UNMC researchers reach milestone in effort to slow or halt progression of Parkinson's

The three key people on the clinical trial were, from left, Dr. Howard Gendelman, Dr. Pamela Santamaria and R. Lee Mosley. UNIVERSITY OF NEBRASKA MEDICAL CENTER▲

By Julie Anderson / World-Herald staff writer
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Researchers at the University of Nebraska Medical Center have reached a new milestone in their efforts to harness the immune system to slow or halt the progression of Parkinson's disease.

In an early clinical trial in humans, the researchers used an existing drug to shift a population of white blood cells from a destructive mode to a protective state that can help defend against brain injury.

While the drug is sometimes used in patients receiving chemotherapy, it has not been used previously in Parkinson's.

Not only did the researchers document the shift through blood tests, molecular studies and brain imaging, but they also saw preliminary evidence of improved motor skills in several patients who received the treatment, including a reduction in the disease's characteristic tremors and improvements in tasks such as buttoning a shirt.

Currently, drugs and other treatments can be used to fight symptoms, but the effects generally give way to the disease in the long run.

The results of the trial indicate that researchers, for the first time, may be able to go beyond treating symptoms to slowing or halting the disease itself.

"It's new, it's exciting, and the mechanism is designed to affect the disease rather than treat symptoms," said Dr. Howard Gendelman, chairman of UNMC's pharmacology and experimental neuroscience department.

Gendelman and R. Lee Mosley, a professor of pharmacology and experimental neuroscience and head of UNMC's movement disorders research laboratory, led the study, a report on which appeared Thursday in the Nature Research journal npj Parkinson's disease. They announced the findings at a press conference Thursday.

Dr. Pamela Santamaria, a neurologist with Nebraska Medicine and founder of Neurology Consultants of Nebraska, said the results offer hope for patients and their families.

"Our study breaks out into a new avenue where it's actually working to try to either halt the progression of the disease, or reduce it," said Santamaria, who treated a little more than half of the patients enrolled in the study. That work wrapped up in January 2016.

Parkinson's is of particular interest to Nebraskans and Iowans because Midwestern states have a high prevalence of the progressive neurodegenerative condition. An estimated one million Americans are living with the disease. More than 15,000 Nebraskans have been diagnosed with it, according to the Nebraska Parkinson's Disease Registry.

Still, both Santamaria and Gendelman cautioned that the study involved a small number of patients and would need to be repeated in a larger number of patients to confirm their findings. The drug, whose trade name is Sargramostim, currently is not available for use by Parkinson's patients.

Gendelman said the researchers wouldn't start a new study for a year or more, after they've reviewed data and improved drug formulation and administration. Such a study likely would involve about 100 patients in Omaha and two other centers.

"This is the first inning of a nine-inning game," he said.

The research also represents a new approach — modulating the immune system — to treating Parkinson's, one that may hold promise for other neurodegenerative disorders, including Alzheimer's disease, stroke and amyotrophic lateral sclerosis, or Lou Gehrig's disease.

Mosley said the study represents the first time, to the researchers' knowledge, that immune transformation was performed on any patient with neurodegenerative disease.

Gendelman said a group of researchers from Taiwan published similar results last week, further validating the Nebraska team's work. The Taiwanese group studied four patients but followed them for two years. At least eight other research groups around the world are pursuing the pathway in a variety of conditions.

Malú Tansey, an associate professor of physiology at Emory University School of Medicine in Atlanta, said the Nebraska study could potentially change the way Parkinson's is treated — if it can be replicated in a larger study.

"It's promising, and certainly it may open up some avenues for immunomodulation, in which you boost the person's own immune system to change a certain population of T cells, or white blood cells, that can change the course of the disease," said Tansey, who is familiar with Gendelman's work but isn't involved in it.

Scott Shandler, chief executive officer of Longevity Biotech in Philadelphia, said there has been a lot of talk in recent years about harnessing the immune system in neurological disorders.

"This is a proof-of-purpose study that bears out what's been talked about for a long time, which is really exciting," said Shandler, who was not involved in the current study.

Shandler's firm has collaborated with Gendelman and his team for about three years. The collaborators recently received renewed funding from the Michael J. Fox Foundation to further the work, focusing on a second-generation product that offers an improvement in the drug and a more patient-friendly route of administration — oral, rather than injection.

But Gendelman stressed that the basic work is homegrown in Nebraska, dating back roughly 20 years, and has been helped along by funding from local individuals and groups. Several attended Thursday's press conference.

The researchers first tested the idea of transforming disease-inciting white blood cells called effector T cells to protective regulatory T cells in cell studies and then validated it in animals.

The results of the human trial are consistent with what they found in mice. Potential therapies often don't make the jump. Gendelman said that roughly 80 percent of what works in mice does not work in humans.

The study involved 20 Parkinson's patients — 10 received the drug, 10 got a placebo. Neither the patients nor the researchers knew who was receiving the drug and who was not. The researchers also studied 17 people who did not have Parkinson's, known as controls, for comparison.

The researchers followed the patients for six months — two months before starting treatment, two months on treatment and two months after treatment ended. Patients generally tolerated the drug well, although some had mild to moderate side effects.

The researchers saw increases in protective regulatory T cells in the blood of patients who received the drug. They did not see the same increases in those who got the placebo.

A research team headed by Tony Wilson, an associate professor of basic and translational research at UNMC, also recorded physiological improvements in specific motor areas of the brains of patients who received the drug using a brain-imaging technique called magnetoencephalography.

In addition, blood metabolites associated with an increased number of T regulatory cells were seen in biochemical studies performed at the Scripps Research Institute in La Jolla, California. A total of 19 scientists and physicians in three locations, including Omaha, participated in the study.

Tim Hoffman, who was diagnosed with Parkinson's in 2007, said he didn't know he'd received the drug until after the trial.

But he did notice that he felt quite a bit better. He could walk better, and his posture and flexibility improved. A home woodworker, he also noticed that his fine motor skills seemed to improve, which he told Santamaria at the end of the study. “I know I was giving her a bad time about, ‘Can I get this stuff?’ because it did appear to give me a positive result,” said Hoffman, who retired in 2016 after a long career as a teacher and school administrator.

He said he feels fortunate that his symptoms have progressed fairly slowly, and he’s focused on doing what he can, including keeping active and maintaining a positive attitude, to keep it that way. He said he was happy to help with the study. “Any progress we can make, the better off all their efforts will make us,” he said.