New technique enables study of 'challenging' proteins

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Researchers from Hull, Bristol and Frankfurt have shown that a new technique for identifying molecular structure can be used effectively on small samples of biological proteins, particularly proteins that are targeted for drug development.

The technique, an enhanced form of nuclear magnetic resonance (NMR) spectroscopy, could enable the structure of a protein to be identified within hours, rather than weeks or months, radically speeding up the process of drug discovery. The findings are published online in the Journal of the American Chemical Society.

Dr Mark Lorch from the University of Hull, who led the research, explains: "Membrane proteins are important targets for the pharmaceutical industry, but they're very difficult to create in large quantities. For some, NMR isn't feasible at all, but even when it is, only small amounts of data can be gained from each small sample, which makes the whole process of identifying the structure very time consuming and expensive.

"Using this technique, we were able to get significant structural data from a small sample of a protein in just 20 hours of NMR time. This is the first time the technique has been shown to work on the size of sample that can be realistically created from any biological protein."

The researchers, from the Universities of Hull, Bristol and Goethe University, used a method known as dynamic nuclear polarisation

(DNP), which boosts the number of nuclei that can be measured through NMR and so increases the signal picked up from the protein.

Although DNP has been used before on large sample sizes of well-studied proteins, the researchers are the first to show its effectiveness in studying a more challenging protein, opening the door to the study of biological samples that are currently inaccessible to conventional NMR.

The study focused on the Sec translocon protein, which transports other proteins either across or into biological membranes. This process is triggered when a signal peptide called LamB binds with Sec translocon and the researchers wanted to identify structural information on how the two interact. This would have been impossible through traditional NMR, as the signal peptide makes up such a small part of the sample to be studied. However, using DNP to enhance the signal from the peptide, the researchers were able to get significant information in a very short period of time.

Provided by University of Hull

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