SIR4 is one of four Silent Information Regulator genes in budding yeast. Sir4p participates in silencing the cryptic mating type loci HML and HMR, and helps maintain a repressed chromatin structure near telomeres. Unlike repressors that act by binding to promoters, the Sir proteins help repress transcription by creating a silent chromatin stucture in a gene- and promoter-independent manner. The Sir proteins do not bind DNA directly, but rather seem to act via histones and other DNA binding proteins. The exact means by which the Sir proteins create a silenced domain is unknown. Silencing at HML and HMR depends on the presence of a regulatory chromosomal domain that binds multifunctional nuclear proteins such as Rap1p, Abf1p, and the Origin Recognition Complex; these proteins help recruit silencing-specific proteins Sir1p, Sir2p, Sir3p, and Sir4p. Sir4p seems to act in the maintenance rather than the initiation of silencing at HML and HMR. Genetic and physical interactions between Sir2p and Sir4p, Sir3p and Sir4p, and Rap1p and Sir4p have been detected. These four proteins act together at telomeres to create a repressed heterochromatin structure. Sir4p has also been shown to interact with histones H3 and H4, consistent with its role in shaping the architecture of the chromatin at HML, HMR, and telomeres. Sir4p seems to play a role in the aging of yeast cells. An allele of SIR4 was found that extends the life span of yeast. In strains with this SIR4 allele, Sir3p and Sir4p are redirected to the nucleolus rather than telomeres. Mutations in SIR4 that lead to a longer life span also result in enhanced rDNA silencing. It may be that the lengthening of life span is due to the prevention of formation of extrachromosomal rDNA circlesthat form through homologous recombination within rDNA arrays, which is inhibited when the rDNA is silenced. A functional homolog of Sir4p exists in Kluveromyces lactis.