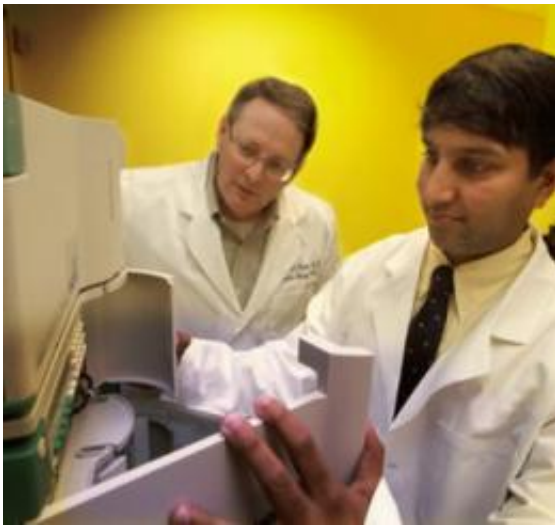


Key player identified in cascade that leads to hypertension-related kidney damage

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This photo shows Drs. David Pollock and Karthik Krishnan. Credit: Phil Jones/MCG campus photographer

A key player in a cascade that likely begins with stress and leads to high blood pressure and kidney damage has been identified by researchers who say the finding may lead to better ways to control both.

Medical College of Georgia researchers have found endothelin, a powerful blood vessel constrictor and inflammatory peptide, increases the number of [T cells](#) in the kidneys, which helps recruit other [immune cells](#), causing inflammation and destruction.

"We think that endothelin somehow causes an increase in T cells which results in renal injury which makes the hypertension worse and harder to control," says Dr. Karthik Krishnan, an MCG allergy/immunology fellow who presents the findings during the 2009 American College of Allergy, Asthma & Immunology Annual Meeting Nov. 5-9 in Miami. Dr. Krishnan was honored with one of three Clement von Pirquet Awards for best scientific paper in allergy/immunology presented by fellows-in-training at the meeting.

The process likely begins in some people when stress, diet or other factors raise levels of the hormone angiotensin II, another powerful blood vessel constrictor, which, in turn, increases endothelin levels. Researchers don't know why endothelin increases T-cell levels in the kidneys. "There are still a lot of mechanistic questions we have," notes Dr. Krishnan.

Inflammation, a part of the normal healing process, also is increasingly identified as a major contributor to a variety of diseases from cancer to cardiovascular disease. "We are starting to look at inflammatory mediators or processes that make hypertension worse with the long-term goal of finding interventions or therapies to counteract these mediators and better control hypertension and prevent organ damage," Dr. Krishnan says.

It's a subset of patients - with mostly uncontrolled hypertension, likely because of a combination of environment and genetics - that tend to have more [inflammation](#) and more resulting [kidney damage](#). Dr. Krishnan hopes that making the endothelin connection will one day help identify these people before their kidneys take a beating.

Standard urinalysis can detect protein in the urine, one of the first signs sign that "the kidneys are falling down on the job," says Dr. David Pollock, renal physiologist in MCG's Vascular Biology Center and a

study co-author. "It's like a cheesecloth that is old and worn out and the holes are getting too big." The body should use all the protein it makes or consumes so none should show up in urine

For the study, mice with normal blood pressures got angiotensin II, which raised their blood pressure and the T cell count in their kidneys. But when researchers also gave an endothelin blocker, T cells numbers in the kidneys did not increase. To double-check the findings, they gave angiotensin II to mice that can't make endothelin and the T cell count stayed down, the researchers report.

For at-risk individuals, endothelin blockers, already on the market for pulmonary [hypertension](#) and under study for some other conditions that result in kidney failure, may help avoid the destruction, Dr. Pollock says.

"We're optimistic that it's important in other forms of renal disease. It looks like this could be useful for essentially anyone with protein in the urine. That's what's really exciting about it," he says.

Source: Medical College of Georgia

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