

New finding could help develop test for kidney disease

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Scientists at The University of Manchester have made an important finding that could help develop an early test for kidney disease.

Dr Rachel Lennon from the Wellcome Trust Centre for Cell-Matrix Research has been studying why some people are more susceptible to <u>kidney disease</u> because of their race and gender.

She explains: "It's well known that impaired <u>kidney function</u> is more common in Afro-Caribbean individuals compared to those from a Caucasian background, and in men compared to women. However, the reasons for the difference in susceptibility are only just being discovered."

Rather than looking at cell function, Dr Lennon and her team wanted to focus on the structure around the cells within the <u>kidney tissue</u> to understand what might be contributing to the development of kidney disease. Their findings have been published in the *Journal of the American Society of Nephrology*.

The researchers used mass spectrometry to analyse the tissue from mice with different genetic backgrounds and sexes, some of which were more susceptible to kidney failure. The sample of tissue was from the kidney filters which control what passes into our urine and what the body holds on to. Each kidney has about a million filters which process up to 180 litres of fluid a day.



The team found there were significant differences in the composition and type of proteins between the mice. The greatest difference was between mice from different genetic backgrounds as opposed to whether they were male or female.

Next the scientists used an electron microscope to get a detailed look at the filters. A normal filter has a scaffold of proteins between two types of cells. The team found that the scaffold part of the barrier in the susceptible mice was abnormal with splits and bulges. So not only was the composition of the filter different but also the structure.

Dr Lennon comments: "The most surprising thing about our findings were that the <u>mice</u> weren't actually exhibiting any symptoms of kidney disease and were all still in full health despite having this different structure in their filters. Their kidneys appeared to be functioning normally."

She continues: "The next question, and the one that we are starting to look at for our next research paper, is when this difference in structure occurs – is it from birth or at a later stage?"

Dr Lennon and her team will also be investigating the reasons behind the difference in structure, and whether there is a mechanism that could be switched off before symptoms of kidney disease become apparent and damage has occurred. They also plan to look at human tissue to investigate whether the same differences are present in our filters.

She says it's likely they will make the same findings: "At the moment we do see these changes in structure when looking at biopsies from kidney patients in clinic but we haven't known what they mean. What we're hoping is that this research will help develop a test that picks up kidney disease or even just a susceptibility to kidney disease before any damage has been done. We're also keen to look at whether we could manipulate



the process which leads to the structural change to develop new, more effective treatments."

More information: "Genetic Background is a Key Determinant of Glomerular Extracellular Matrix Composition and Organization." *JASN* ASN.2014040419; published ahead of print April 20, 2015, <u>DOI:</u> 10.1681/ASN.2014040419

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