Key to tuberculosis cure could lie underwater

March 8 2013

The search for a cure for deadly infectious diseases has led Brian Murphy deep underwater. Murphy, assistant professor of medicinal chemistry and pharmacognosy at the University of Illinois at Chicago, is collecting actinomycete bacteria from water throughout the world in a hunt for new antibiotics.

He and Scott Franzblau, director of UIC's Institute for Tuberculosis Research, are lead investigators on a new, three-year, $1.1 million grant from the Defense Department to find compounds to fight tuberculosis, a disease that killed more than 1.4 million people worldwide in 2011.

As a killer, tuberculosis—caused by a bacterium that most often attacks the lungs—is second only to HIV among infectious agents, according to the World Health Organization. The bacteria lie dormant in about one-third of the population, and 8 million new cases are reported annually.

U.S. military personnel face a much higher risk of tuberculosis than American civilians, due to their frequent deployment in developing countries where infection rates are higher, Murphy said. Some units are stationed in locations where the spread of tuberculosis is a major hazard.

"Novel drug scaffolds that can reduce the spread of tuberculosis throughout the military and quickly address a tuberculosis epidemic are in serious need," he said.

Murphy has so far collected a "library" of nearly 1,000 actinomycete strains, and 1,200 samples of biochemicals they produce, from marine

waters off Massachusetts, Maine, the Florida Keys and Vietnam, and from the freshwater of the Great Lakes.

From his collection, he and Franzblau have identified eight aquatic actinomyces strains that target non-replicating tuberculosis. A promising new class of compounds with drug-like potency emerged from their screenings and is the focus of the new grant, Murphy said. It was isolated from sediment collected 260 feet below the surface of Lake Michigan.

"Freshwater environments are a new frontier for drug-lead discovery," Murphy said. "Actinomycetes have the ability to produce molecules that have a high potential for use as medicines, and very little is known about these bacteria in such environments."

The UIC team will be the first to explore each of the five Great Lakes for antibiotic-producing actinomycete bacteria and will evaluate the viability of freshwater systems as a source for drug-lead discovery.

"If we can understand the capacity for these bacteria to produce new, small-molecule drug leads, it will help guide a global freshwater discovery effort," Murphy said.

Multi-drug and extensively drug-resistant strains of tuberculosis, which are unaffected by first- and second-line drug regimens, are the most serious threat, Franzblau said.

"Perhaps the most problematic aspect of tuberculosis treatment is its duration," said Murphy. Franzblau said lengthy treatment is required to eliminate a persistent population of slow-growing or non-replicating tuberculosis.

Provided by University of Illinois at Chicago