Comparative Analysis of Transcriptional Regulation in Eukaryotic Cell Cycles

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1 Introduction

Microarray technology for global analysis of transcriptional regulation has been developed to offer functional genomics in the post-genome era. This methodology has also been applied to temporal transcriptional dynamics, including cell cycle regulation. Although the cell cycle regulations of eukaryote and prokaryote were individually analyzed, comparative analysis of them has not been accomplished and hence universal genes and processes regarding cell cycles have not been elucidated yet. Here, we analyzed gene expression profiles of the cell cycles over three eukaryotic species to elucidate the common cell cycle regulated genes and processes. Cell cycle regulated genes were extracted from each species and their orthologous relationships were analyzed using KEGG/OC(OrthologCluster). Then we analyzed the common processes associated with cell cycles for each species. Evolution of central programs in the eukaryotic cell cycles is discussed.

2 Method and Results

2.1 Extraction of cell cycle regulated genes

Gene expression profiles of cell cycles of *S.cerevisiae*, *H.sapiens*, and *A.thaliana* were obtained from published papers [1,2,3]. We used the expression profiles of seven time series experiments; three experiments from *S.cerevisiae*, three from *H.sapiens*, and one from *A.thaliana*. Periodically expressed genes within the cell cycles were extracted as cell cycle regulated genes, by applying Fourier Analysis described in [4] to the expression profiles. As for *S.cerevisiae* and *H.sapiens*, we selected the genes, which are extracted from more than one experiment, for further analysis. This yielded 857 *S.cerevisiae* genes and 426 *H.sapiens* genes. For *A.thaliana*, we used all the extracted 1841 genes in the experiment.

2.2 Analysis of orthologous relationships between cell cycle regulated genes

We observed orthologous relationships between the cell cycle regulated genes in each species using KEGG/OC(OrthologCluster) [5,6], which assigns an orthologous identifier to each gene with sequence similarities stored in KEGG/SSDB [6]. We found common genes including 90 *S.cerevisiae* genes, 71 *H.sapien*s genes, and 180 *A.thaliana* genes (Figure 1).

2.3 Cell cycle regulated processes in each species

We also analyzed cell cycle regulated processes in each species. We assigned MIPS functional category [7,8] to cell cycle regulated genes of each species, and transformed the numbers of the genes in each category to Z-scores, by comparing with randomly extracted genes of the same number. In this analysis, we used annotations of MIPS/CYGD [7] for *S.cerevisiae* and MIPS/MAtDB [8] for *A.thaliana*, and we compiled classification for *H.sapiens* by assigning the categories to genes with sequence similarities stored in KEGG/SSDB [6]. Figure 2 shows the Z-scores of the functional categories of *A.thaliana* and *H.sapiens*.

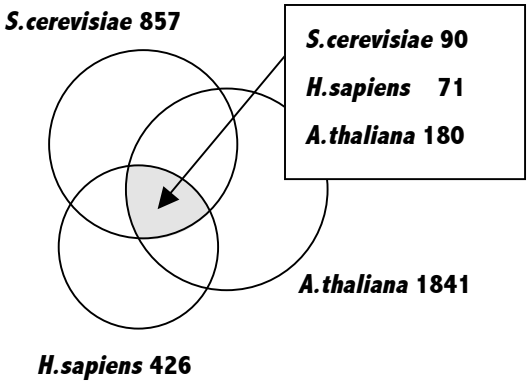

Figure1. The number of the cell cycle regulated genes in each species is shown with each circle. The numbers of the common genes between them extracted by using KEGG/OC were shown in the box.

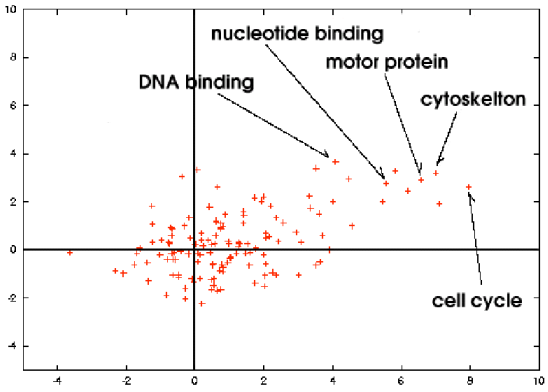

Figure2. Each plot represents a MIPS functional category. Z-score of the number of the cell cycle regulated genes in each category is plotted for *A.thaliana* (horizontal axes) versus *H.sapiens* (vertical axes).

3 Discussions

The common cell cycle regulated genes include checkpoint proteins and DNA metabolism proteins, which are basic cell cycle regulators and effectors. This result confirms evolutionary conservation of cell cycle regulation over eukaryotic species. In addition, vesicle-mediated transporters and mitochondrial transporters are also included in the result, showing that these genes are new candidates for universal cell cycle regulators and effectors. Furthermore, we obtained cytoskeleton, motor proteins, etc. as the common processes. These processes are evolutionary conserved as central programs of the cell cycles. This analysis will serve the basis of comprehensive view for evolution of transcriptional regulation of eukaryotic cell cycles.

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