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GLOMERULAR DISEASE

Albumin endocytosis is caveolin-mediated

New research suggests that podocytes primarily endocytose albumin in a caveolin-dependent rather than a clathrin-dependent manner, despite expressing both factors. This mechanism contrasts with that of the proximal tubule, in which albumin endocytosis is mediated by clathrin.

"Evidence that serum proteins are actively trafficked through podocytes comes from studies in humans and animals with heavy proteinuria, in which protein accumulation within podocytes is a prominent feature," explains lead investigator Judith Blaine.

The researchers used confocal and total internal reflection fluorescence microscopy to track labelled albumin through cultured human urine-derived podocyte-like epithelial cells, which respond to albumin similarly to podocytes. They found that, although albumin had greater access to the apical surface of the cultured cells, endocytosis occurred predominantly at the basal aspect. "This would correspond to the podocyte surfaces adjacent to the basement membrane *in vivo*," explains Blaine. Furthermore, inhibition of clathrin had no effect on the level of albumin endocytosis, whereas caveolin inhibition reduced endocytosis considerably, implicating the latter in the process.

As caveolin-1 is involved in many signalling pathways, and co-localizes with the slit diaphragm proteins nephrin and CD2-associated protein, it might be involved in responses to changes in glomerular haemodynamics. Whether the extracellular albumin load changes these haemodynamics and rates of endocytosis via caveolin-mediated pathways is unclear.

"Understanding the mechanisms of protein trafficking in podocytes and determining how these pathways are altered in proteinuric kidney diseases might one day lead to specific therapies for their prevention," concludes Blaine.

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Original article Dobrinskikh, E. *et al.* Human podocytes perform polarized, caveolae-dependent albumin endocytosis. *Am. J. Physiol. Renal Physiol.* doi:10.1152/ajprenal.00532.2013