

International Partnership Involving UC San Diego Receives \$5 Million to Improve Drug Design Methods

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The University of California, San Diego and two biotechnology companies have joined in a \$5 million effort to improve the methods for determining the three-dimensional structure of proteins used in designing new drugs for a wide range of diseases, including cancer, heart disease and obesity.

UCSD and the two companies-ProSpect Pharma of Columbia, Maryland, and m-phasys GmbH of Tuebingen, Germany-have been awarded a \$5-million grant by the National Institutes of Health to begin the effort, which has implications for improving the efficacy of more than one-half of the drugs now used to treat human ailments, a market greater than \$60 billion per year.

Specifically, the research partners will develop methods for determining the three-dimensional structures of the principal class of drug receptors-proteins on cell membranes called "G-protein coupled receptors" or GPCRs-on which drugs "bind" or attach. Improved knowledge of the structures of these proteins in their native membrane environments will permit biochemists to design drugs that bind better to these receptors and are more effective in treating cancer, heart disease, obesity and other diseases.

"More than half of the drugs currently used in the practice of medicine interact with GPCRs and represent a market of greater than \$60 billion per year," says Stanley J. Opella, a professor of chemistry and biochemistry at UCSD and one of the principal scientists involved in the effort. "Genes for about 500 of these drug receptors have been found in the human genome, yet the structure of only one has been determined, and that is of rhodopsin, the photoreceptor in the eye. The newly-funded partnership will capitalize on the strengths of the participants in the key areas of technology to enable a multidisciplinary approach that overcomes the difficulties inherent in characterizing large membrane proteins."

Other principal scientists in the partnership are Hans Kiefer, chief scientific officer, m-phasys GmbH, and Jonathan Miles Brown, chief operations officer, ProSpect Pharma, Inc. The research effort will be centered at UCSD's Biotechnology Resource for NMR Molecular Imaging of Proteins, also supported by the NIH, which may be unique in having biochemistry laboratories, electronics shop and high field Nuclear Magnetic Resonance spectrometers fully integrated for interdisciplinary research. The facility develops and applies experimental methods and instrumentation of nuclear magnetic resonance spectroscopy to membrane proteins. Recent advances from the UCSD facility involve the structural determination of a mercury transport membrane protein and initial spectroscopic results for GPCRs.

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