SIC1 encodes a cyclin-dependent kinase inhibitorthat regulates the cell cycle at the G1 to S transition by inhibiting the activity of the cyclin-dependent kinaseCdc28p. Sic1p is a potent inhibitor of the cyclin-CDK complexes containing a B-typebut not a G1cyclin. Cells are able to overcome this inhibition and enter S phase by phosphorylating Sic1p and targeting it for degradation via the ubiquitin-mediated proteolysis pathway. Cdc28p is able to phosphorylate Sic1p when complexed with a Cln, thus contributing to the alleviation of its own inhibition. The phosphorylation state of Sic1p is also regulated by other kinases which include Pho85p, casein kinase II, Ime2p, Hog1pas well as by phosphatases such as Dcr2pand Cdc14p. Once Sic1p is phosphorylated on a minimum of six of its nine potential phosphorylation sites, it becomes targeted for degradation. Phosphorylated Sic1p is bound by Cdc4p, which is the substrate recognition subunit of the E3 ligase, SCF-Cdc4. In conjunction with the E2 enzyme Cdc34p, SCF-Cdc4 polyubiquitinates Sic1p on N-terminal residues. Ubc4p can also serve as an E2 for Sic1p in vitro. Once it is ubiquitinated, the polyubiquitin-binding protein Rpn10p targets Sic1p to the 26S proteasome for degradation. The proteins Yrb1p and Rad23p are also required for the efficient degradation of Sic1p.Sic1p is an intrinsically disordered protein that can be found in both the cytoplasm and nucleus. Subcellular localization of the protein is regulated by carbon source. SIC1 is expressed during late mitosis and its transcriptional upregulation is dependent on the transcription factor Swi5p. Overexpression of SIC1 results in cells with elongated budsand sic1 null mutants frequently arrest as large-budded cells, have an extended S phase, and inefficiently segregate sister chromatids which leads to genomic instability. In addition to being a key cell cycle regulator during G1/S, Sic1p also is involved in regulating exit from mitosis and the process of autophagy. Fungal homologs of SIC1 are present in C. albicans and S. pombe. Although lacking sequence similarity, Sic1p is functionally and structurally related to the mammalian Cdk inhibitor Kip1/p27.