Medical Xpress

Research reveals promising strategy for treating tuberculosis

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(Medical Xpress)—Research at Colorado State University reveals that even the most intractable cases of tuberculosis might be effectively battled with a new drug cocktail combining conventional antibiotics and nontoxic compounds that mimic those found in some sea sponges.

Promising initial results of studies by Randall Basaraba and his colleagues recently were published in Pathogens and Disease, the journal of the Federation of European Microbiological Societies. The research is significant because TB, an infectious respiratory disease, kills an estimated 1.5 million people worldwide each year.

"TB remains a dire problem in many resource-poor regions of the world," said Basaraba, an investigator in the world-renowned CSU Mycobacteria Research Laboratories. "With one-third of the human population infected with the bacteria that causes tuberculosis, and with the emergence of drug-resistant strains of the bacteria, there is an urgent need to develop better treatment strategies and to discover the next generation of new antimicrobial drugs."

This message will be among those highlighted during awareness-raising events on World TB Day on March 24.

Basaraba's research project, funded by a $1.8 million grant from the National Institutes of Health, is aimed at developing more effective treatments for tuberculosis. He is directing the study in collaboration with other scientists in the CSU Mycobacteria Research Laboratories and with colleague Christian Melander, a University Faculty Scholar and the Howard J. Schaeffer Distinguished University Professor of Chemistry at North Carolina State University.

Basaraba and Melander began collaborating when they discovered their research groups were working on complementary pieces of the same puzzle: Both are interested in bacteria that cluster together, forming communities that protect them from antibiotics.

Melander's group has worked for several years to develop compounds that could break up these bacterial communities. In the course of this work, they found a remarkably clean sea sponge and successfully modified the responsible compound to create a new class of compounds capable of dispersing communities of bacteria.

Meanwhile, Basaraba's group was focused on developing a new laboratory model for studying Mycobacterium tuberculosis (Mtb), the pathogen that causes TB. Traditional laboratory models allowed scientists to study individual free-floating Mtb, but did not allow bacteria to form communities as they do in human and animal hosts.

The team's unique model allows bacteria to group, permitting the scientists to show that not all Mtb bacteria are equally susceptible to antibiotics. Individual bacteria multiply at a normal rate; when those same bacteria form communities, they adopt a slower multiplication rate.

Basaraba's team found that while the individual bacteria are susceptible to conventional TB drugs, the slower metabolism of the grouped bacteria enable them to survive high doses of antibiotics.

The new class of compounds developed by Melander's group, together with the new laboratory model developed by Basaraba's group, have enabled the researchers to try an approach fundamentally different from other TB treatment strategies: Using the new model, the researchers combined their compounds with antibiotics to study effects on Mtb.

Initial results show that the new compounds successfully break apart communities of bacteria, thereby rendering individual bacteria susceptible to conventional TB drugs. The compounds also inhibited the formation of new Mtb communities.

The scientists will continue testing the novel combination to determine whether the new compounds, combined with antibiotics, can shorten treatment duration and effectively eradicate drug-tolerant Mtb.

"Our hope is that this new strategy will increase the effectiveness of existing antimicrobial drugs by reducing disease relapse, and will prevent the continued emergence of multidrug-resistant Mtb strains," Basaraba said.

Provided by Colorado State University