A matter of degrees. Cold Spring Harbor is launching graduate program in the biological sciences.

man says the degree-granting program will give the lab a more direct role in shaping the education of students on campus. The new program, he says, will help CSH "change the way education is done."

The lab's main innovation, according to Stillman, will be to shorten the time it takes to get a Ph.D.—from the standard 7 years to 4.5 years. CSH hopes to get most of the basic instruction done in the first year, although students would take short courses (some lasting no more than 1 week) throughout their time at the lab. In another change from the standard approach, Stillman says, Ph.D. candidates will have two mentors—one to guide them through the details of preparing a thesis and the other to look out for their intellectual development. The goal, he says, is to ensure "that the research will benefit [the students] and not necessarily reflect what a [National Institutes of Health] study section thinks is important" as an experiment.

The supply of new Ph.D.s is a contentious issue, especially in the life sciences, where recent graduates complain of a paucity of academic positions. In September, a committee of the National Research Council (NRC) of the National Academy of Sciences headed by Princeton molecular biologist Shirley Tilghman argued that there should be "no further expansion" of existing Ph.D. programs and "no development of new programs." This week, a report from the Association of American Universities (AAU)* warns against "the unnecessary proliferation of Ph.D. programs" and says that new programs should meet "a regional or national need."

Tilghman, who is also a trustee of CSH, calls the new graduate program "an interesting demonstration project" that could be an exception to the situation described in the NRC report. If the lab really can train a Ph.D. in less time than "even the best programs in the country" now require, says Tilghman, it will have done something "important." Furthermore, because students at CSH "will not be tied to the research programs of their mentors," Tilghman says, they will gain the degree of independence her panel wanted to encourage.

AAU Executive Vice President John Vaughn, one of the authors of the AAU's new report, says a few universities are now trying to limit the number of years Ph.D. candidates serve as teaching assistants. But it may be difficult to implement such changes at some big state universities, he says, without adding to the pressures students already face.

–ELIOT MARSHALL

* AAU Committee on Graduate Education: Report and Recommendations, October 1998 (www.tulane.edu/~aau/AAUPolicy.html)

CREDITS: (TOP) MARGOT BENNETT/COLD SPRING HARBOR LABORATORY; (BOTTOM) GAMMA-LIAISON

EPIDEMIOLOGY

Pasteur Recruit Resigns In Battle Over New Unit

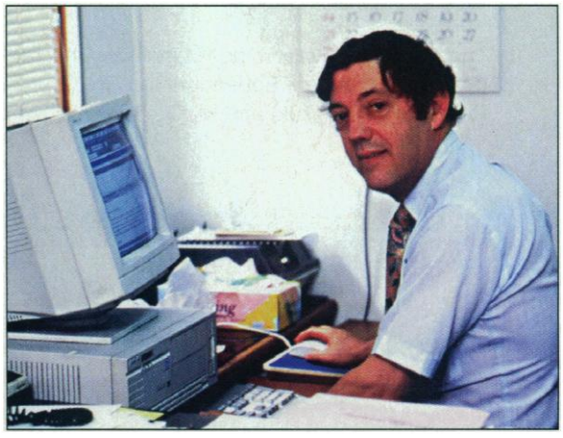
PARIS—Joseph McCormick has worked successfully in a lot of challenging environments. He's chased the Ebola and Lassa fever viruses in the jungles of Zaire and Sierra Leone, and he's battled hepatitis C and cholera epidemics in Pakistan. But none of those experiences prepared him for life at the Pasteur Institute in Paris. On 1 November McCormick resigned as chief of the epidemiology and biostatistics unit he had been hired to create less than a year ago after a tenure committee decided to postpone a decision on granting him permanent status.

McCormick's rapid rise and fall appears to be part of a broader debate over the role of epidemiology at the Pasteur, which traditionally has put a heavy emphasis on basic research. It also reflects the political infighting at the Pasteur in the run-up to elections next year for a new director-general to succeed Maxime Schwartz, who cannot run again and whose leadership style is seen by some as authoritarian. McCormick, formerly of the U.S. Centers for Disease Control and Prevention (CDC), was recruited after a stint in Pakistan by Schwartz and medical director Philippe Sansonetti, who is regarded as a candidate for the top job (*Science*, 13 March, p. 1629).

The trigger for his resignation was a June vote by the tenure committee, an elected body of Pasteur scientists, to delay for 1 year a decision on his status. Unfortunately for McCormick, the scientist who presented his case, microbiologist Patrick Grimont, is often at odds with Sansonetti over the institute's future. McCormick says that Grimont showed little knowledge of the project during a brief visit before the panel's vote, and sources familiar with the committee's deliberations say that his very negative presentation contributed to the 14-0 vote. "McCormick paid the price [for his ties to Schwartz and Sansonetti]," says one Pasteur scientist who asked not to be identified. "He was parachuted in and he didn't know" the score.

Grimont disputes that interpretation of the committee's action. "I did my job [as presenter of McCormick's dossier] as honestly as I could," he says. "There were no political or personal influences" that affected his presentation. Even so, Schwartz says that the panel's vote was "completely unexpected." And Sansonetti views McCormick's departure as a "setback" to his wish to strengthen the institute's public health portfolio.

Administering a setback may in fact be what the committee had in mind. Although most were reluctant to discuss their decision publicly, several told *Science* that they had reservations about McCormick's plans to create a CDC-style epidemiology program at Pasteur. They also felt that McCormick's extensive experience as a field epidemiologist did not fit the academic environment at Pasteur, which prizes more "fundamental" research in epidemiology and biostatistics. Other sources at Pasteur said that McCormick's desire to create a high-powered pathogen laboratory in his unit was seen as too similar to existing research at the institute. "I am surprised that he wanted to have a lab, with a lot of



Pasteurized. Joe McCormick quit as head of the epidemiology unit after failing to win tenure.

equipment," says Grimont. "What was lacking at Pasteur was an epidemiology unit, not a lab looking for bugs."

Despite the dispute over McCormick's plans, committee members say their action was not meant to be a push out the door. "Joe McCormick was not fired from Pasteur or anything like that," says genome researcher Antoine Danchin, a member of both the tenure committee and the scientific council, a separate body that approved McCormick's hiring and the creation of his unit. But McCormick says the decision forced his resignation, as scientists without tenure are not allowed to recruit other researchers for their units. Molecular biologist Moshe Yaniv, also a member of both bodies, agrees that McCormick's inability to recruit people for his unit "would certainly have complicated his life."

Although McCormick's epidemiology unit will be disbanded, Schwartz and Sansonetti still hope to create a new program that will carry out much of the same work. McCormick plans to maintain some ties with Pasteur, serving as a consultant on a variety of projects, including vaccine evaluation. He also hopes to be a liaison to a high-security pathogen lab in Lyons that his virus-hunting wife, Susan Fisher-Hoch, is helping to construct. His background as a field epidemiologist does not seem to bother the Lyons-based vaccine firm Pasteur Mérieux Connaught, which has just hired him to put together an epidemiology program.

Looking back at his short stint at the institute, McCormick says that "if I did something wrong at Pasteur, I don't know what it was." But he confesses that, when it came to politics, "I might have been a little naïve."

–MICHAEL BALTER

MICROBIOLOGY

Genome Links Typhus Bug to Mitochondrion

As recently as the First and Second World Wars, the louse-borne disease typhus swept through armies, ghettos, and prison camps, killing millions of people. Instability and the breakdown of public health measures in Eastern Europe have experts worrying about possible new epidemics of the disease, which is marked by high fever and delirium. But a close look at *Rickettsia prowazekii*, the bacterium that causes the disease, reveals that, in spite of its fearsome reputation, it is a degenerate organism, riddled with nonfunctional genes and gradually losing genes it once needed to function.

In this week's issue of *Nature*, molecular microbiologist Charles Kurland of the University of Uppsala in Sweden and his colleagues describe the complete sequence of the 1.1-million–base pair genome of the pathogen. By helping identify genes that make *R. prowazekii* so deadly, the information may help researchers design better typhus vaccines. The sequence, now one of 18 microbial genomes finished, is also a window to the distant past.

Researchers think that the mitochondria, the small structures that serve as the cell's powerhouses, were derived from bacteria that took up permanent residence in an early ancestor of modern cells. Comparisons of ribosomal RNA genes had indicated that *Rickettsia*, one of the so-called alpha proteobacteria, could be the closest living relative of the mitochondria's predecessor. Now, Kurland says, the new genome sequence "is as confirmatory as you can imagine" about the link between mitochondria and *Rickettsia*. It also illustrates the gene loss that must have marked the mitochondrion's own transition to dependence on the host cell.

Typhus terrorism. During World War II, the military took extreme measures to get rid of lice and lessen the risk of typhus.

Kurland and his colleagues, who began the sequencing project 6 years ago, found 834 genes in the *Rickettsia* genome, a half-dozen of which code for proteins similar to those that make other bacteria virulent. Three of these look like the genes that produce toxic polysaccharides in *Staphylococcus aureus*, which causes boils. The information should help researchers interested in developing new vaccines for typhus find the right proteins to include in their inoculations, Kurland says.

The effort also seems to have paid off in helping pin down the origins of the mitochondria. With the sequence in hand, Kurland, Uppsala's Siv Andersson, and their colleagues compared the *Rickettsia* genes to the DNA still present in modern mitochondria. "We see very strong similarities," says Andersson, particularly in genes involved in energy production. The group also found that many of the pathogen's genes closely resemble genes that code for proteins used by yeast mitochondria—but are found in the nucleus of yeast cells.

This suggests, Kurland says, that somehow "there was an early evolutionary event where there was an off-loading of these genes" from the early mitochondrion to the nucleus. As the ancestral host nucleus took on these genes, the mitochondria would have become more dependent on the host cell, until eventually they could no longer survive except within the cell.

R. prowazekii hasn't taken up permanent residence in cells yet, but it is an obligate intracellular parasite, meaning that it can multiply only in living cells. As a result, Kurland thought its genome might show signs that genes once needed by the organism when it could reproduce independently are being lost. The new sequence indicates he and his colleagues were on the mark. The genome "is a wonderful study in the way genomes evolve to become degenerate," says evolutionary biologist Carl Woese of the University of Illinois, Urbana.

When Andersson surveyed the microbe's existing genes, she found that several key ones, including those needed to make the building blocks of DNA, are missing. Thus, the organism has to depend on the cells it infects to produce these materials. What's more, Andersson adds, the sequence indicates that the "genome is still in the process of getting smaller." She points to an enzyme, called *S*-adenosylmethionine synthetase, which makes a compound that adds methyl groups to a variety of cellular building blocks. *Met K*, the gene that makes the enzyme, has been found in all the microbial genomes sequenced so far except for that of *Chlamydia*, another organism that can thrive only inside other cells. In *R. prowazekii*, however, this gene is altered and is no longer expressed.

Several other recognizable "genes" no longer work because of mutations in their sequences. In fact, Kurland and his colleagues found that functional genes take up only 75% of *R. prowazekii*'s DNA, whereas all of the other bacterial genomes have little extraneous DNA. "With several dead genes and a lot of noncoding DNA, its percentage [of junk DNA] is higher than [that of] any other microbial genome," Andersson says. Woese expects to see more examples of such gene inactivation in the genomes of parasitic microbes. This observation is "probably going to be a trendsetter for the field."

–ELIZABETH PENNISI

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