New nanoparticles could revolutionize therapeutic drug discovery

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A revolutionary new protein stabilisation technique has been developed by scientists funded by the Biotechnology and Biological Sciences Research Council which could lead to 30 per cent more proteins being available as potential targets for drug development - opening up exciting possibilities in drug discovery.

Understanding the structure of proteins is a vital first step in developing new drugs, but to date, drug development has been slowed because due to their instability, proteins are difficult to work with in lab conditions. However, using nanoparticles, scientists from the Universities of Birmingham and Warwick have found a way to preserve membrane proteins intact, enabling detailed analysis of their structure and molecular functions.

These new findings, which have just been published online in the Journal of the American Chemical Society, will give scientists access to previously ignored proteins deemed too unstable to work with.

Professor Michael Overduin, from the University of Birmingham, who led the study, explained: "We have shown how a polymer can wrap around and preserve membrane proteins intact in stable nanoparticles. Membrane proteins are the most valuable but technically challenging targets for drug discovery. Finding a gentle solution that preserves their structure and activity, yet is robust enough for experimental interrogation, has eluded scientists for decades, but is now available."

Using a polymer - styrene maleic acid lipid particles (SMALPs), the researchers solubilised a pair of membrane proteins. They found that not only did the proteins maintain their folded structure, binding and enzyme activities in the SMALPs, but also that using the nanoparticles allowed them to be simply and rapidly used for virtually any laboratory analysis.

Advantages of SMALPs over traditional ways to solubilise proteins such as detergents include enhanced stability, activity and spectral quality of the protein membranes.

Dr Tim Dafforn who jointly ran the study, said: "In the past, studies have concentrated largely on soluble proteins as membrane proteins are so difficult to make. However, the discovery of the SAMLPs removes this barrier and opens up access to membrane proteins - this has exciting clinical implications as it may enable drug discovery on receptors that are currently too difficult to produce or study by current methods."

Commenting on the findings, BBSRC Chief Executive Professor Doug Kell, said: "The attrition rate in developing new drugs is phenomenal. Only a tiny fraction make it into the clinic to benefit patients. Research such as this that can help to increase the number of potential targets will mean a larger pipeline for scientists to develop new drugs from and, ultimately more, better drugs for patients. Fundamental bioscience working in coordination with medical research is vital to deliver new, effective drugs."

More information: pubs.acs.org/doi/abs/10.1021/ja810046q

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