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Cloning and Characterization of cos Mutants Involved in the Cell Cycle Progression and Regulation in *Saccharomyces cerevisiae*

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Eukaryotic chromosomal DNA is replicated exactly once in the S phase of the cell cycle. This is regulated mainly in the initiation step of DNA replication. To understand the mechanisms which control the initiation of DNA synthesis in the cell cycle, we isolated the mutants sensitive to ciclopirox olamine (CPO) which inhibits the cell cycle progression at the G1/S phase. In a screen for CPO sensitivity, we have isolated12 mutants and named them *cos* (*c*iclopirox *o*lamine *s*ensitive; *cos1*~*cos12*) mutants. We determined the sensitivity to hydroxyurea (HU) and methylmethane sulfonate (MMS) of these mutants and subjected them to FACScan analysis to identify their arrest points in the cell cycle. In further analysis, we determined the stable plasmid maintenance in these mutants. Interestingly, the plasmid stability in the *cos11* mutant was decreased. According to these phenotypes, we separated these mutants into three groups as follows : Group I mutants (*cos1, cos3, cos4, cos8*) showed HU and MMS sensitivities and we think these mutants have a role at a checkpoint pathway during the G1, G2 and/or S-phase. GroupII mutant (*cos11*) appeared to be HU and MMS sensitivities, and plasmid loss rate was increased in this mutant. Moreover, plasmid containing one ARS, pDK243, is lost at greater rates than plasmid containing seven ARSs, pDK368-7. This result suggests that *cos11*mutant has a defect in the initiation of DNA replication. Group III mutants (*cos2, cos5, cos6, cos7, cos9, cos10, cos12*) are independent from the cell cycle because they showed the CPO sensitivity only. To further understand these mutants, the genes which complement the *cos3*, *cos*11, *cos*12 mutants were cloned and sequenced. We will report on the characterization of cos mutants and their genes involved in the cell cycle progression.