

PROFILE ANDREW VON ESCHENBACH

Texas Surgeon Vows to Take Next Step in Beating Cancer

The new director of the National Cancer Institute brings his campaign to translate basic research into saving lives to Washington

Andrew C. von Eschenbach says he made "a conscious decision" to spend his first 100 days as the new head of the \$4.2 billion National Cancer Institute (NCI) "listening and learning." But don't confuse that behavior with passivity or a lack of confidence. "I'm a surgical personality," says the 60-year-old urologic surgeon, speaking during a 13 May interview with *Science* from his office on the Bethesda, Maryland, campus. "You consult, then you operate."

As President George W. Bush's pick to run the world's largest cancer research enterprise, von Eschenbach comes to Washington with a bulging budget and a self-imposed mandate to turn those basic research dollars into treatments and cures. The buzzword is translational research, and von Eschenbach, who spent 26 years at the University of Texas M. D. Anderson Cancer Center in Houston, says that he plans to apply that philosophy to everything from proteomics to drug development.

Relatively unknown among bench biologists, von Eschenbach has made a deliberate effort to meet leaders across many fields since taking the NCI helm in late January. He's already won over some of them to his cause. "My contact with him has been very reassuring," says Massachusetts Institute of Technology biologist Phil Sharp, one of several prominent basic scientists with whom von Eschenbach has met. But he adds, "[von Eschenbach's] problem, in my opinion, is going to be satisfying this [basic research] part of the NCI community."

Many scientists say that they are waiting to see how von Eschenbach operates now that his designated probationary period has ended. "I think we are all concerned that NCI without strong and vibrant leadership can drift into a bureaucratic mode," says David Nathan, president emeritus of the Dana-Farber Cancer Institute in Boston, although he emphasizes that his comments are not based on anything that von Eschenbach has or hasn't done.

Von Eschenbach inherits an organization

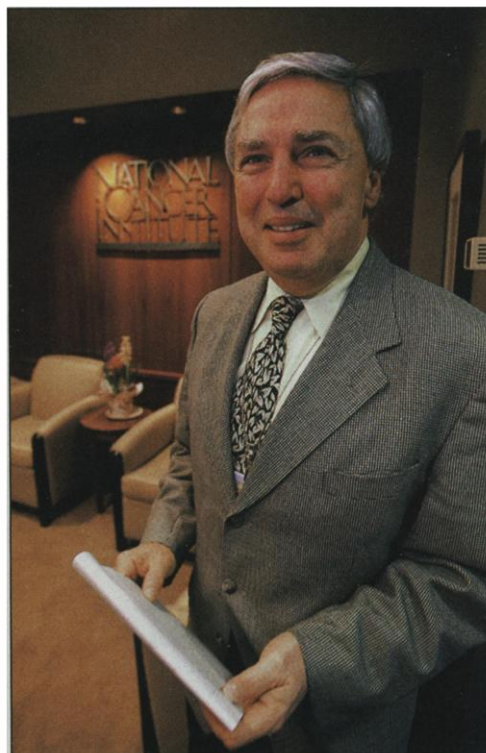
that saw six banner years under Richard Klausner, who overhauled the intramural program and boosted molecular research on cancer before leaving in October 2001. And he will likely get a generous budget in 2003—the president has requested a 12% increase to \$4.7 billion, the largest percentage boost of any entity of the National Institutes of Health (NIH) outside of the 57% rise to combat

bioterrorism proposed for the National Institute of Allergy and Infectious Diseases.

Scribbling diagrams on a notepad as he talks, von Eschenbach comes across as energetic and full of ideas. Despite the challenge of running NCI, he says that he must look beyond NIH to achieve his agenda: "NCI can't do every-

"People are dying, and we've got to make a difference in that."

—Andrew von Eschenbach



In control. Andrew von Eschenbach brings corporate management principles to running NCI.

thing. We have to partner, collaborate, and cooperate." Toward that goal, he made it a condition of his appointment that he continue as a leader of the National Dialogue on Cancer, a forum started by the American Cancer Society (see sidebar). A two-time cancer survivor, he has not yet found time to act upon another employment criterion: that he see patients for half a day a week.

Although few in Washington knew his name until his appointment, von Eschenbach "has been a major force in prostate cancer research," says gene therapy researcher Richard Mulligan of Harvard Medical School in Boston. After attending Saint Joseph's College in Philadelphia and medical school at Georgetown University, he began a fellowship in 1976 at M. D. Anderson, one of the two largest cancer centers in the country. There, he says, he "quickly appreciated that, without basic science, you're not going to solve the problem of cancer." Johns Hopkins University cancer biologist Don Coffey recalls how von Eschenbach "came flying up to Baltimore" one day after reading papers written around 1990 by Bert Vogelstein of Hopkins that linked mutations in the *p53* tumor suppressor gene to human colon cancer. The two proposed looking for *p53* mutations in human bladder cancers, an application of a basic research finding that yielded papers in *Science* and *The New England Journal of Medicine*.

Von Eschenbach's broadest contributions have built on a key clinical observation: Prostate cancer cells tend to metastasize on bone. To investigate this in the lab, von Eschenbach recruited to M. D. Anderson cancer biologist Leland Chung, who showed in the early 1980s that bone cells produce growth factors specific to prostate cancer cells. Von Eschenbach "was very instrumental in bringing forward" the role of such cell interactions in cancer, Coffey says. Subsequent studies have led to phase II and III clinical trials of a prostate cancer therapy that targets bone growth factors.

To support such research, von Eschenbach launched a Prostate Cancer Research Program in 1996 and corralled former President Bush for its board. The program's fundraising was "unusually effective," says M. D. Anderson president John Mendelsohn, netting over \$10 million. The money enabled the university to attract two leading angiogenesis scientists and put the program on the map nationally, he says. The Bushes have a long-standing interest in cancer research, having lost a daughter to leukemia. These interactions, combined with meetings involv-

CREDIT: RICK KOZAK

Tongues Wag as von Eschenbach Keeps Ties to National Dialogue on Cancer

Three years before Andrew C. von Eschenbach became director of the National Cancer Institute (NCI), he helped create the National Dialogue on Cancer. This amorphous private entity, funded by the American Cancer Society (ACS), brings together VIPs and cancer organizations to talk about how to conquer cancer.

It also attracts controversy. The Dialogue has been criticized as unfocused, as well as being a closed shop dominated by one sector of the advocacy community. Some detractors have also suggested that von Eschenbach, who stepped down as ACS president-elect when he was nominated to the NCI post, is too cozy with the group.

As vice chair of its steering committee, von Eschenbach says there's nothing mysterious about the group, despite its meetings behind closed doors. "It's nothing but a forum that allows groups, individuals, organizations, interested parties to ... deal with how they might effectively address cancer as a societal problem," he says. Former President George Bush and his wife Barbara are co-chairs of the Dialogue and have hosted gatherings at their home in Kennebunkport, Maine. The 150-some participants range from celebrities such as CNN talk show host Larry King to politicians, federal officials, biotech executives, and prominent cancer research clinicians.

Proponents admit that the Dialogue has had a slow start, but they believe it's now poised to make a difference in the war on cancer. "Any organization of leaders has to take time to find its niche," says participant Charles Balch, executive director of the American Society of Clinical Oncology, who says the group is now "moving from dialogue to action." Its current plans include finding ways to remove barriers to genomics-based drug development—for example, by developing national standards for tissue banks.



Texas tandem. Von Eschenbach and former President George Bush promote a Dialogue on Cancer.

The Dialogue's most visible accomplishment is launching a spin-off group, or committee, that drafted legislation to rewrite the 1971 National Cancer Act. Senator Dianne Feinstein (D-CA), co-chair of the Dialogue, introduced a version of the bill in February that would increase spending on certain cancer research and prevention programs and create new incentives for companies to develop cancer drugs.

At the same time, the group has been snubbed by some of those it purports to represent. Some prominent advocacy groups have been reluctant to participate in the Dialogue, partly because they say it too closely tracks ACS's views. In particular, some groups chafe at the society's effort to shift the emphasis from research to public health—such as education campaigns encouraging people to adopt healthier lifestyles and be screened for cancer.

The Cancer Letter, a Washington, D.C., newsletter, published a series of articles in the past 2 years questioning some of the Dialogue's activities. These included receiving funds from an ACS government contract with the Centers for Disease Control and Prevention (CDC) that the Dialogue used to fund participants' travel and other expenses. The newsletter argued that the Dialogue was essentially lobbying for CDC, which ACS has asserted should have a greater role in the national cancer agenda. ACS officials dispute that and say there is nothing improper about their use of the funds.

The Bushes are now leading a drive to raise \$15 million to bankroll the Dialogue's projects, and von Eschenbach says that NCI will staff some of these activities. But not everyone is pleased by his decision to commit federal resources. "It's something Rick [Klausner, previous NCI director] would never do," says the leader of one advocacy group. The problem, says the advocate, is that the Dialogue "is really not a shared agenda."

—J.K.

ing then-Governor George W. Bush, "put me in a position to be thought of for other things," notes von Eschenbach.

Von Eschenbach says that he hopes to speed progress at NCI by following the same "circular" approach—moving from clinical observation to the lab and back to the bedside—that he used to understand bone-tumor interactions. Anything less is not acceptable, he says. "If all we do is unravel basic mechanisms, they all pile up. ... People are dying, and we've got to make a difference in that."

Although he remains cautious about his plans, he provided a few details:

• **Translational research.** Von Eschenbach defines translational research as going "all the way" from genomics to clinical trials. One of his ideas is to find ways to get translational researchers to draw on NCI's mouse models consortium as a platform for validating drugs. Von Eschenbach also wants to use genomics tools such as gene arrays to look at

how a person's "host factors"—such as immune, endocrine, and emotional status—help send a cell on the path to cancer. He has set up a clinical center task force to examine other ideas, including having centers collaborate with state health departments in helping doctors enroll more patients in clinical trials.

• **Intramural program.** Von Eschenbach doesn't anticipate a major change in the balance between intramural and extramural research, but he's interested in "integrating" the two by bringing in "small groups" of extramural researchers. He may also follow Klausner's practice of inviting outside scientists for "minisabbaticals." The division of gene-environmental interactions, led by Joseph Fraumeni, is "an extremely important part of the equation," he adds.

• **Management.** Von Eschenbach, who often quotes management guru Andrew Grove of Intel Corp., compares his job to that of a corporate CEO. "When I look at my portfolio of management and leader-

ship responsibly, there's no one single person created that has the skill sets, the energy, the time." He hopes to free himself to explore "NCI's role in the larger cancer community" by hiring two senior managers, one as chief operating officer and the other as chief of staff. Al Rabson, currently deputy director, will function as "chief academic officer," dealing with staff, faculty, and professional societies.

The "content expertise" will come from NCI's six division heads, von Eschenbach says. High on his recruiting list is filling the vacancy left by the recent departure of Robert Wittes as director of the Division of Cancer Treatment and Diagnosis. Von Eschenbach pledges to be more specific about his plans "in the next 60 to 90 days." In the meantime, he hopes that basic researchers can "get excited about the fact that I hope to provide some of the leadership that will help them to do what they do best."

—JOCELYN KAISER