SOUTHWESTERN NEWS

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NIH FUNDS UNIQUE DIABETES PROGRAM THAT COMBINES RESEARCH WITH TECHNOLOGY DEVELOPMENT

DALLAS – Sept. 29, 2000 -- The National Institutes of Health has awarded a $4.6 million, five-year grant that will allow UT Southwestern Medical Center at Dallas technology researchers and biologists to work together to develop new therapies for type II diabetes mellitus.

Under the direction of diabetes expert Dr. Chris Newgard, two biology projects will proceed concurrently with two biomedical technology development projects to find a way to treat adult-onset diabetes.

The "Development of Novel Therapies for Non-Insulin Dependent Diabetes Mellitus" will bring together researchers from the Center for Biomedical Inventions, the Touchstone Diabetes Center, which Newgard co-directs with Dr. Roger Unger; and the Mary Nell and Ralph B. Rogers Magnetic Resonance Center.

The NIH typically does not fund technology development, which makes this grant unique, said Newgard.

"Study sections at the NIH don't often look favorably upon proposals unless there's a very clear hypothesis and there's a very discreet biological problem that you are seeking to solve with methods that are approved by the community at large," said Newgard. "So we really did feel like it was a gamble to go and say, 'We're going to do two biology projects, but we're also going to do two projects that can advance the biology after we develop the technology.' And we were quite pleased and surprised that the site study team viewed it favorably."

In addition to Newgard's work in metabolic gene therapy for diabetes, Unger, Dr. Stephen Johnston and Dr. Thomas Kodadek will direct projects in their respective fields.

Other investigators include Dr. A. Dean Sherry, professor of radiology; Dr. David Mangelsdorf, professor of pharmacology and associate professor of biochemistry; Dr. Robert

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Meidell, associate professor of internal medicine; and Dr. Paul Grayburn, professor of internal medicine.

Dr. Dennis Stone, vice president of the Office of Technology Development, called the team that Newgard has assembled remarkable.

"The planned studies are all the more remarkable because they include not only an expanded investigation of the mechanism of obesity-induced diabetes, but also studies by investigators of the Center for Biomedical Inventions that are designed to create new approaches in the treatment of diabetes," Stone said. "This embodies the true mission of biomedical research: translating basic science into medical therapy."

Newgard, professor of biochemistry, will use viral gene transfer vectors to study fundamental metabolic regulatory mechanisms and the therapeutic use of specific genes in type II diabetes. He will be aided in this work by the application of nuclear magnetic resonance methods for metabolic analysis, developed by Sherry and his co-workers. Two of the specific aims are focused on a newly discovered family of glycogen targeting subunits of protein phosphatase-1.

Unger, professor of internal medicine, will continue his work with leptin, a hormone that appears to cause fat to melt out of tissue. Obesity is a significant risk factor for type II diabetes; more than 80 percent of those with the disease are obese.

He seeks to determine whether lipotoxicity is a mechanism that affects the function of cells other than islet β-cells, using the heart as a new model system. He will also determine whether his observations can be extrapolated to include an alternative animal model of obesity and diabetes (the diet-induced obesity rat) that bears closer resemblance to human obesity and non-insulin dependent diabetes mellitus. As a co-investigator of this project, Mangelsdorf will contribute expertise in molecular biology of genes involved in lipid metabolism.

Johnston, director of the Center for Biomedical Inventions, and Kodadek, professor of

(MORE)

internal medicine and biochemistry, will seek ways to deliver the new treatments that Newgard and Unger develop.

Johnston, professor of internal medicine, will seek to exploit and develop the identification of peptides that bind to specific cell types to target genes and other molecules specifically to islet β-cells. In collaboration with Grayburn, he also will try to develop a novel physical method for targeted gene delivery that has merits on its own but that may also complement the biochemical approach.

Kodadek and Meidell will use their expertise in chemistry and molecular biology to develop a new approach for turning on specific genes in cells that circumvents the requirement for any prior knowledge of the naturally occurring transcription factors for that gene.

"Current therapies for diabetes and obesity are woefully inadequate, and I think it is going to take something bold like this program project to change that," Newgard said.

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