Sequencing the hookworm: Ancylostoma ceylanicum genome provides potential new drug, vaccine targets

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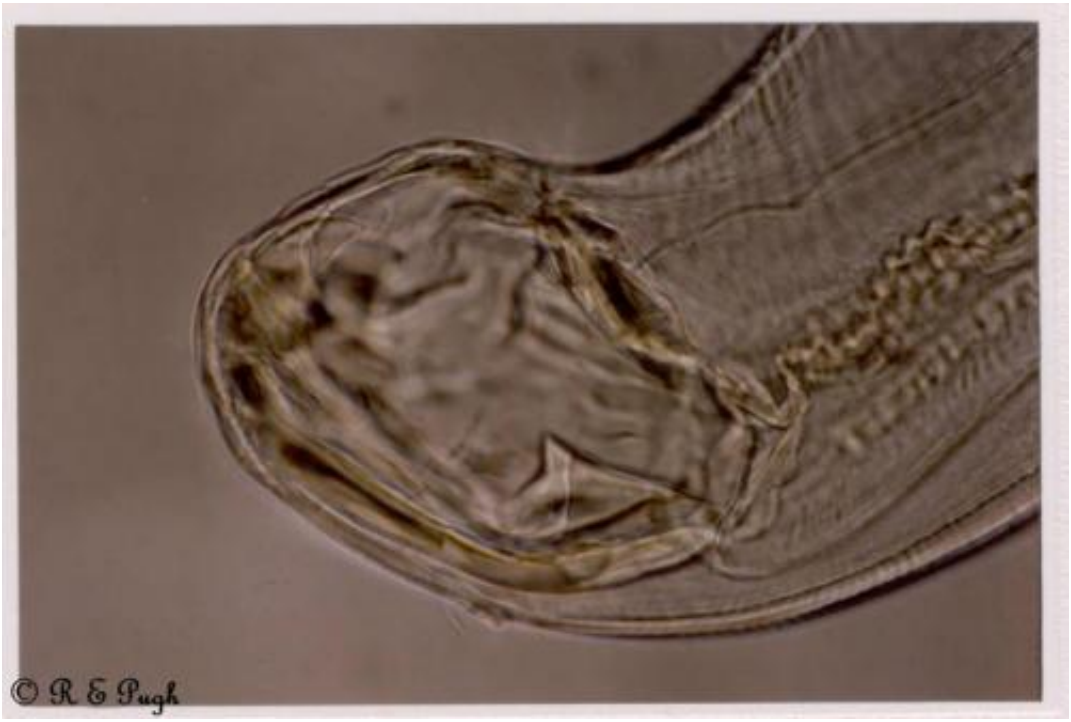

Credit: parasite.org.au , R.E.Pugh

In an advance that may potentially lead to new treatments for parasitic hookworms, scientists at the University of Massachusetts Medical School and Cornell University have sequenced the genome of the hookworm, *Ancylostoma ceylanicum*. The genome of the nematode that, according to some estimates, infects as many as 400 million people

worldwide will help researchers find genes active during infection and devise new drugs or vaccines that target these genes. The study, which also includes researchers from the University of California San Diego and the California Institute of Technology, was published in *Nature Genetics*.

A debilitating tropical disease second only to malaria, hookworms are a leading cause of maternal and childhood morbidity in developing countries. They can live in the small intestine for as long as 10 years, drinking blood, robbing their hosts of iron and protein, interfering with absorption of critical nutrients and suppressing the immune system. Infection can lead to chronic anemia, as well as permanently stunt physical and intellectual development in infected children.

"The health burdens associated with soil-transmitted hookworms, especially in developing countries in Africa and the tropics are enormous," said Raffi V. Aroian, PhD, professor of molecular medicine at UMass Medical School and co-author of the study. "The only drugs we have to combat these parasites were developed to treat farm animals and are only partially effective. There is a tremendous need for a treatment for hookworms in humans that is safe, effective and affordable in the world's poorest countries."

Three species of hookworms can infect humans. People most commonly infected typically reside in poverty stricken areas with poor sanitation and are exposed to the worm through contaminated soil or food. Common in the American south 100 years ago, hookworms were virtually eradicated in the United States through improvements in sanitation and public health efforts during the early part of the 20th century.

Contemporary efforts to study the parasitic nematode have been hampered because the most common species, Necator americanus and

Ancylostoma duodenale, cannot survive outside of a human host. This makes it difficult for researchers to study them in the lab and almost impossible to test new drugs and vaccines. It is why current treatments rely on drugs developed to treat similar worms in farm animals.

Though less common, because *A. ceylanicum* can infect and thrive in animals other than humans, such as rodents, it is an excellent experimental model for hookworm disease that allows scientists to study it in the laboratory. It also opens up the possibility that new drugs or vaccines for human hookworms can be designed and tested using *A. ceylanicum*.

"For this to happen, we first have to know as much as possible about *A. ceylanicum*'s genes and the proteins they make," said Erich M. Schwarz, PhD, senior research associate at Cornell University and co-author of the study. "Until recently this would have been a very expensive and difficult undertaking, but next-generation technologies for analyzing DNA have made it possible for a small number of scientists to sequence and characterize the entire genome of an animal."

Isolating and sequencing DNA and RNA from hookworms during different stages of infection led to several significant findings. The *A. ceylanicum* genome constrains 313 million nucleotides, with 30,738 genes that encode for proteins and show gene activity. Researchers were also able to identify specific genes involved in infection. Among the genes identified were three large families of previously unknown proteins that are strongly synthesized during three different steps of infection. They also found more than 70 genes that likely encode for proteins which the worms need to survive but which are absent from mammals, making them possible drug targets. Finally, they found five genes that are extremely active in adult worms and are promising targets for vaccination because they are likely needed for feeding.

"The sequencing of *A. ceylanicum* adds to a growing number of genomes for parasitic nematodes that collectively infect over a billion people worldwide," said Dr. Aroian. "These genomes are crucial for inventing new drugs and vaccines against parasitic nematodes that rapidly evolve drug resistance and plague large populations in developing countries. With these new genomes we can begin rationally designing and testing treatments in the laboratory that can potentially benefit millions of people."

More information: The genome and transcriptome of the zoonotic hookworm Ancylostoma ceylanicum identify infection-specific gene families, *Nature Genetics* (2015) doi:10.1038/ng.3237 . www.nature.com/ng/journal/vaop … nt/full/ng.3237.html

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