Newly identified enzyme treats deadly bacterial infections in mice

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By the time antibiotics made their clinical debut 70 years ago, bacteria had long evolved strategies to shield themselves. For billions of years, bacteria hurled toxic molecules at each other in the struggle to prosper, and those that withstood the chemical onslaught marched on. Now, with an uptick in antibiotic-resistant bacteria reaching alarming proportions, Rockefeller University scientists have identified an enzyme produced in viruses (called bacteriophages) that could stop these one-celled powerhouses dead in their tracks.

In research published this month in *The Journal of Infectious Diseases*, scientists led by Vincent Fischetti, head of the Laboratory of Bacterial Pathogenesis and Immunology, reveal that the newly identified enzyme, Cpl-1, can successfully treat symptoms of bacterial meningitis in young mice infected with Streptococcus pneumoniae, a highly resistant and deadly strain of bacteria. At a time when antibiotics have continued to prove futile, these findings may provide a solution to one of the more serious public health problems to hit this century.

“We have reached another critical milestone,” says Fischetti, who previously showed that Cpl-1 prevents ear infections in mice. “To argue that these enzymes can be clinically effective, we had to prove that they not only kill antibiotic-resistant bacteria but also reverse their symptoms of disease. And that’s what we did.”

Working with colleagues from the Institute for Infectious Diseases in Bern, Switzerland, Fischetti found that young mice infected with S. pneumoniae and then treated 18 hours later, once symptoms began, survived the potentially deadly infection. Moreover, Cpl-1 destroyed all traces of the most resistant and virulent strains of S. pneumoniae. In a test tube, this eradication took seconds; in the animal, it took a mere four hours and without collateral damage, suggesting that in mice, Cpl-1 is both a selective and safe treatment for drug-resistant bacterial meningitis.

Unlike the guerrilla warfare tactics of antibiotics, which give bacteria time to assemble their resources and develop resistance, phage enzymes strike with blitzkrieg speed and surprise, preventing bacteria from organizing a coherent defense. Without an effective strategy to fight them, bacteria are faced with a war they may not be able to win.

“We have had nothing to control these invasive diseases,” says Fischetti. “This approach may finally give us something.”

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