placed in other NIH institutes and in the Office of the Director.

Many constituents of the NCRR fear for the futures of their programmes in institutes that didn't sign up for them and may not share the NCRR's commitment. "Dr Tabak and Francis Collins say this is going to be budget neutral," says one member of the NCRR's external advisory council. "But when you take a programme from one institute and hand it to another, perhaps without their agreement, you know that within five years or so that orphan programme could be budgeted out of existence."

That concern was especially evident in mid-January, when Tabak's group proposed a 'straw' model — designed to generate discussion — for the dissolution of the NCRR that showed much of its portfolio in an 'interim infrastructure unit'. Some critics were mollified when Tabak issued a revised plan last week, calling the infrastructure entity permanent and placing it in the Office of the Director. The latest plan includes other adjustments: for example, the straw model had divided the NCRR's primate and non-primate animal-model resources, but the revised model keeps them together under the director's office.

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EMORY UNIV.

Stuart Zola's research centre is slated to become the responsibility of the NIH Office of the Director.

Stuart Zola, director of the Yerkes National Primate Research Center in Atlanta, Georgia, which is currently funded by the NCRR, is one of those whose fears were soothed by the adjustments. "Given that we were going to be moved, it makes sense to be moved into another broad-based environment" rather than a disease-specific institute, he says.

"The willingness to listen to the stakeholders is very clearly evident in the new document," says William Talman, president of the Federation of American Societies for Experimental Biology in Bethesda, Maryland, who praises Collins for making a "bold stroke" in launching NCATS. Still, he says: "I don't think I will be comfortable until the test of time determines exactly what the outcome is."

Those seeking to challenge the dismantling of the NCRR will have another opportunity to voice concern at a meeting for stakeholders on 14 March. However, the window of opportunity to stop the process is narrowing. Collins plans to deliver a detailed budget for the new centre to Congress in the coming weeks, and last week he told reporters that he is preparing to search for the future director of NCATS. ■

GENE THERAPY

Targeted gene editing enters clinic

Patients with HIV first to receive experimental gene therapy.

BY HEIDI LEDFORD

A gene-therapy method that specifically disrupts a single gene may have had its first success in the clinic, potentially boosting immune-cell counts in a small number of patients with HIV. The results, presented on 28 February at the Conference on Retroviruses and Opportunistic Infections in Boston, Massachusetts, mark an important therapeutic test for enzymes known as zinc finger nucleases — small proteins that can be designed to bind to and edit specific DNA sequences by virtue of their zinc-bearing structures.

The study, a phase I safety trial, tested a zinc finger enzyme developed by Sangamo BioSciences in Richmond, California. It included six men with HIV who were already taking the standard regimen of antiretroviral drugs. The drugs had kept the virus at bay, but their immune-cell counts remained abnormally low. Researchers removed a sample of $CD4^+$ T cells, the type of immune cells affected by HIV, from each man and used Sangamo's enzyme to disrupt the *CCR5* gene, which encodes a protein that HIV uses to enter $CD4^+$ cells. The engineered cells were then infused back into the patients. Immune-cell counts subsequently rose for five of the six patients who received the therapy.

"It's very exciting," says John Rossi, a molecular biologist at the City of Hope's Beckman Research Institute in Duarte, California. "If they did this several times in a given patient, you could establish a high percentage of resistant cells."

The inspiration for targeting the *CCR5* gene comes from the small percentage of people who, thanks to a natural mutation in the gene, are resistant to most types of HIV infection. At the meeting on Monday, Jacob Lalezari of Quest Clinical Research in San Francisco, California, reported that the engineered cells migrated throughout the body and thrived in the gut mucosa — a key reservoir of HIV. No serious side effects were seen.

The zinc finger nuclease technique is promising for the treatment of many diseases beyond HIV, says Patrick Aubourg, who studies gene therapy at France's national biomedical agency INSERM in Paris. The method could replace the more common technique of inserting modified genes into the genome, in which researchers have less control over the gene in question. But he cautions that the technique still has a relatively low efficiency and might have off-target effects.

Meanwhile, Rossi, who is himself embarking on an HIV study that will use Sangamo's zinc finger nucleases, says that it is not yet clear whether the patients' $CD4^+$ cell count rose because of the *CCR5* disruption or because the extracted cells were activated as part of the protocol for growing them outside the body. And because levels of HIV were already below the threshold of detection in these patients, it is too early to say what effect the therapy could have on patients that have more of the virus. Researchers do not yet know what fraction of a person's $CD4^+$ cells would need to be HIV-resistant to significantly rein in the virus's spread and liberate patients from a lifetime of antiretroviral drugs.

"If they did this several times in a given patient, you could establish a high percentage of resistant cells."

"It's going to take a while to put all of those pieces together," says Carl June, who studies T cells at the University of Pennsylvania in Philadelphia, and is an investigator on another HIV trial involving Sangamo's nuclease. "But it's at least conceivable now." ■