GENE THERAPY

Panel Urges Limits on X-SCID Trials

A U.S. advisory committee last week recommended limits on gene therapy trials in light of a third case of leukemia in a study in France. The panel suggested that U.S. studies of the same disease, X-linked severe combined immunodeficiency (X-SCID), should enroll only patients for whom conventional treatment has failed. However, trials of related diseases, as well as gene therapy trials using similar retroviral vectors, should continue, the panel said. The third leukemia "doesn't change the sense of unease dramatically," said chair Mahendra Rao of the National Institutes of Health (NIH).

Gene therapy trials for SCID have been the field's only success; since 1999 gene therapy has restored the immune systems of at least 17 children with two forms of the disorder. Excitement turned to worry in late 2002, however, when two children developed T-cell leukemia in a trial of X-SCID led by Alain Fischer at the Necker Hospital in Paris; one child died last fall. Although trials put on hold later resumed, a report that a third child in the French trial developed leukemia in January rekindled concerns about the therapy's risks (*Science*, 18 February, p. 1028).

This latest leukemia appears to be different from the previous two. Those occurred after a retrovirus carrying a gene called *gamma c* inserted into the oncogene *LMO2* in bone marrow cells in infants less than 3 months old, noted Food and Drug Administration (FDA) official Carolyn Wilson at a meeting of the FDA Cellular, Tissue, and Gene Therapies Advisory Committee. According to data provided by Fischer and French authorities, the third child, who was treated at 9 months old, does not appear to have an *LMO2* insertion. Although the vector again apparently landed on an oncogene or oncogenes, the insertions occurred at three sites that have not yet been identified.

Success story. Christopher Reid, a patient in a British X-SCID gene therapy trial.

The panel also heard other new data, which offered a mixed message. Last September, a monkey died from a leukemialike cancer at NIH, apparently as a result of being treated in 1999 with a retrovirus carrying two marker genes, reported Cynthia Dunbar of NIH. On the other hand, NIH's Utpal Davé described a report last year in *Science* on a retrovirus-induced mouse ▶

INDIA

Prime Minister Backs NSF-like Funding Body

NEW DELHI—Indian Prime Minister Manmohan Singh has endorsed the creation of an independent agency to support basic research—with a proposed budget that's more than three times the amount the government is now spending.

Scientists have long complained about the current process for winning grants, including inflexible rules and funding decisions that take more than a year. Last week Singh attended the first meeting of the new Science Advisory Council to the Prime Minister and embraced its recommendation for a National Science and Engineering Research Foundation with a mandate to "strongly promote and fund research in all fields of science and engineering." The new foundation "is being patterned on the lines of the acclaimed U.S. National Science Foundation," says C. N. R. Rao, chair of the council, who has campaigned for more than a decade for such a free-standing body. "A foundation that manages its own accounts and is run by a scientist is the only hope for reversing the rapid decline in Indian science," he adds.

The council recommended an annual budget of $250 million for the foundation. That amount would dwarf the $72 million now being spent by the Science and Engineering Research Council (SERC), an arm of the Department of Science and Technology (DST). The management and operating structure of the new foundation would be familiar to most U.S. scientists: five research directorates and a part-time body of distinguished scientists setting its overall direction. The council also recommended that the new foundation be responsible for "assessing the overall health of Indian science" (as NSF does with its biennial *Indicators* report) as well as funding "units of excellence [run by] researchers of exceptional merit" (as NSF does with centers focused on particular research areas).

An evaluation of the existing structures by the prime minister's council was sharply critical of SERC, which was founded in 1972 and supports the bulk of fundamental research done in India. "Science funding in academic institutions and universities has not kept pace with the growing costs of basic research," it concludes. Instead, the process has become "mired in bureaucracy, with complex financial procedures inhibiting efficient operation." Even so, the secretary of DST, Valangiman Subramanian Ramamurthy, say he "has no objections to the new body, since the basic idea is not bad."

A solid foundation. Prime Minister Singh is flanked by top science aides Kapil Sibal (left) and C. N. R. Rao (right).

Science Minister Kapil Sibal has been asked to work out the details, including the fate of SERC. "There is no question of anybody saying no when the prime minister has said 'Yes, it must be set up,' " says Sibal. The change can't come too soon for Rajendra Kumar Pachauri, director general of The Energy and Resources Institute in New Delhi. "An independent foundation," he says, "is vital for resuscitating … a moth-eaten" scientific establishment. —**PALLAVA BAGLA**

CREDITS (TOP TO BOTTOM): GREAT ORMOND STREET HOSPITAL FOR CHILDREN; P. BAGLA

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leukemia that contained insertions in both *LMO2* and *gamma c*, the gene corrected by the X-SCID therapy (*Science*, 16 January 2004, p. 333). The two genes seem to "cooperate" in causing cancer, Davé said, suggesting that gene therapy for diseases not involving *gamma c*—which itself may be oncogenic when expressed by a retrovirus—may be safer.

Indeed, panelists noted, no leukemia cases have yet been seen in trials of ADA-SCID, which does not involve the *gamma c* gene. Nor have leukemias appeared in an X-SCID trial in the United Kingdom that has treated 7 patients. However, the French leukemias appeared roughly 33 months after treatment, and the U.K. patients have not reached that point.

The panel concluded that if two X-SCID trials now on hold in the United States resume, they should enroll only children who have failed bone marrow transplants. "That's going to be a very small number," said panelist Daniel Salomon of the Scripps Research Institute in La Jolla, California. But the panel suggested FDA could lift its hold on a U.S. trial for ADA-SCID. Researchers will be watching closely to see whether any leukemia cases turn up in the British trial. If not, "that would certainly change things" because it would suggest conditions specific to the French trial are leading to the leukemias, concluded Rao.

–JOCELYN KAISER

PALEOANTHROPOLOGY

Skeleton of Upright Human Ancestor Discovered in Ethiopia

Scientists working in the remote badlands of Ethiopia have found the oldest known skeleton of an upright walking hominid, roughly dated to nearly 4 million years ago. The remarkably preserved partial skeleton includes many bones of the pelvis, leg, back, and arms, as a team led by paleoanthropologists Yohannes Haile-Selassie and Bruce Latimer of the Cleveland Museum of Natural History in Ohio announced last week at a press conference in Addis Ababa, Ethiopia.

Early walker. The owner of this shinbone walked upright in Ethiopia 4 million years ago.

CREDIT: ANTHONY MITCHELL/AP PHOTO

The shape of the top of the lower leg bone and pelvis have already convinced the discoverers that this hominid walked on two legs, which is the traditional hallmark of being a member of the human family rather than an ancestor of apes. "It's a once-in-a-lifetime discovery," says Haile-Selassie.

The skeleton so far also includes precisely the anatomical parts below the neck that can allow scientists to distinguish whether it walked like a modern human or in a more primitive manner. "It's a monumentally important skeleton, a real key to understanding hominid origins," says paleoanthropologist Carol Ward of the University of Missouri, Columbia, who cautions that she has not seen the as-yet-unpublished skeleton. "The bits from the skeleton are exactly the pieces we need to see if we came from something like a chimp or something more primitive."

The skeleton was found on 10 February near the village of Mille in the central Afar Depression, where a sharp-eyed fossil hunter named Alemayehu Asfaw spotted an elbow bone. Soon team members found the other part of the arm bone, the pelvis, leg bones, ribs, vertebrae, clavicle, and scapula. Extinct pigs found with the skeleton suggest that it lived 3.8 million to 4 million years ago, a critical time when humans were evolving the ability to walk. The team is now dating samples of volcanic rock taken from layers above and below the fossil and studying fragmentary fossils, including leg and toe bones, from 11 other individuals.

The identity of the new skeleton is still unclear, in part because the specimens are still embedded in matrix and also because most of the known fossils of this age are so fragmentary. There are only four other partial skeletons of human ancestors older than 1 million years. Contenders for the new skeleton's identity include the slightly younger *Australopithecus afarensis*, whose most famous member is Lucy, a partial skeleton that lived 3.2 million years ▶

ScienceScope

Brazil OKs Stem Cell Work

The way is clear for Brazilian scientists to work with human embryonic stem (ES) cells. On 3 March, the Brazilian legislature passed a wide-ranging biosecurity bill that legalizes work with the cells, sending it to President Luiz Inácio Lula da Silva for his signature. It allows scientists who receive permission from a national ethics board to work with existing ES cell lines and to derive new ones from frozen embryos left over after fertility treatments. It also outlaws nuclear transfer experiments using human cells.

Geneticist Mayana Zatz of São Paulo University says she hopes to begin work soon on muscle and nerve studies using ES cells. The bill also allows for the sale of genetically modified seeds.

–GRETCHEN VOGEL

New Trade Rules on Sturgeon

The world's most valuable fish—the beluga sturgeon, a target of human predators who sell its eggs for $100 an ounce—may get help from the U.S. Fish and Wildlife Service (FWS). Officials ruled last week that nations wishing to continue selling beluga caviar to the United States (which consumes 80% of legal exports) must file plans with FWS in 6 months showing how they will stem the species' decline. Those that don't comply will face a trade ban on the fish. Most directly affected are Kazakhstan, Iran, and Russia. Environmentalists decry the new rule, urging an immediate U.S. import ban.

–CHRISTOPHER PALA

Insider Nominated to EPA

A nominee to lead the Environmental Protection Agency (EPA) has succeeded in gaining the unlikely support of both environmentalists and industry groups.

Last week President George W. Bush chose Stephen Johnson, 53, to replace Michael Leavitt as head of EPA. Johnson, who holds a master's degree in pathology, would be the first administrator with scientific training.

Those pleased by the decision include the Environmental Working Group and a pesticide trade group called CropLife America, both based in Washington, D.C.

"He's coming into the job with a stronger grasp of the science than any past administrator," says Lynn Goldman of Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. The main question, she adds, is whether he will have any clout in the White House.

–ERIK STOKSTAD

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Panel Urges Limits on X-SCID Trials

Jocelyn Kaiser

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