MSG5 encodes a dual-specificity protein phosphataseinvolved in the regulation of at least two mitogen-activated protein kinase-mediated pathways. Msg5p dephosphorylates Fus3p, which inactivates this mating response MAPKand targets it for export from the nucleus. Msg5p also dephosphorylates and inactivates the cell wall integrity MAPK, Slt2p, which is activated in response to many growth condition stressors. In addition to down-regulating the activities of both of these MAPKs during desensitization or adaptation to stimuli, Msg5p is also responsible for basal dephosphorylation of Fus3p and Slt2p. Deletion of MSG5 results in induction of many genes normally regulated by the mating or cell integrity pathways, even in the absence of stimuli. MSG5 transcription is induced during the pheromone response, but not under conditions that stimulate the cell integrity pathway. Msg5p and Slt2p are reciprocally regulated on the protein level. Slt2p is a substrate of Msg5p, and dephosphorylation by Msg5p decreases Slt2p activity. Conversely, Msg5p is a substrate for phosphorylation by Slt2p. Phosphorylation of Msg5p is thought to decrease its interaction with Slt2p, thereby reducing the ability of Msg5p to inactivate Slt2p. Msg5p is present in both a shortand a longform. Both isoforms are produced from the same gene via alternative translational initiation sites. Although both forms are equally active on Slt2p, the long form is more efficient at Fus3p inactivation. For technical reasons, SGD sequence annotation currently includes only the longer form of MSG5.