Research targets parasitic worm disease

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Schistosomes, small parasitic flatworms, can live for decades inside the bloodstream of a human. ICredit: Tim Day.

The worms can live inside your body for years, decades even. And it's not the worms themselves that will eventually make you sick. Rather, it's the thousands of eggs they lay.

Schistosomes, small parasitic flatworms that have infected hundreds of millions of people in developing nations, cause chronic illness that damages organs and impairs development in children.

The effects of the disease can last decades, leading Mostafa Zamanian, a postdoctoral scholar in the Iowa State University Department of Biomedical Sciences, to describe the illness as a "slow killer." Zamanian

said the perception of the disease as slow acting is part of the reason the international community has sometimes regarded schistosomes with less urgency than they deserve.

But Zamanian is working with a group of ISU researchers to change that. The team, led by Tim Day, a professor of biomedical sciences, is taking a comprehensive approach to the parasitic worms, working through traditional channels to identify portions of their genome that could be targeted by new drugs. At the same time, they're pursuing unconventional solutions that, if successful, could radically change how the world looks at schistosomes – and maybe other parasites as well.

Slow killers

At least 243 million people required treatment for schistosome infections in 2011, according to the World Health Organization. That number puts it in a category with the most devastating parasitic diseases in the world. For comparison, the WHO estimates that there were about 219 million cases of malaria in 2010.

Schistosomiasis, the name given to the illness caused by schistosomes, is most common in areas of Asia, Africa and South America where populations are exposed to infested sources of fresh water.

Schistosome larvae enter the human body through the skin and travel into blood vessels where they develop into adults. Female adult schistosomes release eggs that can be trapped inside human tissues. The eggs provoke an immune reaction that damages internal organs over the course of years.

"The worms are slow to bring about symptoms," Day said. "That's part of the reason why the financial resources that have been dedicated to finding a cure pale in comparison to the amount of human suffering the

disease has caused."

Tellingly, the WHO uses the term "neglected tropical disease" to describe schistosomiasis and other illnesses like it.

Thinking outside (and inside) the box

Day has been studying schistosomes since before he arrived at Iowa State in 2000. Much of that work has been dedicated to finding molecular targets in the worms that could be susceptible to drugs.

Day said it's fitting that the biomedical sciences program is housed in the ISU College of Veterinary Medicine, because the science behind treating parasitic worms is most often driven by advances in animal medicine. New treatments for humans are often "incidental" to progress in veterinary science, Zamanian said.

Day said only one drug is available in most of the world to combat schistosomiasis, and scientists are finding evidence that worms are developing a resistance to it. As a result, there's a growing need for new treatments. To find them, Day and his colleagues have begun looking in some unconventional directions.

Once inside a host, the worms excrete exosomes containing small ribonucleic acids. Day said it's possible the exosomes play a key role in establishing a link between the parasite and the host. Interfering with those exosomes may disrupt a worm's ability to parasitize the host, he said.

"We've long struggled to understand the relationship between the host and the parasite," Day said. "We couldn't decode it. It's possible some of that takes place through these small RNAs."

Day recently received a Grand Challenges Explorations Grant from the Bill and Melinda Gates Foundation to begin shedding light on the role the small RNAs play in the parasite-host relationship.

Zamanian also received a Grand Challenges Explorations Grant grant to pursue a proposal that takes an even more speculative approach to combating the parasites.

From harmful to helpful

Zamanian is looking into using the latest gene editing techniques to eliminate the worms' ability to produce eggs, thereby eliminating the ability of the worms to cause illness in humans.

Once these "neutral" worms are introduced, Zamanian's thinking goes, the host would develop defenses against harmful worms it may be exposed to in the future. But the proposal doesn't stop there.

If gene editing can turn the worms from harmful to neutral, can the same technique be used to make worms helpful to humans?

"These worms can remain stable in the bloodstream for decades," Zamanian said. "We want to find out if they can be used as a biological platform to release desirable or advantageous molecules."

Doing so could potentially result in reprogrammed schistosomes that, instead of causing illness and misery, serve a medicinal purpose or help to fight off other parasitic infections.

Zamanian will work on the project with collaborating researchers at McGill University in Montreal and Queen's University Belfast. His postdoctoral supervisor, ISU Associate Professor of Biomedical Sciences Michael Kimber, will also have some input into Zamanian's efforts.

Day and Zamanian admit their ideas may sound far out at first blush, but problems of this scale often require bold thinking, Day said.

"Sometimes it's the really aggressive ideas that have the greatest rewards," he said.

Provided by Iowa State University