Colleagues in radiology praise Zerhouni for his intellect and originality, although his research is not widely known outside his field. Brody, who was developing a new MRI machine in Palo Alto, California, before coming to Hopkins, was in California trying to interest people in his new MRI system when he first met Zerhouni. At that time, Brody notes, "people were writing articles about how [the system] wouldn't work." Zerhouni came to evaluate it for Hopkins, and, according to Brody, he concluded that the idea would succeed.

Brody says that Zerhouni may be best known for pioneering noninvasive methods of analyzing the movements of the heart by electrically "tagging" the muscle wall with superimposed magnetic lines and tracking the motions with MRI. Magnetic tagging has enabled physiologists to analyze and compare living healthy and diseased hearts in three dimensions, without surgery. Noninvasive imaging of this sort, says James Thrall, chair of radiology at Massachusetts General Hospital in Boston, has become the "guiding hand of medicine" in the last decade. Thrall also credits Zerhouni for helping support radiologists' efforts to gain a stronger presence on the NIH campus through creation of the National Institute of Biomedical Imaging and Bioengineering. Congress approved it in 2000, despite opposition from former NIH chief Harold Varmus.

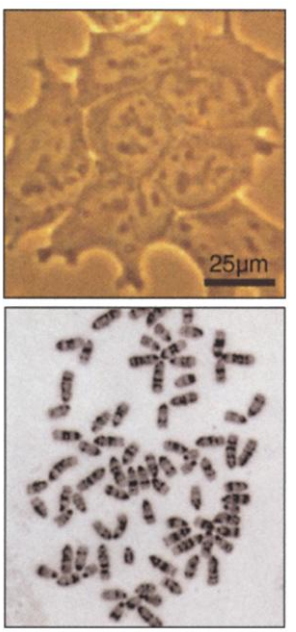
Zerhouni's résumé lists him as "consulting" adviser to the White House during the Reagan Administration, and he currently serves on the scientific advisory board of the National Cancer Institute (NCI). Co-panelist Herbert Kressel, a radiologist and president of Harvard University's Beth Israel Deaconess Medical Center in Boston, calls Zerhouni "one of those people who can see the entire playing field and all the relationships on it." Zerhouni is "personable," Kressel says, but he has never discussed politics or mentioned his views on embryo research.

Former NCI director Richard Klausner, who recruited Zerhouni for advice on tumor imaging, calls him "a clear thinker. … [Zerhouni] is particularly interested in technology," Klausner adds, but he's also "very supportive of science and the culture of science" despite lacking experience as a basic bench scientist. Varmus, now president of the Memorial Sloan-Kettering Cancer Center in New York City, is also upbeat about Zerhouni's talents. He was "smart, insightful, and knowledgeable" about deploying the center's resources during a review of its radiology program, Varmus says: "I hadn't heard of him 3 years ago, but I have a lot of respect for him."

Despite the praise, Zerhouni could run into some flak in Senate confirmation hearings. Questioners will be poised to ask if, as reported, he passed a political "litmus test" on stem cell policy that other candidates flunked. For example, one knowledgeable NIH insider says news reports are essentially correct that another leading candidate, Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, failed to promise to restrict research on human embryonic stem cells.

The idea of measuring an NIH nominee's politics is distasteful to many basic scientists, who worry that such screening could weaken NIH's stature as the government's biomedical crown jewel. "If someone as thoughtful and careful and balanced as Tony Fauci was unacceptable," says Steven Hyman, provost of Harvard University and former mental health chief at NIH, "that really does raise some questions."

–ELIOT MARSHALL



More than enough. Cells that appear to have been "reprogrammed" have enlarged nuclei (*top*) and twice the normal number of chromosomes (*bottom*), suggesting that two cells fused together.

STEM CELL RESEARCH

Studies Cast Doubt on Plasticity of Adult Cells

Opponents of research on human embryos have raised a politically powerful argument against work involving embryonic stem (ES) cells: Such research can be avoided because adult stem cells may offer similar promise. Defying scientific dogma, numerous reports have suggested that adult stem cells can morph into many types of cells, raising hopes that adult cells could eventually be used to treat diseases—without the ethical baggage that accompanies ES cells.

Now two papers in this week's early online publication of *Nature* suggest that some of the surprising plasticity of adult stem cells might be explained by simple cell fusion, not "reprogramming." The new evidence does not explain away all of the potential of adult stem cells, but it does raise a caution.

For years, researchers have assumed that development is a one-way street: A cell that starts down the path to become a neuron, for instance, can become only a brain cell. But studies in the past few years have suggested that cells might indeed be coaxed to turn back and take another path. Nearly a dozen teams have reported that cells from one tissue—blood, muscle, or brain, for example—could, when exposed to the right environment, contribute to an entirely different tissue (*Science*, 8 June 2001, p. 1820).

Although politicians have trumpeted the results, many developmental biologists have been skeptical. In the new papers, two groups, working independently, provide evidence for one alternative explanation. Both report that cells from adult tissues can fuse with ES cells in culture, producing a hybrid that looks like a reprogrammed adult cell but has the pluripotent characteristics of the embryonic cell. The hybrid cells also show chromosomal abnormalities, suggesting that they might not be a reliable source of healthy replacement tissue after all.

Cell biologist Naohiro Terada of the University of Florida College of Medicine in Gainesville and his colleagues were eager to coax adult cells to "dedifferentiate" into cells with unlimited potential. Other work had suggested that some factor produced by ES cells might kick-start the process. To test that idea, Terada, Edward Scott, and other colleagues cultured adult cells from mouse bone marrow tagged with green fluorescent protein together with ES cells that did not carry the marker. The researchers soon found evidence for green cells that behaved like ES cells. But when they looked more closely, they found that all the "dedifferenti-

CREDITS: Q.-L. YING *ET AL.*, *NATURE* ADVANCE ONLINE PUBLICATION, 13 MARCH 2002 (DOI10.1038/NATURE729)

ated" cells had twice as many chromosomes as usual: They were the product of fusion between two cells. Terada doesn't think that fusion explains all the other reprogramming results. "We're not denying any of those data. We're just saying, 'Be careful' " about possible explanations for unexpected results.

Developmental geneticist Austin Smith of the University of Edinburgh, U.K., says he and the team "approached the issue with open but skeptical minds." "All our other data said cells do become lineage restricted" —unable to form new kinds of tissues—as they progress toward becoming a certain cell type. He and his colleagues grew cells from adult mouse brains in a culture that also contained mouse ES cells. They then selected for cells that expressed Oct4 (a protein characteristic of undifferentiated ES cells) and also carried a gene present only in the brain cells. The team recovered more than two dozen cell colonies that seemed to have been reprogrammed. But on closer inspection, the cells had enlarged nuclei and twice as many chromosomes as normal: signs of hybrid cells, not reprogrammed ones.

Several of the original researchers are not dissuaded. "What they're saying is, 'Hey, fusion happens,' " says Diane Krause of Yale University, who has reported that cells from bone marrow can become a variety of tissues when injected into adult mice. Her lab is now checking whether its apparently reprogrammed cells formed from fusion of donor and recipient cells. Jonas Frisén, whose lab reported that brain cells can become a variety of tissues when injected into embryos, is also checking for evidence of hybrid cells, but he does not believe that cell fusion can explain all of their results.

The new papers come on the heels of two others that have cast doubt on the reported malleability of adult cells. In the March issue of *Nature Medicine*, Derek van Der Kooy, Cindi Morshead, and their colleagues at the University of Toronto report that they could not replicate earlier reports that cells from adult brain could become blood cells (*Science*, 22 January 1999, pp. 471 and 534). Instead, they report, cells kept in culture for many generations—as occurred in the original research—tend to accumulate genetic alterations that might lead to an apparent reprogramming.

And in February, Margaret Goodell of Baylor College of Medicine in Houston clarified one of her earlier reports on cells from adult mouse muscle. As she explained in the *Proceedings of the National Academy of Sciences*, the adult cells that seemed to give rise to blood cells were in fact rare blood stem cells that reside in the muscle.

The new results are a needed reminder for the field to stay vigilant, says van Der Kooy. "Our own data fail to replicate transdifferentiation, but there are so many reports out there. I'm still unwilling to believe all of them are false."

–GRETCHEN VOGEL

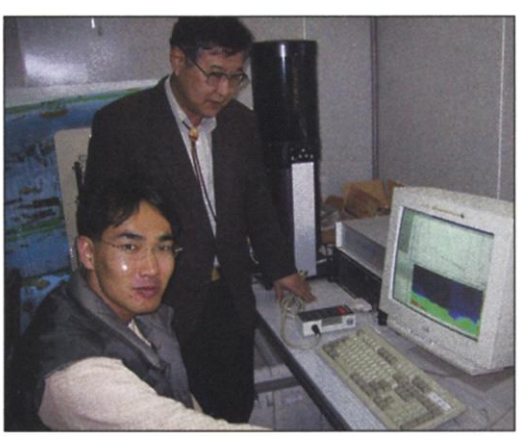
GRADUATE TRAINING

South Korea Scrambles To Fill Ph.D. Slots

SEOUL—Jae-Gwang Won is a member of an increasingly rare breed: a Korean graduate student working on a homegrown science Ph.D. This month Seoul National University (SNU), long considered the country's most prestigious university, failed to fill its quota of graduate slots for the new semester. More embarrassing still, SNU would have fallen short even if it had accepted every applicant.

Korea's postwar economic boom in the 1960s and 1970s certainly benefited from the belief that technical know-how was essential for a rising standard of living. Although many of those scientists were trained abroad, the strategy paid off: By 1995, for example, Korea's economy was the 11th largest in the world, and the country was second behind the United Kingdom in the percentage of its college-age population with technical degrees. "It was a good time for science in Korea," says Sung H. Park, SNU's dean of natural sciences, and there were plenty of good jobs.

Faith in technology as an economic driver hasn't disappeared, but it's being undermined by several factors. One is a loss in status. "When I was in high school, science was prestigious," says 53-year-old Yoon Soon-chang, an SNU professor of atmospheric science and associate dean of planning. "Being a scientist meant being proud." But today's students are more interested in careers that pay well, Yoon says.



CREDIT: SEOUL NATIONAL UNIVERSITY

Minority view. Jae-Gwang Won, seated, with SNU dean Yoon Soon-chang, is part of a dwindling pool of grad students.

ScienceScope

Southern Light Spain is joining the synchrotron club. The science ministry last week approved building Spain's first major facility for probing three-dimensional structures. Plans call for breaking ground next year on the $110 million, 2.5–gigaelectron volt radiation source to open in 2008 near the Autonomous University of Barcelona (UAB). The new center—proposed by a UAB-led team in 1997—will have room for up to 160 research teams, planners say. And it will be open to scientists from across southern Europe, notes Andreu Mas-Colell, head of the Catalán government's research department, which will split the project's cost with the national government.

Protein Probes Biologists who use small molecules to explore how proteins work—an approach known as "chemical genetics" —will soon have a major new resource. The National Cancer Institute has just awarded a $40 million, 5-year contract to Harvard University for a Molecular Target Laboratory. The facility, to be headed by Stuart Schreiber, will be an outgrowth of Harvard's 4-year-old Institute of Chemistry and Cell Biology. It will develop tools such as protein arrays and build a public database that will catalog up to a million small molecules—synthesized by Harvard and other labs—that block or interact with proteins.

The high cost of the robotics, protein assays, and other tools needed to systematically screen sets of molecular probes has prevented chemical genetics from taking off, notes chemist Brent Stockwell of the Whitehead Institute in Cambridge, Massachusetts: "It's not an easy method to implement; this will make it more accessible." Harvard's Rebecca Ward says it's not yet known when the data will go online.

Getting to Basics The U.S. government should fund only basic research that is of high quality, is relevant to government missions, and meets clear performance goals, according to draft guidelines released earlier this month by the White House Office of Management and Budget (OMB) (see www7.nationalacademies.org/gpra). Although no researcher argued with that holy trinity at a recent National Academy of Sciences workshop on the criteria, many wondered about exactly how they will be used to decide which programs deserve cash—particularly when it comes to high-risk research that is bound to stumble. Maybe, OMB's Sarah Horrigan suggested, the guidelines should include "a way to reward scientific failure." That and other changes could be included in OMB's next draft, due out later this year.