

 **PODOCYTE BIOLOGY**

Dynamic control of actin remodelling

Dynamic regulation of the podocyte actin cytoskeleton enables these cells to adapt to changes in their environment and maintain the function of the glomerular filtration barrier. Now Lisa Buvall, Anna Greka and colleagues report that synaptopodin integrates competing signals from upstream tyrosine and serine/threonine pathways to control actin remodelling in podocytes.

“The balance between a stationary and a migratory podocyte is regulated by the intrinsic balance of the small RhoGTPases: RhoA, Rac1 and Cdc42,” explains Buvall. “We previously found that synaptopodin is crucial to maintain podocyte function by promoting a stationary phenotype through RhoA signalling.”

As serine/threonine phosphorylation is known to stabilize synaptopodin, leading to 14-3-3 binding and RhoA-induced stress fibre formation, the researchers used phosphoproteomic technology to investigate whether tyrosine phosphorylation also has a role in the regulation of synaptopodin. They report that in podocytes, EGFR/Src-mediated tyrosine phosphorylation of synaptopodin leads to loss of 14-3-3 binding, resulting in synaptopodin degradation, which promotes Rac1-induced loss of stress fibres.

“Serine/threonine and tyrosine phosphorylation compete for synaptopodin as a substrate and the winner determines the effect on the podocyte cytoskeleton, and ultimately on the integrity of the kidney filter,” says Greka. “If serine/threonine phosphorylation wins, synaptopodin and the filter remain intact, but if EGFR/Src signalling wins, the actin cytoskeleton is disassembled, and consequently, one expects that the filter crumbles. Therefore synaptopodin is a true molecular coincidence detector.”

The researchers believe that the significance of their findings goes well beyond the podocyte. “This work has revealed a mechanism by which cells may utilize a molecular coincidence detector like synaptopodin for the control of Rho protein crosstalk, a mechanism likely to be conserved across many different cell types,” comments Greka.

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synaptopodin is a true molecular coincidence detector



ORIGINAL ARTICLE Buvall, L. *et al.* Synaptopodin is a coincidence detector of tyrosine versus serine/threonine phosphorylation for the modulation of Rho protein crosstalk in podocytes. *J. Am. Soc. Nephrol.* <http://dx.doi.org/10.1681/ASN.2016040414> (2016)