MedicalXpress

# Researchers discover novel pathway to increased inflammation in diabetes patients

November 28 2007

Researchers at UC Davis Health System have discovered a novel pathway that results in increased inflammation of blood vessels in patients with type 1 diabetes. Their findings suggest that, with good diabetes control, this inflammation may be reduced, possibly resulting in a reduction of cardiovascular disease as well.

In a study now available both in the online edition of the *Journal of Clinical Endocrinology & Metabolism* as well on the National Institutes of Health's PubMed, the researchers provide the first-ever demonstration of increased expression and signaling in type 1 diabetics of two key receptors within the body's innate immune system. Called TLR2 and TLR4, they are part of a family of pattern recognition receptors known as Toll-like receptors (TLRs), so-called because of their similarities to the well-defined Toll gene found in much-studied fruit flies.

Type 1 diabetes is a pro-inflammatory state associated with increased cardiovascular mortality. Inflammation plays a pivotal role in all stages of atherosclerosis, the progressive narrowing and hardening of the arteries over time. The UC Davis study found that TLR2 and TLR4 expression and signaling are increased in type 1 diabetes patients and contribute to the pro-inflammatory state.

"It is not unreasonable to speculate that TLR2 and TLR4 promote atherogenesis by contributing to the pro-inflammatory state in type 1 diabetes," said lead author Ishwarlal Jialal, director of the Laboratory for Atherosclerosis and Metabolic Research and professor of internal

medicine at UC Davis. “Inflammation is central to heart disease, playing a pivotal role in plaque formation and stroke. We may well find that a serendipitous byproduct of controlling diabetes is the simultaneous control of this new pathway, leading to less inflammation and lower risk of heart problems.”

The study represents the first-ever demonstration of increased TLR2 and TLR4 activity in type 1 diabetes monocytes, which are part of the body’s immune system, protecting against blood-borne pathogens by moving quickly to sites of infection. The immune system comprises the cells and mechanisms that defend the host from infection by other organisms, accomplishing its defense with the help of such pattern-recognition receptors as TLRs for early detection of specific classes of pathogens.

“This finding provides us with a totally new insight into the causes of inflammation in diabetics,” adds Jialal, who holds the Robert E. Stowell Endowed Chair in Experimental Pathology at UC Davis. “It’s an exciting development in the emerging area of TLR research that has potentially wide-ranging implications.”

Further studies will use mice to examine the molecular mechanisms for increased TLR2 and TLR4 expression and determine their contribution to the pro-inflammatory state of diabetes.

Source: University of California - Davis