that she had been "haunted" by the case and had assembled an entirely new in-house panel to conduct a second inquiry the following month. That group, which did not include Healy, concluded in September 1990 that the scientist did "misrepresent the nature of experimental operations in his laboratory with the intent to mislead." The Cleveland Clinic notified OSI and set up another in-house panel to conduct a full-fledged investigation. That panel, which did not include Healy but considered her testimony, dismissed the charges against the scientist in October 1990.

OSI launched its own review of the case last December. Although NIH has not released the draft report, Suzanne Hadley — OSI's chief investigator at the time — testified last week that the federal probe revealed evidence of misconduct.

Furthermore, she said, "there were significant problems with that first inquiry [led by Healy at the Cleveland Clinic]." For one, Healy's panel included a scientist who had coauthored one of the questioned grant applications, creating a conflict of interest, Hadley said. "And then there was this rather curious concept of anticipatory writing.... The Cleveland Clinic Foundation, in the final analysis, didn't want to call something misconduct when it seemed to be manifestly misconduct as we know it," Hadley told the subcommittee.

Later in the hearing, Healy acknowledged that her preliminary inquiry was "inadequate." She said the scientist under scrutiny told her panel he had included some data that he "anticipated" obtaining before sending the proposals to NIH. Healy called this "inappropriate" but added that she still doesn't know whether the scientist deliberately misrepresented his work.

Dingell pointed out that OSI will next examine whether the clinic's research institute responded adequately to the allegations. "In this case, Dr. Healy's actions as director of the [Cleveland] institute and chairman of the first panel would necessarily be a subject of the investigation," he said. Healy removed herself from any decisions involving the Cleveland case when she joined NIH, but Dingell says the incident may color her judgment of other OSI investigations. Healy calls that suggestion "preposterous."

Several of her actions at NIH have raised concerns on Capitol Hill about OSI's functional independence. At a May 1991 meeting with Hadley and several others at NIH, Healy expressed strong reservations about the way OSI operates, referring to OSI staff as "the keystone cops" and characterizing OSI as "out of control," according to Hadley's testimony.

Hadley also told the subcommittee that Healy demanded a rewrite of a draft report on OSI's continuing investigation of Robert C. Gallo, a prominent AIDS investigator at the National Cancer Institute. Gallo's claim to the discovery of the AIDS virus has long been contested by a French research team. In early June, Healy told Hadley the draft report "reads like a novel," and instructed her to remove editorialized statements and to make it sound more like a scientific paper, Hadley said at the hearing. Hadley objected to the changes in a June 10 memo, saying they would "significantly vitiate the findings of the draft report." In a June 17 memo, Healy replied that she had never intended to change the substance or conclusion of the report, and had merely made some suggestions to improve its style.

At the hearing, Hadley described a recent series of events that she interprets as an attack on her integrity and a threat to her career. One involved her investigation of highly publicized allegations made in 1986 against Boston immunologist Thereza Imanishi-Kari. A draft OSI report, leaked to the press last March, concluded that Imanishi-Kari's lab notebooks contained bogus data (SN: 3/30/91, p.196). In early June, NIH legal adviser Robert B. Lanman asked Hadley for her notes on telephone conversations with Margot O'Toole, the whistleblower in the Imanishi-Kari case. Healy testified that she asked Lanman to obtain the notes because she was concerned that Hadley and O'Toole had developed a friendship that could compromise the ongoing probe. Hadley denied that suggestion and said contact with O'Toole is a necessary part of the investigation.

In late June, said Hadley, OSI Director Jules V. Hallum asked her to return all her files on the Gallo and Imanishi-Kari cases to the central OSI office (she had been working from a satellite office) and told her that Healy had ordered him to "rein in Hadley." The next day, Hadley stopped working on those cases, saying she could not pursue them effectively without her files.

Last week, Healy characterized her actions as managerial decisions necessitated by numerous leaks of confidential draft reports, including the March release of the Imanishi-Kari document. "Everything that I did with regard to OSI was within the context of fulfilling my obligations to the Constitution," she told reporters after the hearing. She added that leaks of preliminary misconduct reports can destroy scientific careers.

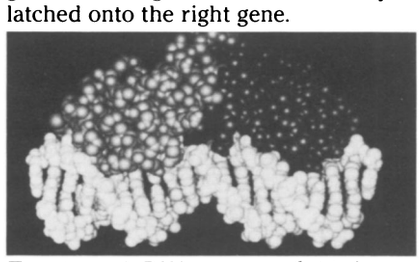
Whether her actions represent managerial solutions or a campaign to undermine OSI remains an open question. But subcommittee staffers say lawmakers have seen enough to make their next move. Several staffers told SCIENCE NEWS that Dingell plans to take steps to remove OSI from the NIH campus and place it under the aegis of the Inspector General's Office at the Department of Health and Human Services — a team known for its aggressive fraud investigations.

— K.A. Fackelmann

A 3-D image reveals a steroid-gene link

In their quest to understand how steroid hormones turn on genes, biochemists have created a picture truly worth a thousand experiments.

Steroids alter the rate of protein production in the body by relying on a separate receptor molecule to find the target gene. In the Aug. 8 NATURE, Paul B. Sigler of Yale University and his coworkers show how a gene fragment binds to the part of a steroid receptor that recognizes specific DNA sequences. Their three-dimensional, computer-generated image, based on X-ray crystallography, reveals that it is not only the binding between DNA and the steroid-receptor molecule, but also the spacing between binding regions, that tells these gene-activating molecules when they've latched onto the right gene.



Sigler/Yale Univ.

Target gene's DNA sequence (white) facilitates the match-up with the two-toned steroid receptor dimer.

Working with Leonard P. Freedman of the Sloan-Kettering Institute in New York City and Keith R. Yamamoto of the University of California, San Francisco, Sigler's team began by modifying the gene fragment: They added an extra unit of DNA, called a base pair, to the middle of its 15-base-pair sequence. Next they synthesized lots of the modified fragment and made multiple copies of the receptor segment that recognized this specific gene fragment.

When one receptor segment latches onto the first six base pairs of the gene fragment, the segment slightly alters its structure, thereby making it easy for a second segment to link with it — forming what is called a dimer. That second segment twists around to home in on the fragment's last six base pairs, whose sequence represents a symmetrical version of the first six. But with the extra base pair in between — making it four instead of three — the dimer fails to line up well with the DNA, so recognition is poor, says Sigler.

When his team repeated the work with unmodified gene fragments, they found that the segments did bind tightly to the DNA. This indicates that the three base pairs in between those that combine with the dimer create the correct spacing that lets the steroid receptor know it has found its target gene, Sigler says. *— E. Pennisi*