

MICROBIAL GENOMICS

TIGR Begins Assault on The Anthrax Genome

team focuses on stitching various HIV genes into *Salmonella*, as well as studying a version of HIV's surface protein that they believe can stimulate potent anti-HIV antibodies. Montagnier has emphasized making vaccines from pieces of HIV's proteins gag, tat, and nef. Gallo says much of the joint work will be done in the lab of the University of Rome's Vittorio Colizzi, who has already been working with Gallo's lab and has had a separate project with Montagnier's foundation.

Gallo, 64, and Montagnier, 69, did collaborate before their famous falling-out. In 1983, when the cause of AIDS remained a mystery, Montagnier published a paper in *Science*, with Gallo's help, that implicated HIV as the cause. But it was not until 1984, when Gallo's lab published four back-to-back papers, also in *Science* (4 May 1984, pp. 497–508), that persuasive evidence linked HIV to the disease. Montagnier and his team felt badly slighted and charged that Gallo inappropriately hogged credit for the discovery. And when analyses proved that the blood test developed by Gallo's lab relied on a sample of HIV supplied by Montagnier, the question then became: Did Gallo's lab deliberately use the French virus without crediting the group, or was it an innocent contamination? A U.S. investigation cleared Gallo of wrongdoing, and Montagnier himself says he does not believe theft occurred. "This is settled now," he says.

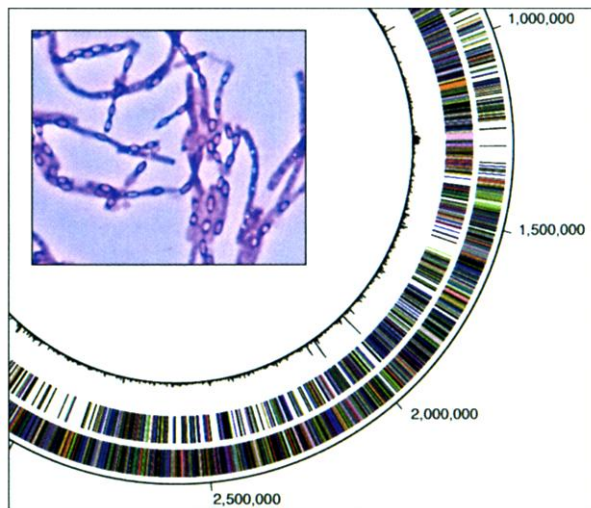
The new collaboration with his longtime rival comes at an opportune moment for Gallo. This month, *Chicago Tribune* reporter John Crewdson published a highly critical book about Gallo's role in the discovery of HIV—*Science Fictions: A Scientific Mystery, a Massive Cover-Up, and the Dark Legacy of Robert Gallo*. "The timing was not calculated," says Gallo, who dismisses speculation that the rapprochement is pure public relations. "They can say that," he says, "but there's substance to the collaboration."

Montagnier also dismisses speculation that the two want to impress the Nobel Prize Committee, which notoriously shies away from researchers embroiled in controversies. "If the prize comes, it will come too late," says Montagnier. "I would have preferred it could have come earlier, and then I think it could have given us more influence to do something in Africa."

Several AIDS researchers who know both Gallo and Montagnier are perplexed by the collaboration, as the two scientists clash not only in style but over substance. Montagnier, for example, contends that HIV relies on cofactors to cause disease, an idea that Gallo soundly rejects. Still, none wanted to comment publicly on the new effort. And both Gallo and Montagnier dismiss the idea that their relationship might devolve into another high-profile tempest. "We're wiser, more mature," says Montagnier.

—JON COHEN

Until recently, microbiologists were elated when the genome of their favorite bug was sequenced. Now, one genome is just not enough: The emerging gold standard is to produce multiple genomes of one species and compare them. Riding the bioterrorism wave, The Institute for Genomic Research (TIGR) in Rockville, Maryland, plans on taking anthrax to this next level. This year, the institute may sequence the genomes of as many as 20 different *Bacillus anthracis* strains from around the world, says TIGR director Claire Fraser—three times more than have been sequenced for any other species.



Circled. The genome of the Ames strain is almost finished, but many others will follow.

Having a wide range of anthrax genome sequences could help investigators nab future bioterrorists and aid in designing drugs and vaccines. But the plan for the vast project was hatched last summer, well before fears of bioterrorism exploded. Charting genetic diversity across a large number of strains is fascinating in its own right, says Fraser: "It's something that we've wanted to do for a very long time, and it has nothing to do with the biodefense issue."

The strains will be selected by anthrax geneticist Paul Keim of Northern Arizona University in Flagstaff, who is involved in the criminal investigation of last fall's attacks (*Science*, 30 November 2001, p. 1810). TIGR and the funder, the National Institute of Allergy and Infectious Diseases, will review the project after the first four genomes are complete, says Fraser, to see how useful the information turns out to be. At the current price of about \$150,000 per genome sequenced to eightfold coverage, the project could cost \$3 million.

TIGR has already produced the sequence of two *B. anthracis* genomes. One, a lab strain called Ames, has been in the works for several years, and the last gaps should be filled within weeks, TIGR's Timothy Read reported at a meeting.* In addition, the institute has determined the draft genome sequence of what is now known as the Florida strain: the anthrax that killed photo editor Robert Stevens of American Media Inc. in Boca Raton last October. Although that microbe, too, belongs to the Ames strain, TIGR says subtle differences set it apart from the first one—differences that may help identify the perpetrators of the attacks.

Not long ago funders scoffed at the idea of comparing the genome sequences of multiple strains. Indeed, geneticist Frederick Blattner of the University of Wisconsin, Madison, re-

calls that funding agencies twice turned down his proposal to sequence a second *Escherichia coli* genome a few years ago, arguing that it would be a waste of money. When its genome was finally sequenced, that second bug—the O157:H7 strain, infamous for causing deadly food-borne outbreaks—turned out to have a million more base pairs than the first strain sequenced and almost 1400 new genes.

Those differences have given researchers countless clues to understanding both microbes, says Fraser. By now, the genomes of five other strains of *E. coli* are being sequenced or have been finished; other pathogens to get

such thorough treatment include *Staphylococcus aureus* and *Chlamydia pneumoniae*, with five strains each. The anthrax project would dwarf those efforts.

Keim, who will also prepare the DNA for the sequencing effort, says he has come up with a list of candidate strains that best represents anthrax's phylogenetic diversity. Comparing the genomes should reveal why some strains are more virulent than others, or why some are better at surviving in the soil, says Martin Hugh-Jones of Louisiana State University, Baton Rouge. "I think you'll see what the really good genes are, and which ones are just coasting along," he says.

With existing tools, however, researchers have so far found very few genetic differences among strains. For instance, using his standard DNA fingerprinting system, which looks at 15 different markers called VNTRs, Keim has been unable to discriminate

* Second Conference on Microbial Genomes, Las Vegas, Nevada, 10–13 February.

among the microbes used in the attacks and other representatives of the Ames strain. At the meeting, Keim reported an advance that may help federal investigators home in on the bioterrorists who sent the anthrax letters last fall. With a new marker discovered in his lab last year and dubbed Homomeric-1 (HM1), Keim says he's able to tell apart five different Ames strains, four collected from research laboratories and one from a goat that died in Texas in 1997.

At the HM1 locus, *B. anthracis* has between 12 and 35 copies of adenine, one of DNA's building blocks, and the number varies for all five isolates. If the strain used in the mail attacks matches one of the strains obtained from laboratories, it could tell investigators where to focus their attention. But Keim, following FBI orders, declines to say which four labs the strains came from, or whether he had checked the Florida isolate for the same marker. —MARTIN ENSERINK

CLONING

Carbon-Copy Clone Is the Real Thing

"While the cloning of companion animals is not yet possible, Advanced Cell Technology is currently able to store cells from your animal now."

—ACT Web site, 15 February 2002.

ACT needs to update its Web site. Last week, scientists in Texas unveiled the first clone of a pet—a kitten named CC, short for Copy Cat (also Carbon Copy). The kitty is the fruit of a privately funded initiative, Operation CopyCat, started a year ago by Mark Westhusin and colleagues at Texas A&M University, College Station. It's actually part of a larger and much more difficult project that aims to clone a dog.

The researchers, who report their feat in the 21 February issue of *Nature*, say cat cloning is just about as efficient (or inefficient) as duplicating mice, cows, sheep, goats, or pigs. Westhusin's team first attempted to use skin fibroblast cells, inserting their nuclei into enucleated cat eggs. Although 82 cloned embryos were implanted into seven surrogate mother cats, only one pregnancy resulted, and the fetus died. In their next try, the scientists created embryos using nuclei from the cumulus cells surrounding the ova of a calico research cat named Rainbow. They implanted five embryos in a surrogate mother—three from cumulus cells and two from the oral mucosa cells. This time, one of the embryos from a cumulus cell made it to term. That puts the success rate at one out of 87.

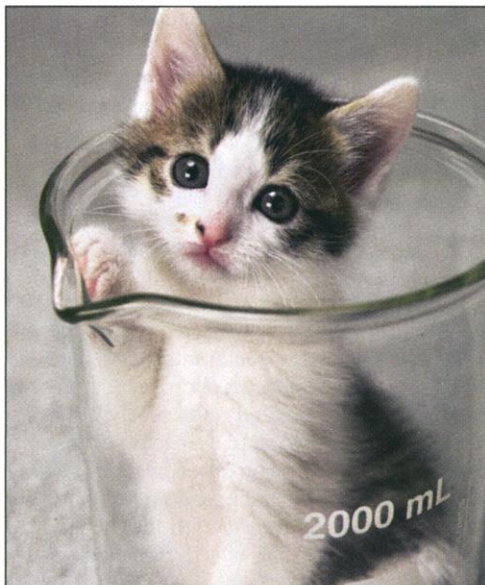
Born by cesarean section on 22 December 2001, CC is a lively, normal-

looking feline, the researchers say. She's not an exact copy of her calico progenitor because these coat markings result partly from random events during development. "I'm not at all surprised at the success of the Texas A&M team; they're an excellent group of scientists," says Robert Lanza, medical director of ACT. He says ACT is moving away from pet cloning and has licensed its technology to the Texas group and others.

CC is the first creation to emerge from the Missyplicity Project. The project was launched 5 years ago by 81-year-old Arizona financier John Sperling, who wants to be able to replace his husky-border collie mix, Missy, when her time is up (*Science*, 4 September 1998, p. 1443). So far, Sperling has put \$3.7 million into the Texas A&M group's cloning efforts through a new company called Genetic Savings and Clone, based in College Station, Texas, and Sausalito, California.

Dog clones, however, are still a long way off, Westhusin cautions. "Assisted reproduction technology in cats has all been worked out," he says. And "you can get them to come into heat when you want." But dogs come into heat more rarely and unpredictably. Dogs also release immature eggs from their ovaries, and researchers have found it very difficult to get them to ripen in a test tube. The focus in this area, says Westhusin, is still "how do you get viable ova."

The public appears willing to wait for dog cloning—and probably to pay \$20,000 or so for it. Lou Hawthorne, CEO of Genetic Savings and Clone—which stores tissue for possible future pet cloning and is gearing up to open its own lab—says the start-up was formed in response to public demand. "When we launched [it] 2 years ago, we got thousands of calls within the first 24 hours," he says. The company hopes to be offering



Copied cat. Two-month-old CC seems normal so far.

ScienceScope

Energetic Discussion U.K. researchers have mixed reactions to a call for a new national energy research center. A government panel reviewing energy policy last week recommended that a new center is needed to energize studies of power use, production, and environmental and social issues. Chemist David King of the University of Cambridge, the government's chief scientist and head of a sub-panel that looked at energy research, says the center would help pull together a "broad menu" of new energy technology studies.

But Ian Fells, an energy expert at the University of Newcastle, favors a more decentralized approach that would boost energy research at "half a dozen" local research centers. That is just one funding model currently being studied by the U.K.'s research councils, which oversee government science spending.

No final decision is expected soon. The energy panel's recommendations are now open for public comment, and a final long-term strategic plan is due later this year.

Oversight Overlords British researchers say pending legislation to prevent the export of sensitive technologies to hostile countries could give the government too much control over what research gets published. According to the lobby group Universities UK (UUK), a revised Export Control Bill now before the House of Lords would give the Department of Trade and Industry (DTI) the right to review new research before it is submitted for publication. DTI would also be able to impose controls on e-mails and instruction manuals covering topics deemed sensitive. The current law applies only to tangible objects and descriptions of certain military technologies.

DTI officials insist that the rules would pertain only to applied research and that additional legislation will define and exempt basic research from export control oversight. UUK, however, wants to see academic freedom enshrined in the export law itself and is seeking support for an amendment during debate next month.

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