Cdc28 is the catalytic subunit of the main cell cycle cyclin-dependent kinase. Homologs include CDK1 in animals and cdc2 in S. pombe. Waves of CDK activity drive events of the cell cycle through phosphorylation of key substrates. To accomplish these waves of activity, Cdc28p associates with different regulators throughout the cell cycle. The expression of several of these regulators is periodic which serves to limit their window of action to the proper time in the cell cycle.The first wave of CDK activity occurs when Cdc28p associates with G1 cyclins and Cks1p. The G1 cyclins are Cln1p, Cln2p, and Cln3p. Cln3p/Cdc28p activity is required for setting the size threshold at which cells pass through START. Once committed Cln3p/Cdc28p inactivates a repressor of G1 transcription, Whi5p, which in turn leads to active SBFand MBF, transcription factors that promote transcription of CLN1, CLN2, and genes required for S-phase. Cln1p and Cln2p are important for initiating polarized growth at the site of bud emergence, promoting spindle pole bodyduplication and inhibiting Sic1p and Cdh1p, two CDK inhibitors. During G1, Sic1p binds and inhibits the growing pool of Cdc28p/B-type cyclin complexes. Towards the end of G1, Cdc28p/Cln1p and Cdc28p/Cln2p complexes phosphorylate Sic1p and target it for degradation.. The absence of Sic1p allows a wave of CDK/B-cyclin activity that drives DNA replication and entry into mitosis.B-type cyclins Clb1p, Clb2p, Clb3p, Clb4p, Clb5p, and Clb6p regulate Cdc28p during S, G2, and M phases. Cdc28p association with Clb5p and Clb6p drives DNA replication. Association with Clb3p, Clb4p, and Clb5p promotes maturation and separation of spindle pole bodies, and proper spindle segregationwhile Cdc28p association with Clb2ppromotes entry into mitosis and triggers a switch in bud growth from polarized to isotropic. The metaphase to anaphase transition occurs when securin, an inhibitor of DNA segregation is destroyed by the proteosome. Mitotic CDK activity is required to target Pds1p for degradation by directly phosphorylating Pds1p and activating the Anaphase Promoting Complex/Cyclosome..Once DNA is segregated, exit from mitosisrequires that mitotic CDK activity be turned off. This is accomplished by degradation of mitotic cyclins and inhibition of remaining mitotic activity by Sic1p. In the absence of mitotic CDK activity, G1 cyclins can once again accumulate.In addition to being regulated by binding partners, Cdc28p is regulated by post-translational modifications. Cak1p phosphorylation of Cdc28p on threonine 169 is essential for CDK activity and is thought to precede cyclin binding. Phosphorylation of Cdc28p on tyrosine 19by Swe1p kinaseinhibits mitotic CDK activity and hence, entry into mitosis. This phosphorylation is removed by the phosphatase Mih1p. Phosphorylation of Y19 is critical for enforcing the morphogenesis checkpoint. When cells experience an environmental perturbation that disrupts bud formation, the morphogenesis checkpoint delays entry into mitosis until a bud is formed. The checkpoint impinges on Swe1p and Mih1p to inactivate the mitotic CDK, insuring that mitosis does not occur in an unbudded cell. Unlike in S. pombe and metazoans, Swe1p and/or Mih1p are not direct targets of the spindle checkpointsor DNA checkpoints.Developmental programs such as mating, meiosis and sporulation, and pseudohyphal growth require alterations in cell cycle control. For example, during mating, pheromone-dependent inhibition of Cln/Cdc28p complexes by Far1p arrests cells in G1 so cell-cell fusion can occur. When sporulation is induced, cells enter meiosis from G1, but CLN1 and CLN2 are repressed by a mechanism that makes meiosis and mitosis incompatible.