Invention will help speed development of drug treatments for heart failure

November 23 2009

Research conducted by University of Minnesota scientists, in collaboration with Celladon Corporation, has led to the invention of technology to more rapidly identify compounds for the treatment of heart failure.

Chronic heart failure is an increasingly important health problem. It is the leading medical cause of hospitalization and is expected to result in an estimated direct and indirect cost to the health care system of $37.2 billion in 2009 alone. About 5.7 million people in the United States have heart failure, and it contributes to or causes some 290,000 deaths annually. However, developing new treatments is an extremely costly and time-consuming process, taking nearly a decade to gain regulatory approval and requiring hundreds of millions of dollars.

The technology, developed by the universitys David Thomas and Razvan Cornea and Celladon Corporations Krisztina Zsebo, allows for increased screening efficiency of compounds capable of disrupting the interactions of proteins implicated in the development of heart failure. Fluorescence resonance energy transfer (FRET) is used to measure disruption of the calcium regulatory system, which has long been implicated in cardiovascular disease. This will provide key information on a particular drugs likelihood of success early in the screening process, since compounds that decrease FRET are good candidates for further development.

"Dr. Cornea and I, along with our students, have worked for more than a

decade developing methods for preparing membranes from purified components, and using FRET to detect changes in protein interactions," Thomas said. "Scientists from Celladon saw the potential for drug discovery, and this resulted in a breakthrough that has added an exciting new dimension to our research program."

The high-throughput assay, developed by the university team, is based on a reconstituted membrane system composed of purified lipid and protein components. This technique is especially important because the interactions of integral membrane proteins are more complex than soluble proteins, making it very difficult to produce a synthetic system that recapitulates the cellular interactions in a large-scale and reproducible manner.

Celladon, based in La Jolla, Calif., has acquired an exclusive license for the technology from the University of Minnesota for the development of molecular therapies for cardiovascular diseases. Celladon also provided funding for the research that allowed Thomas to further refine the assay.

"This technology is very important to the efficient selection and advancement of compounds with the potential to increase cardiac contractility and potentially accelerates product opportunities that will ultimately benefit patients and development partners alike," said Krisztina M. Zsebo, Ph.D., president and chief executive officer of Celladon Corporation. "Celladon's investigation and development of first-in-class CDN small molecules as intravenous and oral drugs for the treatment of acute and chronic heart failure sets us apart in the cardiovascular field and presents multiple partnering opportunities."

Source: University of Minnesota (news : web)