Study by WPI professor produces first edition of a bookworm's genome

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This is a photomicrograph of *Panagrellus redivivus* (*P.redivivus*), known as the bookwork, the beer-mat worm or, simply, the microworm. Credit: Worcester Polytechnic Institute

It has co-existed quietly with humans for centuries, slurping up the spillage in beer halls and gorging on the sour paste used to bind books. Now the tiny nematode *Panagrellus redivivus* (*P.redivivus*) has emerged from relative obscurity with the publication of its complete genetic code. Further study of this worm, which is often called the beer-mat worm or, simply, the microworm, is expected to shed new light on many aspects of animal biology, including the differences between male and female organisms and the unique adaptations of parasitic worms.

Using next-generation sequencing technologies, a research team led by Jagan Srinivasan, now an assistant professor of biology and biotechnology at Worcester Polytechnic Institute (WPI), discovered just over 24,000 putative genes encoded in the worm's DNA—nearly the same number as in the human genome. The team also measured the amount and characteristics of RNA molecules transcribed from those genes to direct cellular processes—that collection of data is called the worm's transcriptome. The genome data published by Srinivasan and colleagues marks the first time a free-living nematode outside of the widely studied *C. elegans* immediate family has been sequenced.

The researchers detail their findings in the paper, "The Draft Genome and Transcriptome of *Panagrellus redivivus* Are Shaped by the Harsh Demands of a Free-Living Lifestyle," published in the April 2013 edition of the journal *Genetics*.

"Humans and nematodes share a common ancestor that lived in the oceans more than 600 million years ago," Srinivasan said. "Many of the basic biological processes have been conserved over the millennia and are similar in Panagrellus and humans. So we believe there is a lot to be learned from studying this organism."

Srinivasan led the *P.redivivus* sequencing project while working as a postdoctoral researcher at the California Institute of Technology in the laboratory of Paul Sternberg, a Howard Hughes Medical Institute investigator and the Thomas Hunt Morgan Professor of Biology at Caltech. Adler Dillman, a graduate student at Caltech, worked closely with Srinivasan on the project and shares first-author status of the new study. Sternberg is the senior author.

Srinivasan joined the WPI faculty in the fall of 2012 and has established his own research program using the microworm and its scientifically more famous cousin, *Caenorhabditis elegans* (*C. elegans*), as model systems to study the neurobiological basis of social communication and how organisms react to environmental cues.

In recent years *C. elegans* has emerged as a star in the biomedical research world. In 1998 it became the first multicellular organism to have its genome sequenced. The experience gained from that work was fundamental to the successful completion of the Human Genome Project. Nobel prizes in 2002, 2006, and 2008 were awarded to researchers who made extraordinary discoveries studying *C. elegans*.

Like *C. elegans*, the microworm *P. redivivus* is a free-living nematode found in many environments around the world. An adult microworm is about 2 millimeters long and has approximately 1,000 cells. Despite its small size, the worm is a complex organism able to do all of the things animals must do to survive. It can move, eat, reproduce, and process cues from its environment that help it forage for food, seek out mates, or react to threats. Unlike *C. elegans*, however, *P. redivivus* is a gonochoristic species, meaning it has male and female individuals who must mate to reproduce. In contrast, *C. elegans* has evolved to be primarily a self-fertilizing hermaphrodite, producing both eggs and sperm in the same individual. (There are some male-only *C. elegans* worms, but they are rare in the wild.)

"Because we see true male and female individuals, Panagrellus will be a powerful model system for studying the differences between the sexes and the processes that the organism uses to find and interact with a mate," Srinivasan said.

Both *P. redivivus* and *C. elegans* are well suited for laboratory research, Srinivasan noted. The worms are easily cultured and have a short lifecycle, growing from embryo to adult in about four days. Adults live for approximately three weeks and can produce as many as 40 offspring each day. This lifecycle makes them ideal for genetic studies. Furthermore, the worms are transparent. Under a microscope researchers can look into a worm's body and see almost every cell in the living animal. They can see the cell nuclei, tag molecules with glowing fluorescent markers, and capture images of biological processes from the moment of fertilization to maturity.

As a free-living species, the microworm is considered to be an ancestor of other small worms that have evolved into parasites and colonize specific plants or animals (including humans) to survive. Studying the differences between the microworm and parasitic species will become another important area of research, Professor Sternberg noted. "Of course we want to know more about parasitic worms, given their impact on people and the environment," Sternberg said. "To know about parasites, however, you have to know about the free-living worms to place the bizarre features of parasites into context."

The current study identified the number, location, and composition of genes and RNA transcript in the microworm, and found significant and surprising differences between the *P.redivivus* genome and that of *C. elegans* even though the worms look nearly identical to the naked eye. For example, the early analysis of the microworm genome suggests that a large collection of genes have evolved as defenses against viruses and other pathogens the worms encounter in the environment—hence the "harsh demands" of their lifestyle as referenced in the paper's title.

"Studying how the genomes differ, and what processes are driven by those differences, should prove to be insightful," Srinivasan said. "Sequencing the genome and transcriptome is an important first step in what we believe will be a rich new field of study for fundamental biological processes that control development and behavior, not only in the worms, but also in humans."

Provided by Worcester Polytechnic Institute