THE CANCER LETTER

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House Committee Begins Investigation Of NCI's National Lung Screening Trial

By Paul Goldberg

The Democratic leadership of the House Committee on Energy and Commerce last week inserted itself into the battle between advocates of lung cancer screening and skeptics who reserve judgment on the procedure pending completion of randomized trials.

Launching an investigation sought by the Lung Cancer Alliance and the Cancer Research and Prevention Foundation, pro-screening groups, the committee has instructed NCI and NIH to report conflicts of interest on the part of extramural scientists involved in the National Lung Screening Trial.

The letter, signed by committee chairman John Dingell (D-Mich.) and Bart Stupak (D-Mich.), chairman of the Subcommittee on Oversight and Investigations, said that "the outcome of this 10-year, randomized case-control [sic.] study could determine whether low-dose CT screening for lung cancer for at-risk individuals should become the standard of care in the United States." The letter is posted at http://energycommerce.house.gov/Press_110/index_110.shtml#Letters.

The investigation focused on two NLST scientists who agreed to testify

(Continued to page 2)

Capitol Hill:

Senate Approves FY08 Labor-HHS Bill Giving NIH A $799 Million Increase

By Kirsten Boyd Goldberg

The Senate voted 75-19 on Oct. 23 to approve a fiscal 2008 Labor-HHS-Education bill that would provide NIH $29.89 billion, a $1 billion or 3.5 percent increase.

The actual increase for NIH programs would be $799 million, a 2.8 percent boost, because the bill requires the institutes to transfer $201 million to the Global AIDS Fund.

NCI would receive $4.91 billion, a $113 million increase over its FY2007 appropriation of $4.797 billion.

The Senate and House are expected to begin conference to reconcile their versions of the Labor-HHS appropriations.

President Bush has said he would veto the bill. The Senate bill, which totals $606 billion, exceeds his budget request by $9 billion. Bush had requested $3.6 billion in cuts to discretionary spending, including a $289 million decrease for NIH.

The Senate vote exceeded the number required to override a veto.

Both Sides Of CT Controversy Testified In Tobacco Trials

(Continued from page 1)

in two tobacco lawsuits. Though they aren't named in the letter, the two are Denise Aberle, co-principal investigator of NLST and professor at the University of California, Los Angeles, and William Black, a radiology professor and principal investigator at the NLST site at Dartmouth Hitchcock Cancer Center and a member of the trial's executive committee.

Aberle and Black were investigated by their institutions, which found no wrongdoing. Both say that their testimony was truthful and in the public interest.

"The other side was making outrageous claims about how CT was proven to be beneficial, and there was a lot of potential harm that could be done," said Black, who withdrew his affidavit submitted for a New York case and returned a $700 check as soon as the controversy surfaced. "I did what was the right thing to do. I haven't done anything unethical, I wasn't greedy. If I am guilty, I am guilty of being naïve, not realizing that somebody could twist this around and make it damaging to NLST and myself."

Aberle, too, said she testified in the interest of public health. "The plan proposed to screen individuals using CT at a time when our only information derives from survival statistics, which misrepresent screening benefit," she said. "The consistent message of my testimony was that we have no data on mortality benefit, there are legitimate risks that may be incurred with CT screening, and we have no clear understanding of the balance between risk versus benefit."

About $30,750 went to Aberle's institution for her testimony. Altogether, she received $11,576 between 2000 and 2003. The money was placed into her professional academic account used to pay medical association dues, journal subscriptions, and other professional expenses. No funds went to support research, she said.

In recent years, proponents of lung cancer screening have been trying to tap into funds from product liability suits against tobacco companies. In 2000, then New York Mayor Rudolf Guiliani announced a CT screening program—the New York Early Lung Cancer Action Program—funded in part with $4 million from the tobacco settlement to screen 10,000 current and former smokers. Last February, the screening program received $8.7 million from a tobacco settlement with flight attendants who had been subjected to second-hand smoke. Now, the New York state legislature is considering a bill that would use $10 million in the state's tobacco settlement funds to set up a CT screening program. Similar bills are pending around the country.

Four researchers affiliated with the International Early Lung Cancer Action Program, which developed the protocols used in the screening demonstration projects, testified for the plaintiffs in the New York case for which Black submitted an affidavit.

The screeners, who are led by Claudia Henschke, of New York Presbyterian Hospital and Cornell Medical Center, argue that CT can find early stage disease better than chest x-ray. Citing data from a large single-arm trial, they claim to produce a 94-percent 10-year survival advantage and argue that this finding makes randomization unethical (The Cancer Letter, Jan. 12).

Skeptics say that CT could be picking up clinically irrelevant tumors, and I-ELCAP findings could be confounded by bias. No major medical organization endorses screening, and recently the American College of Chest Physicians issued a guideline urging that CT screening of former smokers be restricted to well-designed clinical trials with appropriate human subjects protections (The Cancer Letter, Sept. 14).

Though skeptics acknowledge problems with appearances of defending tobacco companies, they note that premature proliferation of CT screening and political attacks on a randomized trial of the technology constitute real threats to public health. "While it's crazy that tobacco might be right, we don't know whether we will be helping these people or hurting them," said Steven Woloshin, associate professor of medicine at

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Dartmouth and an investigator with the Dartmouth Center for the Evaluative Clinical Sciences.

"The irony here is that the people testifying for the tobacco industry are the ones who are protecting public health, and Congress is going to potentially harm people if they derail this incredibly important trial," said Shannon Brownlee, a senior fellow at the New America Foundation and author of the recently published book "Overtreated: Why Too Much Medicine is Making Us Sicker and Poorer."

"This trial is one of the most important randomized, controlled trials that we can do not only because of the public health implications, but also because of the cost," Brownlee said. "This is an attack on evidence-based medicine."

The Question of Equipoise

The Dingell-Stupak letter cites Aberle's testimony at a Louisiana trial on June 18 and 19, 2003, in what appears to be an effort to demonstrate that she had expressed strong opinions about the lack of efficacy of CT screening. An investigator who is convinced that one intervention is better than another cannot ethically continue to randomize patients to a trial.

According to the letter, the defense counsel at the Louisiana trial asked Aberle whether she believed that "doctors who recommend low-dose screening CT for the early detection of cancer are reckless."

"At this time, yes," she replied.

The statement is strong, but appropriate, said Richard Schilsky, chairman of Cancer and Leukemia Group B and president-elect of the American Society of Clinical Oncology. "To me, that implies that she doesn't know whether this is an effective test," Schilsky said. "Reckless may be a pretty strong word, but what she is saying is that she wouldn't recommend it at this time, and that's why we are doing the trial."

In another instance cited in the Dingell-Stupak letter, Aberle was asked whether a delay in screening pending conclusion of a randomized trial would fail to save lives that could otherwise be saved.

"And if you are wrong, you may kill a whole lot more than lung cancer will," she replied.

The letter cites this response as a transgression on Aberle's part: "Inasmuch as there are no published scientific studies that low-dose spiral CT screening will lead to more deaths than lung cancer itself, the basis for her conclusion is also unclear," the letter reads.

This appears to be a misunderstanding of the statement, says Schilsky. Aberle is clearly stating that the worst-case scenario is that mortality from lung cancer would remain unaffected, plus patients could die as a result of follow-up to screening.

"Without the data from the trial, why would you start screening people with this technique?" Schilsky said. "At the moment, there is no evidence that this technique is worthwhile. She is saying that if the trial turns out to be negative and you start screening a bunch of former smokers, some of them may have complications from the follow-on tests."

A review of the transcript not cited in the Dingell-Stupak letter confirms this interpretation.

"Is there any scientific study that has suggested that the low-dose CT kills people?" the plaintiff's attorney parries Aberle's remark.

Her response can be taken as an indication of a strong belief in equipoise:

"There is no study that shows that it kills people, or that it helps people, or that it reduces deaths. In fact, there is no data that it prolongs survival yet. There's no data."

Aberle said her beliefs haven't changed. "How could I do this trial if I didn't believe there were not equipoise?" she said. "I couldn't possibly enroll 18,000 participants unless I believed that there is not a solution. I gave these people consent. I told them I wouldn't hurt them. And the whole reason for having the Data and Safety Monitoring Board is so that if there isn't equipoise, they are going to tell me either to stop the trial or modify the protocol."

Aberle's 2003 testimony is posted at www.cancerletter.com.

Trial Oversight

"The tobacco industry has clear financial interest in the outcome of NLST," the Dingell and Stupak letter states. "If the NLST produces a negative or inconclusive result, the tobacco industry could use these findings to defend itself from litigation seeking low-dose CT screening of lung cancer as a remedy."

This statement is at least as puzzling as the legislators' earlier description of NLST as a "randomized case-control study."

First, there is a technical problem: a superiority trial that reaches an "inconclusive" result is, by definition, a negative trial.

Second, if the trial is negative, why would anyone seek CT screening of lung cancer?

More importantly, if NLST is tainted by outside interests, it's at least as likely that these could be the interests of the radiologists conducting the trial. "You could also make the argument that if a study like this

is positive, it's a potential windfall for radiologists, because presumably there would be a recommendation that anybody who has a smoking history should be getting these tests done all the time," said Schilsky. "That would be good for radiologists, particularly those who own their own facilities and make money every time the scan gets done."

Black said he can't think of any way for any investigator to influence the trial's results.

"It can't be done," he said. "The main outcome in the study is lung cancer mortality, and the way lung cancer mortality is determined is based on a combination of death certificates and an independent death committee that looks at the anonymized medical records of people who have died either from lung cancer or something possibly related to lung cancer or screening. And that's based on an algorithm that's based on the death certificate report and what the CT study results were. So, an investigator has absolutely no control in determining the cause of death. This is complete contradistinction to I-ELCAP. They have no independent review of their deaths or records."

In addition to having a DSMB, the trial, which is funded through a combination of an NCI contract and a grant, has an oversight committee, Aberle said.

"We have an oversight committee that meets with us twice a year to go over any kinds of issues," she said. "This trial has had more oversight and more hands on it than anyone has seen before. The data are strictly separate from me, which is why I don't know anything about these data.

"So even if I were a crazed tobacco lobbyist, as this letter seems to suggest, I could not have hurt this trial," Aberle said.

Dingell and Stupak Seek Disclosures

The letter asks NCI and NIH to review conflicts of interest on the part of all NLST investigators, and to do so using the more stringent criteria applied to NIH employees.

"Given the study's magnitude and commitment of federal resources, it seems prudent for NIH to ensure that the integrity of this study is not compromised," the letter states. "For that reason, the committee respectfully requests that NCI secure and evaluate financial disclosures from each of the NLST site principal investigators and co-investigators using disclosure standards required for NIH federal investigators. To the extent that the Data and Safety Monitoring Board members have not been subject to a careful review, we would urge that as well."

The conflict of interest standards for NIH employees were tightened in February 2005 and now prohibit "even the appearance of influence from extraneous financial interests." Extramural scientists are monitored by their institutions, which review financial interests that could "directly and significantly affect the design, conduct, or reporting" of NIH-funded research.

It's unclear whether NIH would be able to provide the information sought by Dingell and Stupak. "They are citing the intramural federal employee rules as what they want to be applied, and those rules legally may not be applicable," said an NIH official who spoke on condition that his name would not be used. "They may also not be applicable just from a sheer logistics resource requirements. How would we do this? How would we collect personal financial information from every PI across the country in order to assess that information?"

Though the review of conflicts is left to local institutions, the NCI clinical trials cooperative groups have additional disclosure requirements and monitoring procedures that vary from group to group.

"Everyone in the group has to file a COI report for review annually," said Lawrence Baker, chairman of the Southwest Oncology Group. "There are people who are absolutely adamant about saying. 'I will not tell you what stocks I own.' We say to this, 'Okay, then you have to leave the group.'"

After SWOG members submit their statements, their conflict of interest committee reviews them and develops a plan for managing conflicts. These plans depend on the individual's ability to interact with the data, Baker said.

"We will not allow someone to be a study coordinator because of a perception of conflict," he said. "If a [community] physician is going to enter cases into a study and owns Amgen stock, and Amgen's product is involved, we would recognize that. We wouldn't stop him from participating, but we can't imagine that an investigator entering less than one percent of the cases could affect the outcome of the study."

At CALGB, the disclosures of local investigators usually aren't reviewed. "We review the disclosures of someone who is named on the protocol as a leader of a study," Schilsky said. "But when that study goes out to 200 sites, the local person, we don't review their financial disclosures. We assume that they abide by whatever their institutional policies are."

If the groups are conducting registration trials, under FDA rules, they have to collect conflict of interest forms from local investigators and trial leadership.

The principal investigators at the 46 institutions conducting NLST haven't been asked to submit detailed conflict of interest statements, sources said.

Black Never Testified

Black said he has never done any expert witness or industry consulting work.

"I have always wanted to avoid the appearance of a conflict of interest," he said. "One, I don't need it. I make enough money, I am comfortable, I don't have an extravagant lifestyle. I don't want people questioning my work. I've decided just to say no. I can evaluate things, I can make comments, but I just don't want to take money from any industry."

When he was approached by a law firm representing Philip Morris USA, his initial reaction was to say no.

"My desk is covered with papers, I am behind on all fronts, I am trying to do academics, I am trying to do research, I am trying to do teaching and clinical practice," he said. "If I had known that there was any reason not to do this—if I had any excuse—I wouldn't have done it. I felt morally obligated."

Money was irrelevant, he said. It went to the department.

Black threw together an affidavit that incorporated his prior publications and billed the law firm $700 for two hours of work. "I did no new research for them. I was just putting together what I had stated in previous published editorials and papers about screening principles," he said. "It was what 95 percent of the medical community believes in. Nothing at all controversial, all of it published before I ever even met a lawyer."

With Black's permission, the document is posted at www.cancerletter.com. The patients' names have been redacted. Black completed this work in September 2006. In November, at a meeting, a colleague told him that Lung Cancer Alliance was furious about his testimony.

At this point, Black recognized the danger to himself and NLST. "I wondered, would they try to smear me by saying that I worked for a tobacco company and completely distort the record?" he said. "Quite honestly, I never considered myself as being part of tobacco. I considered myself as being against an unreasonable screening program. Everything I have written about tobacco in the medical literature had always been about how it's the leading cause of lung cancer and other preventable deaths."

He hired a lawyer, retracted his affidavit, and wrote a personal check for $700 to the firm that hired him. His affidavit had been provided to the plaintiffs, but was never made part of the court record. Since there was no deposition and no trial, he has never testified.

"Dear Elias"

Advocates of CT screening apparently learned about Black's and Aberle's role from the plaintiffs' attorneys, and on Nov. 22, 2006, LCA President Laurie Fenton and Carolyn Aldige, president and founder of Cancer Research and Prevention Foundation, sent the following email to NIH Director Elias Zerhouni:

"Dear Elias:

"We understand that you are out of the office today and apologize if we are interrupting Thanksgiving holiday activities with your family, but there is a degree of urgency to a situation which we believe represents a serious conflict of interest.

"Two investigators of the National Lung Screening Trial (NLST) have failed to disclose in public forums that they have received payments for testimony and research on behalf of tobacco companies. We are aware of your focus on conflicts of interest at the NIH, and suspect that you are acutely aware of the great sensitivity in the cancer community—particularly in lung cancer—about disclosing even the slightest conflict of interest with the tobacco industry. In fact, most cancer advocacy organizations have long abided by strong and clear policies governing tobacco money and give great scrutiny to working with other individuals or organizations with ties to tobacco.

"Specifically, William C. Black, M.D., principal investigator at the Dartmouth-Hitchcock Medical Center NLST site, and a member of the Executive Committee of the NLST, did research and testified on behalf of Philip Morris USA Inc. in Civil Action No. 06-0224 (CBA) (SMG) on September 16, 2006, in the U.S. District Court of the Eastern Division of New York. On page six of his sworn testimony, he states: 'My compensation per hour for this matter is $350 for record review meetings and testimony.'

"This compensation was not disclosed by Dr. Black on at least two occasions in which he made public statements requiring full disclosure: the [NCI Cancer Intervention and Surveillance Modeling Network] meeting in November 2006 and his submissions for the [Radiological Society of North America] meeting which will be held in Chicago next week.

"Denise Aberle, M.D., principal investigator at the Jonsson Comprehensive Cancer Center, UCLA, site, and co-director of the NLST, testified in Civil District Court of the Parish of New Orleans of the State of Louisiana

in case No. 96-8461, Scott and Jackson vs. American Tobacco Company Inc. et. al….

"We respectfully request that these apparent conflicts of interest be investigated with all due dispatch, especially in light of the fact that each individual will be speaking at the RSNA meeting next week.

"We look forward to discussing our concerns with you at your earliest opportunity; meanwhile, we wish you and yours a lovely Thanksgiving holiday."

The letter contains several factual errors, Black and Aberle say. Allegations notwithstanding, they performed no research for tobacco companies and received no research funds from anyone connected with tobacco. Also, Black didn't testify in the New York case.

As for failure to disclose, the Radiological Society of North America requires disclosure of ties to commercial interests, which, according to disclosure forms, are defined as "any proprietary entity producing health care goods or services, with the exemption of non-profit or government organizations and non-health care related companies." CISNET, a consortium of NCI-funded investigators, has no separate disclosure requirement. "I was a guest at that meeting," Black said. "I never made a presentation."

The NIH response to Aldige and Fenton came from Norka Ruiz Bravo, NIH Deputy Director for Extramural Research.

"It is our responsibility to ensure that the institutions we fund have conflict of interest policies in place and that those policies meet the requirements of the regulations," states the letter dated Jan. 16. "It is the responsibility of the home institutions (in this case Dartmouth-Hitchcock Medical Center and the Jonsson Comprehensive Cancer Center, UCLA) to have a policy in place and to implement that policy to ensure that there is no conflict of interest, or when there is, that there is a means of remediation. We have determined that our responsibilities have been met, as have the responsibilities of the institutions.

"I do understand your concern that there appears to be a conflict of interest. However, if one examines the purpose of the NLST, it is not a trial that is focused on tobacco—even though tobacco is a major cause of lung cancer. The purpose of the NLST is to compare two imaging techniques to determine if either can reduce the mortality of lung cancer through early detection. The trial does not examine how the participants got lung cancer—just the best means to detect that cancer and thus save lives."

I-ELCAP's Ties With Industry, Plaintiffs

On Oct. 8, The Wall Street Journal published a story focusing on the two researchers and the investigation. The story alluded to conflicts on both sides, including General Electric's $100,000 contribution to Lung Cancer Alliance. Readers who turned to the newspaper's Health Blog also learned that General Electric is making royalty payments to Henschke and collaborator David Yankelevitz for an algorithm for detection of lung cancer on CT images.

A subsequent story, on Oct. 23, reported erroneously that "two of the trial's principal investigators have testified as paid experts for tobacco companies."

"Tobacco companies have been pretty evil in what they have done and if I were reading what has been written about me in the Wall Street Journal, I'd say, this guy sounds pretty sinister," said Black. So far, he has spent between $2,000 and $3,000 in legal fees and at least 100 hours providing documentation for investigations conducted by NCI and Dartmouth, and is now facing greater exposure from the Congressional investigation.

Meanwhile, plaintiff's witnesses in the case include four I-ELCAP principal investigators whose names appear on the group's paper published in the Oct. 26 issue of The New England Journal of Medicine. They are: Harvey Pass, of the New York University Division of Thoracic Surgery, Frederick Grannis. Head of the Section of Thoracic Surgery at City of Hope National Medical Center, Steven Markowitz, director of the Center for the Biology of Natural Systems at Queens College, City University of New York, and Albert Miller, professor of medicine at New York Medical College.

"Deni and I were paid expert consultants or paid witnesses," Black said. "They are not only paid witnesses, but if the lawsuit goes their way, they are huge potential beneficiaries."

Gold Standard vs. the Golden Rule

One of these four witnesses, Frederick Grannis, a thoracic surgeon and a PI at City of Hope, who is also a study participant in I-ELCAP, was deposed in the New York case on Dec. 20, 2006.

Excerpts from his deposition follow:

—NLST is "Bad Science": "I can tell you that my point of view is that [NLST] is a trial that I don't think should have been done. I don't think it's a well constructed trial…. I am an ex-smoker who is at personal risk for lung cancer. From my standpoint, when presented with the choice of whether I would participate in the ELCAP trial or in the NLST, it was a very clear and simple decision for me to participate in

the I-ELCAP. Because, first of all, the National Cancer Institute has been telling me for the past 20 years that chest X-ray is not an effective lung cancer screening device, and, second of all, that it might be harmful. So for them to suddenly turn around and offer me that as an arm of a research study struck me as hypocritical at best. And bad science as a second part.

"So that from an ethical standpoint I could not reach equipoise. I could not say that I don't know which of these two treatments is the best. And so I could not recommend that any patient of mine participate in NLST.

--*Randomizing the poor:* "Except in patients who had no health insurance, who were indigent, who could not pay for a lung cancer screen, those patients I told it would be reasonable for you to participate in NLST. It's not social justice, but it's the best you can get in this instance, and you would have a coin flip of getting a good screen, and you would have a second choice of getting a screen that's probably better than nothing, but not as good as a CAT scan, clearly."

—*CT screening outside clinical trials:* "Now that we have the long-term survival rate showing 10 years actuarial survival of patients with screened detected early diagnosed cases of lung cancer were treated appropriately, and 80 percent of all patients who were screened in the study, I think that that is by far good enough information that if an individual comes to me and for some reason doesn't meet the criteria of our research study, then I will say, yes, we'll screen you outside the context of a research study."

—*Current lung cancer treatment strategy:* "The system that we use in the United States today is to do nothing until the patient walks into our office with symptoms of lung cancer. Once we recognize those symptoms and make a diagnosis and treat that patient with the best available treatments we have at our disposal we only cure 15 percent of those people. And, furthermore, that treatment over the past 30 years has resulted in improvement in lung cancer survival from 12 percent to 15 percent. So as far as I'm concerned, that's a failed, bankrupt method of dealing with the problem of lung cancer."

"The method that we have to treat early stage lung cancer are highly effective as reflected in the results of the I-ELCAP trials. Where if you have a patient who can be detected in stage 1A and treated for cure without delay, that the chance of five years—the chance of ten year actuarial survival is 92 percent, which is strikingly different from the 15 percent under what I call the late detection multi-modality salvage strategy that we currently use."

—*Lead-time bias, length-time bias and overdiagnosis bias:* "These biases have been overestimated, overstressed, and they have been used to influence juries, influence the man on the street, influence physicians, influence physicians, influence NCI, NIH, influence organizations to believe that these biases are really important and require the need for a randomized trial and argue against the implementation of lung cancer screening…. These biases are not of major importance in lung cancer screening."

—*Mayo lung trial:* "In the Mayo lung trial the survival in the screened group was twice as good as the survival in the minimally screened group. That survival was statistically significant in a prospective randomized trial…. The reason that it was not accepted as a standard of care … is that experts imputed these biases as skewing the survival data in such a major fashion that lung cancer screening … with a chest X-ray was not only not helpful but was also harmful. And I think that that was a major disservice to mankind.

"There were a number of people, including myself, who felt that the study showed very high promise for reducing the mortality and morbidity of lung cancer, and should have been either implemented into screening the population or followed up by further research. Neither one of those things happened. And a lot of lives were lost in the years intervening.

"They were influenced by the fact that these putative biases, lead-time, length-time, and overdiagnosis bias were so important that they explained away all of the survival benefit in early detection of lung cancer. And I think that's completely wrong. And I think that the subsequent experience in the I-ELCAP study shows clearly that none of those biases have a substantial impact on the results of the trial."

—*A randomized control trial is "not necessarily" the gold standard for determining the effectiveness of a cancer screening method:* "A randomized control trial … often is not the best trial for any kind of research, as well as screening research….

"I'm not as interested in the gold standard as I am about the golden rule. And the golden rule says to do unto others as you would have them do unto you. The price of doing this NLST trial is the terrible suffering and death of at least 75 people. That's what's going to happen. That's what's going to be the end result of this trial. In order to get the answer that they're looking for, it's going to cost the suffering and death of a lot of people, and that's wrong. That's a violation of the golden rule in order to achieve the golden standard."

In the Cancer Centers:

Watson Steps Down After Uproar Over Interview

By Kirsten Boyd Goldberg

Cold Spring Harbor Laboratory announced Oct. 25 that James Watson has retired as chancellor after 40 years of working at the laboratory.

The Board of Trustees suspended Watson's administrative responsibilities on Oct. 18, following news reports that the scientist who shared the 1962 Nobel Prize for describing the double-helix structure of DNA had made derogatory comments about the intelligence of people of African descent.

In a statement, Watson said that at age 79, he is "overdue" to transfer leadership of the laboratory, which he transformed from a small facility when he became its director in 1968 to a renowned research institution specializing in cancer, plant biology, neuroscience, and computational biology. He stepped down as president in 2003, but continued to work on educational programs and fundraising.

"The circumstances in which this transfer is occurring, however, are not those which I could ever have anticipated or desired," he said.

Watson said he will also step down from the board, but he will remain at the laboratory to continue research on cancer. "Final victory is within our grasp," he said. "I wish to be among those at the victory line."

Watson, who had been in London to promote his new book, was quoted in The Sunday Times Magazine on Oct. 14 as suggesting that people of African descent are less intelligent than people of European descent. The article is posted at http://entertainment.timesonline.co.uk/tol/arts_and_entertainment/books/article2630748.ece.

Watson issued a statement apologizing for the comments, saying "there is no scientific basis for such a belief," but he did not say he had been misquoted. He was forced to cancel his U.K. book tour and lectures.

The Times said it stood by the story.

Watson's comments "in no way reflect the mission, goals, or principles of Cold Spring Harbor Laboratory's Board, administration or faculty," CSHL President Bruce Stillman said in an Oct. 17 statement. "The Board of Trustees, administration, and faculty vehemently disagree with these statements and are bewildered and saddened if he indeed made such comments. Cold Spring Harbor Laboratory does not engage in any research that could even form the basis of the statements attributed to Dr. Watson."

The uproar over Watson's remarks also prompted NIH Director Elias Zerhouni to issue a statement. "The comments…are wrong, from every point of view—not the least of which is that they are completely inconsistent with the body of research literature in this area," Zerhouni said. "Scientific prestige is never a substitute for knowledge. As scientists, we are outraged and saddened when science is used to perpetuate prejudice."

Watson has a reputation for making incendiary remarks. In a 2000 lecture at University of California, Berkeley, he suggested that sex drive is related to skin color, and body weight is related to personal ambition.

"That the Cold Spring Harbor Laboratory is now one of the world's premier sites for biological research and education has long warmed my heart," Watson said in his Oct. 25 statement. "So I am grateful that its Board now will allow me to remain along my beloved Bungtown Road. Forty-nine years ago, as a newly appointed young Assistant Professor at Harvard, I gave my first course on this pernicious collection of diseases of uncontrolled cell growth and division. Cancer, then an intellectual black box, now, in part because of research at the Laboratory, is almost full lit. Though important facts remain undiscovered, there is no reason why they should not soon be found. Final victory is within our grasp. Strong in spirit and intensely focused, I wish to be among those at the victory line.

"The ever quickening advances of science made possible by the success of the Human Genome Project will also soon let us see the essences of mental disease. Only after we understand them at the genetic level can we rationally seek out appropriate therapies for such illnesses as schizophrenia and bipolar disease. For the children of my sister and me, this moment can not come a moment too soon. Hell does not come close to describing the impact of psychotic disorders on human life.

"This week's events focus me ever more intensely on the moral values passed on to me by my father, whose Watson surname marks his long ago Scots-Irish Appalachian heritage; and by my mother, whose father, Lauchlin Mitchell, came from Glasgow and whose mother, Lizzie Gleason, had parents from Tipperary. To my great advantage, their lives were guided by a faith in reason; an honest application of its messages; and for social justice, especially the need for those on top to help care for the less fortunate. As an educator, I have always striven to see that the fruits of the American Dream are available to all.

"I have been much blessed."

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