

Ferreting Out Answers to AIDS

Researcher seeks solutions in places where HIV hides

By Delia O'Hara

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The first time [Lena Al-Harhi PhD](#) held an ampule of the HIV virus in her hand, "I was shaking a little bit," she recalls. "We were so extra-careful with it."



Al-Harhi began studying HIV — the virus that causes acquired immunodeficiency syndrome — at the height of the AIDS epidemic in the early 1990s, when a diagnosis with the disease was a certain death sentence. She has remained in the thick of the effort to develop treatments for AIDS and related conditions ever since then.

Now, many people with HIV/AIDS survive for decades — although it still claimed the lives of an estimated 13,712 people in the United States in 2012, according to the U.S. Centers for Disease Control and Prevention. "One of the greatest testimonies in history to basic research is that it has led to allowing people who are infected with HIV to lead normal lives," Al-Harhi says.

However, HIV remains treacherous even after it's treated, retreating to tissues in the body such as the brain, where drugs have limited reach. HIV insinuates itself into a person's DNA and can lie dormant in cell and tissue reservoirs for years, until conditions

are ripe for it to roar back to life. Al-Harhi works to understand how and where the virus moves and hides, and how to stop the damage it causes while operating from these hidden locations.

A wily disease

"The issue with HIV is that while drugs can keep it at bay so that people can live much longer, they develop co-morbid conditions," she explains. For example, up to 50 percent of HIV patients suffer from HIV associated neurocognitive disorders, a spectrum of neurocognitive and motor impairments. HAND, as the condition is known, can cause a range of symptoms, from diminished concentration and coordination to HIV-related dementia, according to Al-Harhi.

Her research has focused on the interactions of this wily disease with its human host — how the virus invades the brain and sets the stage for inflammatory responses that lead to neurologic impairments.

Al-Harhi works on these challenging questions at what she calls the "interface" between the research bench and the clinic. "A cure for HIV/AIDS is the great hope, but we won't have any reasonable approaches to take into the clinic that will work — with acceptable side effects — until we understand what happens in those reservoirs," she says.

Such a cure would be an immense relief to the more than 1.2 million people in the United States who are living with HIV infection, according to the CDC, and the estimated 50,000 more people in the U.S. who become infected each year. Teenagers are especially at risk, as they "may not know how to protect themselves" against a disease typically transmitted by sexual contact, Al-Harhi says.

A cure also would remove the need for the complex drug regimens used to treat HIV/AIDS, which can be difficult for patients to follow faithfully. "There are good drugs that

can effectively keep the disease at bay, but we can't be complacent. Compliance is key," she says. That is, people must faithfully take their prescribed drugs.

Early zest for discovery

Al-Harthi's zest for science, research and discovery started early. By high school, she says, "I loved biology, and I wanted to have an understanding of how things work at the cellular level. I already knew then that I wanted to run my own lab."

She completed her undergraduate studies at American University in Washington, D.C., and received her PhD in microbiology from George Washington University, also in Washington. She was awarded a National Institutes of Health predoctoral intramural training fellowship to conduct her dissertation research in the lab of Robert Gallo, MD, a co-discoverer of HIV, under the mentorship of Suresh Arya, PhD.

She came to Rush for post-doctoral training in the Department of Immunology/ Microbiology, where she joined a team of investigators who were exploring the role of immune activation in HIV pathogenesis and transmission. Al-Harthi welcomed the chance to delve into immunology.

With advances in antiretroviral therapy for HIV, she focused her research on HIV in the brain. She is engaged in identifying mechanisms in the brain that drive HIV neuropathogenesis, that is, the development of diseases in the nervous system.

In particular, Al-Harthi's group studies the role of the Wnt/beta-catenin pathway in HAND. Wnt/beta-catenin is what's known as a signal transduction pathway — a series of biochemical reactions that are initiated by the binding of a protein (in this case, Wnt/ beta-catenin) to its receptor on the cell in order to cause cellular changes.

Wnt/beta-catenin plays critical roles in cell survival, proliferation and differentiation. Al-Harthi has demonstrated that it is an important regulator of HIV replication in

"compartments" that include the brain. Further, her research demonstrated that the Wnt/beta-catenin pathway plays a key role in brain functions that are disrupted by HIV.

Her work has made Al-Harhi a nationally recognized leader in her field. From 2013 to 2015, she chaired the National Institutes of Health study section on NeuroAIDS and other End-Organ Diseases.

She also now is professor and vice chair of immunology/microbiology at Rush. One thing she especially likes about working at Rush is that researchers reach across departments, each with their own "niche and expertise, to make things work. It's very dear to me to be in an environment that values research," she says. Al-Harhi notes that her own team is composed of "many people who have worked to make the research possible."

Culturing diversity in the laboratory

Al-Harhi also serves as principal investigator for a project that is close to her heart, the Initiative to Maximize Student Development. Rush's Graduate College received a nearly \$3 million grant from the National Institute of General Medical Sciences for the program.

The program offers mentoring and professional development, including boosted classroom time, for young, diverse graduate research candidates, who may be the first in their families to go to college. Participants learn how to choose dissertation advisers, manage their time, deploy research tools, create posters and present their findings. They also study the nuts and bolts of running a lab, from writing proposals to obtain funding for a research project to managing a research team.

Al-Harhi, An Arab-American who grew up in North Bethesda, Maryland, says the program will help Rush bring underrepresented minority students on board as researchers-in-training.

"Many larger universities have programs like this, but for Rush to be part of this pool is a testimony to the faculty we have here," Candidates must have "the goods and the will," she says, but "there's a lot of support."

Al-Harthy's gratitude to her own many mentors and exemplars motivated her to take on her role with the program and help foster young researchers. "I am privileged to work with young researchers to create a supportive environment to allow them to succeed," she says. "I am very lucky to have made a career that taps into my passion for education and research and thankful for the opportunities that Rush has provided me over the years."