New technology paves the way for the future of identifying proteins inside cells

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A new technology which enables scientists to identify proteins by making a map of the energy flow inside the protein is revealed today in *Proceedings of the National Academy of Sciences* (*PNAS*) journal.

The scientists behind the new technology hope to develop a tool which can be used to analyse human cells and find out which proteins are present and in what quantities. Being able to sensitively analyse the protein make-up of cells is important because proteins are involved in every process in human cells, from facilitating immune responses to cell-to-cell communication, and when a cell becomes diseased, for example with cancer, the number of different kinds of proteins in a cell changes.

The new research outlines how an imaging technique known as coherent two-dimensional infrared spectroscopy, 2DIR, has been used to successfully identify proteins in laboratory tests. The technique uses an ultra short pulse of infra-red laser light to cause a vibration in one part of the protein molecule. The researchers then track the movement of energy from this vibration as it moves through the protein, building up an energy flow map of the protein which enables them to identify what kind of protein it is.

Professor David Klug from the Single Cell Proteomics project at Imperial College London, one of the authors of the new paper, explains the significance of their study: "We have proved the principle that it is possible to use this type of spectroscopy to identify proteins and we are now looking to use this knowledge to develop a new tool that can be used

to further a broad range of research including drug discovery, diagnostics, biomarker discovery and basic biology.

"This is the first time in over 20 years that a new method for identifying proteins has been discovered, and we're very excited about the possibilities that it will bring to our field."

The technologies under development in the Single Cell Proteomics Project are focussed on improving the sensitivities of proteomic tools to allow single cells to be analysed. Currently, scientists identify and count proteins either by using antibodies or mass spectrometry. The new third potential method, 2DIR, has advantages over the existing methods because it could be more sensitive and provide additional information on how protein activity and function is modulated within cells. "Counting the number of proteins is important, but not enough to understand the biology at work," says Professor Klug.

Potential applications of these methods include the possibility to analyse single cancer cells found circulating in the bloodstream of patients and in the discovery of new biomarkers that might ultimately be used in screening and diagnosis.

The study of proteins, known as proteomics, is the next step for scientists following the identification of all the genes in human DNA in the human genome project. All human cells contain the same 20,000 genes but in different cells different genes are 'switched on' to produce different proteins, and it is the differences between proteins which distinguishes one type of cell from another, and a healthy cell from a diseased cell.

The Single Cell Proteomics (SCP) group at Imperial was established in 2006 with £5 million funding from the EPSRC and BBSRC,.and will run for five and a half years. The project, which is managed under the

auspices of Imperial's Chemical Biology Centre, aims to develop a raft of new measurement tools which will enable scientists to analyse proteins in new ways, with greater clarity and at faster speeds than ever before.

This *PNAS* paper was written in collaboration with Professor Keith Willison, Professor of Molecular Cell Biology at The Institute of Cancer Research, who is a co-holder of the £5M SCP grant. He says: "The development of new single cell, single molecule approaches is vital in the hunt for rare cancer cells."

Source: Imperial College London