In S. cerevisiae, growth and metabolism in response to nutrients, particularly glucose, is regulated to a large degree by the Ras/cyclic AMPpathway. cAMP is synthesized by the Cyr1p adenylate cyclase, which is activated by the Ras GTPases, Ras1p and Ras2p. In turn, these Ras proteins are activated by the Cdc25p guanine nucleotide-exchange factor, which stimulates Ras1p and Ras2p exchange of GDP for GTP. Through its role in regulating cAMP levels, Cdc25p is involved in the processes of fermentative growth, nonfermentative growth, cell cycling, sporulation, and cell size regulation. CDC25 encodes a 180 kDa plasma membrane-bound protein. The Cdc25p N-terminal domain contains an SH3 motif that binds adenylate cyclase and a cyclin destruction box motif that mediates Cdc25p ubiquitin-dependent degradation. The C-terminal domain includes the catalytic domain and a membrane localization signal. The Cdc25p C-terminus is sufficient for full biological activity and is essential for normal growth and viability. Cdc25p is able to form homodimers as well as heterodimers with Sdc25p, another S. cerevisiae Ras-GEF. Mutational analysis suggests that Cdc25p intra- and inter-molecular interactions may be involved in regulation of Cdc25p activity.Cdc25p is also regulated by glucose; the presence of glucose in the media results in Cdc25p phosphorylation, which causes decreased protein association with membranes and decreased interaction with the Ras-GTPases. Mutation of potentially phosphorylated residues in this region leads to changes in the cellular response to glucose. Additionally, when glucose is replaced by a nonfermentable carbon source such as ethanol, overall levels of Cdc25p decrease slightly. Unrelated to carbon source, protein levels also drop when cells are exposed to various stresses such as heat and ethanol shocks and oxidative stress. Deletion of CDC25 is lethal in some S. cerevisiae strains, but null mutants can be rescued by overexpression of SDC25. In the W303 strain background, Cdc25p activity is not necessary for growth in glucose but essential for growth in galactose and non-fermentable carbon sources. While the noncatalytic N-terminal domain of Cdc25p shares no similarity with proteins from other organisms, the C-terminal domain is homologous to the catalytic domain of many Ras-GEFs. Cdc25p homologs include murine Cdc25Mm, Drosophila Sos, and human RASGRF1and SOS1.