

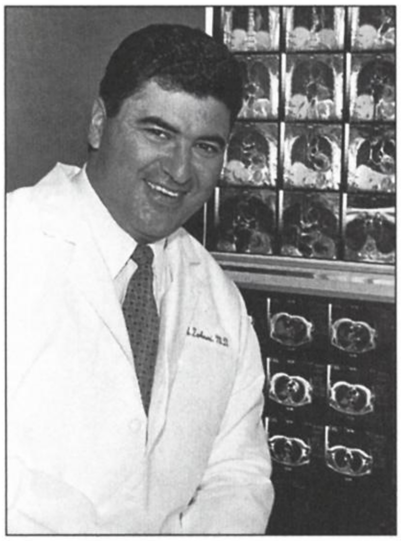


APPOINTMENT PENDING

# Zerhouni Seems Headed for NIH, And New Scrap Over Stem Cells

A Baltimore radiologist with an entrepreneurial bent is expected to be named the next director of the U.S. National Institutes of Health (NIH).

The Washington rumor mill was humming last week with reports that Elias Zerhouni of Johns Hopkins University School of Medicine was in line for the nomination, and although government officials declined to comment publicly as this issue of *Science* went to press, leaders of the U.S. biomedical establishment were taking it as a fait accompli. Former NIH institute chiefs are already showering Zerhouni with friendly comments and expressing their delight that a delay of more than 2 years in filling the top NIH job may soon be over. However, media reports on the expected nomination also pointed to a potential cloud on the horizon: Zerhouni's stance on the politically charged issue of using human embryonic stem cells in research.



**Almost home.** Johns Hopkins's Elias Zerhouni could soon be head of Bethesda-based NIH.

"He's one of these rare triple-threat people, a good researcher, a good clinician, and an incredibly well-organized business leader," says his boss and radiology colleague, Hopkins president William Brody. At the same time, Brody dismisses speculation in *The Washington Post* and elsewhere that Zerhouni had "assured leading social conservatives" that he would not expand the use of human embryonic stem cells in research. That's "absolutely ludicrous," says Brody, noting that Zerhouni helped create and run a new $58 million institute at Hopkins dedicated to stem cell research. "He wouldn't sell out for things he doesn't believe in." (Zerhouni could not be reached for comment; nominees for government posts rarely speak to the press before the U.S. Senate completes the confirmation process.)

Zerhouni, a 50-year-old U.S. citizen, has spent virtually his entire medical career at Hopkins. Algerian by birth and a graduate of the University of Algiers Medical School, Zerhouni came to the United States in 1975 for his medical residency. In 1981 he became an assistant professor in the medical school. After a brief foray to Eastern Virginia Medical School in Norfolk, Zerhouni returned to Hopkins in 1985 as an associate professor, rising to full professor several years later. In 1996 he succeeded Brody as chair of radiology when Brody became Hopkins president. Since 1997 Zerhouni has also served as Hopkins's vice dean for research, guiding several new ventures, including a Hopkins-backed spin-off called Surgi-Vision Inc. in Gaithersburg, Maryland. This private company is developing ideas and patents co-authored by Zerhouni to market magnetic resonance imaging (MRI) sensors small enough to fit inside blood vessels (see sidebar).

## A Spin-Off With Vision

To understand how Elias Zerhouni makes things happen, colleagues say, look at a company he started 4 years ago. Zerhouni and six others founded the outfit, called Surgi-Vision Inc., now based in Gaithersburg, Maryland, with patents licensed from Johns Hopkins University. Their goal was nothing less than to revolutionize the way magnetic resonance images are produced and used, says Nancy Taylor, Surgi-Vision's CEO. Rather than put the patient inside a bulky scanner that captures images from the outside, Zerhouni and colleagues devised a magnetic resonance imaging (MRI) sensor small enough to go inside the gut, heart, or even blood vessels and collect high-resolution data. The resulting cross-sectional images, the inventors reasoned, should be as sharp as x-rays—and wouldn't require ionizing radiation.

"It was [Zerhouni's] vision" that got the project moving, says Taylor. Zerhouni recruited outside talent, including Paul Bottomley, a former General Electric MRI biomedical engineer and M.D., and electrical engineer Ergin Atalar, now both at Johns Hopkins School of Medicine. Zerhouni "came up with the ideas, and I made them work," says Atalar. Zerhouni also chaired a small committee that solicited patentable ideas from faculty members and passed the more promising ones to Hopkins's intellectual property office, says Bottomley, adding that Zerhouni was the "driving force" on investor "road shows" and helped raise more than $15 million in outside money.

**Inside view.** Minisensors gather MRI imagery from within the body.

Surgi-Vision has gotten off to a promising start. The privately held company has formed a distribution partnership with General Electric and won approval from the Food and Drug Administration to begin marketing three types of internal MRI imagers. Zerhouni is on Surgi-Vision's scientific board, says Taylor, declining to comment on his financial stake in the company.

–E.M.

CREDITS: (TOP TO BOTTOM) *JOHNS HOPKINS UNIVERSITY GAZETTE*; SURGI-VISION

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). Copanelist 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

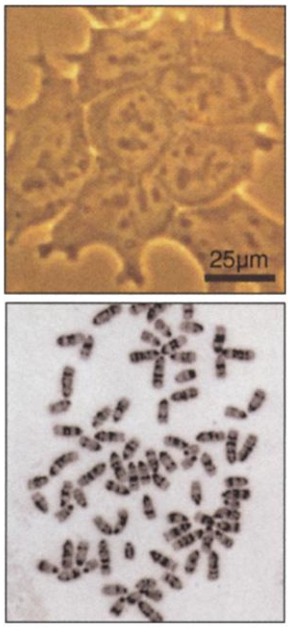
STEM CELL RESEARCH

## 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).




**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.

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)