Scientists devise method to study membrane proteins

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Scientists at the University of Virginia Health System have come up with a protocol to extract proteins from membranes by using chemicals that allow them to be reversibly folded and refolded. The proteins can then be studied using crystallography or nuclear magnetic resonance imaging. Their work is detailed in the March 23 issue of the "Proceedings of the National Academy of Sciences" (PNAS) and also on the cover of the journal. The paper can be found on the web at: www.pnas.org/cgi/content/full/101/12/4065.

"The majority of drugs on the market today are effective because they work on membrane proteins, but our basic knowledge about these proteins lags far behind that of water-soluble proteins," said Lukas Tamm, professor of molecular physiology and biological physics at U.Va. "We need to develop systems to get enough of these membrane proteins expressed in a cell culture so we can measure their thermodynamic, or energetic, stability," Tamm said. "This is of practical interest in designing proteins for therapeutic applications because the proteins need to be kept around for a long time. This protocol developed at U.Va. shows for the first time that these proteins can be taken out of their membrane environment and put back in without losing function," Tamm said. "We also found that the thermodynamic stability, or energy difference, between the folded and unfolded form of membrane proteins depends on the strength of the membrane "rubber band" that the proteins sit in. This energy difference can be predicted, one key variable in the drug discovery process."

In a commentary on the findings, also in the March 23 issue of PNAS, James Bowie, a professor with the Molecular Biology Institute at the University of California, Los Angeles, wrote that “the new work opens another door to a more quantitative description of the energetics protein-protein and protein-lipid interactions in the (membrane) bilayer… We are finally beginning to obtain quantitative information about membrane protein structure.”

Working with U.Va. colleague Heedeok Hong, Tamm used an aqueous (water) system and a compound called urea, that unravels proteins, to carry out folding studies on a membrane protein of the Escherichia coli bacterium called OmpA. Tamm and Hong demonstrated that the folding of OmpA into the lipid bilayers of a membrane is a reversible, two-state process. They also demonstrated that elastic forces in bilayers, such as curvature stress, can affect the folding of membrane proteins.