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学 位 論 文 要 旨
SUMMARY OF DOCTORAL THESIS

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題目 Title: **Analysis of *moc* genes function in *Schizosaccharomyces pombe***

Summary

Meiotic differentiation and the cell growth is mutually exclusive program, and in *S. pombe* this switch between growth and meiosis is controlled by nutrition signals. One of the major signaling pathways that mediate nutritional controls on meiotic initiation is cAMP pathway. Adenylyl cyclase, encoded by the *cyr1* gene, generates cAMP from ATP; trimeric G proteins (Gpa2, Git5, Git11) control the activity of adenylyl cyclase through a nutrient-sensing mechanism of the Git3 receptor; adenylyl cyclase associated protein (Cap1) involves in regulation of Cyr1; and cAMP phosphodiesterase (Pde1) down regulates the cAMP pathway by converting cAMP to AMP.

When nutrient conditions are altered, the *S. pombe* cells are arrested in the G1 phase then the opposite mating types mate, initiate conjugation and subsequently form zygotes. Four genes, *moc1-moc4* (multicopy suppressor of overexpressed *cyr1*) that could bypass the sterility phenotype of the *S. pombe* due to an elevation of cAMP, had been screened out. Moc1/Sds23 and Moc2/Ded1 are known to be a potential regulator of M-phase progression and an essential RNA helicase, respectively. Moc3 (SPAC821.07c) is completely a novel protein containing a Zn-finger (Zn(2)-Cys(6)) motif and Moc4 is found to be identical with a Zn-finger protein Zfs1.

In Chapter 2, it has been described that the strength of inducing ability of sexual development in the same *S. pombe* strain, Moc1 is highest, Moc2 is lowest, and both Moc3 and Moc4 are intermediate inducing abilities. It has observed that the deletion mutant of the *S. pombe moc3* gene is lower in mating rates and forms aberrant asci. In addition, a *moc3* disruptant is sensitive to $CaCl_2$ and DNA damaging agent such as MMS and UV. Those phenotypes are opposing to the phenotypes observe in a *zfs1* disruptant, and quite different from the ones in a *moc1* disruptant. Moc3 localized in the nucleus as observed in Zfs1. Only Moc3 binds with Moc4/Zfs1 weakly in a two-hybrid system, but no other combination of Moc(s) bind each other. Thus, Moc3 is not only involved in sexual development, but also in ascus formation and DNA integrity in an independent manner with Moc1 and Moc2 in *S. pombe* so far studied.

In Chapter 3, functional conservation between *S. pombe moc1/sds23* and its two orthologs *SDS23* and *SDS24* in *Saccharomyces cerevisiae* had been studied. The phenotype of *moc1* disruptant in *S. pombe* are known as longer in cell shape than wild type, partially sterile and sensitive to higher concentration of salt as well as sensitive to higher and lower temperature. These phenotype could be recovered by expressing either

S. cerevisiae SDS23 or *SDS24* which has sequence similarity in amino acids level with *S. pombe moc1/sds23*. Deletion of both *SDS23* and *SDS24* results in producing a large vacuole in *S. cerevisiae* cell that is also reversed by the expression of *S. pombe moc1/sds23*. By these ways it has been noted that *S. pombe* Moc1/Sds23 and *S. cerevisiae* SDS23p or SDS24p are functional homologs. In addition the Δ*sds23* Δ*sds24* diploid strain reduces cell separation in forming pseudohyphal like growth in *S. cerevisiae*. This kind of morphological switch is usual in fungal pathogenesis. In conclusion, the *S. pombe moc1/sds23* and *S. cerevisiae SDS23* or *SDS24* are interchangeable each other but their disruptants are phenotypically dissimilar which is known till to date.

In this thesis, I characterized the fission yeast *moc1* and *moc3* genes and *moc1* orthologs in budding yeast. Although *moc1* and *moc3* genes were expected to play roles in antagonizing the cAMP signaling pathway, the analysis presented in this thesis rather indicated that both genes are involved in multiple cellular events including sexual development, cell morphology and stress response.