Microtubules are conserved cytoskeletal elements that form by the polymerization of alpha- and beta-tubulin heterodimers. The formation of polymerization-competent alpha- and beta-tubulin heterodimers requires that alpha-tubulin and beta-tubulin be properly folded. Specific cofactors are required for the folding of alpha- and beta-tubulin in vitro and homologs of these cofactors have been found in numerous organisms, including S.cerevisiae. CIN4 is a non-essential gene that encodes a small GTPase of the ras superfamily, ADP-ribosylation factorsubfamily. The human homolog of CIN4, Arl2, has been shown to regulate the activity of the post-chaperonin tubulin folding pathway, in part by decreasing the affinity of cofactor Dfor native tubulin. By analogy, CIN4 may play a similar regulatory role in the yeast cofactor pathway, as it genetically interacts with several of the yeast tubulin cofactors, and interacts in the two-hybrid assay with Cin2p/cofactor C. CIN4 was isolated in a genetic screen for mutants that display super-sensitivity to benomyl, a microtubule-depolymerizing drug, and was independently isolated in a genetic screen for elevated chromosome loss. cin4 null mutants are cold-sensitive, show synthetic phenotypes in combination with tubulin mutantsand have defects in nuclear migration and nuclear fusion.