Cell volume regulation: skating through the pathways

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Because every cellular function is integrated directly or indirectly with every other, it is the webs of often highly evolutionarily conserved protein-protein interactions that define the cell (3). Maintenance of structure-function relationships is then prerequi-site for cellular life, and these relationships dictate exquisite control of volume by most differentiated cells (7). It is the perception of the disruption of some aspect of cellular composition (e.g., ionic strength) or structure that serves as the initiating signal for regulatory volume decrease or increase (RVD or RVI, respectively). To offset volume change, an osmotic driving force across the plasma membrane is required that must be generated in response (7). To offset volume change, an osmotic driving force across the plasma membrane is required that must be generated in response (7). To offset volume change, an osmotic driving force across the plasma membrane is required that must be generated in response (7). To offset volume change, an osmotic driving force across the plasma membrane is required that must be generated in response (7). To offset volume change, an osmotic driving force across the plasma membrane is required that must be generated in response (7). To offset volume change, an osmotic driving force across the plasma membrane is required that must be generated in response (7). To offset volume change, an osmotic driving force across the plasma membrane is required that must be generated in response (7). To offset volume change, an osmotic driving force across the plasma membrane is required that must be generated in response (7).

The RVD evoked by hypotonicity in many cell types involves rapid efflux of K⁺ and Cl⁻, as well as osmolytes such as taurine. The solute efflux pathways may be made available by phospho-rylations, subunit associations of existing plasma membrane transporters, and exocytotic insertion of submembrane vesicular transporters into the plasma membrane. The dominant substrate used by skate erythrocytes for RVD is taurine. The taurine efflux pathway elicited by decreased ionic strength in these cells is sensitive to anion-exchange inhibitors, and when the cloned skAE1 is expressed in Xenopus oocytes, it behaves similarly to the taurine osmolyte channel in hypotonically stimulated skate erythrocytes (2). Under isotonic conditions, only a small fraction of the skAE1 is expressed on the plasma membrane extracellular surface of skate erythrocytes; a large part of the remainder is cytosolic in nonionic detergent-insoluble regions, so-called lipid rafts (5). During hyposmotic cell expansion, these appear at the plasma membrane surface with skAE1 in a highly tyrosine-phosphorylated state and largely organized as tetramers with increased binding to ankyrin and decreased binding to band 4.1 membrane scaffolding proteins (6).

The order of progression of the biochemical changes in skAE1 initiated by hypotonicity is unknown. In their most recent paper, Musch and Goldstein (4) have examined these events following inhibition of tyrosine kinase p72syk. Piceatannol is a relatively specific inhibitor of this kinase and has allowed the determination of whether all or part of these events respond to tyrosine phosphorylation. Volume-activated formation of skAE1 tetramers and the transition of exchanger to lipid rafts were unchanged by inhibition of p72syk; however, tyrosine phosphorylation was associated with decreased binding of skAE1 to band 4.1 and increased binding to ankyrin. The results lead the authors to hypothesize that an early step in mediation of taurine efflux by skAE1 is movement to the plasma membrane. Formation of AE1 tetramers may provide a key step in efflux pathway formation, but there is no indication of the position of this conversion in the progression of events. Future studies are to focus on the role of tyrosine kinase-controlled alterations in binding of skAE1 to ankyrin and band 4.1. Alteration of these associations may allow skAE1 to reorganize in lipid raft regions of the membrane.

REFERENCES