Matias Jaureguiberry-Bravo: Exploring a Novel Approach to Preventing HIV-Associated Brain Disorders

Since the advent of antiretroviral drugs in the late 1990s, the medical community has made great progress in stemming the AIDS/HIV epidemic. Previously, patients afflicted with acute HIV infection were at risk for developing dementia. Today, HIV is a more manageable, chronic infection. But HIV-infected patients can still develop milder, lifelong HIV-associated neurocognitive disorders (HAND).

Can buprenorphine, an opioid derivate used to treat opiate addiction, prevent these debilitating conditions, which affect more than 50 percent of the 37 million people worldwide currently living with HIV? Joan W. Berman, PhD, professor of pathology and of microbiology & immunology at Einstein and the Irving D. Kaspas MD Chair for Excellence in Medical Research, recently received a $3.6 million grant from the National Institute on Drug Abuse to explore this question. Matias Jaureguiberry-Bravo, a fifth-year PhD student in Dr. Berman’s laboratory, is an integral member of her research team.
How Does Buprenorphine Work?

Buprenorphine, introduced in 2002 as an opioid replacement therapy, replaces heroin by activating the same receptors, but at a lower level. Like methadone, it blocks cravings for other opioids and helps relieve pain. Since buprenorphine carries lower risk of overdose than methadone, it can be prescribed in a doctor’s office or in a community-based treatment program.

The Berman Laboratory is investigating the mechanisms by which HIV enters the brain and establishes viral reservoirs (sites where the virus accumulates and persists) which lead to the neuronal damage that result in HAND. They are studying whether buprenorphine, which works by binding to the brain’s opioid receptors, can prevent HAND by binding to the opioid receptors of monocytes in the blood.

To test their hypothesis *in vivo*, they are collaborating with David J. Volsky, PhD, and his colleagues at the Icahn Medical School at Mount Sinai. The Volsky Lab has developed mice infected with a modified form of chronic human HIV virus that replicate the neurocognitive impairments seen in HIV patients. “It’s the perfect animal model for us,” says Mr. Jaureguiberry.
A Novel Idea
Mr. Jaureguiiberry notes that understanding how buprenorphine can modify the function of monocytes and its impact on neuro-inflammation is a critical problem.

The study, he explains, highlights an issue at the center of a current scientific debate that revolves around the question: Are opiates immune suppressants as well as immune activators? “We know that opioids modify the immune response,” he says.“It’s really interesting to apply this knowledge in the context of a specific inflammatory disease such as HIV. It’s also interesting that a drug used in one major current public health issue, the opioid epidemic, intersects with another unresolved problem, the HIV epidemic.”

Drug abuse is a major risk factor for HIV-1 infection and opioids have been shown to increase the severity of neuroinflammation, in part by modulating immune cell functions. Some studies have shown that treatment of heroin abusers with buprenorphine results in better cognitive outcomes. The Berman Lab is the first to examine buprenorphine’s effects on CD14+CD16+ monocyte migration to CCL2, which is critical for the development of neuroinflammation.

Mr. Jaureguiiberry often begins his day by processing human blood samples for the experiments he helps to conduct. He isolates the monocytes and cultures them for CD14+CD16+, a subpopulation that can be infected with HIV. These mature monocytes cross the blood brain barrier in response to inflammatory signals including CCL2. This initiates viral seeding in the central nervous system and promotes long-term inflammatory responses that result in neuroinflammation – a process that if targeted could help reduce HAND in HIV-infected opioid abusers and non-opioid abusers.

Several times a week, he commutes to Mount Sinai, where he coordinates meetings with the investigators in the Volsky Lab and works with the mice. “I contribute the immunological cell biology part of the experiments, analyzing the effects on the immune system and the migration of monocytes into the brain,” he explains.

A Scientist Grows in the Bronx
Deciding to pursue his doctorate at Einstein came naturally to Mr. Jaureguiiberry. He was born at Einstein-Weiler Hospital 30 years ago while his parents were PhD students at the College of Medicine. (His dad specialized in immunology, his mom studied cell biology.) When Matias was five, the family moved to Chile, his parents’ homeland. Matias grew up in Santiago and earned his bachelor’s and master’s degrees in biochemistry at the Universidad de Nacional Andrés Bello. He returned to Einstein in 2012 and expects to receive his PhD this December.

His parents were his first professional role models. “More than their expertise it was their passion that inspired me to become a scientist,” he says.

“Matias is an outstanding scientist with an extraordinary work ethic,” says Dr. Berman. “He is extremely bright and full of thought, and understands and appreciates the important details, as well as the broad focus, of a project. He is a wonderful role model.”
He credits Dr. Berman with showing him how “to become a more complete scientist.” “When you’re studying for a PhD you have many questions about yourself,” he says. “Although I’ve had extensive training in research techniques, there are skills beyond the bench that are really important. Joan is a fabulous mentor. In addition to all of the scientific training she gives, Joan encourages us to attend scientific meetings and participate in student activities. Through her I’ve learned how to network and how to communicate about science, especially through writing.”

So far, Mr. Jaureguiberry has served as the lead author or co-author of seven published scientific papers including, most recently, “Opioids and Opioid Maintenance Therapies: Their Impact on Monocyte-Mediated HIV Neuropathogenesis,” in the journal *Current HIV Research*. [https://www.ncbi.nlm.nih.gov/labs/journals/curr-hiv-res/new/2016-03-25/](https://www.ncbi.nlm.nih.gov/labs/journals/curr-hiv-res/new/2016-03-25/) He plans to submit an article this month to the *Journal of Immunology*.

**Future Plans**

“What I like about being a scientist is that every day you do something new and move forward. But it can also be frustrating because you’re doing something that involves the unknown, so you have to figure everything out,” says Mr. Jaureguiberry. “But that’s also what drives me.”
He plans to specialize in neuroAIDS, a field that focuses on a group of neurological disorders caused primarily by HIV damage to the central and peripheral nervous systems. NeuroAIDS combines immunology, cell biology, pharmacology, virology and pathology. Pathology, he notes, “allows you to do basic bench work and translate it into a treatment for disease.”

After he graduates from Einstein, Mr. Jaureguiberry intends to focus on immunotherapy as applied to HIV and other inflammatory diseases including cancer.

“It’s gratifying to know,” he says, “that in the future my research may contribute to improving human health.”