Sensor detects biomarker of early-stage multiple sclerosis

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It can be used to distinguish MS from neuromyelitis optica, another demyelinating disorder. Credit: UFSCar

Researchers at the Federal University of São Carlos (UFSCar) in Sorocaba (state of São Paulo, Brazil) have developed a technique to diagnose early-stage multiple sclerosis, a disease of the central nervous system, and distinguish it from neuromyelitis optica, a rare, yet severe autoimmune inflammatory process also affecting the central nervous system.

The immune system of a person with these diseases produces antibodies that attack and damage part of the myelin sheath, an insulating layer that protects nerves, including those in the brain and spinal cord, and aids the

transmission of electrical impulses. Permanent lesions form in brain regions over time.

Using a nanobiosensor originally developed to detect herbicides, heavy metals and other pollutants, the UFSCar group created a method for observing myelin basic protein (MBP) peptides interacting with antibodies in samples from patients under an atomic force microscope (AFM).

"Atomic force spectroscopy can detect the presence of specific antibodies for each of these two diseases in cerebrospinal fluid and blood serum. If the antibodies are attracted by the peptides deposited on the sensor during the test, this is a sign that the patient has the disease. The device is highly sensitive and can detect a small amount of antibodies, so the method can diagnose the disease at an early stage," said Fabio de Lima Leite, a researcher in UFSCar's Science and Technology for Sustainability Center and last author of an article on the method published in UltraMicroscopy.

Leite began researching nanobiosensors over ten years ago with a Young Investigator Grant from FAPESP and has since continued to study the subject as a principal investigator for UFSCar's Nanoneurobiophysics Research Group (GNN).

His main motivation for shifting his research focus from detecting herbicides to identifying antibodies was the difficulty in diagnosing demyelinating and neurodegenerative disorders. Multiple sclerosis is usually diagnosed clinically on the basis of symptoms reported by the patient and by MRI scanning to identify lesions in certain brain regions.

"Our method is more accurate, avoiding diagnostic errors, as well as being cheaper. An AFM can cost about 20,000 dollars, whereas an MRI machine costs upwards of 400,000 dollars," Leite said.

For researchers, the earlier these diseases are diagnosed, the sooner treatment can begin with less risk of complications. "There's no cure, but early diagnosis can give patients quality of life and better treatment," said Ariana de Souza Moraes, a researcher at UFSCar and a coauthor of the article.

In the study, the researchers used serum and cerebrospinal fluid from patients who were at different stages of multiple sclerosis and receiving treatment at the hospital run by São Paulo State University's Botucatu Medical School (FMB-UNESP) under the responsibility of Doralina Guimarães Brum, a researcher at the school, and Paulo Diniz da Gama, a neurologist affiliated with the Pontifical Catholic University of São Paulo (PUC-SP) in Sorocaba.

The samples were purified by Luís Antonio Peroni's firm RheaBiotech with FAPESP's support under its Innovative Research in Small Business Program (PIPE).

To develop the sensor, it was necessary to synthesize MBP peptides. This was done at the University of São Paulo's Peptide Chemistry Laboratory, headed by Maria Teresa Machini.

"The cerebrospinal fluid and serum were purified, leaving only antibodies in each sample. This enabled us to detect specific antibodies for multiple sclerosis, such as anti-MBP 85-99. If these antibodies are circulating in a patient, they probably have multiple sclerosis. Our next step in the study is to produce a sensor that doesn't require purified samples," Leite said.

In another study published recently in *Scientific Reports*, UFSCar researchers identified patients with neuromyelitis optica and distinguished them from patients with multiple sclerosis. "A biomarker for the disease exists, so it was possible to detect the anti-aquaporin 4

antibody in patient samples by the same method as that used to detect multiple sclerosis," Moraes said.

Neuromyelitis optica can currently be diagnosed by ELISA (enzyme-linked immunosorbent assay), a widely available method that is inexpensive and hence affordable for most patients. "However, this method isn't as sensitive as the nanoimmunosensor and can't detect the disease in its early stages," Moraes said.

Another advantage of the sensor is that it can distinguish the two diseases, avoiding a common diagnostic error. "The two disorders have similar symptoms but different action mechanisms and treatments," Moraes said. "An immunomodulator is recommended for one and an immunosuppressant for the other. An incorrect diagnosis can aggravate the disease. If a patient with neuromyelitis optica is treated for multiple sclerosis, optic nerve inflammation is accelerated and can't be reversed. The sensor is expected to represent a major advance for patients with demyelinating disorders."

More information: Pâmela Soto Garcia et al, Nanoimmunosensor based on atomic force spectroscopy to detect anti-myelin basic protein related to early-stage multiple sclerosis, *Ultramicroscopy* (2020). DOI: 10.1016/j.ultramic.2020.112946

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