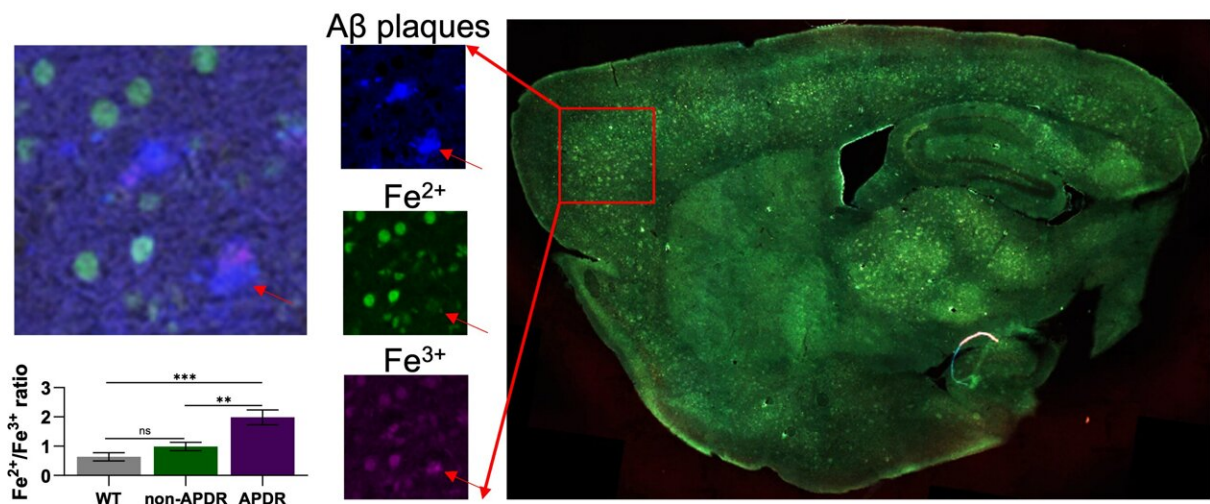


# Newfound link between Alzheimer's and iron could lead to new medical interventions

April 19 2023



Researchers developed DNA-based fluorescent sensors that can detect two different forms of iron ( $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$ ) at the same time in cell cultures and in brain slices from mice genetically modified to mimic Alzheimer's (green image at right). One sensor glows green for  $\text{Fe}^{2+}$  and the other glows red for  $\text{Fe}^{3+}$ . This method has for the first time shown that in the same regions of the brain where the amyloid beta plaques associated with Alzheimer's occur (blue), there is also an increase in the ratio of  $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$ . Credit: University of Texas at Austin

There is a growing body of evidence that iron in the brain may play a role in Alzheimer's disease. Lending weight to that idea, a new imaging probe has for the first time shown that in the same regions of the brain

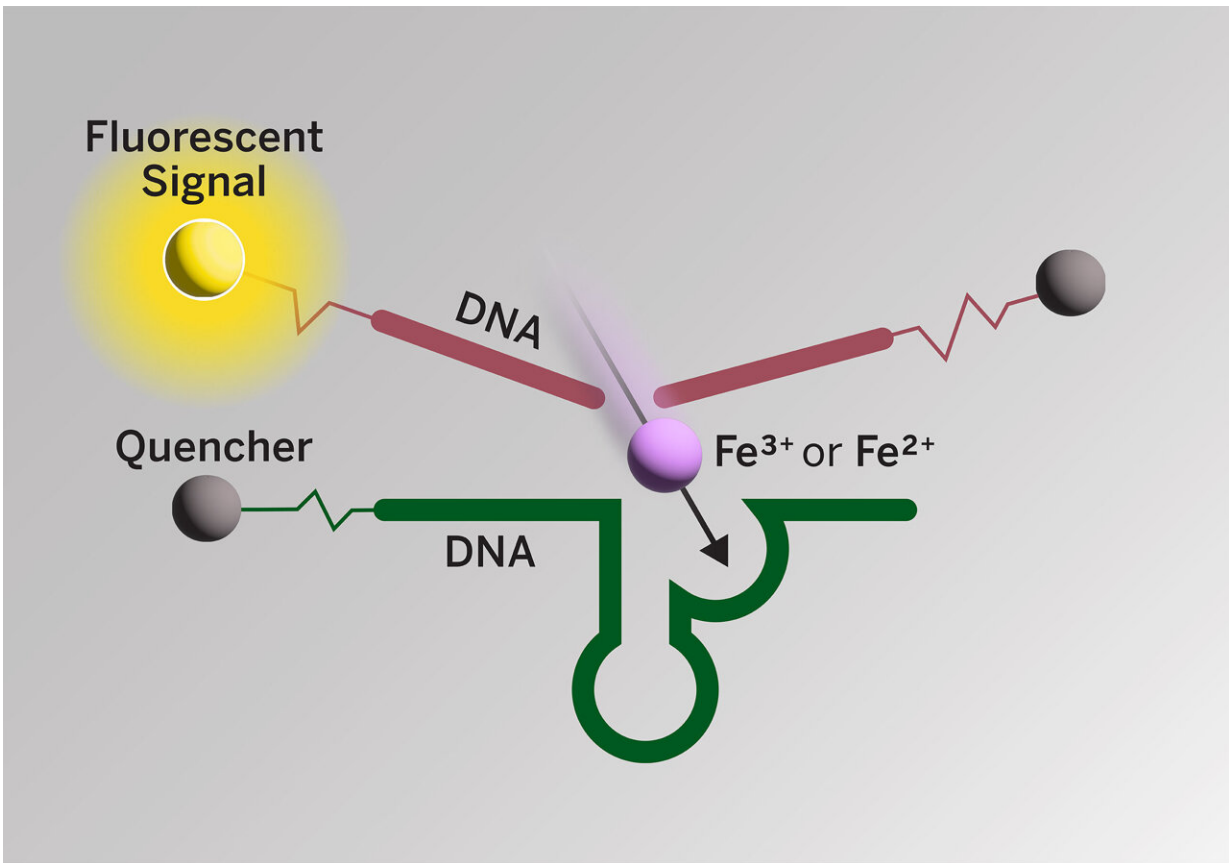
where the amyloid beta plaques associated with Alzheimer's occur, there is also an increase in iron redox, meaning the iron in these regions is more reactive in the presence of oxygen. Their imaging probe could yield even more details about the causes of Alzheimer's and help in the search for new drugs to treat it.

A team from The University of Texas at Austin and the University of Illinois at Urbana-Champaign has published a study today on the new imaging technique and findings in *Science Advances*.

"The link between iron redox and Alzheimer's disease has been a black box," said Yi Lu, corresponding author and professor of chemistry at UT Austin. "The most exciting part to me is that we now have a way to shine light into this black box so that we can begin to understand this whole process in much more detail."

About a decade ago, scientists discovered ferroptosis, a process in the body that is dependent on elevated iron levels, leads to [cell death](#) and plays a key role in neurodegenerative diseases, such as Alzheimer's. Using [magnetic resonance](#) imaging on living Alzheimer's patients, scientists have observed that these patients tend to have elevated iron levels in the brain, although that method doesn't differentiate between different forms of iron. Together, these findings suggested that iron might play a role in destroying [brain cells](#) in Alzheimer's patients.

For the new study, the researchers developed DNA-based fluorescent sensors that can detect two different forms of iron ( $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$ ) at the same time in cell cultures and in brain slices from mice genetically modified to mimic Alzheimer's. One sensor glows green for  $\text{Fe}^{2+}$  and the other glows red for  $\text{Fe}^{3+}$ . This is the first imaging technique that can simultaneously detect both forms of iron in cells and tissue while also indicating their quantity and spatial distribution.



Schematic of a novel iron sensor. When a short strand of DNA called a DNAzyme (green) binds to a specific form of iron (e.g., Fe<sup>3+</sup> or Fe<sup>2+</sup>), the DNAzyme cuts a second strand of DNA (red) and releases a fluorescent signal (yellow) that indicates visually the presence of the specific form of iron. Credit: David Steadman/University of Texas at Austin

"The best part about our sensor is that we can now visualize the changes of Fe<sup>2+</sup> and Fe<sup>3+</sup> and their ratios in each location," said Yuting Wu, a co-first author of the study and a postdoctoral researcher in Lu's lab at UT Austin. "We can change one parameter at a time to see if it changes the plaques or the oxidative states of iron."

That ability could help them better understand why there is an increased ratio of  $\text{Fe}^{3+}$  to  $\text{Fe}^{2+}$  in the location of amyloid beta plaques and whether increased iron redox is involved in forming the plaques.

Another key question is whether the iron redox is directly involved in cell death in Alzheimer's, or simply a byproduct. The researchers plan to explore this question in Alzheimer's mice. If further research determines that iron and its redox changes indeed cause cell death in Alzheimer's patients, that information could provide a potential new strategy for drug development. In other words, perhaps a drug that change the ratio of  $\text{Fe}^{3+}$  to  $\text{Fe}^{2+}$  could help protect brain cells. The new imaging probe could be used to test how well drug candidates work at changing the ratio.

To develop the sensors, the scientists first hired a commercial lab to produce a library of 100 trillion short DNA strands, through a chemical process called oligonucleotide synthesis. They then conducted a screening process to find those strands that recognize—or in chemistry parlance "bind tightly to and conduct a catalytic reaction with"—a specific form of iron and not any other forms. To complete the sensors, other components were added including molecules called fluorophores that glow in a specific color when the probe recognizes the specific form of iron.

Lu, who moved his lab to UT Austin from the University of Illinois at Urbana-Champaign in the summer of 2021, collaborated with researchers there including professor of chemistry Liviu Mirica.

**More information:** Yuting Wu et al, Simultaneous  $\text{Fe}^{2+}/\text{Fe}^{3+}$  imaging shows  $\text{Fe}^{3+}$  over  $\text{Fe}^{2+}$  enrichment in Alzheimer's disease mouse brain, *Science Advances* (2023). [DOI: 10.1126/sciadv.ade7622](https://doi.org/10.1126/sciadv.ade7622).  
[www.science.org/doi/10.1126/sciadv.ade7622](https://www.science.org/doi/10.1126/sciadv.ade7622)

Provided by University of Texas at Austin

Citation: Newfound link between Alzheimer's and iron could lead to new medical interventions (2023, April 19) retrieved 21 June 2024 from <https://medicalxpress.com/news/2023-04-newfound-link-alzheimer-iron-medical.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.