

University of Minnesota retracts pioneering studies in stem cells, Alzheimer's disease

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Years after questions were raised about their integrity, two of the University of Minnesota's highest-profile scientific discoveries have been retracted in one week—one that offered hope over the therapeutic potential of stem cells and the other that offered a promising path toward treating Alzheimer's disease.

The studies are more than a decade old and in some respects superseded by other discoveries in their fields. But the retractions of the [Alzheimer's paper](#) on June 24, and the [stem cell paper](#) on June 17, are setbacks for an institution that has been fighting to move up the U.S. rankings in academic reputation and federal research dollars.

Both studies were published in *Nature* and collectively have been cited nearly 7,000 times in other papers, studies and articles. Researchers worldwide were [using these papers](#) to support their work years after they had been disputed.

That shows the harm in the drawn-out university investigation and the journal's retractions, said Dr. Matthew Schrag, a neurologist who scrutinized the Alzheimer's paper in 2022 outside of his role at Vanderbilt University. "We are squandering not only resources but the credibility and reputation of our profession by failing to address obvious misconduct."

The university said that it has many training and ethics requirements that weren't in place when these papers were published that should prevent future disputes over images, the focus of the questions in both studies, and resulting retractions.

The discoveries were notable in their days because they offered unexpected solutions to vexing scientific and even political problems.

Dr. Catherine Verfaillie and colleagues in 2002 reported that they were able to coax [mesenchymal stem cells](#) from adult bone marrow into growing numerous other cell types and tissues in the body.

Only stem cells from early-stage human embryos had shown such regenerative potential at that time, and they were controversial because they were derived from aborted fetuses or leftover embryos from

infertility treatments. President George W. Bush had banned federal funding for embryonic research, fueling a search for alternative stem cell sources.

Dr. Karen Ashe and colleagues similarly gained global attention in 2006 when they found a molecular target that appeared influential in the onset of Alzheimer's disease, which remains incurable and a leading source of dementia and death in America's aging population.

Mice mimicking that molecule, amyloid beta star 56, showed worse memory loss based on their ability to navigate a maze. Ashe theorized that a drug targeting that molecule could help people overcome or slow Alzheimer's debilitating effects.

The problems leading to the retractions were remarkably similar. Colleagues at other institutions struggled to replicate their findings, which prompted others to look closer at the images of cellular or molecular activity in mice on which their findings were based.

Peter Aldhous first raised concerns in 2006 over the stem cell discovery as a science journalist and San Francisco bureau chief for *New Scientist* magazine.

"The big claim that these were essentially the same as embryonic stem cells and can differentiate into anything, nobody was able to replicate that," he said.

Verfaillie and colleagues corrected the *Nature* paper in 2007, which contained an image of cellular activity in mice that appeared identical to an image in a different paper that supposedly came from different mice. The U then launched an investigation over complaints of image duplications or manipulations in more of Verfaillie's papers.

It eventually cleared her of misconduct, but blamed her for inadequate training and oversight and claimed that a junior researcher had falsified data in a similar study published in the journal *Blood*. That article was retracted in 2009.

Concerns resurfaced in 2019 over the *Nature* stem cell paper when Elisabeth Bik, a microbiologist-turned-research detective, found more examples of image duplication.

Bik also turned out to be a key critic of Ashe's Alzheimer's discoveries, raising concerns about images in her *Nature* paper and several related studies. Much of the blame so far has fallen on co-author Sylvain Lesne, a U neuroscientist who was responsible for the published images. Lesne did not reply to a request for comment, but authorized the university to disclose that it completed its internal investigation into the *Nature* paper without finding any evidence of misconduct. Reviews of other publications from Lesne's lab are ongoing.

Changes over the past decade at the university have sought to reduce academic scandals, including a system added in 2008 for anonymous reporting and for managing accusations. All researchers leading studies at the U must take required training that counsels them on how to avoid conflicts of interest, plagiarism and misconduct.

Even as the papers continue to be cited, researchers have turned to other targets. Ashe has pivoted to the search for a medication that can prevent dysfunctional tau proteins from disrupting the brain's thinking cells, or neurons.

Ashe said she agreed to the *Nature* retraction reluctantly, because she had published [follow-up research](#) that offered fresh proof of her findings and recommended a correction to the *Nature* paper that would have further upheld those findings.

"When the editors decided not to publish the correction, however, I opted to retract the article," she said in an email, adding that "we are encouraged by results of ongoing experiments about Abeta*56, and continue to believe that it could improve our understanding of Alzheimer's disease and the development of better treatments."

Lesne was the only co-author to disagree with the retraction, even though *Nature* stated that the paper contained "excessive manipulation, including splicing, duplication and the use of an eraser tool" to edit the images.

Verfaillie directed the university's stem cell institute and remained involved in its research even after returning to Belgium in 2006. The recent retiree did not reply to an email for comment, but said in a [translation of a Belgium newspaper article](#) that the retraction is "a stain on our reputation." *Nature* called for the correction because Verfaillie and other authors couldn't locate authentic images to prove the validity of their research.

"There is indeed a problem with a photo," she said. "We have not found the correct photo twenty years after the research was conducted. But even without that photo, the conclusion still stands."

The dispute over the utility of mesenchymal stem cells became less important in 2007, when Shinya Yamanaka revealed a process for reprogramming mouse skin cells so that they could mimic the versatility of [embryonic stem cells](#). Others were able to repeat the process, which earned the Japanese researcher a share of the Nobel Prize for Medicine in 2012.

Aldhous said it is disappointing that it took four years to resolve questions over the Alzheimer's paper, and much longer to do the same over the stem cell paper. He said he doesn't believe the university has

adequately solved whether the researchers made repeated mistakes or committed intentional misconduct. The junior researcher blamed for errors in one stem cell paper was not a listed author on other disputed papers, he noted.

However, he said it is arguably more important to quickly correct the scientific record so that faulty or unsubstantiated research doesn't influence other scientists and send them in the wrong directions.

"Why have we had to wait for so long to consign this to the trash can, essentially?" he asked. "This should have happened years ago."

More information: Sylvain Lesné et al, RETRACTED ARTICLE: A specific amyloid- β protein assembly in the brain impairs memory, *Nature* (2006). [DOI: 10.1038/nature04533](https://doi.org/10.1038/nature04533)

Yuehua Jiang et al, RETRACTED ARTICLE: Pluripotency of mesenchymal stem cells derived from adult marrow, *Nature* (2002). [DOI: 10.1038/nature00870](https://doi.org/10.1038/nature00870)

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