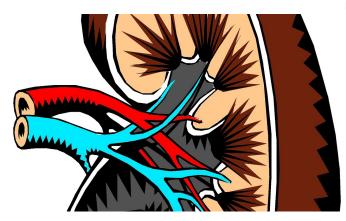


New cellular approach found to control progression of chronic kidney disease

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Researchers have demonstrated for the first time that extracellular vesicles - tiny protein-filled structures - isolated from amniotic fluid stem cells (AFSCs) can be used to effectively slow the progression of kidney damage in mice with a type of chronic kidney disease. The findings, by a research team at the Saban Research Institute of Children's Hospital Los Angeles, provide new insights about the mechanisms of kidney disease and point to a new approach for improved treatments. Results of the study were recently published online in *Scientific Reports*.

Alport syndrome, a type of chronic kidney disease, is an inherited disease that causes damage to the kidneys by the progressive damage to the glomerulus - the area of the kidney responsible for filtering blood. In patients with Alport syndrome, vascular endothelial growth factor (VEGF) - is known to be elevated early on in the disease. Increased VEGF causes scar tissue and severe damage to the cells that line the surface of blood vessels in the glomeruli eventually leading to kidney failure.

"By the time children born with Alport syndrome

reach adult life, they typically need dialysis to clear the waste from their blood and will require a kidney transplant," said Laura Perin, PhD, co-director of the GOFARR Laboratory for Organ Regenerative Research and Cell Therapeutics in Urology and principal investigator of the study.

In earlier studies, Perin's research team demonstrated that injection of AFSCs could delay the progression of renal fibrosis and glomerular sclerosis in particular in mice with Alport syndrome. However, the mechanisms responsible for this therapeutic effect had not been determined.

In the current study, the research team hypothesized that AFSCs provide this protection to the kidney through release of extracellular vesiclestiny membrane surrounded structures that contain receptors on their surface that can bind VEGF and reduce its biological activity on renal cells. The researchers isolated these vesicles and found that they could effectively target the glomerulus to control cellular homeostasis and maintain a stable level of functioning.

"We have demonstrated that these vesicles can be used to regulate VEGF activity and prevent the glomerular capillary damage," said Sargis Sedrakyan, PhD, who is the first author on the paper. "We can efficiently use the vesicles to help restore normal kidney function by curbing the progression of endothelial damage in the filtration unit of the kidney."

While vesicles previously have been shown to be promising targets for developing treatments, this study represents the first time they have been applied to glomerular disease by preventing endothelial damage. The finding represents a potential glomerulus-targeted intervention for chronic kidney disease.

"The advantage of this approach is that we can really modify the amount and the types of



extracellular vesicles that we inject and they seem to be homing to and acting directly in the area that requires treatment," explained Perin.

The team's next step will be to validate the stem cell-derived vesicle in different types of kidney disease with the final aim of finding a therapy that is effective for all patients who suffer from chronic kidney disease.

More information: S. Sedrakyan et al, Amniotic fluid stem cell-derived vesicles protect from VEGF-induced endothelial damage, *Scientific Reports* (2017). DOI: 10.1038/s41598-017-17061-2

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