SOUTHWESTERN NEWS

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UT SOUTHWESTERN NAMED ONE OF 10 NIH CENTERS FOR 'HUMAN PROTEOME PROJECT'

DALLAS – Oct. 9, 2002 – UT Southwestern Medical Center at Dallas is one of 10 U.S. institutions to be awarded a multimillion-dollar National Institutes of Health grant to develop faster methods to study proteins that are critical to drug development.

The grant is part of the NIH's National Heart, Lung and Blood Institute's Proteomics Initiative, a $157 million, seven-year program. The Southwestern Center for Proteomics Research will use the $16 million grant to develop new protein-focused technologies.

The "Human Proteome Project" has been likened to the Human Genome Project, only more difficult. The genome – all the DNA of an organism – is the formula for making proteins. Proteins are the cellular workhorses that carry out genetic orders for major functions like triggering growth and battling diseases. Scientists around the world are now working to describe all the proteins and how they interact with each other.

Dr. Thomas Kodadek, professor of internal medicine and molecular biology and the grant's principal investigator, said the funds from the NHLBI would be used to create tools to study G protein-coupled receptors (GPCRs) and transcription factors. Studies of these proteins have been limited because GPCRs are difficult to isolate and transcription factors are rare in comparison to other proteins.

"For different reasons, those classes of proteins have been under the radar of traditional proteomics, but they are very important for the regulation of physiological responses," Kodadek said.

These receptors are found in cells' outer membranes. They are known to bind signaling molecules and initiate chain reactions that launch genetic programs in the nucleus. Kodadek said a major goal for the grant is to develop GPCRs arrays – flat panels with many different GPCRs arranged in a matrix on the surface. Scientists could introduce a drug or other substance on an array to study multiple GPCRs' responses simultaneously. Because membrane proteins such as GPCRs are difficult to work with biochemically, the construction of such arrays will be technically challenging.

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"Something like half of all drugs are targeted to GPCRs, and receptor specificity is a major issue in evaluating new leads," Kodadek said. "Drug companies could use such arrays to quickly find out how drug candidates affect not only the target receptor, but many other receptors as well."

In order to study transcription factors, Kodadek and his colleagues plan to develop special protein-detecting microarrays. Those also would be flat chips with matrices on the surface, but the matrices would be made up of agents known to bind to certain transcription factors. The binding agents would attract their associated transcription factors, allowing researchers to determine the various volumes and active or inactive states of transcription factors contained in fluid samples taken from study subjects.

To test the tools, Kodadek's team will collaborate with Dr. Masashi Yanagisawa, a professor of molecular genetics who discovered in 1998 that two GPCRs he was studying for appetite regulation in mice also are related to narcolepsy. Not much more is known about the biochemical underpinnings of sleep, which creates a perfect opportunity to test the new technologies, Kodadek said.

"Sleep is one of the few areas in biology where we know almost nothing about the molecular mechanisms that control it," he said.

Other investigators on the NHLBI grant include: Dr. Stephen Johnston, director of the Center for Biomedical Inventions; Dr. Harold "Skip" Garner, professor of biochemistry and internal medicine; and Drs. Ross Chambers and David Fancy, assistant professors of internal medicine. Kodadek also expects to add many new postdoctoral and graduate-student researchers over the next year to work on the project.

The NIH grant is the second major award of funding in less than two years from NHLBI to UT Southwestern. In November 2000, a $13.9 million Program in Genomic Applications (PGA) grant was awarded to advance genomic research related to heart disorders. Johnston is the principal investigator on that grant, and much of the work on both projects will be carried out in the Center for Biomedical Inventions.

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