Proteins involved in blood vessel dysfunction in type 2 diabetes are identified

October 6 2008

According to the American Heart Association, three-fourths of people with diabetes die of some form of heart or blood-vessel disease. Previous studies have shown that cardiac function is compromised and cardiovascular diseases are increased in people with type 2 diabetes. Before vascular diseases develop in diabetics, blood-vessel cell dysfunction occurs. Using precise microscopes, University of Missouri researchers are dissecting coronary microvessels and testing which proteins are responsible for inflammation that causes blood-vessel dysfunction. By identifying the proteins that play important roles in blood-vessel dysfunction, they hope to develop new treatments for blood-vessel dysfunction in people with type 2 diabetes.

"We believe that understanding blood-vessel dysfunction in diabetes is critical because the progression of vascular diseases may be significantly reduced if dysfunction is corrected," said Cuihua Zhang, an investigator in the Dalton Cardiovascular Research Center and associate professor of internal medicine in the MU School of Medicine. "The results of our studies may provide new approaches for the treatment of blood-vessel diseases and disorders in type 2 diabetes, such as the possible use of antibodies that work to stop the proteins responsible for inflammation."

Zhang and other researchers tested their hypothesis that tumor necrosis factor-α (TNF-α), a signaling protein involved in inflammation, was responsible for blood-vessel dysfunction in type 2 diabetes. They observed that diabetic mice had elevated levels of TNF. When diabetic mice lacked TNF, their blood vessels functioned normally. They also

observed that advanced glycation end products and their receptors (AGE/RAGE), which are proteins and lipids that are thought to contribute to various blood vessel complications, amplified TNF production in diabetes. In patients with diabetes, AGEs accumulate more quickly than normal in the blood and arteries.

"We found that the overproduction of AGE and RAGE contributes to blood-vessel dysfunction in type 2 diabetes," Zhang said. "Changes in the blood vessels caused by these proteins cause oxidative stress and vascular dysfunction that leads to diseases such as heart disease and stroke."

Source: University of Missouri-Columbia