FIU researchers develop new pathway to brain for medicine

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Stumped for years by a natural filter in the body that allows few substances, including life-saving drugs, to enter the brain through the bloodstream, physicians who treat neurological diseases may soon have a new pathway to the organ via a technique developed by a physicist and an immunologist working together at Florida International University's Herbert Wertheim College of Medicine.

The FIU researchers developed the technique to deliver and fully release the anti-HIV drug AZTTP into the brain, but their finding has the potential to also help patients who suffer from neurological diseases such as Alzheimer's, Parkinson's and epilepsy, as well as cancer.

"Anything where you have trouble getting drugs to the brain and releasing it, this opens so many opportunities," said Madhavan Nair, an FIU professor and chair of the medical school's immunology department.

In an in-vitro laboratory test with HIV-infected cells, Nair and a colleague, Sakhrat Khizroev, a professor of immunology and electrical engineering, attached the antiretroviral drug AZTTP to tiny, magneto-electric nanoparticles. Then, using magnetic energy, they guided the drug across a cell membrane created in the lab to mimic the blood-brain barrier found in the human body.

Once the drug reached its target, researchers triggered its release from the nanoparticle by zapping it with a low-energy electrical current. The

drug remained functional and structurally sound after the release, according to the experiment findings.

"We learned to control electrical forces in the brain using magnetics," said Khizroev, who designed, oversaw and supervised the entire project. "We pretty much opened a pathway to the brain."

The test findings were published in April in the online peer-reviewed journal, *Nature Communications*. Researchers believe that using this method will allow physicians to send a higher level of AZTTP - up to 97 percent more - to HIV-infected cells in the brain.

Currently, more than 99 percent of the antiretroviral therapies used to treat HIV, such as AZTTP, are deposited in the liver, lungs and other organs before they reach the brain.

While anti-viral drugs have helped HIV patients live longer by reducing their viral loads, the drugs cannot pass the blood-brain barrier in significant amounts, which allows the virus to lurk unchecked in the brain and can lead to neurological damage, said Dr. Cheryl Holder, a practicing physician and FIU professor who specializes in treating patients with HIV.

"We know that even though the viral load is undetectable in the blood, we don't know what's going on in the brain fully," Holder said.

HIV causes constant inflammation, she said, and the virus can pool in areas of the brain where medicine cannot reach, potentially causing damage.

"It's important to get the drug to the brain," she said, "to help prevent dementia in older patients, and inflammation."

But the ability to target drug delivery and release it on demand in the brain has been impossible without opening the skull, Nair and Khizroev said.

Nair, an immunologist who specializes in HIV research, and Khizroev, an electrical engineer and physicist, began collaborating on the project about 18 months ago after winning a National Institutes of Health grant to study the use of magnetic particles.

One of the keys to success was controlling the release of the drug without adversely affecting the brain.

The researchers found their solution in the magneto-electric nanoparticles, which are uniquely suited to deliver and release drugs in the brain, Khizroev said. These nanoparticles can convert magnetic energy into the electrical energy needed to release the drugs without creating heat, which could potentially harm the brain.

The development of a new, less invasive pathway to the brain would open the door to many new medical uses.

Khizroev said he recently returned from a trip to the University of Southern California, where he briefed physicians at the medical school on the technique and its potential for cancer treatment. And Nair said he received a letter recently on behalf of a 91-year-old man suffering from Parkinson's, asking when the technique might become available for use in people.

That may take a while. With the first phase of testing successfully completed using in vitro experiments, the second will take place at Emory University in Georgia, where researchers will test the technique on monkeys infected with the HIV virus.

If researchers complete the second phase successfully, clinical trials on humans could follow, Nair said. Approval from the Food and Drug Administration would be required before the technique becomes commercially available, he said.

FIU researchers have applied for a patent and would receive royalties, they said, though the university would benefit the most, in part because a successful research project could open opportunities for more grant funding on other topics.

For Khizroev, who had previously done research on quantum computing and information processing, the project has offered a way to put his scientific knowledge to use in a way that could have a direct affect on people's health.

"I wanted to apply my knowledge of nanoparticles to something important," he said.