DNA SEQUENCING

Genome of TB Culprit Deciphered

CAMBRIDGE, UNITED KINGDOM—A collaboration of European laboratories has unraveled the complete sequence of the organism responsible for one of the world's biggest scourges, tuberculosis. The sequence, announced last month, was unusually hard to decipher because of peculiarities in the TB genome. It should open new approaches to fighting the disease, which is estimated to kill 3 million people annually. "We have been waiting for a long time for a major advance in tackling this disease," says epidemiologist Paul Fine of the London School of Hygiene and Tropical Medicine.

The organism that causes the disease, *Mycobacterium tuberculosis*, presents a challenge because it is difficult to grow in the lab. "That has led to mycobacterial research lagging behind other fields," says immunologist Gilla Kaplan of Rockefeller University in New York City. "Completion of the sequence pushes *Mycobacterium* research into the mainstream," she says.

Britain's Wellcome Trust, which helped support a successful effort by some of the same researchers to sequence the genome of brewer's yeast (*Science*, 26 April 1996, p. 481), announced backing for projects to sequence *M. tuberculosis* along with the malaria parasite in April last year. Although the *M. tuberculosis* genome is not large, at 4.41 million base pairs, it has some troublesome peculiarities. The organism's gene sequence includes many regions rich in just two bases—guanine and cytosine—out of the four that encode gene sequences in DNA. "Overall, the genome is 65% GC-rich regions, but some parts are as high as 80% to 85% GC-rich," says Julian Parkhill, a sequence analyst at Wellcome's Sanger Centre near Cambridge. This imbalance causes the DNA strand to curl into complex and tortuous secondary structures, which hamper the normal cloning technology used in sequencing.

As a result, the project, headed by Bart Barrell of the Sanger Centre in collaboration with a group led by Stewart Cole at the Pasteur Institute in Paris, initially started as a pilot to determine if such regions could be sequenced reliably. "We were pushed to the limits of current technology," says Parkhill. But the team found that the difficult regions could be sequenced using shorter fragments with considerable effort, so the pilot project became a full-scale sequencing project.

The approach could aid efforts to sequence other genomes. For instance, says Parkhill, "we can also use the lessons learned to help with the human genome, which has specific GC-rich sequences." TB researchers, for their part, are excited at the new prospects opened up by the genome sequence. "Research on the bacterium will now become much more interesting and imaginative," says Kaplan.

Some researchers foresee near-term payoffs in medicine—for example, ways to distinguish the TB organism from the many closely related but innocuous species of *Mycobacterium* that can cross-react with TB tests. "I hope one of the earliest outcomes of the genome project will be the development of more sensitive diagnostic tools which can distinguish between *M. tuberculosis* antigens and those of its relatives," says Fine. Ken Duncan, manager of Action TB at the British pharmaceutical company Glaxo Wellcome in Stevenage, also sees the potential for new therapies. "We now know the sequence of every potential drug target and antigen. It's an enormous boost," he says.

–Nigel Williams

ARCHAEOLOGY

Kennewick Man: More Bones to Pick

Last week, scientists added another bit of bone to the skeleton of Kennewick Man, the oldest, most complete—and most disputed—ancient human from the Pacific Northwest. A partial rib of the 9300-year-old skeleton was found when independent scientists, Native Americans, and the Army Corps of Engineers cooperated in a limited study of the Columbia River beach where the other remains were recovered. But the chip of rib, like everything else connected to this ancient American, is a bone of contention. With the rest of his skeleton, it has been locked away in a vault, pending the outcome of a suit filed by a group of scientists against the corps for the right to study the remains (*Science*, 11 July 1997, p. 173).

Kennewick Man's new bone is the latest twist in a strange saga that occasionally verges on farce, as various groups vie for access to his bones and history. Since the skeleton's discovery about a year and a half ago on corps land leased to the city of Kennewick, archaeologists have longed to study the skeleton, which reputedly has "Caucasoid" rather than modern Native American traits. Native American groups, however, regard the skeleton as the remains of an ancestor, and they want it given to them for burial under the 1990 Native American Graves Protection and Repatriation Act (NAGPRA). Citing NAGPRA, the corps has limited scientists' access to the skeleton, forcing them to subsist on rumors about its significance and even its authenticity—while both Indians and latter-day Norse pagans have visited it.

J. CHATTERS

Disputed territory. Scientists were allowed only limited work along the beach where Kennewick Man was found.

The newest addition to the skeleton, a 2-centimeter-square piece of rib, was found along the reservoir's beach by James Chatters, an independent archaeologist who led the original recovery of Kennewick Man in July 1996. Chatters was part of the weeklong, three-team effort coordinated by the corps to study the site's geology and archaeology.

The rib joins three other bones that have been added to the skeleton since its discovery—and at least one does not belong to Kennewick Man. According to corps spokesperson Nola Conway, the other bones turned up during two corps surveys of the site this past year, done with members of the Umatilla Tribe. A metatarsal, cervical vertebra, and pubis bone were found and put in the vault, says Conway. The Native Americans, in keeping with their beliefs, also put incense cedar boughs in the box with the bones.

All this came to the attention of scientists last fall via newspaper accounts, after members of the Asatru, a group of Norse pagans who claim Kennewick Man was a descendant of early Norse in North America, were allowed to visit their putative ancestor. The scientists criticized the corps for possibly harming the skeleton, saying that moisture from the cedar boughs might