STE20 encodes a serine threonine kinase that functions as a mitogen activated protein kinasekinase kinase kinaseand a histone serine kinase. Originally identified in the yeast signaling pathway for mating, Ste20p has since been found to be involved in the MAPK pathways regulating osmosensing, filamentous growth, bud site selection, polarized growth, actin organization, regulation of exit from mitosis, and apoptosis. Although STE20 is not essential for viability, a null mutation in this gene results in sterility. In its role in signal transduction, Ste20p is activated by the Rho-like GTPase Cdc42p. Cdc42p binds to the N-terminal CRIBdomain of Ste20p, localizing Ste20p to the plasma membrane at sites of polarized growth such as the bud and shmoo tip and relieving the autoinhibitory effect the CRIB domain has on the Ste20p C-terminal kinase domain. Alleviation of inhibition results in Ste20p activation by autophosphorylationor, during budding, phosphorylation by the cyclin dependent kinase-cyclin complexes Cdc28p-Cln1p and Cdc28p-Cln2p. Activated Ste20p subsequently phosphorylates its target, the Ste11p MAPKKK. Maximum Ste20p signaling activity is also dependent on its direct interactions with the scaffolding protein Bem1p and the heterotrimeric G protein beta subunit, Ste4p. During filamentous growth, Ste20p activity is regulated by the protein methyltransferase Hsl7p. More recently, Ste20p activity has been linked to chromatin condensation during apoptosis. Similar to what is seen in apoptotic mammalian cells, hydrogen peroxide-induced cell death in S. cerevisiae requires chromatin condensation resulting from H2B phosphorylation. Upon treatment with hydrogen peroxide, Ste20p translocates to the nucleus and directly phosphorylates serine 10 of histone 2B, even though there is no apparent nuclear-localization signal present in the kinase.Ste20p is the founding member of a large group of protein kinases known as the p21-activated kinasefamily, which is conserved from yeast to humans. The STE20 homolog in Candida glabrata and Ustilago maydis are required for pathogenicityand mutations in human homolog pak3are associated with the disease X-linked mental retardation-30.