

SOUTHWESTERN NEWS

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RESEARCH LINKS GENE TO GLUCOSE SYNTHESIS IN LIVER, WORK MAY BOOST DIABETES RESEARCH

DALLAS – Sept. 17, 2001 – Researchers have discovered that a known gene activates the enzymes that generate glucose in the liver – a surprising new finding that could lead to a breakthrough in diabetes research.

The biochemical and genetic study, reported in the Sept. 13 issue of *Nature* and conducted by scientists of UT Southwestern Medical Center at Dallas and Harvard Medical School, establishes that the *PGC-1* gene turns on several other genes involved in gluconeogenesis, or glucose synthesis from scratch, in the liver, said Dr. Christopher B. Newgard, co-director of the Touchstone Center for Diabetes Research at UT Southwestern.

The findings of this study in mice and rats suggest that *PGC-1* may have a role in diabetes in humans, although this link will need to be established through further research, said Newgard, professor of biochemistry and internal medicine.

For example, a link to non-insulin dependent diabetes, or type 2 diabetes, is possible, given that gluconeogenesis shifts into abnormally high gear in victims of the disease, resulting in secretion of too much glucose into the blood, Newgard said. Type 2 diabetes afflicts more than 16 million Americans.

In this study, researchers at Harvard Medical School, led by Dr. Bruce M. Spiegelman, first established that *PGC-1* expression in the liver is elevated in rats and mice subjected to fasting and others genetically bred to have varied types of diabetes. The finding suggested a link to increased gluconeogenesis, Newgard said.

Then Dr. Guoxun Chen, a postdoctoral researcher in molecular biophysics and molecular genetics at UT Southwestern and a Southwestern Medical School student, worked with Newgard to establish *PGC-1*'s capacity for activating gluconeogenesis in the liver.

The new finding was unexpected because *PGC-1* previously had been described as regulating or stimulating the synthesis of mitochondria, resulting in increased production of energy in the form of heat in muscle cells.

(MORE)

DIABETES RESEARCH - 2

Research into the gene's role in the liver, however, had largely been ignored until now, said Newgard..

Already known was the liver's basic role in balancing its own glucose output with the glucose uptake, or demand, by bodily tissues, including the brain. Normally, gluconeogenesis provides a steady flow of glucose into the blood that provides for the energy needs of tissues.

Also participating in the study were scientists at Vanderbilt University School of Medicine.

The study was supported by the National Institutes of Health and the Juvenile Diabetes Foundation.

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