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TMEM30A downregulation initiate podocyte injury through reducing glycolysis in focal segmental glomerulosclerosis

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Objectives : Podocyte injury plays a critical role in the pathogenesis and progression of focal and segmental glomerulosclerosis (FSGS). Transmembrane protein 30A (TMEM30A) downregulation participates in podocyte injury, but the mechanism remains unclear.

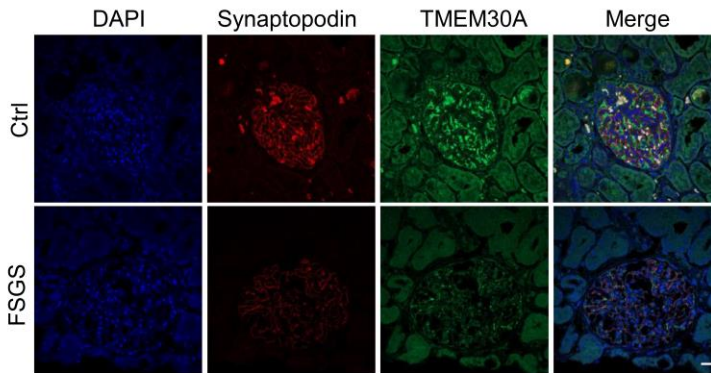
Methods : In our study, we compared Synaptopodin and TMEM30A levels in renal tissues from patients with FSGS to those in normal controls. Through transcriptomic and metabolomic analyses, we characterized Tmem30a knockdown (Tmem30a^{-/-}) and normal mouse podocytes to pinpoint differentially expressed genes and metabolites. Furthermore, Gene Ontology, Kyoto Encyclopedia of Genes and Genomes (KEGG), gene set enrichment analysis (GSEA) and Protein-Protein Interaction (PPI) network were constructed to search signaling pathway and hub genes. We further assessed podocyte (Nephrin and WT1) and glycolysis (ALDOA, HK2, GAPDH, and LDHA) proteins in Tmem30a^{-/-} and normal podocytes.

Results : TMEM30A and Synaptopodin were significantly reduced in the kidney tissues from patients with FSGS. Metabolomics and transcriptomic sequencing analysis of normal and Tmem30a^{-/-} mouse podocytes were enriched into glycolytic pathway by KEGG and GSEA analysis and the levels of glycolytic related genes was significantly downregulated. Furthermore, the expressions of podocyte related proteins and the key glycolytic enzymes were significantly downregulated in Tmem30a^{-/-} mouse podocytes compared to normal mouse podocytes.

Conclusions : The downregulation of TMEM30A, which subsequently impacts glycolysis, contributes to podocyte injury. Our findings clarified the mechanism of podocyte injury in FSGS and have implications for early diagnosis, prevention, and treatment.

Fig.1.jpg

A



B

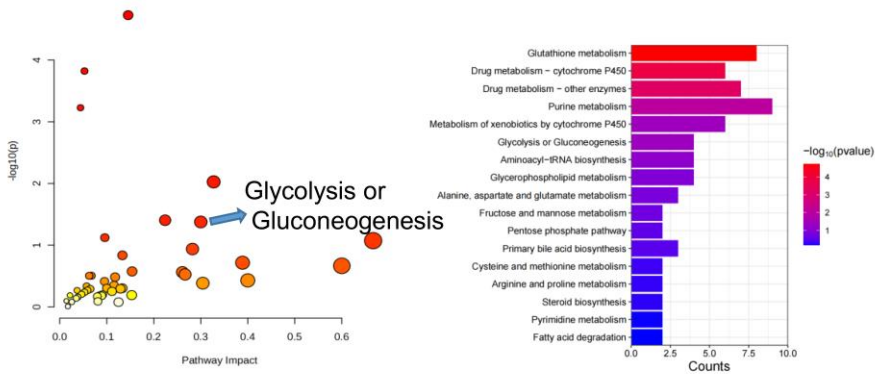


Fig.1.jpg

