INNOVATION ENGINES AT NORTHWESTERN MEDICINE

HIV TRANSLATIONAL RESEARCH CENTER AT NORTHWESTERN MEDICINE

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More than 635,000 people have died from human immunodeficiency virus, or HIV, in the United States since the epidemic was first recognized in 1981. Though the mortality rate has dramatically decreased since then, approximately 1.1 million people in the US are still living with HIV today and this number continues to multiply. Among young people, rates of new HIV infection have, in fact, been escalating in recent years. The epidemic of new infections is not over and is becoming worse among American youth.

As an Innovation Engine at Northwestern Medicine, the **HIV Translational Research Center** (HTRC) is developing new and highly innovative therapies to transform the current treatment method for HIV. Breakthrough therapies involve a shorter course of medicines that will cure HIV infection. Laboratory and clinical studies led by our HIV Translational Research Center researchers are focusing on novel medicines that not only hold great promise for a cure, but can improve how we prevent HIV infection. Antiretroviral treatment (ART) medications are effective at stopping HIV from damaging the immune system, but must be taken for life. If those medications are *ever* stopped, HIV "reactivates" and can again start destroying immunity.

Spearheading Breakthrough, New Approaches to Treat HIV

Over the past two decades, extraordinary medical advances have made it possible for HIV infection to be controlled very effectively with ART. The medicines, however, must be taken consistently and every day for life to suppress or control the virus's activity. If the regimen is not followed strictly, the virus returns to an active state where it can cause harm to one's immune defenses and spread to someone else.

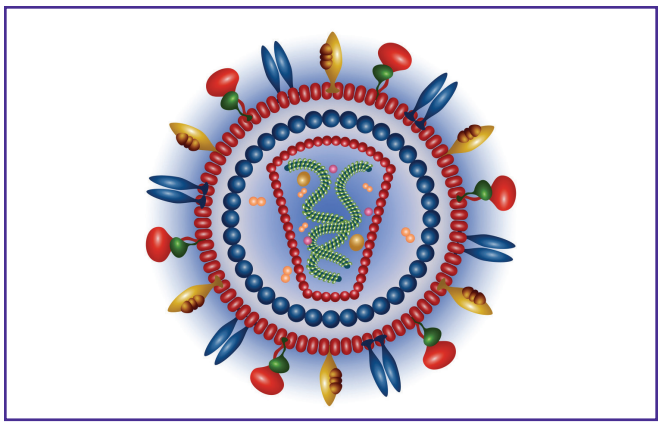
Even if consistently-administered, lifelong antiretroviral therapy can lead to complications such as heart attacks that occur at earlier ages than expected. Experts believe that these complications are attributable to the constant, smoldering inflammation that is caused by residual HIV that persists even during effective antiretroviral therapy. Furthermore, lifelong antiretroviral medications are expensive and can pose a significant financial burden for individuals and countries whose resources are limited.

At the HIV Translational Research Center, we are leading investigations that are driven by our knowledge that, in rare cases, there are "controllers," or patients with HIV who can spontaneously control the virus without antiretroviral therapy. In these "controller" patients, there are fewer cells in which the virus either grows or is dormant, causing no harm to the immune system for decades. We also have evidence that there have been infants and a few adults who were treated with antiretroviral therapy very early after infection who exhibited "prolonged remissions" for months to years after ART medications were stopped. They also have fewer cells with dormant HIV, from which the infection is "rekindled" after ART stops. While other HIV cure research efforts focus on finding and somehow destroying the cells with dormant and reactivatable HIV long after they formed, the Center is unique in attempting to mimic the "spontaneous" control that prevents the cells with dormant HIV from "rekindling" HIV spread throughout the body when treatment ends. The goal is to make now-rare "remissions" much more common and prolonged after a course of medications that work better than current ART.

The HIV Translational Research Center is led with distinction by founding director, Richard D'Aquila, MD, who has been on the front lines of research and care

"Through our HIV Translational Research Center at Northwestern Medicine, we have the exciting potential to revolutionize how HIV infection is prevented and treated across the globe."

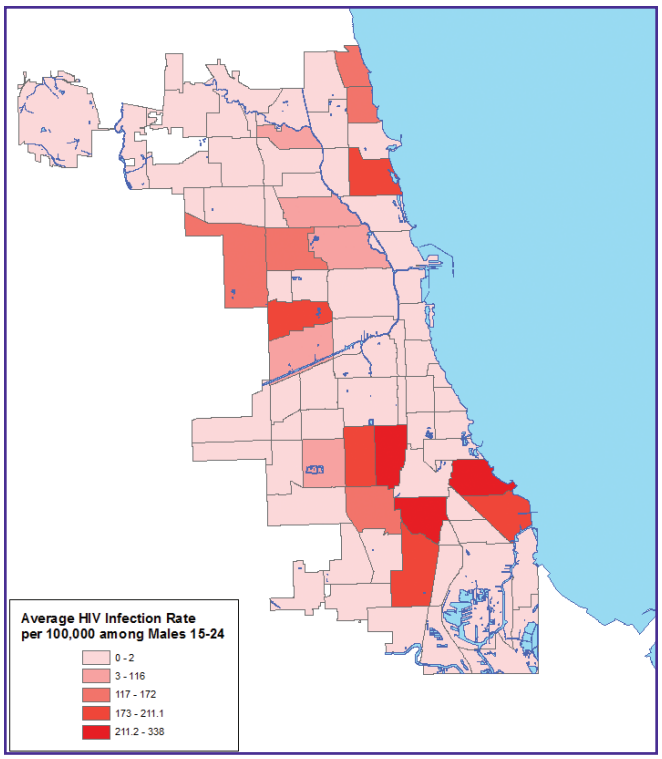
Richard T. D'Aquila, MD, Director, HIV Translational Research Center and Professor of Medicine-Infectious Diseases



Human Immunodeficiency Virus

for HIV infection since he saw some of the first-recognized cases of HIV during his medical residency at the University of Pennsylvania. Our Center has been a forerunner in studying newly identified cellular defenses against HIV, called APOBEC3s. Our studies of rare "controllers" who keep HIV at low levels without ART medicines showed that they have higher levels of this type of cellular defense than other patients. The Center's clinical research is now testing the hypothesis that in most HIV-infected persons, this specific type of cellular defense is depleted by the infection soon after HIV is acquired, but not so in "controllers."

If confirmed, the next step will be to try to boost levels of this APOBEC3 defense in HIV-infected subjects who are not "controllers." The goal is to see if preserving or increasing this defense will decrease HIV's rebound when ART is stopped – and perhaps even diminish the amount of HIV that becomes dormant during the first months of infection. If the theory works, this will turn more of those who receive the Center's developed medicines into "controllers" who have a "prolonged remission" after only a short course of treatment with this new medicine plus today's ART. The ultimate goal is a life-long "functional cure" after a year or so of this novel combination treatment, wherein once this transformational type of antiretroviral treatment is stopped, remnants of dormant HIV remain but will never rebound so as to spread to another person or damage the infected person's defenses. HTRC research has already identified several "lead" small molecules (patent application submitted) that are being improved in the laboratory. An aggressive timeline aims to gain funding needed to start testing them as drug candidates in humans by 2017.



Map of young men in Chicago, by neighborhood (north, west, and south sides of Chicago), who are at high risk of HIV. This map was developed by Feinberg faculty member Gregory Lee Phillips, PhD, MS, who used source data from the Chicago Department of Public Health.

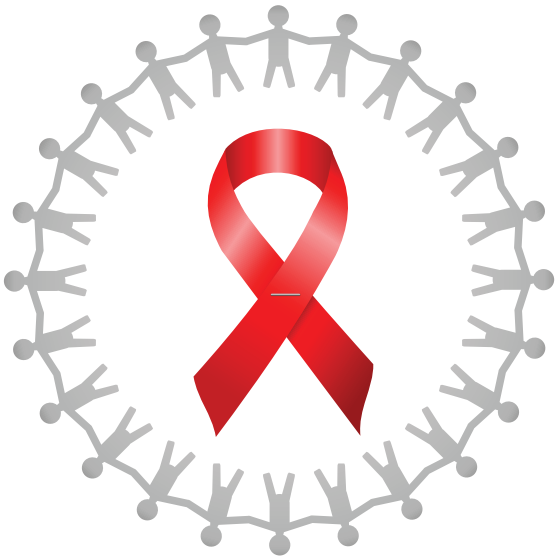
Advances in caring for those who are already infected will be synergistic with efforts to prevent those who are not infected, and at highest risk, from acquiring HIV infection. Northwestern Medicine's HIV Translational Research Center is collaborating with behavioral researchers, including Brian Mustanski, PhD, and Rob Garofalo, MD, MPH, at Northwestern who are the national leaders in studying young men who have sex with men. This is the population group in which most new HIV infections now occur, and from which the Center hopes to learn more about how HIV eludes the body's defenses by becoming dormant in some cells soon after it is acquired. Because the best medicines we have today still allow transmission when doses of daily pills are missed, by functionally curing HIV we will be able to stop HIV from spreading to another person more effectively than ever before.

Helping drive innovation even further, the Center leverages the expertise of other world-leading researchers within Northwestern Medicine as well as across various disciplines. Thomas Hope, PhD, professor in the Department of Cell and Molecular

Biology, Patrick Kiser, PhD, from the McCormick School of Engineering and the Department of Obstetrics and Gynecology, and Steven Wolinsky, MD, chief of the Division of Medicine-Infectious Diseases, are a few examples of the outstanding partners we are honored to work with at the Center.

The HIV Translational Research Center's collaboration with institutions beyond Northwestern is markedly robust as well. In leading an initiative spanning Northwestern, the University of Chicago, the Chicago Department of Public Health, and several key community based organizations, Dr. D'Aquila has built a "team of rivals" to bolster the infrastructure supporting HIV/AIDS research throughout Chicago.

Looking beyond Chicago, we are especially enthused about applying results of our research to resource-limited settings. This will be made possible by closely working with several other Northwestern experts. The Center for Global Health, led by Robert Murphy, MD, as well as the closely-collaborating Center for Innovation in Global Health Technologies at the McCormick School of Engineering, led by Matthew Glucksberg, PhD, will help extend the Center's reach around the world. With a steadfast confidence in the innovative spirit and academic excellence of our team and collaborators, the HIV Translational Research Center at Northwestern Medicine is looking forward to ending the HIV epidemic, not only locally in Chicago but also across the US and the globe.



THROUGH NORTHWESTERN MEDICINE, WE ARE CREATING A NATIONAL EPICENTER FOR HEALTHCARE, EDUCATION, RESEARCH, COMMUNITY SERVICE, AND ADVOCACY.

NORTHWESTERN MEDICINE

Northwestern Memorial HealthCare and Northwestern University Feinberg School of Medicine comprise Northwestern Medicine. Together we aspire to be the destination of choice for people seeking quality healthcare. We are building support to advance that care through leading-edge treatment and breakthrough discoveries.

Our commitment to transform healthcare and to be among the nation's top academic medical centers can only be accomplished through innovation and excellence as exemplified by our **HIV Translational Research Center at Northwestern Medicine**. We invite interested friends to join us in supporting our new Center by providing gifts of endowment and outright support that will help to accelerate our research studies, support state-of-the-art care, and advance the training of our next generation of experts.

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