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

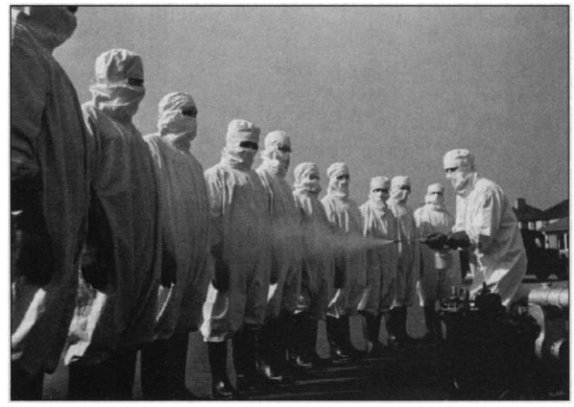
MICROBIOLOGY

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