

# Comparative Analysis of Conditional Regulation Across the Yeast Genomes

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## 1 Introduction

Biological processes are driven by complex genomic regulation which is known to be flexible across species. Cross-species comparison of gene regulation aids in the understanding of such regulatory plasticity. Here, we analyzed the transcriptional regulation of the yeast genomes, *S.cerevisiae* and *S.pombe* under biologically identical conditions. We compared genes whose transcription is regulated in stress response, mitosis, and meiosis of the yeasts. Shared and unshared regulated genes across two yeast genomes were detected, and the numbers of the shared genes were evaluated under each condition. Stress-repression of expression is strongly conserved in orthologous genes, which may reflect the negative selection on the gene regulation under the survival condition. On the other hand, gene regulation in meiosis is not conserved, which may reflect regulatory optimization for proliferation.

## 2 Method and Results

### 2.1 Genes with conditional regulation

We extracted genes with conditional regulation under each of the conditions of stress response, mitosis, and meiosis.

#### 1. Stress-induced (S-I), stress-repressed (S-R) genes

Gene expression profiles of stress response of *S.cerevisiae* and *S.pombe* were obtained from the literature [1,3]. Expression profiles with identical stress conditions were selected (hydrogen peroxide, heat shock, MMS stress, and sorbitol osmotic shock). Genes with  $\geq$  four-fold change were extracted as S-I genes. Similar processes were conducted with  $\leq$  1/4-fold change for S-R genes.

#### 2. Periodically transcribed genes within mitosis (Mi genes)

Gene expression profiles of mitosis were obtained from the literature [6,8]. Periodically transcribed genes within the mitotic cycle were extracted as Mi genes by applying the Fourier Analysis described in [7].

#### 3. Meiosis-induced (Me-I) and meiosis-repressed (Me-R) genes

Gene expression profiles of meiosis were obtained from the literature [2,4]. Genes with  $\geq$  four-fold change were extracted as Me-I genes. Similar processes were conducted with  $\leq$  1/4-fold change for Me-R genes.

### 2.2 Comparative analysis of gene regulation across species with orthologous information

We compared the transcriptional regulation of orthologous genes over two yeast species. Orthologous relationships were extracted from reciprocal best hits based on KEGG/SSDB [10]. Such relationships are explored in each gene subset across the two species. To evaluate their significance of overlap, their numbers expected by chance and their Z-scores are obtained by randomizing orthologous relationships (Figure 1).

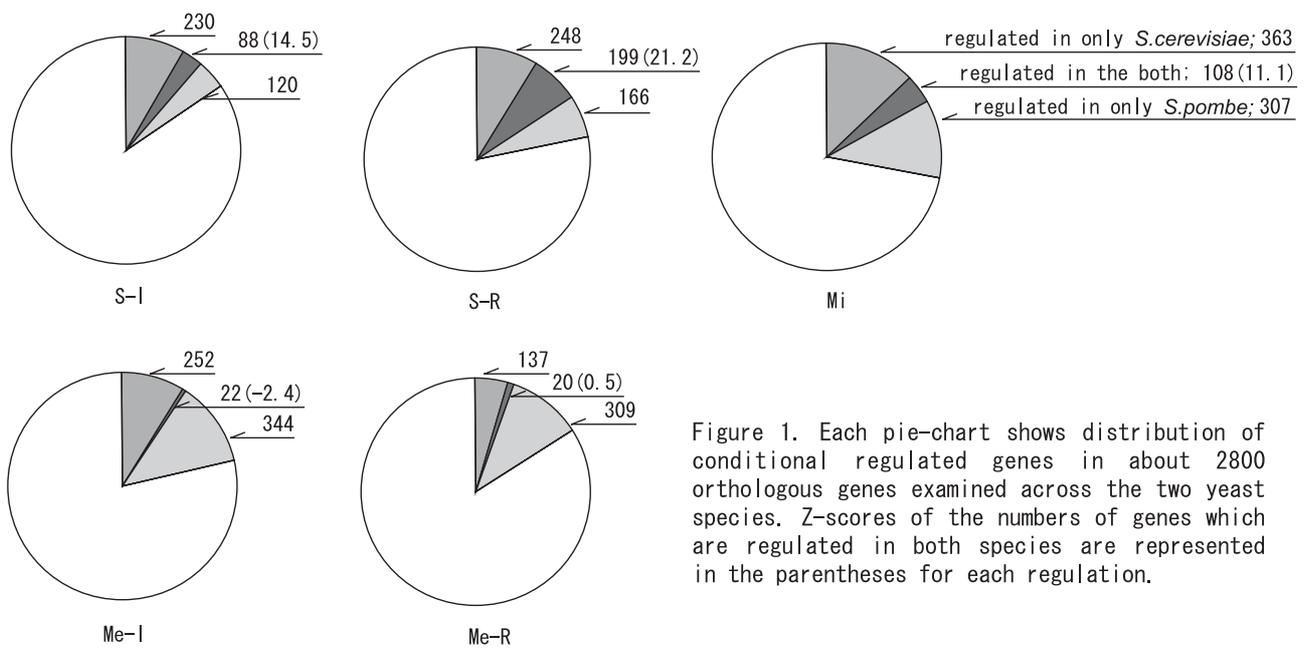


Figure 1. Each pie-chart shows distribution of conditional regulated genes in about 2800 orthologous genes examined across the two yeast species. Z-scores of the numbers of genes which are regulated in both species are represented in the parentheses for each regulation.

### 3 Discussion

Although many studies have reported selective forces within protein sequence conservation or divergence, a few studies have reported selective forces for gene regulation as a possibility for a general cause of conservation or divergence in gene regulation [5]. We found relatively strong conservation in S-I and S-R transcription, which may reflect negative selection on gene regulation under survival conditions. Weak conservation in Me-I and Me-R transcription may reflect positive selection for the optimization of proliferation. Such positive selection is recognized as the cause of the divergence of many eukaryotic reproductive protein sequences [9], which makes this a candidate as a contributor to the weak conservation of regulation in meiosis.

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