Scientists unite to warn against flawed chemical reagents

Community-driven website hopes to flag up poor-quality tools and prevent wasted experiments.

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21 July 2015

A band of more than 50 scientists has created a website to help biologists avoid poor-quality chemical reagents that undermine experiments in molecular biology and drug discovery.

“Shitty reagents generate shitty science. They waste money and waste careers,” says biochemist Aled Edwards, head of the Structural Genomics Consortium, a public–private partnership to study proteins important to drug-discovery efforts. Although the literature is rife with reports about the flaws of individual chemical tools, scientists continue to use them, he says. “The current way of doing things can't fix it. There is a systems failure in how we communicate information about molecules.”

The Chemical Probes Portal, which Edwards and dozens of co-authors describe in a commentary published in *Nature Chemical Biology* on 21 July[1], is an attempt to create a community tool to improve the situation.

Chemical probes are small molecules designed to bind to a specific protein and disrupt its function. They are valuable tools for biologists trying to find out what a particular protein does in a cell, or for drug-discoverers gauging whether interfering with a function could form the basis of a therapy. But probes often interfere with unintended proteins, and their reliability can vary by cell type and by species. That can lead scientists who rely on such probes to make — and publish — unwarranted conclusions.

Grand failures

Unreliable probes have led to thousands of papers with uninterpretable results as well as a failed clinical trial for breast cancer that involved more than 500 people in 2009–11, says Edwards. For example, one probe, initially described as inhibiting a particular protein called PI3 kinase, was described more than a decade ago as having potent effects on many other proteins. Better probes for PI3 exist, but nearly all chemical vendors advertise the original probe for use against PI3, and more than a thousand papers have been published on the outdated probe's use with PI3 since 2014.

The new portal will recommend probes for use with particular proteins as well as specify recommended experimental systems and concentrations at which to use the reagents. “Our contribution is going to be sorting through the chaff and saying ‘here's the wheat,’” says Edwards.

“I do think a database will be a helpful tool,” says Kip Guy, a chemical biologist at St. Jude Children's Research Hospital in Memphis, Tennessee. Finding appropriate information in the scientific literature is onerous, he says. He anticipates using the portal both for designing his own experiments, as well as when reviewing grants and scientific papers.

At the moment the portal is populated with entries for a mere seven probes, notes William Zuercher, a chemical biologist at the University of North Carolina at Chapel Hill, and a co-author on the commentary. The portal has £50,000 (US$78,000) of seed funding from the London-based biomedical charity the Wellcome Trust, and a small group of the co-authors have pledged to curate and enter data on probes. The team hopes to hire someone to lead the project in the next few weeks. The success of the portal will depend on experts turning their frustration with inconclusive work into action, says Zuercher. “To make the resource sustainable, we will need community input.”

Nature | doi:10.1038/nature.2015.18027

References

1. Arrowsmith, C. H. *et al*. *Nature Chem. Biol.* **11**, 536–541 (2015).