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ISOLATION AND CHARACTERIZATION OF FISSION YEAST GENES INVOLVED IN TRANSCRIPTION REGULATION OF CELL CYCLE EVENTS

(A SHORT COMMUNICATION)

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Previous efforts in understanding cell cycle controls were focussed on regulatory molecules that drive the cell through different phases of cell division. As a consequence, the major regulatory pathways that transit the cell from G1 to S and from G2 to M phases are presently known [1]. Recently, partly because the genome-wide transcription analysis became available, a great deal of interest was generated to understand how genes are regulated during cell division. Yeasts, as model organisms of cell cycle research which have contributed to the discovery of cell cycle regulatory pathways, also play a key role in understanding gene expression during cell cycle.

Because of its mode of cell division, which is highly similar to the mammalian cell division, the fission yeast *Schizosaccharomyces pombe* has become one of the two crucial yeast model organisms to study the control of cell cycle. Its cylindrical cells grow at their tips and divide by medial fission. Several stages of its cell cycle were studied during the course of decades of research. Thus, considerable amount of information has been accumulated about the regulatory pathways leading to mitosis and about the molecules guiding the cell to exit from mitosis [2]. Recently, a key pathway was also discovered which regulates the physical division of daughter cells at the end of cell cycle [3].

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However, little is known about the regulation of gene expression during cell cycle, although it is believed that a large number of genes are expressed in a cell cycle dependent manner. Recently, from the investigation of the other yeast model, *S. cerevisiae*, using the powerful DNA microarray approach, some knowledge were added [4], supporting the view that large regulatory units might exist in eukaryotes, and play a key role in the correct execution of different cell cycle events.

To gain more information on gene expression regulation during cell division in the fission yeast, a mutagenesis screen was carried out in the hope to find regulators of cell cycle events. A large number of mutants were isolated and subjected to further analysis. The majority of them exhibited complex phenotypic characteristics, including defects in cytokinesis, mitosis and even in sexual differentiation, suggesting that multifunctional regulators might be defective in the mutants. As the mutations primarily affected cell separation, they were named *sep* (separation) mutants [5].

To elucidate the molecular function of the *sep* genes, a cloning program was initiated. Until now, five *sep* genes were cloned, all of them were putative regulators of transcription.

Sep1, the first gene cloned, encodes a sequence specific transcription factor of the fork-head family, the majority of those involved in development and differentiation of higher eukaryotes [6]. Sep1 is a nuclear protein in accordance with its function [7].

Sep9 encodes a homologue of SPT8 [8], a subunit of the *S. cerevisiae* SAGA-complex [9], which functions as a guide in helping to remodel the chromatin structure prior to transcription.

Sep10 is a conservative protein that shows strong homology to proteins from a number of higher eukaryotes, including human, worm and fruit fly, and possibly involved in a transcription complex [10]. *Sep15* [11] and *sep11* [10] are also members of a transcription complex, named as mediator complex. This complex has been conserved in structure during evolution, and functions in the regulation of genes required for development, differentiation and cell cycle, although little is known about its targets and mechanism of action [12].

With the exception of *sep15*, none of the genes is essential for normal growth, but some of the combinations of deletions cause lethality, suggesting overlapping functions. *Sep9*, *sep10* and *sep11* seem to be involved in the activation of regulation of differentiation and possibly also exhibit other regulatory roles.

The current data available suggest a common and interacting role for the *sep* family of genes, which might form a regulatory unit that connects a variety of signals to the transcription machinery in order to coordinate the regulation of genes throughout cell cycle and differentiation.

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