New Antibiotic Dulls Bacterial Senses

To perceive the world and react to it, people rely on their eyes, ears, and other sensory organs, which send electrically coded information via nerve cells to the brain. In contrast, bacteria tend to use much simpler, two-protein relays to govern their responses to changes in the external environment.

"These two-component systems are the eyes and ears of the bacteria," says microbial geneticist Thomas J. Silhavy of Princeton University. "[They] control the expression of all the genes that are important for survival in various environmental circumstances."

Investigators searching for new antibiotics have now found a compound that seems to inhibit the first half of these signaling systems, a family of proteins known as kinases. In test-tube experiments, the compound stalls the growth of many bacteria, even recalcitrant strains that have acquired resistance to other antibacterial drugs. James A. Hoch of the Scripps Research Institute in La Jolla, Calif., and his colleagues report their findings in the April 28 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

As antibiotic resistance has grown steadily into a pressing issue, scientists have sought drugs that take aim at different bacterial targets than those attacked by traditional antibiotics. The two-component signal pathways, which consist of a kinase and a protein called a transcription factor, make an appealing choice because bacteria use the pathways but animal cells do not.

Researchers have recently found that although some microbes have no two-component signal pathways, others employ several dozen of these kinase–transcription factor relays.

The pathways usually govern bacterial virulence genes, whose activity is vital to establishing an infection or causing disease in a host. For example, when certain bacteria reach a person's lungs, a particular kinase is activated. The kinase then chemically modifies its partner transcription factor, enabling it to bind to DNA and turn on the genes required to initiate a lung infection.

To identify potential new antibiotics, Hoch's team, working with scientists at the R.W. Johnson Pharmaceutical Research Institute in Raritan, N.J, searched for compounds that would prevent the activation of a bacterial kinase, KinA, which is part of a two-component relay. The investigators identified a compound that thwarts the growth of many strains of bacteria—including troublesome ones that resist antibiotics such as penicillin and vancomycin—and kills a drug-resistant strain of *Staphylococcus aureus*.

Hoch and his colleagues also found that bacteria develop resistance more slowly to the KinA inhibitor than to a traditional antibiotic. They speculate that the compound may inhibit several kinases, making it difficult for bacteria to develop mutations that overcome the drug.

Some researchers have expressed skepticism about developing drugs that target the kinases in signaling systems, arguing that such compounds wouldn't kill bacteria directly. However, a few recent studies have shown that some of these two-component pathways are essential for the survival of bacteria.

Moreover, reducing a bacterium's virulence could give a person's immune system time to eliminate the microbe before it causes problems. "If you had an inhibitor of a large number of the kinases, the bacteria would be deaf, dumb, and blind," Silhavy says. While such an inhibitor sounds promising, he cautions that it must prove itself through tests in animals and eventually people. —*J. Travis*

Language origins may reside in skull canals

The evolutionary roots of speech and language have long inspired heated scientific debate. Much of it concerns whether anatomical features necessary for talking emerged only in modern *Homo sapiens*, sometime between 40,000 and 100,000 years ago, or in other, earlier members of the 5- to 6-million-year-old human evolutionary family (SN: 4/24/93, p. 262).

A new analysis of ancient and modern skulls, the first to focus on the size of a bony channel that funnels a major nerve to the tongue, indicates that human ancestors living 400,000 or more years ago—not to mention Neandertals, who first appeared around 135,000 years ago—may have been able to talk much as humans do today.

"Humanlike speech capabilities may have appeared much earlier in time than the first archaeological evidence for symbolic behavior [around 40,000 years ago]," contend anatomist Richard F. Kay of Duke University Medical Center in Durham, N.C., and his colleagues.

Kay's group examined a bony tube located at the bottom of the skull, called the hypoglossal canal, through which the hypoglossal nerve passes. This nerve originates in the brain stem and fans out, sending movement commands to all but one of the tongue's muscles.

Although several smaller nerves also traverse the hypoglossal canal, the Duke researchers argue that its enlargement in fossil hominids reflects growth of the hypoglossal nerve to coordinate the tongue movements needed for speaking.

The scientists first observed that the area of the hypoglossal canal relative to the mouth's overall size averages nearly twice as large in 48 modern human skulls as in comparable samples of chimpanzee and gorilla skulls.

Moreover, three fossil skulls attributed to *Australopithecus africanus*, a hominid dating to more than 2 million years ago, possess hypoglossal canals in the same relative size range as those of chimps, Kay and his colleagues report in the April 28 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES.

In contrast, hypoglossal canals comparable in size to those of modern humans appear in two Neandertals placed at roughly 60,000 to 70,000 years old, a 90,000-year-old "early" *H. sapiens*, and two *Homo* specimens ranging from 300,000 to 400,000 years old.

"This is exciting work," comments anthropologist Erik Trinkaus of Washington University in Saint Louis. "It suggests that fine neurological control over the vocal tract necessary for spoken language emerged during a time of major revolutions in hominid adaptive patterns," around 500,000 to 100,000 years ago.

Other recent evidence suggests that the size of hominid brains increased dramatically during that period (SN: 5/24/97, p. 322), when populations of human ancestors achieved impressive social and technological feats (SN: 1/4/97, p. 12).

Boosts in brain size reflect a greater reliance on meat and other high-protein foods, Trinkaus asserts. Spoken language would have helped ancient hominids share critical information about local food sources and develop timely survival plans, he says.

Neandertals may have died out around 30,000 years ago because their adaptive strategies differed from those of modern humans in subtle, but ultimately fatal, ways, Trinkaus theorizes.

"Language is not what made modern humans successful," he contends. "The critical issue was how language was elaborated and employed in different populations of Neandertals and modern humans." —*B. Bower*