Whole-genome expression analysis of snf/swi mutants of Saccharomyces cerevisiae

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The Saccharomyces cerevisiae Snf/Swi complex has been previously demonstrated to control transcription and chromatin structure of particular genes in vivo and to remodel nucleosomes in vitro. We have performed whole-genome expression analysis, using DNA microarrays, to study mutants deleted for a gene encoding one conserved (Snf2) or one unconserved (Swi1) Snf/Swi component. This analysis was performed on cells grown in both rich and minimal media. The microarray results, combined with Northern blot, computational, and genetic analyses, show that snf2Δ and swi1Δ mutations cause similar effects on mRNA levels, that Snf/Swi controls some genes differently in rich and minimal media, and that Snf/Swi control is exerted at the level of individual genes rather than over larger chromosomal domains. In addition, this work shows that Snf/Swi controls mRNA levels of MATα-specific genes, likely via controlling transcription of the regulators MATα1 and MCM1. Finally, we provide evidence that Snf/Swi acts both as an activator and as a repressor of transcription, and that neither mode of control is an indirect effect of the other.

There is substantial evidence that the structure and position of nucleosomes can control transcription in eukaryotes. Both in vivo and in vitro experiments have shown that nucleosomes can cause repression of transcription by blocking transcription factor binding (1). In recent years, several studies have shown that the conserved protein complex, Snf/Swi, can relieve this repression by perturbing the structure of nucleosomes (2). This remodeling probably allows transcription factors to bind to their sites, facilitating transcription initiation. Since the discovery of the Snf/Swi complex, other classes of nucleosome remodeling complexes have been discovered throughout eukaryotes (3, 4), suggesting that nucleosome remodeling is a general mechanism for controlling transcription in vivo.

Several studies in Saccharomyces cerevisiae have demonstrated that Snf/Swi is required for the normal transcription of only a subset of genes. First, although snf/swi mutants exhibit many mutant phenotypes, including poor growth, the inability to use particular carbon sources, and a defect in sporulation, Snf/Swi is not required for viability (3). Second, Northern blot analyses have demonstrated transcriptional defects at merely a handful of genes (5). Finally, a recent study of the expression of all S. cerevisiae genes in a snf2 mutant demonstrated that only a small percentage of mRNAs have altered levels when cells are grown in rich medium (6). The requirement for Snf/Swi in S. cerevisiae cells grown in less nutritious media has not been examined.

Snf/Swi is a multiprotein complex, and the roles of the different members of the complex are not well understood. Among the Snf/Swi complexes studied in S. cerevisiae, human, and Drosophila, only a subset of Snf/Swi proteins are conserved, including Snf2/Swi2, Snf5/Sc3, and Swp73 (1). All of the Snf/Swi complexes have been demonstrated to possess ATP-dependent nucleosome remodeling activity in vitro (7–9). Three of the conserved subunits in the human Snf/Swi complex have been demonstrated to constitute a “core” set of Snf/Swi factors (10). This core complex, which includes Snf2/BRG1, a DNA-dependent ATPase, Snf5/IN1, and Swi3/BAF155/BAF170, can carry out nucleosome remodeling activity in the absence any other Snf/Swi component. The other Snf/Swi subunits could be required for nucleosome remodeling activity in vivo or for other unknown aspects of Snf/Swi activity, such as response to signals or interactions with transcriptional regulators.

The factors that determine the dependence of a gene on Snf/Swi are not understood. Several studies have indicated that Snf/Swi may be targeted to particular promoters by physical interactions with specific transcriptional activators or repressors (11–18). However, it seems likely that such interactions cannot be the sole determinants of Snf/Swi-dependence. For example, Pho4 activates both PHO5 and PHO8, yet PHO5 transcription is Snf/Swi-independent whereas PHO8 transcription is Snf/Swi-dependent (19). Other factors, such as a particular chromatin structure (3) or promoter strength (20), may also play a role in determining Snf/Swi action. In addition, Snf/Swi-control could be exerted at the level of chromosomal domains rather than specific genes. This model predicts that the genomic location of a gene would influence its dependence on Snf/Swi.

Recent studies have suggested that, in addition to its role in transcriptional activation, Snf/Swi may also play a role in transcriptional repression. This idea has come from a combination of gene expression studies (21–24), biochemical analysis of nucleosome remodeling by human Snf/Swi (25) and the Snf/Swi-related S. cerevisiae complex, RSC (26), and from whole-genome expression studies (6). It is unclear whether Snf/Swi-mediated repression is a direct or indirect effect of Snf/Swi activity and whether it involves nucleosome remodeling.

Therefore, several fundamental issues remain unresolved concerning Snf/Swi function. The introduction of methods to measure the mRNA levels for every S. cerevisiae gene (27) has provided the tools to answer some of these questions. We have used whole-genome DNA microarrays to identify the entire set of S. cerevisiae genes dependent on two subunits of the complex, Snf2 and Swi1. Using two different media conditions, we have identified several genes by microarray and subsequent Northern blot analyses that are good candidates for being directly controlled by Snf/Swi. One of these genes is the essential gene MCM1, the yeast homologue of human serum response factor (28). Our studies also show that Snf/Swi-dependent genes are scattered throughout the genome, indicating that Snf/Swi controls transcription at the level of individual genes and not at the level of chromosomal domains. Finally, we provide further evidence that Snf/Swi is required for transcriptional repression at some genes, and our genetic analysis strongly suggests that this repression is not an indirect effect of Snf/Swi activation.

Materials and Methods

Yeast Strains and Methods. S. cerevisiae strains are isogenic to S288C (29) and were constructed by standard methods (30).

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They are FY2 (MATa ura3-52), FY20 (MATa ura3-52), FY31 (MATa ura3-52 hisΔ200 snf2Δ1::HIS3), FY32 (MATa ura3-52 hisΔ200 snf2Δ1::HIS3), FY57 (MATa ura3-52 his4-9126 lys2-1288), FY458 (MATa ura3-52 his4-9126 lys2-1288 hisΔ3200 snf2Δ1::HIS3), FY710 (MATa ura3-52 leu2Δ1 his4-9126 lys2-1288 (hta1-hbh1)Δ1::LEU2), FY724 (MATa ura3-52 leu2Δ1 his4-9126 lys2-1288 (hta1-hbh1)Δ1::LEU2 snf2Δ1::HIS3), FY1254 (MATa ura3-52 hisΔ3200 lys2-1288 leu2Δ1 swi1Δ1::LEU2), FY1357 (MATa ura3-52 arg4-12 lys2-173RII leu2Δ1 snf2Δ1::LEU2), FY1882 (MATa ura3-52 leu2Δ1 swi1Δ1::LEU2), FY1885 (MATa ura3-52 leu2Δ1 (hta1-hbh1)Δ1::LEU2), FY1885 (MATa ura3-52 leu2Δ1 (hta1-hbh1)Δ1::LEU2 snf2Δ1::HIS3).

Microarray Analysis. FY2, FY31, and FY1882 were grown in rich medium (yeast extract/peptone/dextrose containing 2% glucose) or in synthetic minimal medium (yeast nitrogen base without amino acids plus ammonium sulfate), supplemented with uracil and 2% glucose, to a cell density of 1–2 × 10⁷ cells/ml (30). Total RNA was prepared by using hot phenol extraction (31). poly(A)+ RNA was prepared by using Oligotex resin from Qiagen (Chatsworth, CA). Microarray analysis of poly(A)+ RNA was carried out as described (27). cDNA made from poly(A)+ RNA from the wild-type strain was fluorescently labeled with Cy5 (represented as red), and that from the mutants was labeled with Cy3 (represented as green). The two labeled cDNA pools were mixed and hybridized simultaneously to a microarray. Each set of hybridizations was performed with an independent RNA preparation. Statistical analyses were carried out using the statistical toolpak software available with Microsoft Excel.

Northern Hybridization Analysis. Strains listed in the figure legends were grown in rich or minimal medium supplemented with appropriate amino acids to 1–2 × 10⁷ cells/ml. RNA was prepared from 10-ml samples and was analyzed (32). The probes used for hybridization were 32P-labeled using primers purchased from Research Genetics (Huntsville, AL) and PCR amplified from pIP45, which contains the SPT15 fragment of S. cerevisiae. The computer programs Multiple EM for Motif Elicitation (MEME) (33) and Aligns Nucleic Acid Conserved Elements (ALIGNACE) (34) were used to search for putative sequence motifs, with 600 bp 5′ of each gene as input. Analyses of genome-wide distributions of promoter orientations and intergenic distances with respect to gene expression in snf2Δ swi1Δ mutants were done with the assistance of B. A. Cohen and R. Mitra (personal communication).

Results

Measurement of mRNA Levels in snf2Δ and swi1Δ Mutants by Microarray Analysis. We have used whole-genome DNA microarrays with the goal of identifying all of the genes in S. cerevisiae that are controlled by the Snf/Swi complex. By this method, the mRNA levels in wild-type and snf2Δ swi1Δ mutant strains were determined for each S. cerevisiae gene, and the results are expressed as ratios of mutant:wild-type mRNA levels. Our microarray analyses included two variables. First, to determine whether loss of two different Snf/Swi subunits causes the same transcriptional defects, we analyzed mRNA levels in both snf2Δ and swi1Δ mutants. Snf2 and Swi1 may have different roles in vivo because Snf2 is a conserved core member of Snf/Swi, capable of carrying out nucleosome remodeling in vivo (10), whereas Swi1 is not conserved and is not required for this core activity in vitro. Second, to determine the requirement for Snf/Swi under two different nutrient conditions, we analyzed expression of strains grown in rich and minimal media. In minimal medium, S. cerevisiae cells induce transcription of several sets of genes, such as those required for amino acid biosynthesis, whereas the expression of those genes is repressed in rich medium (35). Therefore, we reasoned that the requirement for Snf/Swi may differ between the two growth conditions.

Several independent measurements of mRNA levels were performed for cells grown in rich and in minimal medium. The data set and statistical analysis is available at http://genome-www.stanford.edu/swisnf. In addition, Northern hybridization analysis was carried out for several cases of particular interest as described below. Of the ∼6,014 genes tested, ∼1% show greater than a three-fold change in mRNA levels in both snf2Δ and swi1Δ mutants (Fig. 1). In both media conditions, some genes have decreased mRNA levels whereas others have increased mRNA. A similar effect was observed in a previous whole-genome expression study of an snf2 mutant grown in rich media (6). We have analyzed the altered expression in snf2Δ swi1Δ mutants by several criteria as described in the following sections.

We examined the list of genes affected in snf2Δ swi1Δ mutants to learn of possible additional mutant phenotypes. We noticed that HAP4, which encodes a factor that controls the transcription of genes required for lactate utilization (36), has five-fold reduced mRNA levels in both snf2Δ and swi1Δ mutants (Fig. 1). In both media conditions, some genes have decreased mRNA levels whereas others have increased mRNA. A similar effect was observed in a previous whole-genome expression study of an snf2 mutant grown in rich media (6). We have analyzed the altered expression in snf2Δ swi1Δ mutants by several criteria as described in the following sections.

Snf2 and Swi1 Are Likely Required for Transcription of the Same Genes in Vivo. Based on the microarray analysis, loss of Snf2 or Swi1 causes similar changes in mRNA levels (Fig. 1). The small number of differences observed could be caused either by variation in the microarray measurements or by real differences between snf2Δ and swi1Δ mutants. We studied one of these genes, SER3, in greater detail. By Northern analysis, SER3 mRNA levels are increased 23-fold in snf2Δ and only 8-fold in swi1Δ (Fig. 2A). Thus, although a small number of genes may differ with respect to the magnitude of the effect in either snf2Δ or swi1Δ, most Snf/Swi-regulated genes seem to depend on both subunits of the complex. These results suggest that Swi1 plays as...
import an important role as Snf2 in S. cerevisiae under the conditions tested.

Snf/Swi Dependence Can Differ in Rich and Minimal Media. The microarray analysis revealed that some genes are more strongly Snf/Swi-dependent in one type of medium than the other. For example, genes encoding hexose transporters, HXT1, HXT3, HXT6, HXT7, have decreased mRNA levels only in minimal medium. In contrast, several amino acid biosynthetic genes, particularly several MET and ARG genes, have increased mRNA levels only in rich medium. We performed Northern blot analysis on two genes, SAG1 and SER3, whose Snf/Swi-dependence is affected to different degrees in rich and minimal medium. These results (Fig. 2) verify that SAG1 mRNA levels are more severely decreased in minimal medium compared with rich. SER3 mRNA levels are increased in snf2Δ and more significantly increased in rich medium compared with minimal. Another medium-specific effect is described in the next section.

**Effects on Two Gene Families: The Acid Phosphatase Genes and the** MATα- **Specific Genes Are Snf/Swi-Dependent.** Members of a small number of gene families show changes in mRNA levels in snfΔ/swiΔ mutants. For example, mRNA levels of the inducible genes encoding acid phosphatase (PHO5, PHO11, PHO12) and the high-affinity phosphate permease (PHO84) were decreased 5- to 10-fold in rich medium but were unaffected in minimal medium in which their expression is significantly lower (Table 1; W. Hörz, personal communication). Transcription of the acid phosphatase genes is normally induced in medium with low inorganic phosphate (Pi) levels and is repressed by high Pi levels (38). It has been recently observed in an independent study that the basal transcription of PHO5 that occurs in high Pi depends on Snf/Swi whereas the derepressed levels in low Pi are Snf/Swi-independent (W. Hörz, personal communication). The snf/swi effect on the transcription of these genes is unlikely to be an indirect effect of decreased levels of their transcriptional activators, Pho2 and Pho4, as PHO2 and PHO4 mRNA levels are not altered in snf2Δ and swi1Δ mutants (Table 1). Therefore, our microarray results suggest that Snf/Swi directly controls the promoters of the acid phosphatase genes in rich medium.

A second gene family observed to be Snf/Swi-dependent contains the four known MATα-specific genes, STE3, MFC1, MFC2, and SAG1. By microarray analysis, three of these genes have decreased mRNA levels in snfΔ/swiΔ mutants in rich and minimal media (Table 2). To confirm these results, we measured the mRNA levels for these four genes by Northern blot analyses. These results (Fig. 3; Table 2) are close to those from the microarray analysis. Thus, three members of the MATα-specific gene family are affected by snf2Δ and swi1Δ mutations.

To address whether the Snf/Swi control of MATα-specific genes is direct or indirect, we investigated expression of their three known regulators, MATα1, MCM1, and STE12 (39). These results (Fig. 3B; Table 2) showed that both MATα1 and MCM1 mRNA levels are reduced in snfΔ/swiΔ mutants whereas STE12 mRNA levels are unaffected. MATα1 mRNA levels were decreased approximately three-fold in both snf2Δ and swi1Δ strains compared with the wild type. The expression of MCM1 in snf2Δ and swi1Δ was more complicated. MCM1 has been previously reported to encode three transcripts, 1.0, 1.2, and 1.6 kb in length (40), although the 1.0-kb transcript was not detectable in our
analysis. Interestingly, the 1.2- and 1.6-kb MCM1 transcripts show different Snf/Swi-dependence: the 1.6-kb MCM1 mRNA level is reduced approximately three-fold in snf/swi mutants whereas the 1.2-kb MCM1 mRNA level is unaffected. These results strongly suggest that the MCM1 and the MATa1 promoters are controlled by Snf/Swi and that the decrease in MATa1-specific gene transcription in snf/swi mutants is caused by decreased expression of both MATa1 and MCM1.

Promoter Analysis Reveals No Motifs Common to Snf/Swi-Dependent Genes. Snf/Swi has been shown to possess nonspecific DNA binding activity (41). However, no specific DNA sequence has been shown to confer Snf/Swi-dependence to a promoter. We wanted to determine whether Snf/Swi-dependent promoters had any common sequence motifs. Such motifs could target Snf/Swi to the promoter or could serve as binding sites for a common set of activators. We utilized two sequence analysis programs, MEME (33) and ALIGNACE (34) to analyze promoter sequences. Analysis of promoter sequences from all genes affected in rich medium revealed several motifs that are found upstream of the amino acid biosynthesis genes, like the MET gene family or upstream of some PHO genes (data not shown). However, neither program revealed any other motif that was specifically found in Snf/Swi-dependent genes. These negative results suggest that no single motif confers Snf/Swi-dependence to a promoter.

Transcriptional Control by Snf/Swi Is Gene-Specific. It is not clear whether Snf/Swi regulates transcription of individual genes or whether it exerts control over larger regions ranging from pairs of genes to extensive chromosomal domains. This issue can be addressed by examining the genomic positions of Snf/Swi-dependent genes. A clustering of the affected genes would support the possibility of Snf/Swi-controlled chromosomal domains of expression. Analysis of the positions of genes that show greater than a two-fold change in mRNA level in either swi1Δ or snf2Δ mutants shows that Snf/Swi-dependent genes are spread throughout the genome (http://genomewww.stanford.edu/swisnf) and demonstrate that there are no Snf/Swi-dependent chromosomal domains in the genome under the media conditions examined here.

Although Snf/Swi-dependence appears to be exerted at the level of individual genes, there are a small number of cases in which adjacent genes are both Snf/Swi-dependent. Therefore, we examined whether this co-dependence correlates with either the relative orientation of the two genes—for example, with divergently or convergently transcribed genes—or the distance between the genes. We found no correlation with either the orientation of the genes or the intergenic distance (data not shown). This analysis provides additional evidence that Snf/Swi control is specific to an individual gene and that the impact of its remodeling activity does not spread over the region to affect neighboring genes.

Evidence That Snf/Swi Repression and Activation Occur by Different Mechanisms. One surprising result from whole-genome expression analysis of snf/swi mutants, both from our studies and those previously described (6), is that the mRNA levels for many genes are elevated in snf/swi mutants, particularly in rich medium. In addition to these studies, there was some prior indication of a negative role for Snf/Swi in controlling transription (21–24). The possibility of both positive and negative roles for Snf/Swi in transcription are consistent with recent biochemical results suggesting that Snf/Swi and related nucleosome-remodeling complexes can catalyze nucleosome remodeling from “repressive” to “remodeled” and vice versa (25, 26). However, the expression studies also raise the possibility that some of the effects observed may be indirect. For example, an apparent positive effect of a snf/swi mutation could result from decreased levels of a repressor whose expression is Snf/Swi-dependent.

Previous studies have demonstrated that particular classes of mutations in histone genes—for example, a deletion of one copy of the two H2A-H2B-encoding loci in S. cerevisiae, (hta1-hbt1)Δ—can partially suppress all of the phenotypes of snf/swi mutants, including the decrease in transcription observed at some genes (42). To understand whether the decreased expression of a repressor is responsible for the increased transcription of genes in both snf2Δ and swi1Δ, we analyzed mRNA levels of two genes, SER3 and YOR222W, whose mRNA levels are greatly increased in a snf2Δ mutant. If transcription of these genes is increased indirectly, because of reduced transcription of a repressor in snf/swi mutants, then repressor levels would be restored in the (hta1-hbt1)Δ snf2Δ double mutant and we should observe suppression of this snf/swi effect. However, Northern blot analysis (Fig. 4) demonstrates that the snf/swi effect on both SER3 and YOR222W is not suppressed by the (hta1-hbt1)Δ mutation as they have similar mRNA levels in both snf2Δ and (hta1-hbt1)Δ snf2Δ strains. Because the (hta1-hbt1)Δ mutation usually suppresses all of the known activation defects in snf/swi mutants, these results suggest that the increased transcription of these genes is not the result of decreased transcription of a Snf/Swi-dependent repressor but rather a direct effect of Snf/Swi action on SER3 and YOR222W. In contrast, the decreased
levels of the $SAG1$ and $MATA1$ mRNAs are suppressed by $(hta1\text{-htb1})\Delta$ (Fig. 4). Thus, our results suggest that Snf/Swi may use different mechanisms for the activation and repression of transcription.

**Discussion**

We have combined the approach of whole-genome expression analysis with Northern blot, computational, and genetic analyses to understand more about the role of the Snf/Swi complex in controlling transcription in *S. cerevisiae*. These studies have provided information on Snf/Swi function in vivo. First, although only a small percentage of *S. cerevisiae* genes are strongly dependent on Snf/Swi, the set of Snf/Swi-controlled genes depends on growth conditions. Second, the loss of either of two different Snf/Swi components, Snf2 or Swi1, generally causes the same changes in mRNA levels. Third, Snf/Swi controls transcription at the level of individual genes, rather than targeting larger chromosomal domains. Fourth, Snf/Swi, which is nonessential for growth, contributes to the transcriptional control of at least one essential gene, $MCM1$. Finally, Snf/Swi appears to act as both a transcriptional activator and repressor in vivo, and our genetic evidence suggests that these opposite roles occur by distinct mechanisms. In these studies, the combination of whole genome expression analysis with more traditional methods has provided a productive approach to obtain a more complete picture of the *in vivo* roles of this transcription complex.

We have compared our results to those of a previously described whole-genome expression analysis of a snf2 mutant grown in rich medium (6), and we find both similarities and differences. In both studies, it was observed that a snf2 mutation causes increased and decreased mRNA levels. Both studies also concluded that a small subset of genes are strongly affected (greater than three-fold) in snf/swi mutants, although there is only partial overlap between the two studies (http://genome-www.stanford.edu/swisnf). The different findings can be attributed to the many differences between the two studies, including the experimental method, the genetic background of the *S. cerevisiae* strains used, and the particular snf2 allele tested.

The limited requirement for Snf/Swi among all *S. cerevisiae* genes is likely caused by at least two different factors. First, most studies have concluded that Snf/Swi is not very abundant, existing at $\sim100–200$ complexes per haploid cell (7, 43, 44) (compared with an estimated 3,000 molecules of RNA polymerase II holoenzyme) (44). Snf/Swi is $\sim$10-fold less abundant than a closely related *S. cerevisiae* nucleosome remodeling complex, RSC (43). In addition, Snf/Swi has been shown to be partially redundant with other nucleosome modifying proteins, including Gcn5, a histone acetyltransferase required for transcriptional activation of some genes (45–48).

Whole-genome expression studies (6) have shown that a gen5D mutation, similar to snf/swi mutations, causes transcriptional effects on a small percentage of *S. cerevisiae* genes. A significantly greater number of genes would likely be affected in gen5D snf2A double mutants.

Growth medium affects the set of Snf/Swi-dependent genes. There is a wealth of evidence that nutritional conditions alter gene expression (35, 38). A previous whole-genome expression study demonstrated that changing one environmental condition, the transition from glucose-rich to glucose-poor conditions, causes large-scale changes in the pattern of gene expression in *S. cerevisiae* (27). However, some of the differences that we found were surprising and may unveil previously unknown aspects of regulation. For example, the different control of the *PHO* genes in rich and minimal media, both containing high phosphate levels, is not understood. It seems likely that testing the requirement for Snf/Swi for cells grown under other conditions, such as low glucose or stress conditions, will uncover other sets of Snf/Swi-dependent genes.

A small number of gene families exhibit transcriptional changes in snf/swi mutants. Our results suggest that the Snf/Swi dependence of three $MATA\alpha$-specific genes is an indirect effect as Snf/Swi controls expression of the genes encoding two $MATA\alpha$-specific gene activators, Matal1 and Mem1. Because Matal1 and Mem1 assist each other’s binding (39), the observed effects on their mRNA levels could cause a significant effect on activation. One of the $MATA\alpha$-specific genes, *MCM1*, does not appear to be Snf/Swi-dependent. The reasons for this difference are not currently understood. Similarly, it has recently been shown that, although *PHO5* and *PHO8* are both regulated by Pho4, the first is Snf/Swi-independent whereas the latter is Snf/Swi-dependent (19). The reduced mRNA levels for *MCM1* were not detected by the microarray analysis; the *snf/swi* defect was probably obscured by the fact that there are two detectable *MCM1* mRNAs and only one of the two is Snf/Swi-dependent. This effect on just one of the two *MCM1* mRNAs is reminiscent of the Snf/Swi control of *SUC2* mRNA (49).

An effect on *MCM1* expression may account for several *snf/swi* mutant phenotypes. Mem1 acts as either an activator or a repressor at several loci, including the $MATA\alpha$-specific, $MATA\beta$-specific (39), arginine anabolic, and arginine catabolic genes (50, 51). Previous studies have shown that several members of the *ARG* gene family exhibit defective repression in *mcm1* mutants (50, 51), suggesting that the increased mRNA levels of several *ARG* genes, observed in our studies (see http://genome-www.stanford.edu/swisnf), may be a result of decreased *MCM1* expression. It is also intriguing that both snf/swi and mcm1 mutants impair the mitotic stability of minichromosomes con-
taining particular DNA replication origins (ARS) (40, 52). In addition, the slow growth of snf/swi mutants could be caused by reduced expression of MCM1, an essential gene.

Analysis of promoter sequences of Snf/Swi-dependent genes did not identify any common sequence motifs. This negative result fits with recent evidence that suggests that Snf/Swi may be targeted to the HO promoter by the Swi5 transcription factor rather than by particular promoter sequences (11, 53). Although it is likely, then, that Snf/Swi is targeted to promoters at least in part by interactions with transcriptional activators (or repressors) (12–18), it is still possible that Snf/Swi acts as both an activator and as a repressor. These results fit well with other recent expression studies that have suggested that nucleosome remodeling complexes such as Snf/Swi and RSC are involved in transcriptional repression (21–24). In addition, they agree with biochemical studies that have demonstrated the bi-directional nature of the Snf/Swi and RSC remodeling activities in vitro (25, 26). Our genetic tests have provided strong evidence that, between activation and repression by Snf/Swi, one is not likely to be an indirect effect of the other. Taken together, these results support the emerging view that nucleosome remodeling complexes modulate nucleosome structure in vivo to help facilitate a dynamic and reversible transcriptional state (2). Further genetic and biochemical analysis of Snf/Swi repression will help us understand the mechanisms by which it controls transcription, as well as its roles in controlling transcription in vivo.

Finally, the genome-wide transcription profiling studies described here and by Holstege et al. (6) have provided evidence that Snf/Swi acts as both an activator and as a repressor. These results fit well with other recent expression studies that have suggested that nucleosome remodeling complexes such as Snf/Swi and RSC are involved in transcriptional repression (21–24). In addition, they agree with biochemical studies that have demonstrated the bi-directional nature of the Snf/Swi and RSC remodeling activities in vitro (25, 26). Our genetic tests have provided strong evidence that, between activation and repression by Snf/Swi, one is not likely to be an indirect effect of the other. Taken together, these results support the emerging view that nucleosome remodeling complexes modulate nucleosome structure in vivo to help facilitate a dynamic and reversible transcriptional state (2). Further genetic and biochemical analysis of Snf/Swi repression will help us understand the mechanisms by which it controls transcription, as well as its roles in controlling transcription in vivo.

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