

# Insulin Suppresses Receptors that Cause Cascade of Inflammation, Study Shows

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(PhysOrg.com) -- Researchers at the University at Buffalo -- the first to identify the anti-inflammatory and cardioprotective properties of insulin -- now have discovered one pathway through which the hormone produces this effect.

Insulin appears to suppress a particular group of inflammatory mediators known as toll-like receptors, or TLRs, which are critical to the inflammatory process.

TLRs are a variety of pattern-recognition receptors that identify bacterial and viral products and other pathogens.

UB researchers have found that insulin interferes with the expression of several types of TLRs, likely by suppressing a specific transcription factor known as PU.1, which is known to regulate TLR expression.

"We reported earlier that an infusion of low-dose insulin exerts a quick, powerful anti-inflammatory effect in diabetic patients," said Paresh Dandona, M.D., Ph.D., UB Distinguished Professor of Medicine, chief of the Division of Endocrinology in UB's Department of Medicine, School of Medicine and Biomedical Sciences, and senior researcher on the project.

Dandona also is chief of Kaleida Health's Division of Endocrinology and director of Kaleida's Diabetes-Endocrine Center of Western New York, where he conducted his research.

"Knowing that toll-like receptors are major determinants of the body's inflammatory response to viral and bacterial pathogens, we set out to see if these receptors were susceptible to insulin's effect," said Dandona.

"We've now shown for the first time that an infusion of low dose insulin suppresses expression of five TLR subtypes and the DNA binding of PU.1."

Husam Ghanim, Ph.D., research assistant professor in UB's Division of Endocrinology, Diabetes and Metabolism, is first author on the study, which was published online June 12 in *Diabetes Care* ahead of print.

TLRs have been shown to play a role in many inflammation conditions, including atherosclerosis, endotoxin shock, insulin resistance and diabetes, lupus, the destruction of insulin producing cells and insulin resistance in type 2 diabetes.

The current study was conducted in 24 patients with Type 2 diabetes. Researchers infused 10 obese Type 2 diabetics with a low dose of insulin plus a sugar solution to maintain correct glucose levels, while a similar group of 14 received either a sugar or saline solution to serve as controls. Both groups were infused for four hours.

Expression of TLRs was measured in white blood cells prepared from blood samples collected before the start of the infusion, and at 2, 4 and 6 hours after the infusion began.

Results showed that the levels of TLRs dropped significantly within 2 hours in the insulin group and reached the maximum reduction at 4 hours. Specifically, at 4 hours insulin suppressed levels of TLR 1, 2, 4, 6, and 9 by approximately 24 percent, 21 percent, 30 percent, 28 percent and 27 percent, respectively. At the same time, the DNA binding of PU.1 was suppressed by 24 percent.

Meanwhile, neither TLR expression nor PU.1 DNA binding were affected in those who received dextrose or saline.

"These data further support the concept that insulin is anti-inflammatory and that it may have potential use in treating various infective inflammatory conditions as well as acute coronary syndromes," Dandona said. "This includes acute myocardial infarction and cardiac surgery, where inflammation plays an important role."

Priya Mohanty, M.D., Rupali Deopurkar, M.D., Ph.D., Ching Ling Sia, Kelly Korzeniewski, Sanaa Abuaysheh, and Ajay Chaudhuri, M.D., all from Dandona's research group, also contributed to the study.

Provided by University at Buffalo

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