THE GALLO PROBE

HHS Cancels Gallo's Moment in the Sun

Ever since the National Institutes of Health (NIH) formally opened a misconduct probe into Robert Gallo's early AIDS research more than two and a half years ago, Gallo has remained uncharacteristically silent, at least in public—the result of a gag order from his superiors. Last week, however, Gallo was scheduled to get his moment in the spotlight, courtesy of NIH director Bernadine Healy. Convinced that he had defended himself well in a closed-door session with the directors of NIH's institutes, she had arranged for him to appear on 24 June at an open meeting of the National Cancer Advisory Board Subcommittee on AIDS to answer questions from committee members and the public (*Science*, 15 May, p. 955). Gallo was certain to get all the exposure he needed and maybe more: At least 30 news organizations had planned to send reporters, and CNN had even arranged to cover the meeting live.

Let's call the whole thing off. Michael Astrue.

But the day before the meeting was to begin, NIH called it off, citing legal concerns raised at the last minute by Michael Astrue, general counsel of NIH's parent body, the Department of Health and Human Services (HHS). On 23 June, Astrue wrote to Nobel Prize–winning biologist Howard Temin of the University of Wisconsin, who chairs the AIDS subcommittee, to inform him that the meeting "exceeds the statutory authority of your committee and therefore must be canceled."

A top-level HHS official involved in the decision, who spoke on condition that he not be identified, cited two main reasons for the cancellation. First, the meeting "essentially amounted to an investigation of the underlying facts in the Gallo case"—an investigation Temin's subcommittee had no authority to conduct, the official said. Furthermore, such a public forum could have been "unfair" to Gallo, the official said, since in addition to the NIH investigation he also faces probes by Representative John Dingell's (D–MI) oversight subcommittee, the General Accounting Office, and the HHS inspector general—all of whom would have been watching his public statements closely. The meeting "was just a bad idea to begin with," the official concluded.

Whether a bad idea or not, the meeting had certainly promised to be highly unusual—and potentially explosive. For one thing, it would have marked the first time the federal government had provided the subject of an ongoing misconduct investigation a public platform to make his defense. For another, it could have touched on issues that are still the subject of international dispute, such as the validity of a multimillion dollar Franco-American patent on the AIDS blood test. U.S. lawyers for the Pasteur Institute, in fact, had scheduled a press conference immediately following the advisory board meeting "to respond to anything Gallo was going to say," says Michael Epstein, a lawyer at the New York firm of Weil, Gotshal, and Manges, which represents the institute.

Temin insists that the meeting could have steered clear of such potential land mines. The idea, he says, was "to enable Dr. Gallo to present, in his own voice, information relative to this controversy" and "to have a discussion of some of the lessons that can be learned from this controversy about the processes of scientific discovery, scientific management, and scientific administration." The meeting was "expressly" not a review of the misconduct investigation or the harsh criticism of Gallo offered by an outside panel of advisers chaired by Yale biochemist Fred Richards (*Science*, 8 May, p. 738), Temin says.

Despite such protestations, however, Temin's own statements suggest that the meeting would have covered some of the same ground as the NIH probe. For example, Temin says that Gallo had been asked to respond to six specific charges, among them that he may knowingly have used LAV, an HIV isolate he received from the Pasteur Institute, to make his AIDS blood test in 1983 and 1984; that he had repeatedly denied growing LAV in his laboratory; and that he may not have given the French credit for knowledge he gained by growing LAV. Several of these charges have been addressed in NIH's misconduct report or by the Richards panel.

The decision to call off the meeting doesn't mean that Gallo has lost his chance to make his case publicly—just that he can't do so at the government's expense. Says the HHS official: "If [Gallo] wants to pick a forum and present his views as a private individual, the department has no problem with that." So far, however, Gallo hasn't said whether he's willing to emerge from NIH's protective cocoon to get his side of the story out on the table.

–David P. Hamilton

DRUG REGULATION

Do Antidepressants Promote Tumors?

As if cancer patients don't already have enough to worry about, a new animal study conducted by a team of Canadian researchers has raised a disturbing possibility. The study, which is published in the 1 July issue of *Cancer Research*, shows that two widely used antidepressants, Elavil and Prozac, act as "tumor promoters" in rats and mice. That means that the drugs, although they are not carcinogens by themselves, accelerate the growth of existing tumors in those animals.

While there's currently no evidence that the antidepressants promote tumor growth in humans, the new results are troublesome because cancer patients are more likely to suffer from depression—and thus to be prescribed antidepressant drugs—than members of the general population. Says oncologist Lorne Brandes of the Manitoba Institute of Cell Biology in Winnipeg, the leader of the team that did the work: "I think that the antidepressants are valuable drugs. But the message is disturbing, and there's no way around that."

Indeed, officials at both Canada's Health Protection Branch and the U.S. Food and Drug Administration (FDA) are taking a look at the Brandes group's results. Agnes Klein, chief of the Health Protection Branch's Oncology Division, characterizes the work as "interesting" and "well done," although she declined to comment on what action, if any, her agency is considering. And Gregory Burke, director of the FDA's Division of Oncology and Pulmonary Drug Products, says he too is interested, because the Brandes team's results bear on the wider issues of how tumor promoters work and how to assess the cancer risks of such compounds. At present, for example, carcinogen screens aren't set up to detect promoters. "The agency and the whole world are trying to design better tests," says Burke, who has invited Brandes to FDA headquarters to discuss his results.

Brandes and his colleagues decided to undertake the animal studies as an outgrowth of their research on an intracellular receptor known as the "anti-estrogen binding site" (AEBS), which was identified by Robert Sutherland and his colleagues at the Ludwig Institute in Sydney, Australia, on the basis of its ability to bind Tamoxifen, the anti-estrogen drug used to treat breast cancer. The Manitoba group wanted to pin down the role the AEBS plays in the cell, and to do this they needed a compound that would bind specifically to the receptor and tweak its activity. Tamoxifen itself wasn't suitable be-

cause it also binds to the estrogen receptor and has other cellular effects as well. But the researchers thought that by tinkering with Tamoxifen's structure they might be able to come up with a specific AEBS binder. They eventually hit on a compound called DPPE that seemed to fit the bill.

DPPE proved to have several effects on cell growth, including stimulation of tumor growth in rats and mice. And Brandes noticed something else as well: DPPE is structurally similar to the antihistamines, which led the researcher to suggest that all or part of the AEBS might be a novel type of histamine receptor, an idea supported by further work. Previously discovered histamine receptors mediate allergic reactions, among other things, but not cell growth.

But the antihistamines aren't the only compounds that DPPE resembles. It is also structurally similar to antidepressants, including Elavil and Prozac. And since DPPE proved to have tumor-promoting activity in rodents, the question then was, might the antidepressants have similar activity. The answer, according to the current study, is yes. The researchers found, for example, that when they used the chemical carcinogen known as DMBA to induce mammary tumors in rats, animals treated with either antidepressant, in doses comparable to those given to human patients, developed the cancers both more rapidly and in greater numbers than controls. That led Brandes to ask one of the paper's co-authors, cell biologist Robert Warrington of the University of Saskatchewan in Saskatoon, to test the drugs in another cancer model in which melanoma cells are transplanted into mice; they also stimulated the growth of those cells. Brandes suggests the drugs are promoting tumor growth by virtue of their ability to bind to the intracellular histamine receptor.

What everyone agrees are needed now are more studies. "It would be interesting to see if the [intracellular histamine] receptor has the activity in human cells," says FDA's Burke. If it does, the information might be helpful in designing better screening tests.

It would also heighten concerns about antidepressants. Brandes calls for epidemiological studies aimed at determining how the fates of cancer patients who take the antidepressants compare to those of patients who don't. Although some previous studies have indicated that depressed individuals are at higher risk of developing cancer than people who aren't depressed, other studies haven't shown any differences between the two groups. Brandes says, however, that none of these studies appeared to take antidepressant use into account. And then there's the question of whether any of the antihistamines might themselves be tumor promoters. As Burke says, "[Brandes] has a lot of interesting experiments to do."

–Jean Marx

WOMEN IN SCIENCE

Congress Focuses on Job Discrimination

What do a garbage truck driver, a maintenance shop engineer, a neurologist, and a mathematics professor have in common? If they are women, they may find it tough to succeed in a man's world: Women from these four diverse occupations testified to Congress last week that they have been sexually harassed or discriminated against on the job. The four decided to go public with their cases to urge Congress to approve two new bills aimed at helping women enter—and stay in—what they called "male-dominated" jobs. One of the bills is designed specifically to address the problems women face in scientific and technical fields. "Whether women are scientists or truck drivers, physicians or plumbers, they often face isolation, hostility, and harassment in a male-dominated environment," charged Representative Constance A. Morella (R–MD), author of the proposed legislation.

Their stories represented "extreme" situations—such as former National Institutes of Health neurologist Maureen Polsby's account of refusing to go to bed with a man who recruited her for a medical fellowship. But other speakers, including Radcliffe College President Linda S. Wilson, testified that while "overt sexism is less pervasive than in the past," many women still experience subtle forms of discrimination. It is high time, they argued, that Congress, industry, and academia took steps to show that they value having women in the workplace; the witnesses advocate policies that go beyond banning sexual harassment to making sure that women who complain are protected and have means to redress their grievances. "The U.S. is the only industrialized nation in which basic workplace policies assume that women are not in the workplace," says Wilson. She says that American institutions ought to show they value female employees by offering leave and child-care services that recognize that men and women have familial obligations.

In academia, the problem is most glaring in the sciences, where the image of the "ideal scientist" is a man who works 80 hours a week because he has no conflicting family obligations, says Wilson, herself a chemist. Mathematics professor Jennifer Harrison—who failed to get tenure at the University of California at Berkeley and has filed suit against the university—hammered the point home in her testimony. A recent survey of the nation's top 10 math departments found that they have five tenured women, compared with 281 men with tenure. And where women do break into scientific professions, they consistently earn less money and hold lower ranking jobs than men. In medicine, which is considered to be relatively hospitable to women, less than 10% of the faculty are women, says Catherine Didion, executive director of the Association for Women in Science, who adds that only one American medical school has a female dean.

Those statistics have caught the attention of Congress: A half dozen congresswomen spoke at last week's hearing to try to stir up support for the two bills introduced last October by Morella. One bill, H.R. 3476, with no price-tag, would set up a 17-member commission to study the problems women face in entering and succeeding in technical professions. The panel's recommendations would go to the President and Congress. Another bill, H.R. 3475, would provide about $1 million to the Department of Labor for technical assistance to employers and unions to train and assist women in "nontraditional jobs," such as electronics technicians, maintenance engineers, and carpenters.

Complaint registered. Jennifer Harrison *(top)* and Rep. Constance Morella.

But before those bills can go anywhere, the Congressional Caucus for Women's Issues may have to deal with a problem close to home—namely, how to change attitudes in Congress, another male-dominated institution. Despite the attention last week's hearing on sexual harassment received, it is still unclear whether Congress is ready to enact legislation that would help women break into and keep "nontraditional jobs." Neither bill has been scheduled for a vote before the Labor Committee, though the women's caucus has been pushing for one. As Representative Patricia Schroeder (D–CO) looked around at the mostly female audience at the hearing, she quipped: "Part of the problem is, look at the audience. We have got to get more men into nontraditional audiences."

–Ann Gibbons