AN INTERVIEW WITH ELIAS ZERHOUNI

Piloting High-Flying NIH To a Soft Landing

As the budget-doubling campaign ends, the new NIH chief discusses biodefense needs, large-scale biology, and stem cell research

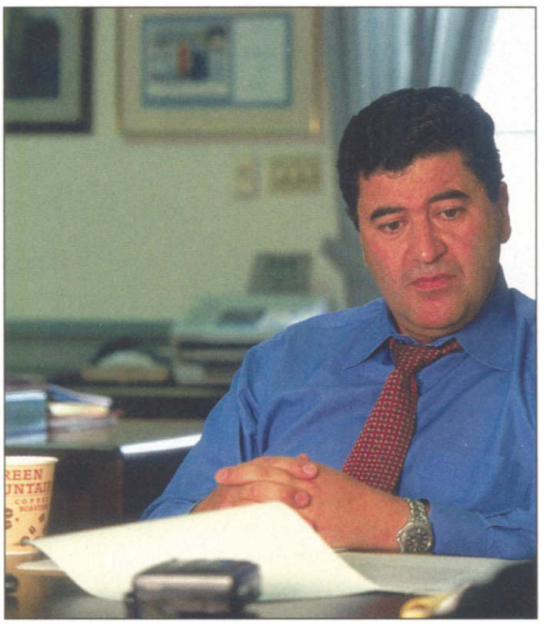
The Bush Administration took a year before naming Elias Zerhouni to lead the National Institutes of Health (NIH). But after he was nominated on 26 March, the Johns Hopkins radiologist moved through the Senate at light speed. Zerhouni appeared 30 April before a confirmation committee, where a predicted brouhaha over NIH funding of human embryonic stem cell research never materialized. Instead, Zerhouni won the Senate's approval on 2 May and was sworn in 18 days later.

Congress might have moved swiftly in part because it felt that NIH needs strong leadership to manage its ballooning budget and 27 sprawling institutes and centers. NIH is set to receive $27 billion in 2003, a doubling of its budget since 1998. Zerhouni is expected to face much tighter budgets in future years, at a time when NIH will be taking on new responsibilities in bioterrorism research. This will present a management challenge—one for which the Algeria native appears to be well qualified. A former executive vice dean at Johns Hopkins University School of Medicine in Baltimore, Zerhouni boasts a versatile background that includes work as a clinician, inventor, entrepreneur, and biomedical engineer.

In an interview last week with *Science* in his office on the NIH campus in Bethesda, Maryland, Zerhouni, 51, who favors dark business suits, outlined his goals 4 months into the job. He said he aims to make sure that biomedical research results are translated into public health benefits. But he took pains to explain that that does not mean less attention to basic research: "I am absolutely committed to making sure that NIH has a very balanced portfolio."

This summer Zerhouni brought together 100 scientists—ranging from intramural bench scientists to industry researchers—to meet in focus groups. The "ground rules," he said, were to identify needed resources, "roadblocks," and "gaps in knowledge" that no single NIH institute could tackle in areas such as bioinformatics, molecular libraries, systems biology, and clinical research. Zerhouni intends to develop action plans for the next 3 to 5 years.

Earlier this month, Zerhouni appointed directors for two institutes: mental health and alcoholism. That leaves three slots to fill (drug abuse, neurological disorders, and general medical sciences). He has initiated a review of the intramural research program and NIH's management. Zerhouni also noted that Deputy Director Ruth Kirschstein, whom he described as "a treasure for the institution," will become his adviser. "She's done so much for this place; I think a senior advisory position to the director would be terrific," Zerhouni says.



CREDIT: RICK KOZAK

A transcript of questions and answers, edited for brevity and clarity, follows.

Q: What are your first priorities?

A: I thought [there were several] important things a new director could do after two and a half years of transition. Funny things happen in large organizations when you have a long transition. Decisions are not made, clear strategic directions are not spelled out, recruitments are sort of delayed.

One was to reenergize the place, recreate momentum. ... I had an immediate need to recruit excellent directors. I really challenged both the internal community and the outside community over the summer to try to define [key issues] that only the NIH director could activate. ...

I had 100 scientists over the summer from outside, from inside, and organized five what I call "road map" meetings. ... These scientists were from basic science, translational research, clinical research, social, behavioral. ... And once we did this, it was very obvious that there were issues that just hadn't been attended to.

There's a major change in the way science is conducted. I don't have to tell you about the explosion in data, the scaling up of research technologies. So that essentially became a topic: How do we generate facilitating and enabling resource support, whether it be bioinformatics, molecular libraries, structural biology resources, and so on?

[Another] recurring theme across institutes is this issue of making sure that our science is relevant to the public. ... I tend to look at it as a systems problem. ... We're suffering because you see a much longer timeline between [the discovery and the use of new ideas in medicine]. Clearly that is something you hear from the scientists, who feel that they do not have access to the resources to validate their approach or get the proof of concept. You [also] hear it from the pharmaceutical industry: They quote statistics that a few years back, 40% of drugs that went to phase III trials would eventually fail. Now it's 80% of drugs that go to phase III trials fail. ... It tells you that we have a problem.

Q: What will you do with these action plans?

A: We'll follow up. We'll have meetings with the directors, and each one of the items that is identified will then be analyzed in depth in terms of really having data and having a good quantitative understanding.

Q: Is the model of the traditional NIH grant going to change? Will there be more networks like the Alliance for Cellular Signaling [which received a large "glue grant"]?

A: It won't change. It will evolve into different shapes, because multidisciplinary science requires you to have collaborations. ... But at the end of the day, you also need [principal investigators] who themselves have an inherent understanding of [multiple] fields so they can ask the right questions. Before I even came to NIH, I heard about the glue-grant idea, and I thought that was a terrific idea. [It goes] way beyond the capabilities of any

one laboratory. And we're going to face more and more problems of this nature. I understand [the glue-grant group is] doing well; I'm going to watch it carefully. Is that a model that we need to implement? I don't know, but it's really exciting, I think.

Q: You have said NIH needs to explain how it has spent its funds. How are you going to do that?

A: Congress, the public, patient advocacy groups [are] saying, "We've doubled our investment; what does that mean, where's it going to, what are we getting for it?" There's a huge outcry out there about the public health impact of the budget. And there is a sense that perhaps we're not as good at communicating what those impacts have been. So I really think that we need to as an institution do better and be more proactive in explaining in detail what it is we're doing.

Q: How does NIH come down with a "soft landing" from budget increases of up to 15% for the past 5 years to projected increases starting in 2004 of 2%?

A: I think it's a challenge. ... When the doubling was going on, you had a very vibrant economy, you had a federal surplus, you had no crisis like biodefense. This is a totally different environment. We can't defy gravity and expect 15% numbers every year.

[But] I'm working as hard as I can with the Administration. I can tell you, I'm advocating for NIH as strongly as I can, because I think we have the justification. ... If you look at our nation and the growth rate of health care costs considering our current health care system, ... we're entering a race between the growth of that health care cost and the need for discovering new approaches that will drastically change the cost structure in major, major diseases. So my view is that it is a strategic imperative to invest aggressively in research.

Q: Is there an imbalance in federal support for biomedical science versus physical and other sciences? There is a proposal to double the budget of the National Science Foundation.

A: There's no doubt that we need to have more investment in the quantitative sciences in this country. ... But I wouldn't say that means stop investing in biomedical sciences. ... I find that these approaches—double, triple, let's do it, me too—don't appeal to me intellectually. What is it that you want to do strategically? That is my question. It's a good slogan, though.

Q: Can NIH spend $1.7 billion on bioterrorism research wisely in 1 year, and is it smart to keep spending at that level if there are no new bioterrorism incidents?

A: I'm absolutely convinced [that the funds can be spent wisely]. First of all, you have to give credit to NIH ... for coming up with a very cogent research agenda within 90 days of request. Now, as we're starting a new field, we absolutely need to have a huge investment in infrastructure. ... If you look at the magnitude of the problem, $1.5 billion, $1.7 billion is probably going to be the base investment in biodefense.

"As we're starting a new field [biodefense research], we absolutely need to have a huge investment in infrastructure."

Q: How will you promote translational and clinical research?

A: I think we have a systemic issue. We really need to have common data standards. We need to have a better computer infrastructure, information infrastructure for conducting clinical investigations in the country. We need to have a strategy that looks at new models, new validated research methods in clinical investigations. ... For example, there are some scientists who feel that Bayesian statistics should be used in clinical trials early on. ... You know, the approaches that we use—the double-blind randomized study—is the mainstay of clinical investigations, and we've used that successfully. But in a day and age when you can really combine data on large-scale populations, ... should we look at that and reengineer our clinical research and clinical investigation system in this country? That's a question that I'm going to look into.

Q: What's happening with the office of the director? Do you anticipate some changes?

A: Yes. I took my time to evaluate the office. I think we definitely need to have more capabilities to present what our results are, analyze our portfolio, evaluate our portfolio, be able to communicate that portfolio. So I'm very interested in building an advanced analysis capability so that when NIH provides results or provides plans, they're well supported by coherent analysis of the data.

Q: What do you think of the proposal being explored by a National Academy of Sciences (NAS) panel to consolidate NIH institutes?

A: I don't see how you could do it politically. I have to tell you, in 4 months I've learned enough. I opened the meeting of the national advisory council of the Eye Institute. Somebody started raising the issue, saying, "Well, we want to talk to you about the NAS study." I said, "Yes, actually, I wanted your input. Which institute would you want to be merged with?" There was a silence in the room.

Q: What is the mission of the stem cell SWAT team headed by [deafness institute director] James Battey? Will it consider creating an NIH stem cell repository?

A: I wanted ... the action of NIH to become more strategic: Review the state of the science, review exactly what the pathway to progress should be. What are the stumbling blocks? Do we have enough scientists? Do we have enough access to cells?

There is ... informal talk [about creating a repository], because one of the issues that you absolutely need to tackle is this issue of full characterization, standardization of the cell lines so that you can compare results across laboratories. ... [But] remember, we don't own the cell lines.

Q: Do you intend to stay at NIH a certain length of time?

A: No, I don't have a particular agenda. I really don't. I had a great job where I was. I have to tell you, if you had told me a year ago that I would be here, I would have said, "You're dreaming." I would turn down offers to consider jobs. ... I did mention one time that the only job worth doing is this one. So it's probably what got me the nomination.

—JOCELYN KAISER

CREDIT: RICK KOZAK