Anti-aging hormone Klotho inhibits renal fibrosis, cancer growth

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A natural hormone known to inhibit aging can also protect kidneys against renal fibrosis, UT Southwestern Medical Center researchers have demonstrated.

Scientists led by Dr. Makoto Kuro-o, associate professor of pathology, showed in mice that the anti-aging hormone Klotho suppressed both renal fibrosis – a common complication of chronic kidney disease – and the spread of cancer. The findings are available online in the Journal of Biological Chemistry.

More than 26 million people in the U.S. are affected by chronic kidney disease. Researchers say Klotho also helps patients with acute injury of the kidney that obstructs urine outflow or causes a drop in blood flow to the kidney. Nearly half of the patients in hospital intensive care units have some form of kidney injury due to drugs, surgery, bleeding or dehydration, said Dr. Kuro-o, the study's senior author who discovered Klotho more than a decade ago.

"Within a few days after injury, renal function can be completely gone," he said. "We show that Klotho injection in a drip infusion could be effective not only as an initial treatment for acute kidney injury, but also to prevent its progression into chronic kidney disease. This offers real hope for patients with renal disease."

The UT Southwestern researchers focused on mesenchymal cells: multipotent cells that can differentiate into a variety of cell types. These

are essential for development and growth, but when the cells are out of balance, they can morph into a pathological form that causes fibrosis (toughening of the tissue layers) and metastasis in cancer cells, said Dr. Kuro-o.

Scientists involved in this study also found that Klotho prevents cancer migration and metastasis. In the study, they blocked a ureter to cause renal fibrosis or introduced human cancer cells in laboratory mice. Secreted Klotho was effective in blocking three signaling pathways – TGF-?1, Wnt and IGF-1 – that can cause tissue fibrosis or cancer metastasis.

The researchers reported for the first time that Klotho binds to the cells' transforming growth factor receptor and inhibits signaling required for epithelial-to-mesenchymal transition (EMT), a "master switch" that causes cells to morph into a more pliable form. EMT cancer cells can squeeze into surrounding tissue and eventually into the bloodstream, leading to metastatic spreading of cancer.

"This is further evidence that Klotho is an understudied tumor-suppressor and really quite important because it's secreted and flows through the body," said Dr. David Boothman, professor of radiation oncology and pharmacology, associate director for translational research and an author of the study. "It could be a major surveillance mechanism for blocking tumor formation and progression."

Provided by UT Southwestern Medical Center