Scientists Find Promising Treatment For Neglected Killer Diseases

University of Washington
Yale University

A University of Washington and Yale University collaboration yields a set of chemical compounds that may hold the key for treating infectious parasitic diseases including Chagas' disease and malaria. The compound was licensed to a nonprofit pharmaceutical company that is developing a drug for use in Latin America.

> *Some of the world's most intractable diseases are predominant in the developing world. These illnesses are known as neglected diseases because, though they have a significant impact on vulnerable populations, they receive little attention from the medical community or the pharmaceutical industry.*

One of these neglected killers is called Chagas' disease. Chagas' disease is an insect-borne, parasitic illness that infects and kills millions of people every year, according to the World Health Organization. Chagas' is endemic in 21 Latin American countries and a major cause of heart failure in the region. Caused by the parasite Trypanasoma cruzi, it is

most often transmitted by an insect known as the kissing bug. Humans, as well as wild and domestic animals, carry the parasite, and the insects infected with T. cruzi frequently live in the thatched walls and roofs of homes, making it especially challenging to eradicate.

Controlling the disease is difficult, costly and risky. It depends largely on treating homes in affected areas with residual insecticides and, in general, improving housing by replacing traditional thatch-roofed dwellings with more modern plastered walls and metal roofs. Management of the illness now entails blood screening to prevent transmission through transfusion. Some drug treatments are available as well.

Finding a Treatment for the Disease, Not Just the Symptoms

But the standard drug treatments for Chagas' leave much to be desired. Most are aimed at fighting the infection, which manifests in the heart and gastrointestinal tract of the victim. The drugs are difficult to administer and highly toxic, leading to severe side effects in many patients. And no existing medicines have consistently cured patients, according to a report from the Institute for OneWorld Health, a nonprofit pharmaceutical company whose purpose is to develop affordable treatments for neglected infectious diseases around the world.

A collaborative research effort among scientists at the University of Washington and Yale University recently brought forth a non-toxic drug therapy for Chagas'. The team included Andy Hamilton and Junko Ohkanda, both chemists at Yale; and Fred Buckner and Wesley Van Voorhis, infectious disease experts, and Michael Gelb and Kohei Yokoyama, chemists, at University of Washington.

"It was a wonderful collaboration between organic chemists and parasite biologists that came about through reading the literature and recognizing potential connections," says principal investigator Andy Hamilton, who has since become a provost at Yale. "Big problems nearly always involve collaborative solutions because no one person or institution can have all the answers."

Fred Buckner, of the University of Washington Medical School, agreed. He has worked for years with a group of chemists led by Michael Gelb to develop compounds to treat infectious diseases caused by protozoan pathogens.

"They would make the compounds and we would test them against the parasites to see if they would do anything. Some turned out to be active against targets that were different that what we designed them to do, but we determined the mechanism of action and showed them to be active in an animal model," Buckner says.

Collaboration Goes Beyond the Laboratory

The original patent application described "compounds and methods for treating infections caused by bacterial protozoal and fungal agents," says Aline Flower, of the University of Washington TechTransfer Invention Licensing.

"We developed, in collaboration with parasitologists, compounds that target the Chagas' disease agent in animal models, and we are seeing some very encouraging data," Hamilton says when asked about the potential application of the compound.

Buckner and his colleagues had made inroads targeting these diseases, working toward cures or vaccines. "We had discovered that protozoan parasites contain the enzyme protein farnesyltransferase," he says. "This same enzyme plays an important role in cancer cells, which meant a lot of research laboratories were developing drugs against it. We were working on the hypothesis that protein farnesyltransferase inhibitors might work against parasites," Buckner says.

In the meantime, Hamilton and his colleague at Yale were working on a similar problem from another angle. “This was the result of many years of fundamental research in trying to get a novel molecular structure to target a specific enzyme,” Hamilton says. “It’s a question of how one synthetic molecule could recognize a biological molecule in a process called molecular recognition.”

Perhaps just as important as the chemical compound the researchers discovered, Hamilton says the two universities and the nonprofit pharmaceutical company have developed an integrated model for drug development. “We hope, as we make progress in the pre-clinical stage, OneWorld Health will help us pull together the necessary funding to allow the clinical and preclinical development of these compounds,” he says.

Alan Carr, senior licensing associate at the Yale Office of Cooperative Research, says that an inter-institutional agreement between the University of Washington and Yale enabled the institutions to structure a deal with OneWorld Health to license the compound affordably.

Like the drug compound, this model for drug development, borne of innovative university technology transfer, could well have a lasting impact on people around the world.

This story was originally published in 2006.

To see available technologies from research institutions, click here to visit the AUTM Innovation Marketplace.