

Prevent diabetic kidney function deterioration

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Since the progress of diabetic kidney disease is difficult to slow, many patients have to undergo dialysis or kidney transplantation. However, researchers at Karolinska Institutet have managed to prevent diabetic kidney function deteriorating in mice using a new treatment method, and are confident that it could be a possible treatment for humans as well. The study is published in the journal *Cell Metabolism*.

Diabetic kidney disease (or diabetic kidney failure) is the most common reason for dialysis. The clearest indication is the leakage of different plasma proteins into the urine, but there is also insufficient cleansing of waste products from the blood, impaired filtration and reduced urine production. There are currently few treatments available that can prevent the progressive deterioration of kidney function in patients, who often have no choice but to undergo dialysis or kidney transplantation.

It has long been known that people with <u>diabetic kidney disease</u> have an accumulation of lipid droplets in the kidneys, but scientists have not known what causes this phenomenon or the extent to which it exacerbates the disease. The researchers at Karolinska Institutet previously demonstrated that a special growth factor called VEGF-B (vascular endothelial growth factor B) controls the uptake of fats into muscles by regulating the ability of the cells coating the inner blood vessel walls to transport fat.oped

Newly developed drug candidate

By studying mice with diabetic kidney disease, the team has now uncovered a correlation between VEGF-B in the kidneys and the degree of pathological severity. When they blocked the biological effect of VEGF-B in mice with diabetic kidney disease using a newly developed drug candidate, they found a decrease in accumulated lipids in the kidneys. They subsequently managed

to make special cells in the renal filtration apparatus called podocytes respond again to insulin signalling and thus prevent further deterioration in kidney function.

"We've also been able to see from kidney biopsies that people with diabetic kidney disease also have raised levels of VEGF-B," says Professor Ulf Eriksson at the Department of Medical Biochemistry and Biophysics. "This suggests that our treatment, in which we 'freeze' the effect of the disease, could work on people so that they are spared dialysis. But the drug candidate that we've used has to be shown to be safe and free from unacceptable adverse effects."

Hope to extend treatment

The researchers now hope to extend their treatment concept to other kidney diseases that also cause the leakage of <u>plasma proteins</u> into the urine.

Since diabetic kidney failure is also a significant risk factor in serious cardiovascular disease, Professor Eriksson was awarded the Heart and Lung Foundation's grand prize in 2012.

"Without the resources I then had at my disposal I would probably not have been able to complete this project," he says.

More information: Annelie Falkevall et al. Reducing VEGF-B Signaling Ameliorates Renal Lipotoxicity and Protects against Diabetic Kidney Disease, *Cell Metabolism* (2017). DOI: 10.1016/j.cmet.2017.01.004

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