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# Will Zerhouni become the new NIH director?

Who is Elias Zerhouni? Prior to last month, more people seemed to have heard of Keyser Söze than the Algerian-born radiologist who is reportedly the Bush Administration's favored candidate for National Institutes of Health (NIH) director. Zerhouni's appointment will end the two-year void created by Harold Varmus' departure. However, much depends on Zerhouni's views on human embryonic stem (ES) cell research—they are not only key to his approval by the Senate, but will be equally pivotal in the future direction of the NIH, the world's largest biomedical research organization.

Zerhouni is the executive vice dean of the Johns Hopkins University School of Medicine in Baltimore, and demonstrated the administrative talent required to run NIH by being the driving force behind last year's creation of the $60 million Institute for Cell Engineering at Hopkins.

The institute conducts cell research with the goal of turning cells into therapeutic transplants. Speaking in February 2001, Zerhouni said the use of such cells holds "enormous untapped potential to treat currently incurable diseases," and the research must be performed. "Somebody has to do it," he said. "We as an institution cannot deny to our patients the investigation of the potential of these therapies for them." A team of Hopkins scientists led by John Gearhart was among the first to create permanent stem-cell lines (Proc. Natl. Acad. Sci. USA ***10****, 13726; 1998*).

Despite his apparent support last year for the reprogramming of human cells to yield therapeutic tissue, if appointed, Zerhouni would be expected to honor Bush's restrictions on federal funding for ES cell research and somatic cell nuclear transfer. And rumors abound within the biomedical research community that Zerhouni may have had a change of heart and may now be leaning toward a rejection of therapeutic cloning and ES cell research.

He will almost certainly face questions on these lines of study before being confirmed by the Democrat-controlled Senate, who may seek to block his appointment if they feel his views on the field will impede progress in medical research. He will first appear at hearings run by Senator Edward Kennedy (D-MA). Kennedy said he had never heard of Zerhouni until his name surfaced as a candidate.

Being pro-ES cell research is believed to have scuttled the directorship chances of more prominent candidates such as Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, since this does not sit well with the anti-abortion, pro-life Bush Administration. Fauci, in fact, was the first choice of Health and Human Services Secretary, Tommy Thompson, and his rejection is not the first time Bush has overruled the disgruntled Thompson, who is rumored to be on the verge of leaving.

For or against ES cell research?

With a projected FY2003 budget of $27 billion, the degree to which NIH participates in the area of stem-cell research is vital to international advancement of the field. "The strength of the NIH has always been derived from its focus on making investments in clear, scientifically based priorities," says Robert Schooley, an AIDS researcher who heads the division of infectious diseases at the University of Colorado Health Sciences Center. "If it strays from this, this will threaten one of the areas where the US has been pre-eminent since the end of World War II."

Former director Varmus won the 1989 Nobel Prize for discovering the cellular origin of retroviral oncogenes, and is credited with restoring NIH's basic scientific mission and putting real muscle into its research budget. Zerhouni's own research currently focuses on the development of imaging techniques for cardiac disease. For example, he has been developing the method of magnetic resonance imaging with tissue tagging as a non-invasive technique for measuring 3-dimensional motion and deformation of the heart. One NIH scientist commented that although Zerhouni may lack detailed knowledge of the clinical trials process, "…maybe it's not a bad idea for someone to head NIH who has a technology focus. It would be an unusual change, possibly a positive one."'

While NIH employees called by *Nature Medicine* said that Zerhouni was well known to them, other scientists queried expressed some puzzlement over his possible appointment. Schooley reflects the views of many: "He is not someone who is widely known in the biomedical research community. He faces big challenges, not least the fact that a large number of key positions are vacant at NIH."

Six of the NIH institutes now lack directors, including biomedical imaging, neurology, mental health, drug abuse, alcohol abuse and general medical sciences. And the Bush Administration also is grappling with other national health vacancies, including the Food and Drug Administration, Surgeon General and the Centers for Disease Control and Prevention.

**Marlene Cimons, Washington, DC**

# Poor sales trigger vaccine withdrawal

Poor sales have prompted GlaxoSmithKline (GSK) to withdraw its Lyme disease vaccine, LYMErix, from the United States market. Lawsuits relating to adverse effects of the vaccine have been filed since its introduction, but the US Food and Drug Administration (FDA) found no proof that LYMErix is dangerous. It appears that lack of demand, not safety concerns, is the reason for the withdrawal.

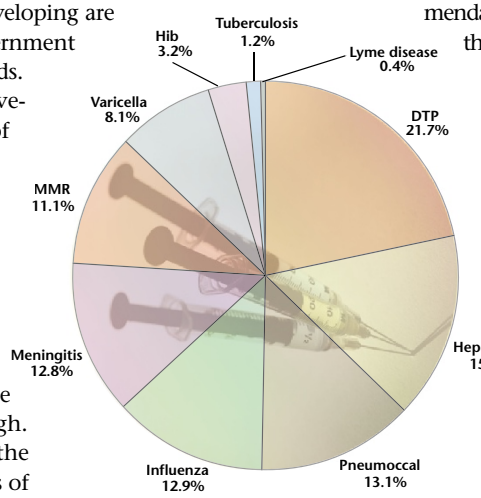
Importantly, the move shows that even though the global vaccine market is expected to increase by 25% within the next five years—from a value of $4,800 million to $6,400 million—vaccine manufacturers are not immune to financial forces, which signals a troubled future for new vaccines against rare diseases such as West Nile virus (WNV) and Ebola if they complete development.

LYMErix was approved by the FDA at the end of 1998, and earned $40 million in peak sales during its first year on the market. In 1999, 16,273 cases of Lyme disease, concentrated mostly in the northeastern states, were reported to the US Centers for Disease Control and Prevention (CDC). However, GSK withdrew LYMErix following predictions that less than 10,000 people would be vaccinated in 2002.

According to a recent report by industry analyst group Datamonitor, LYMErix represented only 0.4% of the global vaccine market sales in 2000. "Companies need to

assess which of the markets will maximize their revenue," says analyst Amber Gibson, author of the report. "Companies should also establish strong relationships with governments and ensure that the vaccines they are developing are in line with government priorities," she adds.

A cost-effectiveness analysis of the Lyme disease vaccine by the CDC indicates that the use of LYMErix vaccine is justified only in areas in which the incidence of Lyme disease is high. They found that the mean net savings of vaccination per case averted is $3,377 if the probability of contracting Lyme disease is estimated at 0.03. However, the probability of contracting Lyme disease is, in all but a few areas, less than 0.005.




Disease breakdown of the global vaccines market (2001). Source: Datamonitor

Vaccine expert Stanley Plotkin, who presently consults for Aventis Pasteur, calls the withdrawal of LYMErix "regrettable." He says, "This vaccine was developed because of a perceived demand by the public for protection against a common infection," but he remembers that the CDC gave the vaccine at best a "lukewarm" recommendation. They proposed that it "should be considered" only for persons aged 15–70 years with frequent or prolonged exposure to tick-infested habitats or travelers to these areas. Indeed, the 1999 cost-effectiveness analysis by the CDC remark-ed, "Ours is not the only study to suggest that the vaccine not be used universally," and cited an Institute of Medicine report that gives a Lyme disease vaccine the lowest ranking in terms of priorities for vaccine development.

Plotkin believes that the vaccine's withdrawal means there never will be a Lyme disease vaccine and that other vaccines against diseases such as WNV might never reach the market. "No company is going to spend hundreds of millions to develop a vaccine that will not be recommended and therefore will not sell," he points out.

But these new vaccines are making their way through the academic research pipeline nonetheless, including a combined vaccine against WNV and dengue virus (*Proc. Natl. Acad. Sci. USA* **99**, 3036; 2002). The Datamonitor report indicates that WNV vaccines are unlikely to be strong candidates for widespread immunization programs. "However, the susceptibility of infants and the over-50s to the more severe manifestations of this disease mean that in endemic regions vaccines could be considered for both childhood and elderly immunization programs," they point out.

Gibson suggests that development of novel technologies in vaccine discovery, formulation and delivery will be critical for attaining market share. When assessing the value of a vaccine, various factors, such as the severity of the disease and the mortality rate, must be considered, but so must the cost of treating the disease. "Basically, if the cost of immunizing every individual is lower than the cost of treating the number who get the disease, then you can justify its use," she says.

**Emma Hitt, Atlanta**

## Tech transfer pays off

Technology transfer is starting to pay off for North America's universities and hospitals according to a new survey released by the Association of University Technology Managers (AUTM). After five years of annual growth at a rate of 20%, income from license agreements jumped to 47%, amounting to $1.26 billion, for the last fiscal year analyzed, which was 2000.

"Some of it is simply a maturation of the [biotech] industry," says AUTM president-elect Patricia Harsche, of Fox Chase Cancer Center in Philadelphia. "Many of the licenses that were entered into eight to ten years ago are now products."

Several one-time events, however, have inflated the total figure. The biggest—$200 million—was the University of California's settlement of two patent infringement lawsuits against biotech company Genentech for human growth hormone. But even without that settlement, license income across the board for these institutions grew 23% with most of the money coming in the form of product royalties.

Several institutions earned more than $30 million in royalties, and two—the University of California and Columbia—topped $100 million. Queen's University in Kingston, Ontario, whose royalty payments came to $5.4 million (up 800% on the previous year) can thank the Food and Drug Administration's approval of Levulan, a photodynamic therapy system for precancerous skin lesions, and European sales of erectile dysfunction drug Uprima contributed, as well as unspecified royalties from Bristol–Myers Squibb for patents on the cancer drug Taxol.

Increase in tech transfer deals for US and Canadian academic institutions and hospitals

| | 1997 | 1998 | 1999 | 2000 |
|---|---|---|---|---|
| Adjusted gross license income (millions) | 611 | 725 | 862 | 1,263 |
| Invention disclosures | 11,303 | 11,784 | 12,324 | 13,032 |
| Patent applications filed | 6,629 | 7,714 | 8,802 | 9,925 |
| Start-ups formed | 333 | 364 | 344 | 454 |

Source: Association of University Technology Managers Licensing Survey: FY 2000

Income from redeemed ownership of shares in companies rose from $25 million to $165 million, or 15% of total income. For example, Dartmouth College sold $60 million in equity from the monoclonal antibody company Medarex, which was cofounded in 1987 by Dartmouth Medical School; and Georgetown University received $26 million for Aventis' allergy drug Allegra which was invented by Georgetown's Raymond Woosley.

2000 also saw a 32% increase in the number of academic startup companies, a trend that's likely to continue, says Mark Chalek, director of the office of corporate research at Boston's Beth Israel Deaconness Medical Center, which tripled its income in 2000. "People have realized you can do these things thoughtfully, deal with the conflicts of interest, and create firewalls between companies and academic labs appropriately," he says.

**Ken Garber, Ann Arbor**

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