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RESEARCH NEWS

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Gilliam Fellow Finds a New Twist on How Some Parasites Move

In 1843, the Hungarian scientist David Gruby—considered the founder of medical microbiology—was studying a microscopic parasite in frog blood. The parasite seemed to propel itself forward like a corkscrew, so he named the creature *Trypanosoma sanguinis*, after the Greek word "trypanon," or augur. The name stuck, and the term Trypanosome is now used to describe a genus of unicellular parasites that move in a similar way.

But new research is challenging Gruby's description of the parasite's movement. José A. Rodriguez, an HHMI-funded doctoral student at the University of California, Los Angeles, and a multidisciplinary team of colleagues have found that the parasite *Trypanasomabrucei*, which causes African sleeping sickness, doesn't move in just one direction like a corkscrew. Instead, it rocks left then right and back again, without changing the direction it is trying to go.

This video shows the parasite *T. brucei* swimming in blood drawn from an infected mouse, with images obtained every millisecond. Credit: Jose A. Rodriguez

"It's a much more sophisticated and efficient way to move," says Rodriguez, who is first author on a paper published the week of October 19, 2009, in *Proceedings of the National Academy of Sciences*. "We underestimated these guys. We have to give them more credit for how they regulate their behavior."

Rodriguez is a molecular biology graduate student who works on cancer research in the UCLA lab of Manuel Penichet. Rodriguez is funded by an HHMI Gilliam Fellowship, which goes to exceptional students from disadvantaged backgrounds who are pursuing a Ph.D. in the sciences. As an undergraduate, Rodriguez majored in biophysics at UCLA, and he is putting that background to use in Penichet's lab using ultrafast single particle imaging, a technique that lets him take high-speed pictures of biological events as they happen. In Penichet's lab, Rodriguez looks at molecules that interact with receptors on cancer cells, but the technique can also be used to look at many other biological processes.

Rodriguez— along with fellow biophysicists John Miao and Robijn Bruinsma—began collaborating with Kent L. Hill, a microbiologist at UCLA, whose team studies the movement patterns of *T. brucei* and other trypanosomes. Hill and Miao saw an opportunity to apply Rodriguez's expertise in ultrafast single particle imaging to help in getting high-speed pictures of *T. brucei* as it moves.

This video shows the parasite *T. brucei* swimming in a culture medium used to maintain the cells outside their host. The images were taken a rate of one every millisecond. Credit: Jose A. Rodriguez

When Rodriguez snapped images of *T. brucei* —one thousand pictures every second—they didn't show what Hill expected. Ordinarily, corkscrews turn in a single direction: clockwise. But these images show that *T. brucei*moves forward by turning both clockwise *and* counter-clockwise, Rodriguez explains. This left-to-right rocking—or "kink-driven motility"—generates waves that flow from the tip of the parasite's flagellum to the base of its body.

Rodriguez hopes the finding is more than just biological curiosity. It might point to a new cure for sleeping sickness by targeting the proteins that *T. brucei* relies on to move. If drugs could impede this complex movement, they could keep the parasite from getting into the brain, Hill says. "Sleeping sickness has two stages. It starts in the blood, and makes patients sick. And then it goes the brain, where it turns lethal," he explains. "We don't have good drugs for treating sleeping sickness in the central nervous system. So what we'd like to do is prevent the parasite from getting there in the first place."

Meanwhile, Rodriguez is becoming known around UCLA as an enthusiast of high-speed photography of microscopic objects. "This was a fruitful collaboration with several other laboratories," Penichet says of his graduate student's foray into trypanosome biology. "This will be (José's) second, first-author publication, and he's got several more in our cancer cell research that hopefully will be published soon."