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Molecular Mechanism of Salt- and Osmo-Tolerance in Yeast (II)

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Summary

Adaptation to high salt and high osmolarity conditions is a fundamentally important biological response of all types of cells, ranging from bacteria, fungi, plants, and animals. In yeast, for example, external high salt and high osmolarity conditions activate the HOG (High Osmolarity Glycerol) MAP kinase (MAPK) pathway, which is essential for yeast to adapt to and survive on those conditions.

MAP kinase cascades are conserved signaling modules composed of three sequentially activated kinases (MAPKKK, MAPKK, and MAPK). The yeast high osmolarity glycerol (HOG) pathway can be activated by either of two upstream pathways, termed the SHO1 or SLN1 branches. When stimulated by high osmolarity, the SHO1 branch activates an MAP kinase module composed of the Ste11 MAPKKK, the Pbs2 MAPKK and the Hog1 MAPK.

To investigate how osmostress activates this MAPK module, we isolated and characterized constitutively activated alleles in three key genes involved in the pathway, namely *STE11*, *STE50*, and *SHO1*. We found that Cdc42 not only activates the upstream kinases in the HOG pathway, Ste20 and Cla4, but also binds to Ste11-bound Ste50, thereby bringing activated Ste20/Cla4 and their substrate Ste11 together. Subsequently, activated Ste11 and its HOG pathway-specific substrate, Pbs2 MAPKK, are brought together by binding of the Ste50-Ste11 complex to the cytoplasmic domain of Sho1, to which Pbs2 is also bound. Thus, both Sho1 and Ste50 act as adaptive docking proteins that restrict the flow of the osmostress signal from Ste20/Cla4 to Pbs2, via Ste11.