

Strategy Discovered for Fighting Persistent Bacterial Infections

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DENVER — Researchers at National Jewish Health have discovered a promising strategy for destroying the molecular scaffolding that can make *Pseudomonas* bacterial infections extremely difficult to treat in cystic fibrosis patients, wearers of contact lenses, and burn victims. [Jerry Nick](#), MD, Associate Professor of Medicine at National Jewish Health, and his colleagues report in the April 2009 issue of *The Journal of Medical Microbiology* that a long string of aspartic acid molecules disrupts the molecular bonds that hold together the structure supporting *Pseudomonas* biofilms.

"Once a bacterial community forms a biofilm it becomes much more difficult to treat," said Dr. Nick. "We think our discovery will pave the way for more effective treatment of *Pseudomonas aeruginosa* infections, which can wreak so much havoc in cystic fibrosis patients."

Biofilms are a form of bacterial colony in which bacterial cells attach to and live within an extracellular matrix, where medications and the immune system have difficulty reaching them. As a result, these infections become very difficult to treat effectively. *Pseudomonas* biofilms form and cause lung damage in most cystic fibrosis patients as they grow older. *Pseudomonas* biofilms can also form on the corneas of contact lens wearers, and in wounds and burns.

Dr. Nick and his colleagues previously showed that formation of *Pseudomonas aeruginosa* biofilms is enhanced by the remains of immune system cells known as neutrophils, which accumulate in vast numbers to the site of infection, then die and spill their contents. *Pseudomonas* builds the extracellular matrix from neutrophils' DNA, the actin structural molecules, and histones, the molecules around which DNA normally wraps inside the cell nucleus.

DNase, an enzyme that breaks long strands of DNA, is already used to help thin the thick mucus that plagues cystic fibrosis patients. Dr. Nick believes it may also break up the *Pseudomonas* biofilms. But it is clearly not enough, because *Pseudomonas* biofilms remain one of the most vexing problems for cystic fibrosis patients as they age.

Dr. Nick and his colleagues thought that a negatively charged molecule might help break up the biofilms by bonding to the positively charged histones and preventing them from contributing to the molecular scaffolding, and by breaking apart actin bundles. So, they added aspartic acid polymer, long strings of the negatively charged molecules, to cell cultures of *Pseudomonas aeruginosa* and neutrophils.

In one experiment, a 48-hour-old *Pseudomonas* biofilm was reduced by 42 percent when exposed to DNase for 10 minutes. The aspartic acid polymer alone could not reduce the density of the 48-hour-old biofilm. But when both DNase and the aspartic acid polymer were applied to the biofilm, it was reduced by 78 percent. Several other experiments with varying doses and exposure times of DNase and the aspartic acid polymer on different *Pseudomonas* strains and biofilms had similar results.

"The DNase and aspartic acid worked together synergistically to break down the biofilm," said Quinn Parks, PhD, lead author on the research paper. "We are now experimenting with different aspartic acid polymers to find the most effective ones. This may be an important new therapeutic strategy for combating *Pseudomonas* infections."

National Jewish Health is the leading respiratory hospital in the nation. Founded 120 years ago as a nonprofit hospital, National Jewish Health today is the only facility in the world dedicated exclusively to groundbreaking medical research and treatment of patients with respiratory, cardiac, immune and related disorders. Patients and families come to National Jewish Health from around the world to receive cutting-edge, comprehensive, coordinated care. To learn more, visit the [media resources page](#).

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