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Michigan Health Watch

## A blow to Michigan Alzheimer's patients after research fraud claim





Kathleen Mangi was diagnosed with Alzheimer's disease about 15 years ago. Both she and her husband, Jim, were scientists. She no longer recognizes him. (Bridge file photo by Erin Kirkland.)

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- *A whistleblower claims fraud in a landmark 2006 study into the cause of Alzheimer's*
- *If true, the deception likely misdirected years of medical research and resources*
- *Michigan scientists say other research continues to show promise.*

The fight to find a cure for Alzheimer's disease faces yet another setback following allegations that a foundational study into the cause of the illness — the basis of years of research and billions of dollars in investment — may have been fraudulent.

The revelations, [published last week in Science](#) magazine, are a gut punch to the scientific community, which fears that if the allegations are true they will erode trust in medical research while having the effect of [discouraging robust funding for other avenues of research](#) for more than a decade.

The report will surely prove devastating as well to [more than 190,000](#) Michigan residents now living with Alzheimer's. Jennifer Leopard, president and CEO of the Michigan chapter of the Alzheimer's Association, called the news "unfair to people living with the disease and those who support them."





An allegation of scientific misconduct is “heartbreaking” for people with Alzheimer’s disease and their families, said Peter Lichtenberg, director of the Institute of Gerontology at Wayne State University. (Courtesy photo)

“For the scientific community — and even for the non-science person — this is more than outrageous” if fraud is proven, said Peter Lichtenberg, director of the Institute of Gerontology at Wayne State University.

“It’s not that fraud or any scientific conduct wipes out the good work that’s been done,” he said, “but it’s heartbreaking.”

Still, Lepard, Lichtenberg and others say, there's more research now than ever that could lead to the eventual big win over this disease.

In its article, Science reported that a whistleblower had raised allegations that a University of

Minnesota-based Alzheimer's researcher, Sylvain Lesné, had included scores of doctored images in his seminal 2006 study of Alzheimer's.

Alzheimer's research has long focused on [amyloids](#) — sticky proteins that clump together to form plaques that collect between neurons and disrupt brain cell function. Lesné's widely cited work went further. It isolated a subtype of the protein, A $\beta$ \*56, and injected it into young rats. The result: the rats' ability to recall things they knew, such as the location of a platform on a maze, nosedived.

Lesné's research was transformative, igniting millions of dollars in a new trajectory of research chasing down this specific species of amyloid, according to Science.

But over the years, [some began to suspect](#) amyloid's role in Alzheimer's had been mischaracterized or inflated. There has been, for instance, debate among researchers over whether amyloid clumps found on the brains of Alzheimer's patients were the cause of the disease or merely a marker of its progress.

When other researchers attempted to replicate the results, they couldn't. That failure followed years in which Alzheimer's patients and their families were encouraged by a succession of [seemingly promising clinical studies that eventually faltered](#).

Dr. Henry Paulson, director of the [Michigan Alzheimer's Disease Research Center](#) at the University of Michigan's Michigan Medicine, part of a national network of 31 centers, said he "pretty much dismissed" Lesné's findings several years ago. And he noted that the Michigan research efforts — part of a collaboration of scientists across the state — take a "[beyond amyloid](#)" approach to Alzheimer's research.

While amyloid "is clearly an important component of Alzheimer's," Paulson said, "it's not the only component, and it's not the end-all component."

In other words, there are other areas of research to be pursued.

"I'm less concerned about this discovery of fraud putting holes in our understanding of the pathology of Alzheimer's disease than I am in how those outside of science might somehow think they can no longer trust it," he told Bridge Michigan Wednesday.

The ugly truth is that fraud in science does happen, said Paulson, who helps edit academic journals and said he, himself, has called out other scientists whose work is questionable.

Science is rigorous and unforgiving when it rights itself, he and others suggested. Papers and funding get yanked, research rebuked, and a disgraced scientist likely will never get that lifeblood research funding again. A career is in shambles.

"It's rare, but it's real," he said. "And we're constantly on the lookout for it."

## For families

Still, allegations of fraud are tangential to families dealing with Alzheimer's and the services they need now: Better screening, better treatment, and perhaps one day a cure.

Instead, they've had hopes dashed again and again this past year.

A 10-year clinical trial of the drug crenezumab, ended in [disappointment in June](#). Swiss drugmaker Roche announced it was pulling the plug on a clinical trial for crenezumab after it [failed to significantly](#) slow or prevent cognitive decline in people at risk of a rare, inherited form of Alzheimer's.

The news followed dashed hopes last year of Biogen's Aduhelm. That drug also failed to show significant power against advancing Alzheimer's, but the U.S. Food and Drug Agency nonetheless approved it — essentially because there has been so little other hope in the field for decades.

The hope was that Aduhelm's introduction to the market — however tentative its promise — would spark other research that had been mostly dormant for decades.

Lepard, at the Alzheimer's Association, said Lesné's findings were a small piece of a much larger research picture. In fact, the [Alzheimer's Association International Conference](#) convenes this week in San Diego — a collection of researchers and advocates, including more than 50 from Michigan, she said.

And Lichtenberg of Wayne State said there is more research to be pursued through a behavioral sciences lens. That includes the [FINGER study](#), a long-term trial examining whether lifestyle choices like exercise, diet and social support help keep dementia at bay.

Lesné's work into a specific amyloid species doesn't diminish these other efforts, and it certainly doesn't topple an entire field, Lepard said.

"If you picture research as a pyramid, this is not a bottom block," she said.





With research underway in countless areas of dementia treatment and care, Paula Duren, founder of Universal Dementia Caregivers, said she believes science will find an effective treatment for Alzheimer's. (Bridge file photo)

Paula Duren, who runs Universal Dementia Caregivers, based in Farmington Hills, said people who inquire about treatments are often diagnosed too late for current drugs to be effective in stalling the disease.

Research setbacks are expected, said Duren, a psychologist by training whose parents both died of dementia-related disease. She is often asked about treatments that she knows don't yet exist.

"I tell them that if they keep this (research) up, somebody's going to find a cure," she said.

Jim Mangi said he also believes a cure will be found, eventually. His wife, Kathleen — an environmental scientist like Jim — was diagnosed with Alzheimer's 15 years ago. She has since lost her ability to walk, use a fork or to recognize the man who still calls her "my sweetheart."

She is content, though, he said, and smiles when she sees him when he visits her at a long-term care facility in Saline.

Science has made Mangi a realist; Alzheimer's may have cemented it.

"There is a sadness," he said. "There are drugs that treat the symptoms, but that's all they do. Alzheimer's never resolves. So there is a point where — for every person with dementia — the disease overwhelms what drugs there are."

As a man whose wife fades a little more every day, "I'm chagrined. I'm sad," he said. But "as a scientist, I'm not surprised."

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