New visual technique could advance early detection of neurodegenerative diseases

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Introduction and overview of Cap-QuIC method. Credit: npj Biosensing (2024). DOI: 10.1038/s44328-024-00003-0

Researchers at the University of Minnesota have developed a new visual
diagnostic technique that can be used to advance early detection of neurodegenerative diseases like Parkinson's disease and similar diseases that affect animals, including Chronic Wasting Disease in deer.

The research is titled "Visual detection of misfolded alpha-synuclein and prions via capillary-based quaking-induced conversion assay (Cap-QuIC)" and published in npj Biosensing.

Named Cap-QuIC (Capillary-enhanced Quaking-Induced Conversion), researchers will now be able to distinguish infected samples with the naked eye, which makes testing more accessible and cost-effective. This new method builds upon the researchers' previous groundbreaking diagnostic technique that allowed for faster and more accurate disease detection.

"The simplicity and efficiency of Cap-QuIC could lower the barriers to routine screening for neurodegenerative diseases, ultimately leading to earlier intervention and better patient outcomes," said University of Minnesota Professor Hye Yoon Park, a senior co-author of the paper and professor of electrical and computer engineering in the College of Science and Engineering.

Parkinson's disease is characterized by the accumulation of misfolded alpha-synuclein proteins—proteins found in nerve cells in the brain. The disease affects millions worldwide and poses significant challenges in early diagnosis and treatment.

Most diagnoses today come from the observation of a person's external symptoms in clinical settings during advanced stages of disease. Late detection can limit the potential therapeutic options. Current early diagnosis relies on fragile and expensive equipment for testing that limits access in some areas, especially in developing countries.
The differential action, first discovered by Peter Christenson, an electrical and computer engineering postdoctoral researcher and first author on this paper, is influenced by the protein's surface characteristics, which vary significantly between healthy and diseased states.

"I remember I was in the lab using an expensive fluorescent reader to determine if my samples were positive or negative. As I continued the experiment, I was able to predict the status of each sample before putting it into the reader," Christenson said.

"Then it hit me, 'Why do I even bother using this expensive piece of equipment if I can tell the status of samples by eye?' This was the breakthrough moment that led us to developing our new misfolded protein detection assay."

The Cap-QuIC visual method leverages simple action to detect misfolded alpha-synuclein proteins. The team demonstrated that they could use glass capillaries—small test tubes designed to hold biological materials—to distinguish between normal and disease-associated proteins by observing differences in liquid movement within the tubes.

"This method is not only applicable to Parkinson's but could also accelerate the diagnosis of other similar diseases, including Chronic Wasting Disease in deer," said Peter Larsen, an associate professor of veterinary and biomedical sciences in the College of Veterinary Medicine.

The researchers tested the technique on tissues from wild white-tailed deer infected with Chronic Wasting Disease and showed that Cap-QuIC could classify samples with high sensitivity and specificity.

"Our Cap-QuIC procedure represents a major advancement in point-of-
care neurodegenerative disease diagnostics," said Professor Sang-Hyun Oh, a McKnight Professor and Bordeau Chair in the College of Science and Engineering's Department of Electrical and Computer Engineering and senior co-author of the paper. "By simplifying the detection process, we can potentially diagnose Parkinson's disease earlier, which is crucial for effective management and treatment."

Larsen and Oh lead the University's Minnesota Center for Prion Research and Outreach (MNPRO) that brings faculty and external team members together from across various disciplines to study protein misfolding diseases such as Alzheimer's disease, Parkinson's disease, Chronic Wasting disease, and ALS.

In addition to Park, Christenson, Larsen, and Oh, the team involved in this paper included University of Minnesota researchers Hyeonjeong Jeong, Hyerim Ahn, Manci Li, Rachel Shoemaker, and Gage Rowden.

More information: Peter R. Christenson et al, Visual detection of misfolded alpha-synuclein and prions via capillary-based quaking-induced conversion assay (Cap-QuIC), npj Biosensing (2024). DOI: 10.1038/s44328-024-00003-0

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