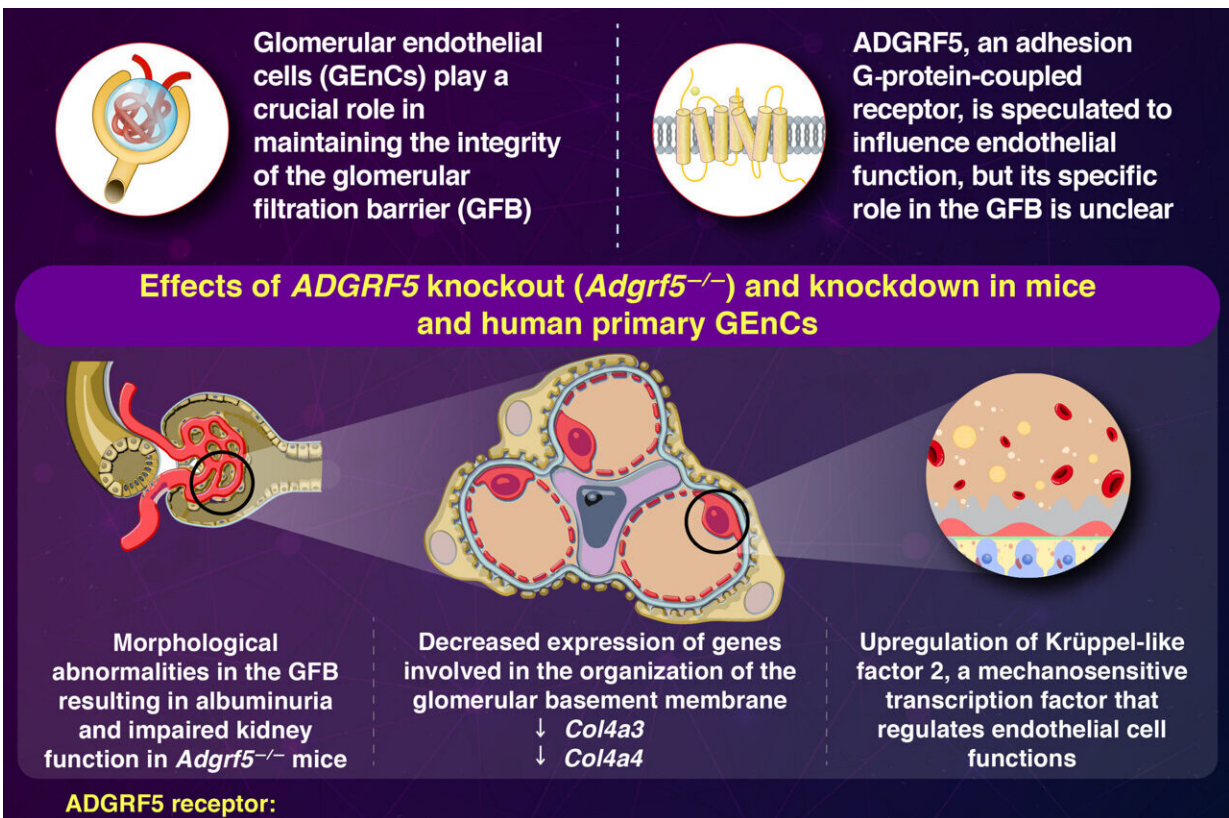


Unraveling the role of ADGRF5: Insights into kidney health and function

June 21 2024



ADGRF5 is crucial for maintaining GFB integrity and function, with its deletion causing significant kidney defects and impaired function. Credit: Tokyo Tech

Glomerulus, the fundamental filtering unit of the kidney, is an intricate network of capillaries—small blood vessels that regulate the movement

of ions, water, and metabolites while maintaining impermeability to essential macromolecules such as proteins.

The selectively permeable capillary wall, known as the glomerular filtration barrier (GFB), consists of three main components: glomerular endothelial cells (GEnCs), the glomerular basement membrane, and podocytes. GEnCs line the inner surface of the capillary wall and are covered by a thin layer of glycoproteins and other carbohydrate-based moieties.

Adhesion G-protein-coupled receptor F5 (ADGRF5), a transmembrane cell receptor expressed in GEnCs, is implicated in influencing the integrity of the GFB, potentially playing a role in its structural and functional maintenance. To elucidate the precise role of ADGRF5 in maintaining the integrity of the GFB, a collaborative research study was undertaken by scientists from Tokyo Institute of Technology (Tokyo Tech) and Kyorin University. Their findings were [published](#) in the *Journal of the American Society of Nephrology* on June 6, 2024.

The research team led by Associate Professor Nobuhiro Nakamura from the School of Life Science and Technology, Tokyo Tech, Japan, and Professor Miki Nagase from the Department of Anatomy, Kyorin University School of Medicine, Japan, conducted a series of genetic knockout and knockdown experiments in mice and human primary GEnCs to investigate the specific role and underlying mechanisms of ADGRF5 in maintaining the GFB.

Explaining the motivation behind the present research, Dr. Nakamura says, "During our analysis of renal gene expression profiles using the Nephroseq v5 database, we observed a reduced expression of ADGRF5 mRNA in the glomeruli of patients with diabetic nephropathy. Additionally, there was a positive correlation between glomerular ADGRF5 expression and the estimated glomerular filtration rate."

Initially, the researchers observed the specific expression of ADGRF5 within [endothelial cells](#) that line the glomerular capillary wall. In mice with genetic knockout of ADGRF5, the GFB was affected by morphological abnormalities like splitting and thickening of the glomerular basement membrane and GEnC detachment. The overall integrity of GFB was severely impacted leading to albuminuria—presence of albumin proteins in urine.

Furthermore, deletion and knockdown of the ADGRF5 gene in mice and human primary GEnCs, respectively, revealed alterations in the expression of genes crucial for maintaining the integrity of the GFB. Specifically, knockout/knockdown of ADGRF5 significantly downregulated type IV collagens (Col4a3 and Col4a4) that comprise the GFB and influence GFB permselectivity. In addition, Krüppel-like factor 2 (KLF2), a mechanosensitive transcription factor that regulates endothelial cell functions, was found to be upregulated.

Taken together, their findings highlight the critical functions of ADGRF5 in maintaining the integrity of GFB. Emphasizing the potential impact of the research work, Dr. Nakamura says, "This study reveals a novel mechanism that maintains the GFB. Insights into the role of ADGRF5 aids the understanding of glomerular disorders and significantly contributes to the advancement of future research."

Unlocking the novel functions of the ADGRF5 receptor holds promise for pioneering therapeutic breakthroughs in treating glomerular filtration barrier dysfunctions, notably proteinuria.

More information: Miki Nagase et al, Glomerular Endothelial Cell Receptor ADGRF5 and the Integrity of the Glomerular Filtration Barrier, *Journal of the American Society of Nephrology* (2024). [DOI: 10.1681/ASN.0000000000000427](https://doi.org/10.1681/ASN.0000000000000427)

Provided by Tokyo Institute of Technology

Citation: Unraveling the role of ADGRF5: Insights into kidney health and function (2024, June 21) retrieved 26 June 2024 from <https://medicalxpress.com/news/2024-06-unraveling-role-adgrf5-insights-kidney.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.