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Mechanism underlying selective albuminuria in minimal change disease

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The glomerular capillary wall has charge and size barriers with sieving coefficient of 0.00062 for albumin and 0.98 for low molecular weight proteins (Am J Physiol 1992;263:F601). A normal human glomerulus filters approximately 3 g of albumin per day, more than 97% of which is reabsorbed by megalin in the renal tubules (Kidney Int 2013; 84:861). selective proteinuria is associated with foot process effacement in minimal change disease (MCD), whereas nonselective proteinuria results from slit membrane damage and podocyte detachment. The amount of proteinuria increases with increasing percentage of foot processes effacement lining the capillary walls, and the number of slits decreases with tight junction formation between podocytes in MCD. Through which part of the podocytes is albumin filtered? SDS-PAGE analysis of urinary proteins showed that albumin and transferrin were selectively detected in MCD without high-molecular-weight proteins, but interestingly, no low-molecular-weight proteins were observed. This phenomenon cannot be explained by the damage of the slit membrane size barrier. We therefore hypothesized that albumin is transported by vesiclar endocytosis and exocytosis with albumin receptors (Kidney Int 2011;80:1328, Med Mol Morphol 2008;41:92). In the MCD animal models, there are many vesicles in podocytes and the motor molecule dynein 1 and microtubules are increased in podocytes, suggesting that albumin-containing vesicles may be transported along microtubules (Med Mol Morphol 2017; 50:86). To confirm the role of vesicle transport along the microtubules in podocytes in MCD, we induced MCD in mice with a genetic mutation in the microtubule anchoring protein APC, and found that cytoplasmic dynein 1 and vesicle trasport in the podocytes decreased, resulting in decreased albuminuria (Int J Mol Sci. 2021; 22(24):13412). The NADPH oxidase inhibitor apocynin also inhibited podocyte FcRn albumin receptors and reduced albuminuria (KI 2011;80:1328).
In conclusion, regulation of vesicular transport in podocytes may be a novel therapeutic strategy for nephrotic syndrome.