UB Chemist's Diligence Leads to Corrections in Scientific Press

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Experiments conducted in the laboratory of University at Buffalo chemist John P. Richard were spotlighted recently in the national scientific press, including a news article in the journal Nature, because they led to the retractions of two important scientific papers.

Richard's role in pointing out errors in the published research drew praise from the scientific community "because it highlighted the importance of working through the scientific process in pursuit of proving the veracity of advances in science," said Jorge V. José, UB vice president for research.

For the past three decades, John P. Richard, Ph.D., professor of chemistry in the UB College of Arts and Sciences, has been interested in understanding how enzyme catalysts make slow reactions fast.

So he was intrigued in 2004, when a major advance in the development of a "designer enzyme" was reported. In a paper published in Science, Homme W. Hellinga, James B. Duke Professor of Biochemistry at Duke University, reported to have transformed a ribose-binding protein into an active enzyme. The publication was widely hailed in the scientific press as a milestone in the field of protein design.

The idea that a protein could be designed essentially de novo was not something people thought was possible, Richard recalled. He contacted Hellinga to obtain materials needed to express this protein.

"We were interested in the wild type catalyst from living systems that catalyzes the same reaction," he said. "We spend a lot of time thinking about how these catalysts work and wondered how Hellinga's designed catalyst differed from the wild type catalyst.

"Then we found out it wasn't different," he said.

That surprising result came after Astrid Koudelka, a UB research technician, had been working on the experiments for several months with Tina Amyes, Ph.D., a UB adjunct professor of chemistry, and Richard.

The UB scientists led by Richard had spent considerable time purifying the Hellinga "catalyst" only to find that the purified protein did not reproduce the published work; instead, they found that

Hellinga's protein was inactive and that the activity was due to a contaminating enzyme from the host organism.

"We did the experiment several times, probably more times than we needed to," said Richard. "We didn't want to level accusations without being sure they were well-founded."

Richard and his colleagues found that the error lay in the Hellinga lab's failure to properly purify the proteins. He communicated his lab's results to Hellinga, as well as to editors at Science and the Journal of Molecular Biology, which had published similar work by Hellinga.

Hellinga concurred that the papers contained errors, and both journals published retractions. Duke University's subsequent investigation into the matter cleared one of his graduate students of any wrongdoing.

An editorial in Nature pointed out that while this instance seems to prove

that things have gone right with the scientific process, a closer look indicates there also may be some problems:

"In effect, Richard and his two co-workers wasted seven months and tens of thousands of dollars failing to reproduce the results from Hellinga's lab. Richard's subsequent efforts to correct the scientific record thus came at considerable cost, with no discernable benefit to his own career.

"This is a perennial problem in science. Many researchers who come across non-reproducible work save themselves extra hassle and money by simply not pursuing it further. Meanwhile, those who refuse to let it go -- like Richard -- gain nothing," the editorial said.

But Richard and Amyes, who have been continuously funded by the National Institutes of Health for more than 20 years, would do it again. "This is the way science works," said Richard, who added that Science and Nature typically publish about half a dozen retractions each year.

Reporting errors is critical, he said, because publications influence grant-funding decisions. When scientists are doing related work and their proposals come up for discussion in study sections, reviewers will wonder why they aren't having similar successes to those that have already been published, he noted.

"The idea being: if other scientists can do it, then why can't you?" he said.

"You try to get things right," Richard concluded. "If you know an important result is wrong, then you are obliged to bring it to people's attention."

In addition to the Nature news article about the Richard lab's work,

stories about it also were published in Chemical & Engineering News; The Chronicle of Higher Education online and the Scientist.

In the meantime, Richard's lab continues to provide critical insights into catalysis.

His recent publication in Accounts of Chemical Research about strategies that proteins might adopt to catalyze reactions may prove useful in designing catalysts, an emerging field that has attracted attention because of its potential to transform countless industrial processes in the chemical industry.

Source: University at Buffalo