Radical chemistry research makes waves

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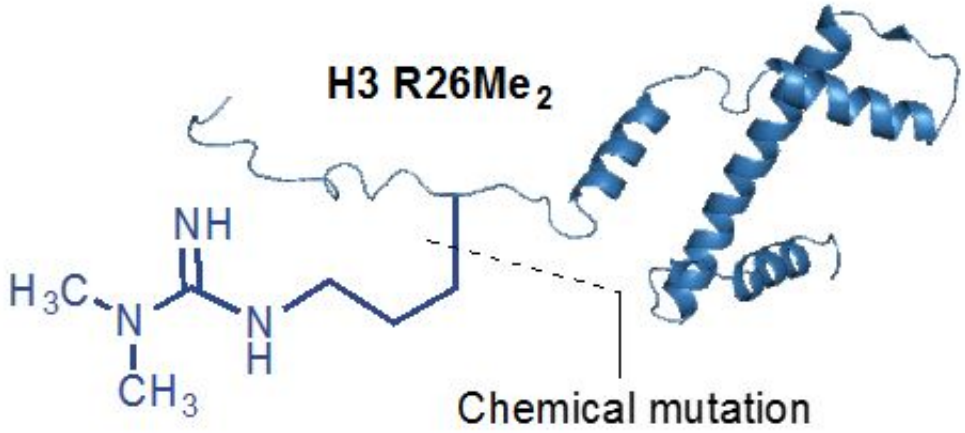


Credit: Flinders University

SA Young Tall Poppy of the Year, Flinders University's Dr Justin Chalker, has been part of an international research effort which opens the door to new drug development and a range of other applications in biochemistry.

After almost a decade of research, the pioneering work in protein mutation could rapidly unlock some of the mounting problems in human health such as the basis for cancer and neurodegenerative diseases.

The team used this breakthrough to access proteins that are highly valued in biology and medicine, yet not accessible through traditional techniques.

"The study and new technology may facilitate the production of new protein-based drugs, or biologics," says Dr Chalker.

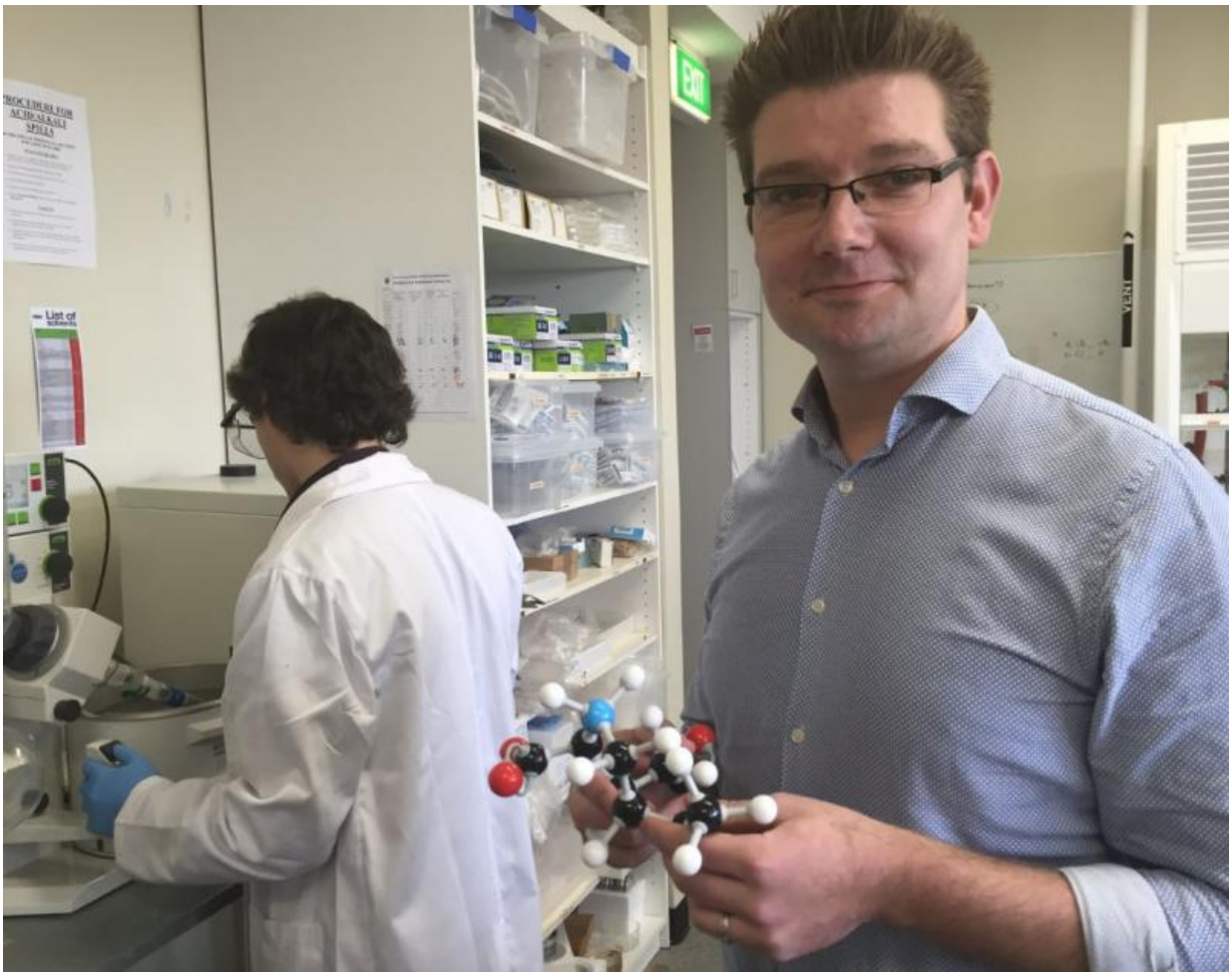
"Importantly, it's a fundamental technique that will enable biochemistry labs around the world broad and unprecedented access to these modified polypeptides.

"The technology allows for new insights into proteins – the molecular machines that power life."

Dr Chalker says the method bypasses the central dogma of biology because the changes to the protein are not carried out at the genetic level, but on the protein itself.

The Oxford University-based research team found a new way to mutate proteins directly using selective single-electron or so-called radical chemistry.

Dr Chalker, now lecturer in synthetic chemistry and ARC Discovery Early-Career Research Award Fellow at Flinders' School of Chemical and Physical Sciences, is a co-author on a study reported in the latest issue of *Science*.



Dr Justin Chalker at the Chalker Lab at Flinders. Credit: Flinders University

Accessing these proteins allowed the team to make further discoveries about how genetic material is packaged in the cell and how certain enzymes carry out important reactions.

Commencing in 2007, Dr Chalker and Oxford co-authors Dr Gonçalo Bernardes (now Cambridge University) and Professor Ben Davis first invented and patented the core technology, which has since been assigned to US-based biotech and novel drug developer Catalent Biologics.

Over the intervening years, a team of more than 20 scientists have studied, expanded and refined the technique so that it is generally useful on diverse proteins.

Directed by Royal Society Fellow Professor Davis and led by Oxford PhD student Tom Wright, the Science paper features the fruits of these efforts, with more than 50 protein mutants prepared for diverse purposes in biochemistry and medicine.

The long-term commitment of the research team is reflected in the thoroughness of the study which features a whopping 289 pages of experimental details.

Dr Chalker says the publication was just in time.

"An independent lab was hot on our heels with a related study, also published in the same issue of *Science*," he says.

"Together, these studies are an important advance in the study of protein structure and function."

The study, titled "Posttranslational mutagenesis: A chemical strategy for exploring protein side-chain diversity," has been profiled in *Science*, *Nature Methods* and *Chemical & Engineering News*.

More information: T. H. Wright et al. Posttranslational mutagenesis: A chemical strategy for exploring protein side-chain diversity, *Science* (2016). DOI: 10.1126/science.aag1465

A. Yang et al. A chemical biology route to site-specific authentic protein modifications, *Science* (2016). DOI: 10.1126/science.aah4428

Provided by Flinders University