

Marie-Louise Hammar-skjold, MD, PhD, and David Rekosh, PhD, are molecular geneticists. For the last 20 years, the couple has worked steadily and quietly to unravel the genetic mysteries of HIV as co-directors of the Myles Thaler Center for AIDS and Human Retrovirus Research at the University of Virginia.

And they've had their share of success: Thaler Center scientists—currently four faculty members working in molecular genetics, immunology, virology and vaccine development—have made critical discoveries that have advanced the understanding, not only of how HIV works, but of some basic functions of all cells.

Hammar-skjold's and Rekosh's work with HIV rev gene, for example, which is essential to replication of the virus, has been part of a revolution in understanding about the important role RNA plays in regulation within the cell. Their work also includes a patent on some potential compounds that might inhibit the HIV virus.

But these researchers have never been so focused on their own bench work that they haven't been aware of what's going on in the rest of the world.

"More than 25 years ago, we changed our careers from working on other viruses to working on HIV," Hammar-skjold said. "We felt that this was one of the most urgent issues where we had expertise. Our hearts have always been in doing the right thing, whatever we can do and wherever our resources are needed the most."

Thinking Globally

More recently, as drug development, treatment and education have helped stabilize the AIDS crisis in the U.S., Hammar-skjold and Rekosh have turned some of their attention to the epidemic that is still devastating other



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Written by Linda J. Kobert
Photographs by Jackson Smith



parts of the world. More specifically, they've turned their attention to Africa.

According to the World Health Organization's 2010 global estimates, about 34 million people worldwide are infected with HIV; three-quarters of those (22.9 million) are in Sub-Saharan Africa. Seroprevalence of the infection in the region in adults ages 15-49 (5%) is higher by a factor of ten than the average of all other regions of the world.

In the country of South Africa, however, the picture is even more grim: adult seroprevalence in 2009 was estimated at 17.8%. These numbers vary widely, depending on the region, but according to Rekosh, in antenatal clinics in cities such as Durban, HIV infection rates in women ages 15-25 are as high as 60-70%.

"The types of viruses that are circulating in Africa are actually different than the main type of virus that is circulating in the U.S.," Rekosh said. "We know a tremendous amount about the U.S. viruses and how they develop drug resistance, but we know very little about the viruses that are causing the world epidemic. So part of our long term research is to look directly at the viruses that are circulating in Africa and to apply the same kinds of questions we've been asking about the U.S. viruses."

Acting Locally

Through UVA's Center for Global Health, Hammarskjold and Rekosh developed a collaboration with Pascal Bessong, who chairs the microbiology department at the University of Venda (Univen) in northeastern South Africa. While Univen does not have a school of medicine, Bessong has spent his career surveying the HIV epidemic in this region in Limpopo Province, which remains one of the poorest in the country. His goal is to develop a molecular biology program at the

Change



Tshifhiwa Tambani



Tshifhiwa Nefefe

Replicating the Skills of Science

For South African student Tshifhiwa Tambani, coming to UVA to participate in a ten-week research internship at the School of Medicine was a transforming experience on many levels. For one thing, she thought she wouldn't measure up to the American students at this leading university.

"I thought, I'm inferior and they're going to be top students," Tambani said. "But I'm just like them. They struggle as much as I do."

Tambani and her classmate Tshifhiwa Nefefe are graduate students in microbiology at the University of Venda (Univen), a traditionally black university in rural Limpopo Province in northeastern South Africa. The two were selected through a competitive application process to participate in UVA's Summer Research Internship Program (SRIP), which includes lectures by distinguished faculty members, exposure to a variety of advanced research techniques and, most importantly for these individuals, hands-on research in the lab.

Tambani's and Nefefe's participation in this program was part of an ongoing collaboration between Univen's head of microbiology Pascal Bessong and UVA researchers Marie-Louise Hammarskjold, MD, PhD, and David Rekosh, PhD. Because of this collaboration, Univen was able to acquire a grant from the South African government to support this project.

"We've had several students from SRIP in our lab," Rekosh said. "That's where we got this idea to get students from Univen to come here to participate in this program that takes students from small colleges and shows them what research is like and gives them some lab experience."

The students designed their own projects that they pursued

during their time at UVA. Tambani worked in Hammarskjold's and Rekosh's lab, infecting cells with HIV mutated in a specific gene to determine how it would affect viral growth. Nefefe, whose interest is in the effects of medicinal plants on the immune system, spent time in the lab of Janet Cross, PhD, in the Department of Pathology, doing in vivo and in vitro studies with isothiocyanates, naturally occurring substances that appear to inhibit tumor growth.

Because their university is among the most economically and academically disadvantaged, the skills Tambani and Nefefe developed here are invaluable, not just for them personally, but for their university. When they return, they are expected to teach their newly developed skills to others and to advance ongoing research projects at the university.

"Now I can see that there is a lot I can do within science," Nefefe said. "Now I'm thinking my life will be totally based on doing research and sharing the knowledge I have with others. I am starting to see science as a career."

Tambani agrees. "Back at home they always discourage you from doing graduate work," she said. "They think when you do a masters' or PhD that you're over qualified for any job. But by being here, I know I can actually do research. When I go back, I'll be more serious about getting my PhD, and all the knowledge I acquired here I will pass on to other students and motivate them to learn more and become more educated."

university that will prepare skilled scientists who can take on the task of tracking and treating the local infection.

"In addition to the research we're doing, which is geared toward understanding the epidemic and is being carried out with a small number of people who work in Pascal's lab," Rekosh said, "we realized we could do something else, which we consider as important or more important in fighting the AIDS epidemic. And that is helping this university to build capacity by getting involved in teaching there and to set up a program to bring students here."

Over the past six or seven years, Hammarskjold and Rekosh have participated in several exchanges between the two universities, hosting students and scientists from Univen who have come to Virginia to work in their lab and traveling to Univen, sometimes with other UVA scientists, to teach molecular biology concepts and methods to South African students and faculty. They've also helped establish a program for Univen students to participate in a UVA internship program where they learn research skills that they can take back and teach to others. And recently they've been invited to speak to high school students in Limpopo about molecular biology.

"We've started this [collaborative research] project that they run in South Africa, but we provide a lot of expertise and training," Rekosh said. "They're trying to understand the pattern of drug resistance in the area and trying to understand the kind of [HIV] viruses that are circulating there. So it's a very hands-on, applied epidemiological project, which is very different from the other things we do, trying to understand the way the genes work."

"They're just barely coping with being able to treat people," Hammarskjold added, noting that before 2005 there were virtually no antiretrovirals available in the developing world. "So we're really trying to increase the

level of expertise so that, now that they have treatment, they can address drug resistance up front."

Helping Others Help Themselves

Capacity building is a unique approach in global health initiatives. More often, experts from the developed world come to disadvantaged places like Limpopo to work in the community on projects such as providing services in a local AIDS clinic or building clean water facilities. Sometimes there is buy-in from the community, sometimes there is not.

While these projects are worthy, Hammarskjold's and Rekosh's focus is different. Rather than doing something for the people living in Limpopo, their mission is to increase the quality of teaching at the university, to build the skills of faculty and students so that they are better equipped to help their own local community. And while these initial efforts are modest now, they hope their work at Univen serves as a model that others can use to help disadvantaged communities help themselves.

"When we first came to UVA we had no idea that we were going to be involved in global education," Hammarskjold said. "Since our main goal has always been to fight AIDS, when we see what is happening with the epidemic we now feel that this kind of education has become a very big thing, maybe more important right now as far as fighting AIDS is concerned than what we're doing in the lab."

"We do this because it is the right thing to do," Rekosh added. "We really believe that there can be an AIDS-free generation in South Africa, but in order for that to happen what's absolutely key is education and training and sophisticated science. That has to be developed in places like the University of Venda. We see this as pivotal to the whole thing: if the people of South Africa can't do this themselves, then any effort by the outside is not going to be sustainable."

Thaler's Legacy

Construction of a new, modern hospital at the University of Virginia occupied much of the 1980s. Myles Thaler, a distinguished graduate of the University's School of Architecture and head of landscape architecture at the vice president's home in Washington, D.C., lent his services to the project by designing and planting a meditation garden near the link between the old hospital and the new one.

During that time another medical phenomenon was building: the emergence of the HIV/AIDS epidemic. The UVA School of Medicine was not involved in the wave of research that swelled to study the epidemic then, but when Thaler was diagnosed with HIV—at that time the diagnosis was essentially a death sentence—he wanted to inspire his beloved University to start studying the condition.

The Myles Thaler Center for AIDS and Human Retrovirus Research was established at the University in 1992 through a series of generous gifts from anonymous donors in honor of Thaler.

"Myles knew he wouldn't be around much longer and he wanted this Center to be his legacy," said David Rekosh, PhD, who serves as the Myles H. Thaler Professor and co-directs the Center with his wife, Marie-Louise Hammarskjold, MD, PhD.

At the time it was started, the Thaler Center was unique at the University. It was unsolicited, and it jump-started a research program that did not exist at the University before that. Over the past 20 years, the Thaler family has continued to be intimately involved in the Center's activities, and their continued support has helped the Center develop new initiatives.

"The donors were very enlightened," Rekosh said. "They realized that the Center would probably never grow to be very big, given that we're not in an urban area. But they realized the importance of basic research, and they understood that the kind of research we carry on as we try to understand how HIV works has implications for lots of other diseases besides HIV."

"My parents probably still hold some hope that this Center is actually going to help me," Thaler told Hammarskjold and Rekosh before he died. "I'm realistic about this. I know it's not, but your Center is going to be like the children and grandchildren I'll never have. I just want to do some good. It's not about me."