The trafficking and transport of manganese in *S. cervisiae*

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Manganese is a redox active metal that is an essential element for all forms of life. Yet the requirement for manganese (like many other metals) in life has imposed a need for exquisite homeostatic regulation and trafficking of manganese, as it is also a potentially toxic metal. Cells have evolved elegant mechanisms for regulating the uptake and distribution of manganese into cells (metal utilization pathways) and the directed excretion of excess intracellular manganese (metal detoxification pathways).

In the baker yeast, *S. cerevisiae*, manganese is transported into cells by two members of the Nramp (natural resistance associated macrophage proteins) family of proteins that transport divalent metal cations; Smf1p and Smf2p. Smf1p is a manganese transporter expressed on the cell surface under manganese starvation conditions; under manganese replete conditions it is trafficked to the vacuole for degradation. This movement to the vacuole in response to manganese involves ubiquitination of Smf1p by Bsd2p. While Smf1p can transport a number of divalent metal cations (e.g. Fe^{2+}, Cu^{2+}, Co^{2+}), only manganese ions can regulate the protein at the post-translational level. The second Nramp transproter, Smf2p is observed in yeast cells in as yet unidentified vesicles, and is required for activation of Mn-enzymes such as superoxide dismutase in the mitochondria and Golgi sugar transferases. Like Smf1p, Smf2p is also targeted to the vacuole for degradation is response to manganese.

The mechanism by which Smf transporters sense intracellular manganese and respond by a shift in their intracellular location is not well understood. The work here combines yeast molecular genetics and cell biology to probe the relationship between manganese in the excretory pathway of cells and the feedback mechanisms for regulating manganese homeostasis.