S19-4 Strict regulation of zinc homeostasis by zinc transporters

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Zinc transporters are essential for various physiological functions like immune response and early development, and have turned out to be implicated in various pathological processes like breast cancer metastasis, diabetes and Alzheimer diseases *etc*. Zinc transporters that physiologically function in eukaryotic cells are assigned to SLC30A or SLC39A families. Urinary loss of zinc is extremely low, and therefore zinc balance is primarily maintained in zinc absorption through the intestine. Dietary zinc is absorbed from intestinal epithelial cells where ZIP4 is functional as an essential transporter for zinc uptake. During zinc deficiency, ZIP4 protein levels are increased and ZIP4 is localized on the apical membranes after the extracellular amino-terminal half of the protein is proteolytically removed. In contrast, ZIP5, highly homologous to ZIP4 and also expressed in intestinal epithelial cells is targeted to the basolateral membranes of these cells only in zinc-replete condition. This reciprocal regulation of ZIP4 and ZIP5 expression would be important for zinc homeostasis in the body. On the other hand, specific zinc transporters regulate zinc homeostasis in cellular or subcellular levels through their specific function. Thus, the coordinated regulation of zinc transporters is indispensable for homeostatic maintenance of zinc.