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New findings contribute to understanding of diabetic kidney disease

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A gene called PVT1 may help reduce the kidneys ability to filter blood, leading to kidney disease, kidney failure and death, according to a study published today by researchers at the Translational Genomics Research Institute (TGen).

The TGen team found PVT1 expression levels increased up to 5-fold in response to hyperglycemia, or high blood sugar, a condition that often accompanies diabetes.

But by knocking down or reducing the expression of the PVT1gene, TGen researchers lowered the amount of proteins associated with the excessive accumulation of extracellular matrix (ECM) in glomeruli, part of the basic filtration unit of kidneys, according to the TGen study published today in the online scientific journal *Public Library of Science (PLoS) ONE.*

The accumulation of excessive ECM within the mesangial cells, which regulate blood flow in capillaries inside the kidney, is a hallmark of diabetic nephropathy, or kidney disease, which is the leading cause of reduced life expectancy among the nation's growing numbers of diabetics.

"The goal of this study was to identify possible molecular mechanisms by which PVT1 may contribute to the development and progression of diabetic nephropathy in mesangial cells," said Dr. Johanna DiStefano, the study's senior author and Director of TGen's Diabetes,

Cardiovascular and Metabolic Diseases Center.

"Despite the growing magnitude of the disease, the molecular mechanisms underlying the etiology of diabetic nephropathy remain poorly understood," Dr. DiStefano said.

PVT1, also known as plasmacytoma variant translocation 1, was previously identified by Dr. DiStefano's team as a candidate gene for End Stage Renal Disease (ESRD), or kidney failure. Too much PVT1 also has been associated with breast and ovarian cancers, in which it may help cause cells to multiply out of control and fail to go through the normal process of cellular death.

Through RNA interference, which helps control which genes are active and the degree of their activity, researchers reduced the expression of PVT1, which in turn reduced the protein levels of ECM components.

In a related finding, TGen scientists discovered that PVT1 affects the expression of other genes — FN1, COL4A1 and PAI-1 — in a manner that is at least partially independent of TFFB1, a gene associated with tissue fibrosis, or tissue damage.

"Delineation of the relationship between TGFB1 and PVT1 represents a critical component toward understanding the molecular mechanisms underlying the regulation of ECM in diabetic nephropathy," said Dr. Lucrecia Alvarez, the study's lead author and a TGen post-doctoral fellow.

Provided by The Translational Genomics Research Institute