Serum- and glucocorticoid-inducible kinase (SGK) interacts with the chloride channel ClC-5 to regulate renal albumin uptake

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The reuptake of albumin from the glomerular filtrate by the renal proximal tubule is a constitutive receptor-mediated endocytic process. This process requires a number of key membrane proteins including the scavenger receptor megalin, the Cl^- channel ClC-5 and the Na-H exchanger NHE3 that are thought to form the endocytic complex. In addition, albumin uptake is regulated by a number of accessory proteins including cofilin, Nedd4-2 and the PDZ (PSD95/Dlg/ZO-1) scaffold NHERF2. We have recently found that the serum- and glucocorticoid-inducible kinase SGK-1 regulates albumin uptake. Overexpression of SGK-1 significantly increased albumin uptake (114 ± 3.7%). In contrast, overexpression of ligase defective SGK-1 inhibited albumin uptake by 81 ± 3.1% (n=4, $P < 0.05$). SGK-1 has been previously reported to bind to NHERF2 *via* a PDZ binding motif. Therefore, we investigated if the effects of SGK-1 on albumin uptake were mediated by an interaction with the ClC-5-NHERF2 complex. An SGK-1 antibody was used to probe OK cell lysate and it was found that ClC-5 co-immunoprecipitated with SGK-1. However, when GST-pulldown experiments were performed using the C-terminus of ClC-5 (which binds NHERF2) there was no binding of SGK-1 detected. Interestingly, there are potential SGK-1 phosphorylation sites on the intracellular N-terminus of ClC-5 and we are currently investigating whether SGK-1 binds to this portion of the channel. Alternatively, SGK-1 may be exerting its effects *via* phosphorylation of as yet unidentified accessory proteins. These data suggest a novel role for SGK-1 in regulating albumin endocytosis *via* mechanisms that may not involve PDZ scaffold interactions.