Membrane complexes take flight

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Against currently held dogma, scientists at the Universities of Cambridge and Bristol have revealed that the interactions within membrane complexes can be maintained intact in the vacuum of a mass spectrometer. Their research is published in this week's edition of *Science Express.*

The researchers were surprised to discover that membrane complexes could remain associated as it has always been assumed that they would not survive once transferred to the alien conditions inside the mass spectrometer.

"Even if interactions between proteins within the membrane could be maintained we would not have expected them to remain associated with proteins in the cell's interior," says Carol Robinson, Principal Investigator and Royal Society Research Professor at the University of Cambridge's Department of Chemistry.

Cellular membranes surround cells and provide the ultimate in cellular security; nothing can get into a cell without the say so of membrane proteins - the worker molecules that reside in the membrane wall and provide tightly regulated entry points. This natural home of membrane proteins excludes water, yet methods available to study proteins at high resolution revolve round aqueous environments. The ability to "fly" intact membrane proteins in a mass spectrometer paves the way for weighing the proteins and identifying the molecular partners they work with in nature.

The new research, funded by the Biotechnology and Biological Sciences Research Council, will enable scientists to investigate membrane complexes with from a variety of sources and with a range of small molecules. Since about 60% of all drug targets are membrane proteins this is a significant discovery.

Ever since Professor Robinson first flew soluble protein complexes in a mass spectrometer in 1996, she has wanted to do the same with membrane complexes. Collaborating with a membrane biochemistry group in Bristol, led by Professor Paula Booth, she began to think of ways of studying these most challenging assemblies.

Dr Nelson Barrera a post-doctoral researcher in Chile, though experienced in membrane biochemistry, was a new recruit to mass spectrometry. He was largely unaware of the difficulties that had previously been encountered and approached the problem in a new way. Rather than trying to remove the detergent (used to keep the protein intact in solution once outside the natural membrane) he maintained the detergent in unusually high amounts. He then deliberately destroyed this protective detergent layer once in the gas phase. This allowed him to liberate the intact assembly. He was also able to remove units from the modular assembly in the gas phase, just as in solution.

Professor Robinson adds: "I am very excited by this finding given the importance of membrane complexes in guarding the entrance and exit to cells. The type of proteins we have been studying, for example, are involved in drug resistance in cancer cells and antibiotic resistance of bacteria.

"I look forward to exploiting this discovery to the full; not only in characterising the many membrane complexes for which controversy exists but also in discovering new assemblies and in investigating the potential of this approach in drug discovery."

Professor Paula Booth, at the University of Bristol added: "This is a major advance that helps us understand how nature constructs cellular life. The membrane wall of cells is a precision-made, complex and highly regulated structure. We are now much better equipped to understand this incredible, natural self-assembly feat."

Citation: 'Micelles protect membrane complexes from solution to gas phase' will be published in the 12 June 2008 edition of Science Express.

Source: University of Cambridge