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Use of NIH funds placed under a spotlight

WASHINGTON DC

Congressman Joe Barton wants to know whether biomedical researchers funded by the US National Institutes of Health (NIH) are spending their grants haphazardly — overpaying research assistants, for example, or winning funds for phantom projects that they then use to do other research.

Barton, a Republican representative for Texas, heads the committee in the House of Representatives that oversees the NIH. After the committee's investigation of conflicts of interest inside the agency, revised ethics rules made their debut last month. Now the focus is on scientists outside the agency, at research hospitals and universities, who work with NIH funds.

After reading a 16 August article in the *Wall Street Journal* about a whistle-blower at

Cornell University's medical school in New York, and after receiving direct complaints, Barton's office sent two letters to Daniel Levinson, the inspector-general at the NIH's parent department, Health and Human Services.

One letter asks for a broad investigation into large grants to clinical-research centres, which can be worth many millions of dollars and cover many activities. The second asks for an investigation into whether NIH grant monies are being used to pay graduate research assistants unreasonably high salaries. This suspicion is based on complaints the committee received saying that some graduate assistants at the University of California, Davis, receive salaries and tuition waivers that amount to six times the salary of a postdoc.

Chris Harrington, director of communica-

tions in the University of California's federal-relations office, says he believes that the university complies with federal law.

And Norika Ruiz Bravo, deputy director for extramural research at the NIH, says she would be happy to cooperate with an investigation, but is not convinced there is a problem. "We're careful stewards of taxpayer funds. I would be surprised if there is widespread misuse of them," she said.

"You have to remember that these are grants, not contracts," she adds. "There is a certain amount of discretion left to the investigator on how to approach a scientific problem."

It remains to be seen whether Barton will agree. He has called for the investigation as his committee considers a draft of a sweeping reauthorization bill, which would affect the NIH's basic organization. ■

Emma Marris

"These are grants, not contracts. There's a certain amount of discretion."

Pioneering HIV treatment would use interference and gene therapy

Scientists have unveiled plans to test an HIV treatment based on a much-touted technique that hasn't yet been tried on people.

The treatment is based on a mechanism called RNA interference (RNAi), which can be used by cells to shut down invading viruses. Scientists and the biotechnology industry believe the interference pathway is a tremendously promising target for a variety of therapies. Two clinical trials of RNAi therapies have already begun, but the HIV proposal goes a step further, combining RNAi with gene therapy. It will be a closely watched test of whether the field can fulfil its potential.

Leaders of the trial described their plans to the US Recombinant DNA Advisory Committee (RAC) on 21 September. The committee gave generally favourable reviews, but recommended further safety tests before the study begins.

One of the trial's leaders is John Rossi, a molecular biologist at City of Hope's Beckman Research Institute in Duarte, California. Rossi says his team will perform

these extra tests before asking the Food and Drug Administration (FDA) for approval to begin the trial.

If the FDA says yes, Rossi and his team will test the therapy on five HIV patients who have a blood cancer called lymphoma. They will treat the patients' lymphoma with aggressive chemotherapy and a bone-marrow transplant — a normal procedure. But before the transplant, they will use gene therapy to add stretches

of DNA to stem cells in the bone marrow. It is hoped that molecules encoded by the added genes will trigger the cells' RNAi defences against HIV.

The trial is different from the RNAi trials already under way, because the molecules used in those studies remain in the body for only a short time. The City of Hope researchers will deliver DNA packaged into a gene-therapy vector that could persist in patients

for months or even years.

The RAC is cautious for that reason, and because the trial will set another precedent: it is the first in which researchers will use a lentivirus to deliver therapeutic genes to patients' stem cells. Lentiviruses are related to retroviruses, which were used in gene-therapy trials that caused cancer in three children with a rare immunodeficiency disease (see *Nature* 433, 561; 2005).

"We need to be careful, because now we have a study that's using a vector in the same family as the retrovirus, it's going into stem cells, and it's going into immunodeficient patients," says Diane Wara, who chairs the RAC.

The City of Hope team will monitor its patients to see whether the therapy causes cancerous mutations. The preliminary experiments are promising, Wara told *Nature*, emphasizing that she was speaking for herself, and not for the RAC. "John Rossi's work is beautifully done, and his data are very compelling." ■

Erika Check

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Interfering with HIV: a clinical trial of a combined treatment is under review.