HHMI
HOWARD HUGHES MEDICAL INSTITUTE

RESEARCH NEWS

JULY 22, 2009

Primate Form of HIV Kills Chimps Early

Image Title: Rebecca Rudicell, a graduate student at the University of Alabama at Birmingham, prepares a piece of the simian immunodeficiency virus, a close relative of HIV, to be sequenced. Rudicell extracted the virus's genome from the feces of a chimpanzee from Tanzania. - Steve Wood-UAB Creative

Sometimes dirty work pays off. For Rebecca Rudicell, almost three years of studying chimpanzee feces has led to new insight into how an AIDS-like disease develops in wild African chimpanzees.

“I have the very glamorous job of spending my days (studying) chimpanzee feces,” jokes Rudicell, a student in an Howard Hughes Medical Institute-funded program to teach graduate students about medicine at the University of Alabama at Birmingham (UAB).

African primates are naturally infected with more than 40 different strains of simian immunodeficiency viruses (SIVs), two of which have crossed the species barrier to give rise to human immunodeficiency virus (HIV). HIV infection is well known to cause AIDS but until now it was thought that SIV infection in its various primate hosts did not cause disease.

"The thought had always been that this virus didn't hurt chimpanzees, but it looks to us like they are dying at higher rates. We were not expecting this."

- Rebecca Rudicell

Rudicell and her colleagues have used chimpanzee droppings to learn more about the distribution of apes infected with SIV. Over the past three years, Rudicell has processed and analyzed about 500 specimens collected by trackers at the Gombe Stream National Park in Tanzania, the research home of chimpanzee expert and conservationist Jane Goodall. Rudicell extracts DNA from the feces to confirm the chimp's identity. Then she analyzes the samples for the presence of SIV. "It's a labor-intensive process," she says. "But there's something thrilling about working with a sample from a wild chimpanzee living halfway around the world."

That effort paid off with a stunning finding: Some chimps infected with SIV develop AIDS-like symptoms and die early. Previously, researchers believed SIV was harmless in apes and monkeys, a dogma that Rudicell and her mentor, Beatrice Hahn, a professor of medicine and microbiology at UAB, are now beginning to overturn with research findings published July 23, 2009, in the journal *Nature*. Goodall and several of her Gombe colleagues are co-authors on the paper.

"The thought had always been that this virus didn't hurt chimpanzees, but it looks to us like they are dying at higher rates," Rudicell says. "We were not expecting this."

Learning about Medicine Rudicell came to Hahn's lab and UAB because of her interest in the school's Med into Grad program, which is part of an initiative at 13 universities nationwide. HHMI began the Med into Grad program in 2005 to encourage universities to develop graduate training programs that incorporate an understanding of the principles of medicine and disease. Each school in the program receives a four-year grant from HHMI, which provides $650,000-$1 million of total support. UAB's program, called the Hughes Med-Grad Fellowships, helps train science graduate students in

basic biomedical science and modern clinical medicine.

The program “sounded fascinating, exactly what I wanted to do,” says Rudicell, a Pensacola, Florida, native who majored in chemistry and biology at Warren Wilson College in Asheville, N.C.. “I like the idea of doing translational research, of using actual specimens from patients or subjects.”

In the past, graduate programs have been completely focused on teaching one subject to the exclusion of almost everything else, says Danny Welch, a professor of pathology and current director of UAB’s Med-Grad Fellowships. “People get so into their favorite molecule that they don't understand the disease,” Welch says. “We want our Med-Grad students to communicate more effectively with people in other disciplines” so they can work with doctors to help treat patients and understand the complexities and interrelationships involved in a disease. HHMI will announce a second round of Med into Grad programs in October.

At UAB, the 27 Med-Grad students take classes where clinicians and patients offer real-world perspectives on diseases and current treatments. Students pick the diseases they want to learn about, find clinicians working in that area, invite patients to class, and sometimes visit hospitals and clinics. For example, during their class on HIV, a UAB clinician walked the class through the history of HIV and AIDS, explained the challenges of treating HIV infection, and introduced the students to a patient activist.

In addition, the students spend time at a drug discovery firm, the Southern Research Institute, learning how to screen for new disease treatments. Welch says it’s vital for students to be exposed to career opportunities outside of academia. “A lot of science graduate students will end up working in other settings, in industry, at foundations, and so on,” he says. “Those places are structured very differently than a university lab.”

The program’s directors also help place students in labs that ask basic science questions about human diseases. When Rudicell arrived at UAB, she began rotating in different labs before making a decision about what she wanted to study. Former Med-Grad program director Tom Clemens encouraged Rudicell to work with Hahn, a renowned biologist who first traced the origin of HIV to chimps in west-central Africa. Rudicell started with a ten-week rotation, and Hahn invited her to stay. Rudicell says she was thrilled at the opportunity to work with Hahn on such groundbreaking research.

Chimp HIV Hahn began working on the problem of SIV years before Rudicell came to UAB. In 1999, Hahn reported that two of the four subspecies of chimpanzees were infected with a particular type of SIV, SIVcpz. Members of one of these chimpanzee subspecies, *Pan troglodytes troglodytes*, harbored viruses closely related to HIV-1, which pointed to that subspecies as the likely source of HIV-1. To identify the chimpanzee

reservoir of HIV-1 in the wild, Hahn set out to survey the geographic spread and genetic diversity of SIVcpz across the African continent. Since chimps are endangered and cannot be tested in the wild, she and her lab members developed techniques to test chimpanzee feces for SIV, and they teamed with Goodall, who has been observing the Gombe chimps since 1960, and her colleagues there.

After four years of study, Rudicell and the other team members analyzed their data and realized that the infected chimpanzees were dying early. After lots of double-checking – including laborious re-testing each sample of chimp feces– the team learned that the infected chimps were dying about 10 to 16 times faster than those not infected with SIV. The team used tissues samples from chimps who had died in Gombe Park to confirm that they had symptoms of an AIDS-like disease, including a damaged immune system. Hahn's team also used their knowledge of which chimps had SIV to show that female chimps infected with the virus had fewer babies and those babies were more likely to die. "It's probably been going on forever and a day," Hahn says. "We just didn't know about it."

For now, Rudicell is continuing her work on the distribution of SIV in chimps and finishing up her graduate degree. "I handed the torch to Rebecca about a year ago, so now she is in charge of the study," Hahn says. Rudicell, who is in her fourth year of graduate school, is not sure where her nascent career will lead. She enjoys her current work and might opt to continue studying HIV in apes and monkeys. Or she might try her hand at science policy. "I'm keeping my (options) open," she says.

Either way, Welch says completing the Med-Grad fellowship will help her. "If we equip the students with a handful of skills that put them at a competitive advantage, they'll have better careers," he says. "And society will get more bang for its educational buck."