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Study finds molecular link between insulin resistance and inflammation

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An exploration of the molecular links between insulin resistance and inflammation may have revealed a novel target for diabetes treatment, say scientists at the John G. Rangos Sr. Research Center, Children's Hospital of Pittsburgh of UPMC. Their findings were published earlier this month in the online version of *Diabetes*, one of the journals of the American Diabetes Association.

Signs of low-grade systemic inflammation are not uncommon among people who have the pre-diabetic condition known as metabolic syndrome, as well as in animal models of obesity and type 2, or insulin-resistant, diabetes, said senior author H. Henry Dong, Ph.D., assistant professor, Department of Pediatrics, University of Pittsburgh School of Medicine.

"But it's not yet clear if there is a cause-and-effect relationship between chronic exposure to low-grade inflammation and the onset of insulin resistance," he explained. "Other studies have shown that in patients who have inflammation and diabetes, insulin-sensitizing drugs seem to reduce inflammation while anti-inflammatory therapies improve sensitivity to insulin."

Dr. Dong's team examined the role played by a protein called Forkhead Box 01 (Fox01), which his previous research showed contributes to elevations in triglycerides in an animal model of obesity and diabetes.

In the current paper, the researchers found in cultured cells and mouse

experiments that Fox01 stimulates inflammatory white blood cells called macrophages, which migrate to the liver and adipose, or fat, tissue in insulin-resistant states, to increase production of a cytokine called interleukin-1 beta (IL-1B). The cytokine in turn interferes with insulin signaling. Insulin typically inhibits Fox01, setting up a feedback loop in healthy tissues that helps regulate insulin levels.

"The findings suggest that when there is a lack of insulin or when cells such as macrophages are resistant to its presence, there are no brakes on Fox01's stimulation of IL-1B and its further interference with insulin signaling," Dr. Dong said. "That might explain why chronic inflammation often is coupled with obesity and type 2 diabetes. Also, a drug that acts on Fox01 might be able to better control blood sugar."

According to the ADA, an estimated 24 million Americans have type 2 diabetes, formerly known as adult-onset diabetes. As obesity becomes more common, however, the prevalence is rising in children. In type 2 diabetes, the body becomes resistant to the effect of insulin, leading to elevated blood sugar levels.

Source: University of Pittsburgh Schools of the Health Sciences (news : web)

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