

News:

# Retracted: highly cited paper

Posted by [Jef Akst](#)

[Entry posted at 26th April 2010 08:14 PM GMT]

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Two papers (one highly cited) on the mechanism of estrogen signaling have been retracted after an investigation by Wyeth found that the research data of its former employee Boris Cheskis were "unreliable."

The retractions do "clear up an area of uncertainty," said molecular endocrinologist [David Ray](#) of the University of Manchester School of Medicine, whose studies on a related topic conflicted with the now-retracted findings. "You don't want [to spend] your whole career refuting other people's work; you want to be figuring out entirely new stuff for yourself."

The primary action of steroid receptors, such as the estrogen, progesterone, and glucocorticoid receptors, is to regulate transcription when bound by a natural or drug ligand. When the ligands bind, however, there are many cellular effects that occur more rapidly than could be mediated through gene expression, Ray explained, suggesting these receptors may have other ways of effecting changes in the cell. Then researchers discovered that the progesterone receptor could bind directly to c-Src -- a signaling kinase that can activate a variety of pathways in the cell.



Image: Wikimedia commons

In 2002, Cheskis and colleagues published that they had identified a way that the estrogen receptor could also affect c-Src activity -- through interactions with a protein they called MNAR (modulator of nongenomic action of estrogen receptor). Their report, published in *Proceedings of the National Academy of Sciences* and cited 190 times, according to ISI, suggested that the estrogen receptor (ER) interacted with MNAR, which in turn mediated the activity of various signaling kinases and downstream signaling molecules, including c-Src. At the time, MNAR was the first molecule identified that linked a nuclear hormone receptor to the intracellular communication system. It was a "novel interacting molecular mechanism," Ray said.

Last July, the paper was retracted by the authors, who claimed that the data demonstrating the activation of the cellular signaling cascade by MNAR were "unreliable," although the physical interactions between the ER, MNAR, and Src were "valid." Daniel Salisbury, the managing editor of *PNAS*, told *The Scientist* that the journal retracted the paper on the request of the authors, and declined to go into any further detail.

The retraction helped validate the work of Ray and his colleagues on the structurally similar glucocorticoid receptors (GR), which had found that MNAR was not required for the activation of Src. At the time, Ray and his colleagues just chalked up the difference to the fact that they were studying a different receptor system. The GR and the ER "are similar, not identical," he said. "So we weren't unduly alarmed when it was different." But with the mechanism reported by Cheskis being retracted, "it now appears that they're rather more similar than we'd given them credit for."

"In general, the retraction of this specific mechanism does not have a major impact in the scientific field," molecular gynecologist [Tommaso Simoncini](#) of the International Society of Gynecological Endocrinology and the University of Pisa, Italy, who recently cited the *PNAS* paper, told *The Scientist* in an email. But it does negate "one potentially important advancement in the molecular understanding of the interaction."

A *Molecular and Cellular Biology* report, cited 27 times since 2007, which further detailed the mechanism of MNAR's interactions with the ER and Src, was also retracted due to

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"unreliable" data. *MCB* did not respond to requests for comment.

Wyeth (now Pfizer) declined to comment further on the details of their internal investigation, but did confirm that Cheskis is no longer employed by Wyeth or Pfizer.

Cheskis was also found [guilty of research misconduct](#) by the Office of Research Integrity, having falsified four figures in two National Institutes of Health grant applications, according to a report in the Federal Register earlier this month.

"It's unfortunate," said cell and molecular biologist [John White](#) of McGill University in Québec, who cited one of the retracted papers in a recent publication. "None of this knocks any pillars out from under our understanding of how the estrogen receptor functions," he added, "but the notion that there was misconduct [is] itself upsetting."

As a result of the ORI's finding of misconduct with respect to the two NIH grants filed, Cheskis signed a voluntary settlement agreement which states that he is responsible for the figure falsifications. For the next two years, he may receive funding from the US Public Health service, but only under supervision "to ensure the scientific integrity of his research contribution," according to the Federal Register.

Cheskis could not be reached for comment.

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**comment:****High citations: Cited for what?**

by Shi Liu

[Comment posted 2010-04-27 14:35:58]

I am wondering why this highly cited 2002 paper got retracted so late. I am also wondering why this paper would be cited by the other researchers if it is doomed to be unreliable. Just because it is a PNAS paper and thus makes it a desirable reference? I know that some papers on how to write scientific papers have taught some tricks on how to cite literature which includes citing the top journals to boost the value of the later work? /////

More ironically, the 2007 Molecular and Cellular Biology paper "further detailed the mechanism of" the 2002 PNAS paper also got retracted even though it self has received 27 citations. Does this mean flawed science is actually infectious? /////

What citation means and how much value should we give to the citation counts?

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by Augustus White

[Comment posted 2010-04-27 13:40:03]

I got interested in the scientific misconduct business a few years ago when I read everything I could find on Piltdown Man. That body of information teaches one a good deal about the motivations involved, how the scientific community deals with suspect data, and how misconduct might have been prevented or discovered earlier.

Unfortunately, the tendency now is to publish only sanitized, uninformative, legalistic summaries, evidently negotiated by counsel. Some incidents in Canada have been almost completely buried because of privacy and defamation concerns.

Personally, I don't care about the identity of the persons or institutions. However, the process has rather little point if the details are so sanitized that we can learn absolutely nothing from them about possible red flags, failed procedures, and what checks on accountability do and do not work.

If the lawyers (and I am one of that breed) are worried, than eliminate the names. That's a concern only for a few people, who don't need the factual details. But the point is not to shun evil-doers or cast out demons. The point is prevention and detection of future misconduct. For that we need far more information. If we have to choose, give us the facts and forget the hand-wringing, anathemas, and public burning of heretics. But tell us what actually happened.

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by Mitchell Wachtel

[Comment posted 2010-04-27 13:36:15]

You folks deserve an award for bringing such cases to the attention of all instead of letting them slip beneath the waters. One item that should be reported in such articles is that the co-authors were not held responsible, if that was indeed the case.

A pathologist like me may well take photographs of a rat's lungs. If the molecular biologist first author studying multiple genetic changes faked the results, there is no reason on earth for me to know this. Also, if you work with people in other laboratories and, nowadays, on other continents, you cannot be responsible for their work unless again you are the senior author.

One reason to carefully explain the culpability is to encourage co-authors who have suspicions about someone on the team to report them to the senior author or to an ethics

committee.

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**comment:**

**Deja' vu**

by Nancy Bowling

[Comment posted 2010-04-27 13:07:34]

Isn't this just sounding a little familiar? Didn't Charles B. Nemeroff [ACNP] do the exact same thing in the Science publication Neuropsychopharmacology when he was exalting the Cyberonics VNS device? Isn't that why HE was forced to step down? That device has been killing people and disabling them for years now. I should know. It almost took my sisters' life. Now this registered nurse and single mom will be disabled for the rest of her life. Not because she has a seizure disorder, mind you. But rather, because she believed what she had read about that device and thought it might honestly help her. Do these idiots even consider just how many lives they are destroying because of their deceptions? Are they even aware just how many people are dying because of it? Do any of them even care? I had a mother contact me and tell me how her precious child died on her kitchen floor from a seizure after having that device implanted, and she was so beside her self, not understanding how this could have happened. I'll tell you how it's happening. People whos' opinions we trust are more concerned with what's going into their wallets, then who they're pushing into early graves. This is so pathetic.

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**comment:**

**Bizarre world**

by James Sacco

[Comment posted 2010-04-27 12:00:41]

I can never understand how scientists who are caught (or admit to) falsifying data can still receive funding from the US public health service.

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