

Scientists announce major breakthrough against rare kidney disease

May 19 2015



This image shows a cross section of a kidney. Credit: Holly Fischer/Wikipedia

Scientists at The University of Manchester and Central Manchester University Hospitals NHS Foundation Trust have made a significant breakthrough in the fight against Membranous Nephropathy (MN) – a rare kidney disease which can lead to kidney failure.

Their research was funded by Kidney Research UK – the UK's largest funder dedicated to kidney research and kidney problems in the UK.

PLA2R is a [protein](#) found in cells in the kidney, and is involved in the development of MN. This disease occurs when the immune system causes antibodies to attack the PLA2R protein which then results in the thickening of the [capillary walls](#) in the kidney filters leading to kidney failure.

The team in Manchester have found the precise region of PLA2R where antibodies attack, and have discovered molecules which can block antibodies from binding to the PLA2R protein and causing damage.

Now the team know where the antibody attacks they can design treatments to remove it, or to block it from attacking the kidney with [small molecules](#) known as peptides.

80% of adults with MN will produce antibodies against PLA2R, so it was vital for the team to find out how the antibodies bind to the protein and cause damage. To do this, the team needed to know the exact structure of the protein so they built a three dimensional model.

They then discovered that they could stop the antibodies from binding to the PLA2R protein by making a small replica of the binding site so that the antibodies attacked the decoy and not the real protein.

Dr Rachel Lennon commented: "This opens up possibilities for two new treatments for MN patients. We may be able to use a decoy as a drug to block the anti-PLA2R antibodies from attacking the kidney, or we could use small molecules called peptides to remove the anti-PLA2R antibodies from the body.

"Our research should eventually lead to the development of a specific

treatment for patients with MN that will reduce the severity of the condition, prevent progression to [kidney failure](#), and reduce the risk to patients from existing immunosuppressive treatment."

Professor Paul Brenchley says "This research project shows the benefit of University and NHS researchers working closely together to improve treatments for patients. We now know how to remove these damaging [antibodies](#) and our research group will develop a specific and safer therapy over the next three years if we can attract the next round of funding".

Elaine Davies of Kidney Research UK said: "This is a significant breakthrough in the fight against [kidney](#) disease and we have awarded additional funding through a PhD studentship announced in April 2015, to Dr Lennon's team to further investigate how to stop autoantibody binding using small molecule inhibitors. These experiments and the team's work in general will be vital when developing future treatments for patients with Membranous Nephropathy. However, more funding for research into [kidney disease](#) is desperately needed, so we can continue to make important breakthroughs like this which give hope to patients."

A recent paper, 'Identification of a Major Epitope Recognized by PLA2R Autoantibodies in Primary Membranous Nephropathy', published in the *Journal of the American Society of Nephrology*, contains further information on this research.

More information: "Identification of a Major Epitope Recognized by PLA2R Autoantibodies in Primary Membranous Nephropathy." *J Am Soc Nephrol.* 2015 Feb; 26(2): 302–313. doi: 10.1681/ASN.2014050502

Provided by University of Manchester

Citation: Scientists announce major breakthrough against rare kidney disease (2015, May 19)
retrieved 26 April 2024 from

<https://medicalxpress.com/news/2015-05-scientists-major-breakthrough-rare-kidney.html>

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