

Embargoed: 13:15 CEST, Saturday, 25 May 2024

New technique detects novel biomarkers for kidney diseases with nephrotic syndrome

A groundbreaking study, presented today at the 61st ERA Congress, has uncovered a significant breakthrough in the diagnosis and monitoring of kidney diseases associated with nephrotic syndrome.¹

Using a hybrid technique, researchers identified anti-nephrin autoantibodies as a reliable biomarker for tracking disease progression, opening new avenues for personalised treatment approaches.

Nephrotic syndrome, characterised by elevated protein levels in the urine, is linked to kidney diseases such as minimal change disease (MCD), primary focal segmental glomerulosclerosis (FSGS), and membranous nephropathy (MN). The primary cause behind nephrotic syndrome is damage to podocytes, the cells responsible for filtering the kidneys, which allows protein to leak into the urine.²

Children diagnosed with MCD or FSGS often receive a diagnosis of idiopathic nephrotic syndrome (INS), where the cause of the nephrotic syndrome is unknown. This is frequently because children with high protein levels in their urine rarely undergo a kidney biopsy, which is how the cause is typically determined.³

Traditionally, diagnosing these conditions has posed challenges due to overlapping histological features and hesitancy to conduct invasive kidney biopsies, particularly in children. While anti-nephrin autoantibodies have been observed in certain patients with MCD and FSGS, their precise role in the advancement of these diseases is not fully understood.^{4,5}

The study, conducted across Europe and the USA, introduced a novel approach combining immunoprecipitation with enzyme-linked immunosorbent assay (ELISA) to reliably detect anti-nephrin autoantibodies.

The findings revealed that anti-nephrin autoantibodies were prevalent in 69% of adults with MCD and 90% of children with INS who had not been treated with immunosuppressive drugs. Importantly, the levels of these autoantibodies correlated with disease activity, suggesting their potential as a biomarker for monitoring disease progression. The antibodies were also rarely seen in the other diseases under examination.

To further investigate the impact of nephrin immunisation on kidney function and disease, researchers administered laboratory-made nephrin protein to mice, creating a condition akin to MCD in the mice. Immunisation led to the phosphorylation of nephrin and notable alterations in cell structure, indicating the involvement of antibodies targeting nephrin in podocyte malfunction and nephrotic syndrome.

Remarkably, unlike other models necessitating multiple immunisations,⁶ this model induced swift disease manifestation with a single immunisation, even at low antibody concentrations.

Dr. Nicola M. Tomas, co-lead author of the study, commented, "The identification of anti-nephrin autoantibodies as a reliable biomarker, coupled with our hybrid immunoprecipitation technique, enhances our diagnostic capabilities and opens new avenues for closely monitoring disease progression in kidney disorders with nephrotic syndrome."

Professor Tobias B. Huber, lead author of the study, furthered, "By providing insights into underlying mechanisms, these findings lay the groundwork for personalised interventions and pave the way for a new era of precision medicine for these complex conditions."

The study is being published today in the New England Journal of Medicine and presented at the 61st ERA Congress in Stockholm, Sweden.

ENDS

Notes to editors:

A reference to the ERA Congress must be included in all coverage and/or articles associated with this study.

For more information or to arrange an expert interview, please contact press@era-online.org

About the lead study authors:

Professor Tobias B. Huber is a Professor of Medicine, Chair of the III. Department of Medicine at the University Medical Center Hamburg-Eppendorf, Director of the Hamburg Center for Kidney Health and President of the International Society of Glomerular disease.

Dr. Nicola M. Tomas is a Senior Attending Physician and Principle Investigator at the III. Department of Medicine at the University Medical Center Hamburg-Eppendorf.

About the European Renal Association (ERA):

With more than 25,000 active members, the ERA is one of the biggest nephrology associations worldwide leading European nephrology, and one of the most important European Medical Associations. It organises annual congresses and other educational and scientific activities. The ERA also collects data and performs epidemiological studies through its Registry. The Society supports fellowships and educational/research projects through its committees and working groups. Its publications are NDT, CKJ (Open Access journal), and the online educational portal NEP.

The 61st ERA Congress takes place between 23-26 May 2024, both virtually and live in Stockholm, Sweden.

Website: www.era-online.org

References:

1. Autoantibodies Targeting Nephrin in Podocytopathies, Huber T. B (2024). Presented at the ERA Congress 2024.
2. Tapia, C., & Bashir, K. (2023). Nephrotic Syndrome. In StatPearls. StatPearls Publishing.
3. Eddy, A. A., & Symons, J. M. (2003). Nephrotic syndrome in childhood. *Lancet (London, England)*, 362(9384), 629–639. [https://doi.org/10.1016/S0140-6736\(03\)14184-0](https://doi.org/10.1016/S0140-6736(03)14184-0)
4. Watts, A. J. B., Keller, K. H., Lerner, G., Rosales, I., Collins, A. B., Sekulic, M., Waikar, S. S., Chandraker, A., Riella, L. V., Alexander, M. P., Troost, J. P., Chen, J., Fermin, D., Yee, J. L., Sampson, M. G., Beck, L. H., Jr, Henderson, J. M., Greka, A., Rennke, H. G., & Weins, A. (2022). Discovery of Autoantibodies Targeting Nephrin in Minimal Change Disease Supports a Novel Autoimmune Etiology. *Journal of the American Society of Nephrology: JASN*, 33(1), 238–252. <https://doi.org/10.1681/ASN.2021060794>
5. Shirai, Y., Miura, K., Ishizuka, K., Ando, T., Kanda, S., Hashimoto, J., Hamasaki, Y., Hotta, K., Ito, N., Honda, K., Tanabe, K., Takano, T., & Hattori, M. (2024). A multi-institutional study found a possible role of anti-nephrin antibodies in post-transplant focal segmental glomerulosclerosis recurrence. *Kidney international*, 105(3), 608–617. <https://doi.org/10.1016/j.kint.2023.11.022>
6. The classical pathway triggers pathogenic complement activation in membranous nephropathy. Seifert L, Zahner G, Meyer-Schwesinger C, Hickstein N, Dehde S, Wulf S, Köllner SMS, Lucas R, Kylies D, Froembling S, Zielinski S, Kretz O, Borodovsky A, Biniaminov S, Wang Y, Cheng H, Koch-Nolte F, Zipfel PF, Hopfer H, Puelles VG, Panzer U, Huber TB, Wiech T, Tomas NM. *Nat Commun.* 2023 Jan 28;14(1):473. doi: 10.1038/s41467-023-36068-0.