

UCLA researchers identify markers that may predict diabetes in still-healthy people

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In the first large scale, multiethnic study of its kind, researchers at UCLA have confirmed the role played by three particular molecules known as cytokines as a cause of Type 2 diabetes, and further, have identified these molecules as early biological markers that may be used to more accurately predict future incidences of diabetes among apparently healthy individuals.

Reporting in the August 15 issue of the journal *Archives of Internal Medicine*, Simin Liu, professor of epidemiology and medicine with a joint appointment in the School of Public Health and the David Geffen School of Medicine at UCLA, and colleagues have identified three inflammatory cytokines (cytokines are messenger molecules) tumor necrosis factor-alpha (TNF- α); interleukin-6 (IL-6); and high-sensitivity C-reactive protein (hs-CRP) that may be one of the causes of type 2 diabetes which afflicts roughly seven percent of the U.S. population.

Type 2 diabetes is the most common form of diabetes; about 90 to 95 percent of people who have diabetes have type 2. People with this condition produce insulin, but either their bodies don't make enough of it, or can't effectively use it.

Low-grade chronic inflammation of the body, which is reflected by elevated levels of inflammatory cytokines in the blood stream, may promote insulin resistance in the liver, muscles, and the vascular endothelium cells, the layer of thin, flat cells that lines the interior surface of blood vessels. Such inflammation can last for years before

leading to type 2 diabetes, cardiovascular disease, or hypertension.

A blood test that looks for high levels of inflammatory cytokines could serve as an accurate predictor of diabetes in still-healthy people, years ahead of the traditional risk factors of obesity or insulin resistance. The finding also has implication for cancer research as well, said Liu, since people with diabetes are at greater risk of developing breast and colon cancers.

“This is a final confirmation of earlier studies about the underlying biology behind type 2 diabetes,” said Liu, who is also a member of the UCLA Jonsson Comprehensive Cancer Center. But those studies, he said, were either very small or animal studies. By comparison, he said, their study was more extensive in scale and involved human study volunteers. “Our study identified 1,600 new cases of diabetes and measured the blood markers before they developed the disease.”

The researchers took advantage of the Women’s Health Initiative Observational Study (WHIOS), an ongoing, long term study that was designed to examine the association between behavior, socioeconomic status, diet, and other factors and the effect on a woman’s health. Liu and colleagues took baseline level measurements of inflammatory cytokines in apparently healthy women without any signs of diabetes who were between the ages of 50 and 79 years-old, then tracked their health for the next six years. The WHIOS study involved some 82,000 postmenopausal women who cut across multiple ethnicities, including whites, blacks, Hispanics, and Asian/Pacific Islanders. At the time of follow-up, Liu and colleagues compared 1,584 women, now diagnosed with type 2 diabetes, and matched them by age, ethnicity and other factors to 2,198 other women in the study who remained free of the disease.

While all three cytokines were found to be significantly related to an increased risk of clinical diabetes, hs-CRP appeared to be a more

consistent predictor of increased risk in all four ethnic groups. These associations were independent of traditional risk factors such as obesity or elevated levels of glucose and insulin, previously reported by Liu and colleagues in the same multiethnic sample.

“The pro-inflammatory state is often linked to obesity,” said Liu, “which can lead to insulin resistance. So, identifying these markers by a simple blood test well before a disease begins not only can help improve mechanistic understanding of the disease, but also offer alternatives to lifestyle—hitting an optimal balance of nutrition, for example, and engaging in more exercise - relatively simple things that can prevent disease.”

Source: University of California - Los Angeles

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