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## New Institute for Tuberculosis and HIV Research Created in South Africa

A groundbreaking partnership between the Howard Hughes Medical Institute (HHMI) and the University of KwaZulu-Natal (UKZN) in South Africa will establish an international research center focused on making major scientific contributions to the worldwide effort to control the devastating co-epidemic of tuberculosis and HIV and on training a new generation of scientists in Africa.

“This initiative adds a new dimension to HHMI’s commitment to international research,” said Thomas R. Cech, president of HHMI. “Our cross-Atlantic partnership reflects a shared view that direct and substantial investment in basic, clinical, and translational research in the heart of the pandemics of HIV and TB will yield significant discoveries that will alleviate the human suffering caused by these diseases.”

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The creation of the KwaZulu-Natal Research Institute for Tuberculosis and HIV (K-RITH) reflects nearly two years of discussion between HHMI and UKZN and was announced at simultaneous events in Washington, D.C., and Durban, South Africa. HHMI has committed \$60 million to the initiative over the next 10 years.

“The HHMI-UKZN partnership is a major and unique investment into one of humanity’s major global health challenges, that of HIV and TB co-infection. The partnership is addressing a real problem that affects real people,” said Professor Malegapuru William Makgoba, vice chancellor of the university.

The South African Ambassador to the U.S., His Excellency Welile Nhlapo, joined Cech and Makgoba for the announcement in Washington. A simultaneous event was held in Durban.

The institute will be located on the campus of the Nelson R. Mandela School of Medicine in Durban in a six-story facility that will include two floors of high-level biosafety (BSL-3) laboratories equipped for TB research. HHMI will provide \$20 million (R218 million) toward the construction of the new building with UKZN and LIFE Lab, a biotechnology center of the government of South Africa, making substantial commitments for the project. The total cost of the project – which will be integrated with the existing Doris Duke Medical Research Institute – is estimated at about \$30 million (R308 million). Construction is expected to begin in late September.

HHMI awarded seed grants totaling more than \$1.1 million to scientists in the U.S. and South Africa in 2008 as part of the long-term plan to develop K-RITH. This year, the Institute will provide an estimated \$3 million in grant funding and support construction of temporary laboratory facilities to support the TB research program. The Institute has committed to providing substantial ongoing research support to K-RITH for 10 years.

“This initiative is one of the most challenging we have embarked upon in our international program,” said Robert Tjian, who will become HHMI’s president on April 1. “I look forward to seeing how K-RITH realizes the potential for developing new strategies to combat the dual scourge of HIV and tuberculosis – both for South Africa and the entire world.”

South Africa has more residents infected with HIV than any other nation in the world. By 2007, the nation accounted for 17 percent of the global HIV disease burden– an estimated 5.4 million people are infected – and it has one of the highest per capita rates of tuberculosis in the world. Tuberculosis, a major problem in the pre-AIDs South Africa, emerged as a public health crisis in its own right, particularly with the emergence of both multi-drug resistant (MDR) and extensively drug resistant (XDR) strains of tuberculosis in persons already infected with HIV.

KwaZulu-Natal province, home to more than 10 million people, bears an even greater burden of disease than the nation as a whole and as much as 40 percent of the population may be positive for HIV. When an outbreak of extensively drug resistant or XDR- TB was reported in the rural area of Tugela Ferry in 2006, the region became a focus of international concern even as additional cases of XDR-TB surfaced elsewhere in the world.

“The projects defined in the K-RITH program are there to address important research questions that would provide greater insights, understanding and the potential for solutions. All these should bring hope to people who are infected and affected,” said Makgoba. “Most critically, this partnership is an investment into the future, in the training of a new generation of scientific leaders in this important area of health research.”

HHMI and UKZN will jointly recruit a permanent director for K-RITH. Barry R. Bloom, former dean of the Harvard School of Public Health, and a well-known TB researcher, will chair the search committee.

But the commitments by HHMI and UKZN go beyond the financial. Two leading HHMI investigators with longstanding expertise in TB and HIV research will participate actively in the program: William R. Jacobs, Jr., of the Albert Einstein College of Medicine and Bruce D. Walker of the Massachusetts General Hospital, who directs the HIV Pathogenesis Program in Durban, a joint initiative of Harvard University and UKZN. Walker also directs the newly formed Ragon Institute, which will focus on development of a vaccine against HIV. UKZN scientists helping to direct and plan K-RITH are A. Willem Sturm, a noted TB researcher and dean of the Mandela School of Medicine who serves as K-RITH's interim director and Salim S. Abdool Karim, UKZN Pro Vice-Chancellor (Research) and director of the Center for the AIDS Program of Research in South Africa.

“K-RITH will leverage HHMI's deep experience in fundamental research and its financial resources with UKZN's own programs in HIV and TB research in the context of ongoing efforts to manage HIV and TB in KwaZulu-Natal,” said Cech. “K-RITH scientists will have an unparalleled opportunity to collaborate with their colleagues at clinical sites in and around Durban in research efforts that focus on the diagnosis, pathogenesis, treatment, and prevention of TB and HIV.”

K-RITH will initially focus on four major research areas, led by teams of U.S. and South African scientists and their clinical collaborators:

- Development of rapid and more effective tests for tuberculosis that will be built with the use of engineered bacteriophages, viruses that infect bacteria. Better diagnostics will save lives. Tuberculosis is a slow-growing organism and difficult to culture, which means that tests used to diagnose patients or identify those with drug resistant strains of the disease take too long. Some newer tests are more rapid, but miss resistant strains or require too much high-tech equipment. The lack of effective diagnostic tools poses a particular threat to individuals vulnerable to infection because their immune systems are weakened by HIV or other diseases. Principal investigator: William Jacobs Jr.
- Characterization of the genotypic and phenotypic characteristics of drug resistant strains of tuberculosis – both MDR and XDR – as a step toward understanding the biological factors that drive bacterial pathogenesis. This research will be coupled with clinical and epidemiological data on strains of tuberculosis as a step toward developing a comprehensive understanding of the role that each plays in determining patient outcomes. Ultimately, this research may lead to rapid genetic testing for drug resistance. Principal investigator: A. Willem Sturm.
- Analysis and characterization of the complex immune response to tuberculosis –specifically among individuals already infected with HIV –

with a goal toward understanding the factors that may predict disease progression or long-term control of the TB infection. Understanding how the immune system responds to TB will be essential to the development and testing of vaccines for both HIV and TB. Principal investigator: Bruce Walker.

□ Study of recurrent tuberculosis in patients with HIV to assess the nature of the recurrence: Is it a function of re-infection with TB or has the patient's latent TB infection become reactivated? This research has important public health implications because each scenario requires a different treatment response and poses different risks – for example, as South Africa greatly expands highly active retroviral therapy (HAART) in the coming years, what will be the best strategies for managing large numbers of individuals at high risk for TB in a crowded clinic? Principal investigator: Salim S. Abdool Karim.

K-RITH builds on a strong foundation of other cross-Atlantic collaborations that have linked scientists in KwaZulu-Natal and their colleagues around the world with clinical researchers in the province. These initiatives – supported by the government; universities in South Africa, the U.S. and United Kingdom; the U.S. National Institutes of Health and Centers for Disease Control and Prevention; and philanthropic funding – have made significant scientific and clinical discoveries that have advanced the treatment of HIV and, more recently, the treatment of tuberculosis.

HHMI's commitment to international science began 18 years ago with an initial program focused on Canada and Mexico. Today, the Institute provides grants to 104 international research scholars with a focused program on infectious and parasitic diseases.