The protein kinase regulator Ste50p is involved in mitogen-activated protein kinasepathways governing mating, filamentous growth, osmoregulation, and nitrogen starvation, all of which also depend on the MAPK kinase kinaseSte11p. Ste50p and Ste11p interact constitutively via their N-terminal regions, each of which contains a single SAM domain, and Ste50p fulfills an essential role in the activation of the Sho1p branch of the high-osmolarity glycerol responsepathway by acting as an integral subunit of the Ste11p MAPKKK. The SAM domain, or Sterile Alpha Motif, is an evolutionarily-conserved protein-binding domain present in single copies in over 300 eukaryotic proteinsthat are involved in signal transduction, transcriptional activation and repression, and regulation of various developmental processes. Effective regulation of Ste11p by Ste50p also depends on the Ste50p conserved C-terminal \"Ras-association\"domain, which is required for delivery of Ste11p to the plasma membrane in the filamentous growth signaling pathway, and is also essential for invasive growth and HOG signaling. Ste50p disrupts an association between the Ste11p catalytic C-terminus and its regulatory N-terminus, and also appears to modulate Ste11p autophosphorylation and is itself a substrate of the Ste11p kinase. The interaction between Ste50p and Ste11p is a prerequisite for key signal transduction events, and is differentially required for Ste11p activity, as well as modulation of Ste11p function during mating, filamentous growth, and HOG signaling, but has a lesser role in pheromone response.Ste50p functions in cell signalling by determining the extent and duration of mating pheromone-induced signal transduction, thereby leading cells to hormone-induced differentiation, and acts downstream of the Ste2p alpha-pheromone receptor, between the pheromone receptor-bound heterotrimeric G proteinand Ste11p. Ste50p serves as an adaptor that links the Cdc42p-Ste20p kinase complex to effector kinase Ste11p, by tethering Ste11p to the plasma membrane via association with Cdc42p, thereby permitting the encounter of Ste11p with Ste20p for activation, which is required for the intiation of signaling. Inactivation of STE50 leads to sterility and attenuation of mating pheromone-induced signal transduction, whereas overexpression of STE50 intensifies the pheromone-induced signaling. Defects in filamentous growth and mating exhibited by ste50 mutants can be suppressed by the overexpression of STE11. Mutations in the SAM domain of STE50 that prevent the heterotypic Ste11p-Ste50p association present signaling defects in the pathways for mating, filamentous growth and osmotolerance. Homologs of STE50 are found in other fungi, including Saccharomyces kluyveri, Hansenula polymorpha, Candida albicans, and Neurospora crassa.