

After Amyloid

Seminal Alzheimer's 2006 paper retracted after Science investigation. Can we trust any researchers anywhere anymore?

June 5, 2024 By [Mike Barr](#)

TL;DR: The most-cited Alzheimer's paper ever published — a landmark 2006 Nature study identifying a protein called A β *56 as a primary driver of memory loss — has been retracted following a Science magazine investigation into alleged image manipulation by its first author, Sylvain Lesné. The retraction implicates not just one paper but potentially 16 years of Alzheimer's research, hundreds of millions in NIH funding, and the credibility of the broader amyloid hypothesis itself. And Amyloid Inc., as Mike Barr calls it (it's also been called the Amyloid Mafia), is not going quietly.

- The paper: Published in Nature in 2006, cited nearly 2,500 times — the most-cited paper ever retracted, according to [Retraction Watch](#).
- The misconduct: A 2022 Science investigation by whistleblower Matthew Schrag found extensive evidence of doctored and manipulated images across Lesné's body of work.
- The fallout: 16 years of misdirected research, ~\$287M in annual NIH amyloid-oligomer funding, and ongoing approval of drugs (Leqembi) that at best modestly slow decline — and at worst cause fatal brain bleeds.
- The bottom line: "You can cheat to get a paper. You can cheat to get a grant. You can't cheat to cure a disease. Biology doesn't care." — Matthew Schrag, MD, PhD

[IMAGE: Brain scan or amyloid plaque microscopy image — something that evokes the science at the center of this story]

Amyloid Inc. Will Not Go Quietly

Do not expect Amyloid Inc. to go gently into that good night — not from just this one, albeit quite scandalous, blow. I will update this post as more perspectives and reporting come in. While it does not directly affect people living with HIV/AIDS, there are corollaries, spinoffs, and implications — to say nothing of further tarring an industry (pharma + NIH + FDA, which one could argue persuasively have become one giant conglomerate) purported to have our best interests and the

advancement of science as their goals.

And as I mentioned in an earlier post: if you have not yet read Karl Herrup's "[How Not To Study A Disease](#)," summer beach season might be a good time.

The Retraction (June 2024)

Authors of a landmark [Alzheimer's disease research paper](#) published in Nature in 2006 have agreed to retract the study in response to allegations of image manipulation. University of Minnesota neuroscientist Karen Ashe, the paper's senior author, acknowledged on the journal discussion site [PubPeer](#) that the paper contains doctored images.

The study has been cited nearly 2,500 times — making it the most-cited paper ever to be retracted, according to [Retraction Watch](#).

Ashe wrote: "Although I had no knowledge of any image manipulations in the published paper until it was brought to my attention two years ago, it is clear that several of the figures have been manipulated ... for which I as the senior and corresponding author take ultimate responsibility."

After initially arguing the paper's problems could be addressed with a correction, Ashe agreed to retraction — with the exception of first author Sylvain Lesné, a protégé of Ashe's who was the focus of [a 2022 investigation by Science](#). Lesné did not agree to the retraction, did not reply to press requests, and — as of this writing — remains a University of Minnesota professor still receiving NIH funding.

"It's unfortunate that it has taken two years to make the decision to retract. The evidence of manipulation was overwhelming." — Elisabeth Bik, scientific integrity consultant

That debate has continued alongside the approval of the anti-amyloid drug Leqembi, which at best modestly slows cognitive decline and at worst results in [serious or fatal brain swelling or bleeding](#).

The Backstory: How Matthew Schrag Unraveled It

In August 2021, Matthew Schrag — a neuroscientist and physician at Vanderbilt University — received a call that would pull him into a maelstrom of possible scientific misconduct. A colleague connected him with an attorney investigating Simufilam, an experimental Alzheimer's drug whose developer, Cassava Sciences, claimed it improved cognition. The attorney's clients — two prominent neuroscientists who were also short-sellers — believed some supporting research may have been fraudulent.

Schrag, 37, had already gained notoriety by publicly criticizing the controversial FDA approval of

the anti-amyloid drug Aduhelm. Applying his technical knowledge to published images, he identified apparently altered or duplicated images in dozens of journal articles. That thread eventually led him somewhere far more consequential: to the seminal 2006 Nature paper by Lesné and Ashe.

A [six-month investigation by Science](#) validated Schrag's suspicions. Independent image analysts and several top Alzheimer's researchers reviewed his findings and concurred. Some of the apparent manipulations were described as "shockingly blatant."

What the 2006 Paper Claimed — and What It Cost

The paper identified a previously unknown amyloid protein subtype — A β *56 (pronounced "amyloid beta star 56") — and appeared to prove it caused memory impairment in rats. The finding was hailed as a breakthrough. Ashe called it "the first substance ever identified in brain tissue in Alzheimer's research shown to cause memory impairment." Nature called it "a star suspect."

In the 16 years that followed, NIH funding for research labeled "amyloid, oligomer, and Alzheimer's" rose from near zero to \$287 million annually. Lesné and Ashe helped spark that explosion.

"The immediate, obvious damage is wasted NIH funding and wasted thinking in the field — because people are using these results as a starting point for their own experiments." — Thomas Südhof, Nobel laureate, Stanford University

Crucially: only a handful of independent research groups have ever reported detecting A β *56. Several labs tried and failed — but rarely published their negative results, since journals are typically uninterested in them and researchers are reluctant to contradict a famous investigator.

The Amyloid Hypothesis: Wounded, Not Dead

Scientists remain divided on whether the broader amyloid hypothesis — the idea that amyloid plaques are the primary driver of Alzheimer's — survives this blow. Harvard's Dennis Selkoe, a longtime amyloid proponent who has cited the Nature paper 13 times, reviewed Schrag's dossier and found it credible. He calls the apparent falsifications in corrected papers "shocking" — but still believes the amyloid hypothesis is viable.

Others are less charitable. The amyloid hypothesis has been compared to "the Ptolemaic model of the Solar System" — with amyloid playing Earth at the center, while the true drivers of the disease

orbit unseen. Scientists who have advanced alternative causes — immune dysfunction, inflammation, metabolic dysfunction — have long complained of being sidelined by the “amyloid mafia.”

“If current phase 3 clinical trials of drugs targeting amyloid oligomers all fail, the amyloid hypothesis will be under extreme duress.” — Dennis Selkoe, Harvard University

The Institutions That Failed

The University of Minnesota investigated Lesné’s work beginning in June 2022 — and concluded, with remarkable restraint, that it found “no findings of research misconduct pertaining to these figures.” The statement did not address several other questioned figures in the same paper.

“How is manipulating figures not misconduct?” asks Elisabeth Bik, whose image analysis validated Schrag’s findings. Cases like this, she argues, should be investigated by independent bodies — not the accused scientists’ own universities, which face profound financial and reputational conflicts of interest.

Journals fared little better. The Journal of Neuroscience published five suspect Lesné papers. Nature declined to comment on its own image integrity standards or plans. As of this writing, Lesné received a coveted NIH R01 grant — four months after Schrag delivered his concerns to NIH, reviewed by an NIH program officer who was a co-author on the very paper under scrutiny.

The Whistleblower’s Verdict

Schrag — who grew up home-schooled in a tiny cow town in eastern Washington, volunteered in a nursing home as a teen, and spent years running experiments over and over in a neuropharmacology lab — says he went public despite the personal and professional risks because the stakes were simply too high to stay quiet.

His office displays an antique microscope, an homage to predecessors who applied painstaking bench science to medicine’s endless enigmas. A small sign on his desk reads: “Everything is figureoutable.”

So far, Alzheimer’s has been an exception. But Schrag remains clear-eyed about what this episode means.

“You can cheat to get a paper. You can cheat to get a

degree. You can cheat to get a grant. You can't cheat to cure a disease. Biology doesn't care."

For those who want the full, riveting backstory: the [original 2022 Science investigation](#) is actually more gripping than this June 2024 update. Put on a fresh pot of coffee.

Mike Barr, a longtime POZ Contributing Editor and founding member of the Treatment Action Group (TAG), is a science writer, functional medicine practitioner and herbalist in NYC. [Reach out to him here](#). Or sign up for his curated professional-grade supplement dispensary — 30% off your first order, 25% off all auto-refills — [here](#).
