New and Notable

Remarkable Results in Study by Riethmüller et al.

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Human kidneys filter 180 liters of blood daily to eliminate toxic waste. Valuable solutes are pumped back into the bloodstream and aquaporins (AQP) ensure that water flows back as well. Driven by the osmotic gradient, the major water flux is transported by AQP1, the first water channel protein identified by Nobel Prize Laureate Peter Agre in 1992. The remaining water reabsorbtion takes place in the collecting duct, and is mediated by AQP2 in the apical membrane of the principal cells. This flux is controlled by the antidiuretic hormone arginine-vasopressin (AVP). Binding of AVP to its receptor at the basolateral side of the collecting duct cells leads to activation of cAMP-dependent protein kinase A, which phosphorylates AQP2 at residue Ser-256. Phosphorylated AQP2 tetramers are recognized by a cellular transport machinery that relocates the AQP2-containing vesicles to the apical membrane, where they fuse and thus enhance the water permeability. This transport process is key to water homeostasis, is highly complex, and still not well understood.

In this issue on page 671, Riethmüller et al. describe atomic force microscopy imaging and force-mapping of primary epithelial cells from collecting ducts. They show on living cells that their Young's modulus decreases by 51% after addition of AVP, suggesting a reorganization of the cytoskeleton. Riethmüller et al. then address the question whether AVP induces actin depolymerization, thereby opening a path for the transport of AQP2-containing vesicles toward the apical membrane. Force-mapping was performed on cells whose actin cytoskeleton was stabilized by jasplakinolide, but amazingly no inhibition of the AVP-induced vesicle transport was observed. In contrast, blebbistatin, a myosin II inhibitor, completely suppressed the AVP response.

These are remarkable results, because they shed some light on the mechanism of vesicle movement. They demonstrate that it is not the proposed depolymerization of F-actin that allows for the displacement of AQP2-containg vesicles to the apical membrane, but that it is the relaxation of actomyosin interaction that facilitates vesicle translocation. It will be interesting to explore the nature of the latter mechanism and to identify the components of the entire transport machinery.

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