen ions, or plasma, is held inside a big vacuum chamber by magnets and heated to millions of degrees by passing electrical currents through it or firing beams of atoms into it.

Doughnut-shaped tokamaks, such as JET and Princeton's Tokamak Fusion Test Reactor, have managed to achieve fusion, but the amount of energy put in to keep the reactor running far exceeds the amount of energy produced. To reach or even exceed the breakeven point and produce excess energy, researchers say they will have to build the biggest tokamak so far, the $4.2 billion International Thermonuclear Experimental Reactor (ITER). Governments around the world are currently considering whether to go ahead and build the machine.

Proponents of spherical fusion, however, think it can be done more simply and cheaply. A brace of papers in this week's issue of *Physical Review Letters* shows that the Mega Amp Spherical Tokamak (MAST), also in Culham, and the National Spherical Torus Experiment (NSTX) in Princeton have both made first base by achieving high plasma confinement mode, or H-mode. Like a river that regains its composure downstream from white-water rapids, the H-mode is a smooth, dense flow of plasma that is twice as good as the lower density, more turbulent flow at retaining heat. "All the tokamak reactor proposals use H-mode," says Cordey. Alan Sykes, head of the physics team at MAST, adds: "It wasn't obvious that spherical tokamaks would be able to access this higher mode of confinement."

Interest in spherical tokamaks began in the early 1980s when Martin Peng and Dennis Strickler of Oak Ridge National Laboratory in Tennessee suggested reshaping the torus. Their work attracted little attention until experimenters at Culham cobbled together a baby spherical tokamak. "That was very successful indeed, and the world saw that spherical tokamaks seem to produce good, high-quality plasmas," says Sykes. The upshot was a whole new generation of spherical machines, of which MAST and NSTX are the largest.

The potential advantage of the spherical tokamak is that it takes less magnetic field to give the same level of plasma control. This is because the magnetic field lines in a tokamak spiral like a helical spring down around the central hole before looping back from bottom to top via the outer reaches of the container. Crucially, it's the spiral around the hole that imparts stability to the plasma. Because a spherical tokamak turns the central hole into a long, narrow tube, the magnetic field lines can not only wrap round more tightly, but they do so over a much greater distance. Hence spherical tokamaks make much more efficient use of their magnetic fields and are better able to resist the plasma's urge to break free, says Rajesh Maingi, who led the NSTX search for the H-mode. This improved efficiency translates into as