Pho80p is one of 10 cyclins that interact with the cyclin-dependent kinase Pho85p. Pho80p, Pcl6p, Pcl7p, Pcl8p, and Pcl10p belong to the Pho80p subfamily of cyclins, which primarily regulate the response to nutrient levels and environmental conditions. Pho80p provides the substrate specificity for the Pho85p kinase. Under non-stress conditions, Pho80p-Pho85p phosphorylates key regulators of genes that are necessary for survival under stress. Phosphorylation prevents the translocation of these regulatorsto the nucleus, thus repressing their activity.Pho80p-Pho85p plays a central role in regulating the response to phosphate limitation. Under high phosphate conditions, Pho80p-Pho85p phosphorylates the transcription factor Pho4p, preventing its localization to the nucleus. Under low phosphate conditions, Pho80-Pho85p is inactivated by the CDK inhibitorPho81p as well as by the small molecule inositol heptakisphosphate. Inactivation of Pho80p-Pho85p allows an unphosphorylated Pho4p to translocate to the nucleus and activate the transcription of genes involved in phosphate uptake and storage. Because Pho80p-Pho85p regulates Pho4p, which in turn regulates genes required for phosphate storage in the vacuole, pho80 mutants have vacuolar morphology and inheritance defects.In addition to Pho4p, other substrates of Pho80p-Pho85p are involved in regulating the response to nutrient levels and environmental conditions. Pho80p-Pho85p phosphorylates Rim15p, a key protein kinase controlling the entry into stationary phase, suggesting that phosphate levels influence the decision to enter G0. In the absence of stress conditions that activate calcium signalling, Crz1p is phosphorylated by Pho80p-Pho85p, preventing its nuclear localization and activation of genes necessary for the stress response. In addition, Pho81p and Pho80p-Pho85p appear to effect the expression of stress response genes controlled by post-diauxic shift independent of their role in regulating Pho4p localization.Pho80p is phosphorylated by Pho85p; this phosphorylation is necessary for its function. Pho80p is a stable protein, with a half-life of more than 30 minutes.