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PROSPECTS

Recruitment of Chromatin Remodeling Machines

Craig L. Peterson[1]* **and Colin Logie**[2]

[1]Program in Molecular Medicine and Department of Biochemistry and Molecular Biology, University of Massachusetts Medical School, Worcester, Massachusetts 01605
[2]University of Nijmegen, Department of Molecular Biology, 6525 ED Nijmegen, The Netherlands

Abstract The assembly of eukaryotic DNA into folded nucleosomal arrays has drastic consequences for many nuclear processes that require access to the DNA sequence, including RNA transcription, DNA replication, recombination, and repair. Two types of highly conserved chromatin remodeling enzymes have been implicated as regulators of the repressive nature of chromatin structure: ATP-dependent remodeling complexes and nuclear histone acetyltransferases (HATs). Recent studies indicate that both types of enzymes can be recruited to chromosomal loci through either physical interactions with transcriptional activators or via the global accessibility of chromatin during S phase of the cell cycle. Here we review these recent observations and discuss the implications for gene-specific regulation by chromatin remodeling machines. J. Cell. Biochem. 78:179–185, 2000.

In a typical interphase nucleus, the majority of genes are packaged into highly condensed chromatin structures that range in size from 100–200-nM-diameter fibers. Although these structures are required to package DNA into the tiny space of the nucleus, it seems obvious that this condensed state creates accessibility problems for enzymes that must locate particular DNA sequences. In the past decade, a combination of yeast genetics and old-fashioned biochemistry has led to the discovery of the "holy grail" of the chromatin world—enzymes that modulate the accessibility of chromatin at a gene-specific level. The first of these "chromatin remodeling enzymes" to be identified was the *Saccharomyces cerevisiae* SWI/SNF complex. Subunits of this 2 million dalton protein complex were first identified through yeast genetics as positive regulators of transcription with genetic ties to chromatin components (e.g., histones) [for review see Winston and Carlson, 1992]. Subsequently the purified SWI/SNF complex was found to be a DNA-stimulated ATPase, which hydrolyzes ~1,000 ATPs/minute to disrupt histone-DNA interactions [Côté et al., 1994]. Although the mechanism by which SWI/SNF disrupts nucleosome structure is not known, this "remodeling" reaction leads to an enhanced accessibility of nucleosomal DNA to Dnase I [Côté et al., 1994; Owen-Hughes et al., 1996], restriction enzymes [Logie and Peterson, 1997; Logie et al., 1999], and sequence-specific DNA binding proteins [Côté et al., 1994; Utley et al., 1997]. Additional ATP-dependent remodeling enzymes have been identified in yeast (RSC, Cairns et al., 1996; ISW1 and ISW2, Tsukiyama et al., 1999], Drosophila [ACF, Ito et al., 1997; CHRAC, Varga-Weisz et al., 1997; NURF, Tsukiyama and Wu, 1995; brm, Papoulas et al., 1999], human [hSWI/SNF, Kwon et al., 1994; NURD, Tong et al., 1998; Xue et al., 1998; Zhang et al., 1998; RSF, LeRoy et al., 1998], and frog [Mi-2, Wade et al., 1998]. In the case of the yeast SWI/SNF, Drosophila brm, and human SWI/SNF complexes, ATP-dependent remodeling is required for transcriptional regulation of target genes in vivo [reviewed in Kingston and Narlikar, 1999]. The actual role of these other remodeling complexes remains elusive.

The second type of remodeling enzyme consists of the nuclear histone acetyltransferases that covalently modify lysine residues within the flexible N-terminal domains of the histone proteins. Acetylation of the histone N-terminal domains can disrupt the higher order folding of nucleosomal arrays as well as control the bind-

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*Correspondence to: Craig L. Peterson, 373 Plantation St., UMMS, Worcester, MA 01605. E-mail: craig.peterson@umassmed.edu

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ing of nonhistone proteins to the chromatin fiber. As is the case for the ATP-dependent enzymes, a yeast protein, Gcn5p, is the paradigm for the nuclear histone acetyltransferases. *GCN5* was first identified in several mutant screens as a gene product required for transcriptional control [Georgakopoulos and Thireos, 1992; Marcus et al., 1994; Pollard and Peterson, 1997], and subsequently the *Tetrahymena* homolog of *GCN5* was purified as a histone acetyltransferase [Brownell et al., 1996]. Gcn5p is the catalytic subunit of several large, multi-subunit acetyltransferase complexes [e.g., ADA and SAGA; Grant et al., 1997; Pollard and Peterson, 1997; Saleh et al., 1997], which like SWI/SNF, are conserved from yeast to man [Ogryzko et al., 1998]. In mammals, there appear to be two homologs of *GCN5, hGCN5* and *P/CAF;* both have been implicated in transcriptional regulation [Candau et al., 1996; Yang et al., 1996, Xu et al., 1998].

Although chromatin is expected to impose constraints on the expression of all genes, *SWI/SNF* and *GCN5* are only required for transcription of a small subset of yeast genes. For instance, global genome analyses indicate that expression of only 5–7% of the ~6,000 yeast genes is reduced 2-fold or more by inactivation of SWI/SNF or Gcn5p [Holstege et al., 1998]. The gene-specific effects of *swi/snf* or *gcn5* mutants have led to the view that these enzymes must be targeted to specific loci where they then control gene expression. Below we review recent studies that lead to a simplified model for recruitment of chromatin remodeling enzymes, and then discuss how this model impacts the question of why expression of only a few genes requires these chromatin remodeling enzymes. We also discuss how the global remodeling of chromatin during S phase of the cell cycle might be misinterpreted as a targeted change in chromatin structure.

RECRUITMENT OF CHROMATIN REMODELING ENZYMES BY TRANSCRIPTIONAL ACTIVATORS

One model evoked to explain how chromatin remodeling enzymes might be recruited to target genes proposed that these enzymes were subunits of an RNA polymerase II holoenzyme. In this case, gene-specific transcriptional activators would bind and recruit PolII holoenzyme that would "carry with it" all of the necessary chromatin remodeling enzymes to facilitate transcription. Consistent with this model, both yeast and human SWI/SNF complexes have been shown to co-purify and co-immunoprecipitate with Pol II holoenzyme [Wilson et al., 1996; Cho et al., 1998; Neish et al., 1998], and a mammalian PolII holoenzyme contains the CBP and P/CAF histone acetyltransferases (P/CAF is one of two mammalian Gcn5p homologs) [Cho et al., 1998; Neish et al., 1998]. However, most yeast holoenzyme preparations do not contain SWI/SNF or Gcn5p [Myers et al., 1998], and purified SWI/SNF and Gcn5p complexes lack holoenzyme components [Côté et al., 1994; Cairns et al., 1996; Grant et al., 1997). Furthermore, several mutations that disrupt holoenzyme, such as a deletion of *SRB2* or *GAL11,* do not yield characteristic Swi$^-$ or Gcn5-phenotypes (i.e., a defect in *HO* expression; Peterson, unpublished observations).

Two recent biochemical studies also seem inconsistent with the "Holoenzyme Model." First, Natarajan and colleagues failed to detect significant co-immunoprecipitation of SWI/SNF and yeast PolII holoenzyme, whereas strong interactions were observed between SWI/SNF and the Gcn4p activator [Natarajan et al., 1999] (see below). Secondly, Yudkovky et al. [1999] used yeast nuclear transcription extracts to assemble functional preinitiation complexes on an immobilized DNA template. They then investigated whether SWI/SNF was recruited to the promoter along with PolII holoenzyme. Although SWI/SNF was sequestered onto the immobilized DNA template, recruitment was independent of promoter sequences, TBP, or PolII holoenzyme. Thus, SWI/SNF recruitment is unlikely to require an obligatory association with PolII holoenzyme, but it still remains a possibility that SWI/SNF (or Gcn5p) does interact functionally with PolII holoenzyme at one or more steps in the transcription cycle (e.g., during transcription elongation) [see Brown et al., 1996].

In contrast to the holoenzyme model, an explosion of recent data supports a simple model in which gene-specific activators directly recruit SWI/SNF and Gcn5p HAT complexes to target genes (Fig. 1). Purified yeast SWI/SNF or Gcn5p-containing HAT complexes have been found to directly interact with a variety of transcriptional activators, including mammalian glucocorticoid receptor, yeast Gcn4p, Swi5p, GAL4-VP16, and GAL4-AH [Ikeda et al., 1999;

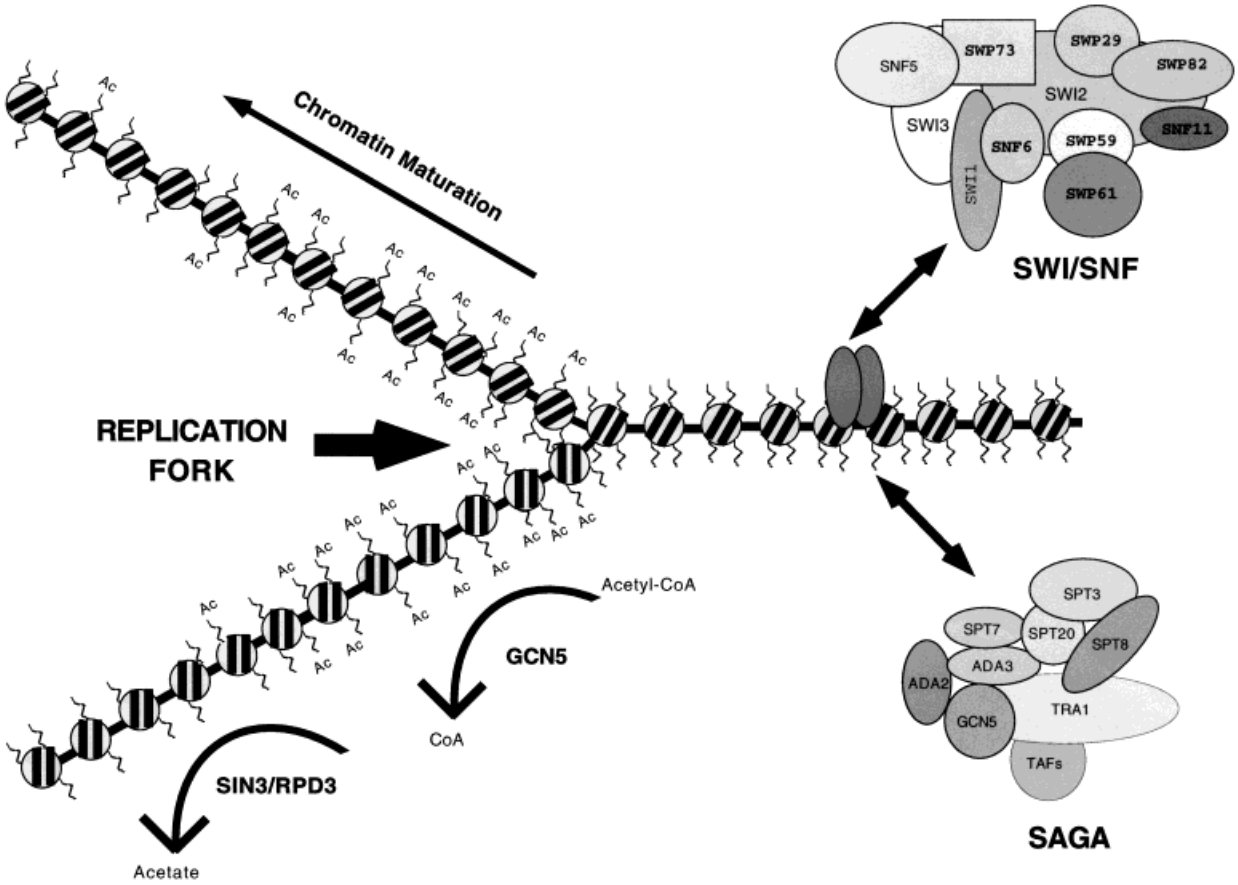

Fig. 1. Gene-specific targeting and genome-wide activity of chromatin remodeling enzymes. Schematic of chromatin in front and behind an advancing DNA replication fork. DNA-bound ovals ahead of the fork depict a transcriptional activator that is able to directly recruit the SWI/SNF or SAGA chromatin remodeling complexes. Chromatin immediately behind the replication fork is shown as highly acetylated, due to a combined action of cytoplasmic histone acetyltransferases and the nuclear Gcn5p acetyltransferase. As chromatin matures behind the fork, histone deacetylases, such as Sin3p/Rpd3p, remove the replication-associated acetylation events.

Neely et al., 1999; Wallberg et al., 1999; Yudkovsky et al., 1999]. Furthermore, these interactions are mediated by the transcriptional activation domain and are sensitive to mutations that cripple activation function [Ikeda et al., 1999; Neely et al., 1999; Wallberg et al., 1999; Yudkovsky et al., 1999]. The in vitro association of SWI/SNF and Gcn5p HAT complexes with activation domains is functionally significant since activators can also recruit SWI/SNF remodeling activity and Gcn5p HAT activity to nucleosomal substrates in vitro [Utley et al., 1999; Yudkovsky et al., 1999] and this recruitment stimulates RNA polymerase II transcription from such templates [Ikeda et al., 1999; Neely et al., 1999].

Activator-dependent recruitment of both yeast and human SWI/SNF complexes has also been observed in vivo. Nasmyth and colleagues used a chromatin immunoprecipitation technique to demonstrate that the cell cycle regulated association of yeast SWI/SNF with the *HO* locus required the prior binding of the Swi5p activator [Cosma et al., 1999]. Likewise, the human SWI/SNF complex associates with the glucocorticoid receptor in vivo, and this interaction is required for hormone-dependent changes in chromatin structure surrounding the receptor binding sites [Fryer and Archer, 1998]. In addition, human SWI/SNF is recruited to the adult β-globin gene in erythroid cells via the EKLF transcription factor [Lee et al., 1999] and to myeloid genes via association with the C/EBPβ transcription factor [Kowenz-Leutz and Leutz, 1999]. Thus, the emerging view is that SWI/SNF and Gcn5p-containing

HAT complexes are targeted to specific genes via direct interactions with gene-specific activators.

WHY DO SWI/SNF AND Gcn5p CONTROL EXPRESSION OF A LIMITED NUMBER OF GENES?

Although the activator recruitment model may appear to yield a simple solution to the problem of targeting a limiting amount of remodeling enzyme to a few genes, it raises some glaring problems. First, it appears that all members of the "acidic" class of transcription activation domain can interact with either yeast SWI/SNF or Gcn5p HAT complexes. For instance, even the generic acidic activators, GAL4-VP16 and GAL4-AH, can recruit SWI/SNF in vitro. However, it is firmly believed that transcription of all ~6,000 yeast genes requires an "acidic" class of activator. Thus, if all acidic activators can recruit SWI/SNF and Gcn5p in vitro, why is it that SWI/SNF and Gcn5p appear to control expression of only a few genes in vivo? One possibility is that recruitment in vivo is restricted to only a subset of activators. Alternatively, SWI/SNF and Gcn5p may indeed be recruited to every yeast gene whose expression is controlled by an acidic activator. In this scenario, we envision two explanations for why mutations that inactivate SWI/SNF or Gcn5p might lead to decreases in expression of only a subset of these genes. First, the chromatin remodeling activities of SWI/SNF and Gcn5p may be redundant either with each other or with additional remodeling enzymes. Consistent with this view, neither SWI/SNF nor Gcn5p are essential for yeast growth, but inactivation of both SWI/SNF and Gcn5p is a lethal event [Pollard and Peterson, 1997; Roberts and Winston, 1997]. Likewise, by taking advantage of ts alleles in SWI/SNF subunits, two groups have reported that *swi/snf gcn5* double mutants do in fact have a more global effect on yeast transcription than does either single mutant [Biggar and Crabtree, 1999; Sudarsanam et al., 1999].

A second possibility is that SWI/SNF and Gcn5p are recruited to all genes, but that their remodeling activities do not control a rate-determining step required for expression. Evidence for this type of model comes from studies of the yeast Gal4p activator. At the *GAL1* locus, Gal4p binds to four low-affinity sites that are located in a nucleosome-free region, and expression of *GAL1* does not depend on either *SWI/SNF* or *GCN5*. However, if two of these low affinity Gal4p binding sites are positioned within a nucleosome, Gal4p binding and transcription becomes *SWI/SNF* and *GCN5* dependent [Burns and Peterson, 1997; Biggar and Crabtree, 1999]. Furthermore, if a nucleosome positioning sequence is used to re-position nucleosomes away from the low-affinity Gal4p sites, transcription again becomes *SWI/SNF* independent [Burns and Peterson, 1997]. Thus, a dependence on chromatin remodeling enzymes does not correlate with promoter strength (the eventual transcriptional outputs are the same) but on the nucleosomal context of the low affinity Gal4p binding sites. Since Gal4p can recruit SWI/SNF in vitro, the data are consistent with a model in which Gal4p recruits SWI/SNF (or Gcn5p) to all promoter derivatives, but that the requirement for remodeling is only rate-determining for gene expression when nucleosomes are an obstacle for GAL4 binding. This type of model may hold for all *SWI/SNF* and *GCN5* dependent genes. For example, positioned nucleosomes cover key upstream regulatory sequences of the *HO* and *SUC2* loci [Gavin and Simpson, 1997; Wu and Winston, 1997] (Krebs and Peterson, unpublished data), and in the case of the *HO* gene, *SWI/SNF* and *GCN5* are required for binding of the Swi4p/Swi6p activator to nucleosomal sites [Cosma et al., 1999] (Krebs and Peterson, unpublished data).

GENOME-WIDE RECRUITMENT OF REMODELING ENZYMES IN S PHASE

In addition to the targeted changes in chromatin structure described above, global changes in chromatin structure also occur during each cell cycle. For instance, during S phase chromatin structure must be duplicated after passage of the DNA replication fork, and during mitosis, chromosomes undergo extensive condensation events that are required for correct chromosome segregation. Nucleosomes that are deposited after passage of the replication fork contain high levels of acetylated histones H3 and H4 due to the action of cytoplasmic histone acetyltransferases. As the newly replicated chromatin matures, acetyl groups are removed by histone deacetylases, yielding bulk chromatin in G2 that contains a baseline level of histone acetylation [for review see Fletcher and Hansen, 1996]. This S phase-

dependent hyperacetylation of yeast chromatin can lead to a high "background level" of acetylation as detected in chromatin immunoprecipitation studies, which can mask or lead to an under-representation of targeted acetylation events [see Kuo et al., 1998].

Chromatin must also unfold during DNA replication, which leads to a transient period of enhanced chromatin accessibility. This can create a "window of opportunity" for binding of transcriptional regulators as well as enhance the nontargeted action of nuclear chromatin remodeling enzymes (Fig. 1). For instance, we recently found that genome-wide histone H3 acetylation during S phase was significantly reduced in a *gcn5* mutant [Krebs et al., 1999]. This global acetylation by Gcn5p was not restricted to genes transcribed by RNA polymerase II, since even the ribosomal locus (transcribed by RNA polymerase I) contained less acetylated histone H3 during S phase in a *gcn5* mutant. In addition to the effects of *GCN5* on global acetylation, we also found that the Sin3p/Rpd3p deacetylase complex is required for much of the global deacetylation of histone H3 following S phase [Krebs et al., 1999]. Thus, in *sin3*-cells bulk chromatin is hyperacetylated throughout the yeast cell cycle. This genome-wide modification of chromatin is unlikely to be restricted to acetylases and deacetylases. ATP-dependent remodeling complexes may also function at a genome-wide level during S phase, and these remodeling activities may have an important role in establishing the correct spacing and positioning of nucleosomes after replication fork passage. Nucleosome positioning can play a key role in expression of some genes, and thus we expect that the absence of such genome-wide activities might alter the expression of a subset of genes.

Do the genome-wide acetylation or deacetylation events catalyzed by Gcn5p and Sin3p/Rpd3p have any significant consequences for the regulation of gene expression? In wildtype cells, these events may have only a minor effect on chromatin structure or gene expression, since the combination of these two activities may lead to only small changes in histone acetylation status. However, this balance of power would be disrupted in *sin3* or *gcn5* mutants, which might lead to abnormal effects on gene expression. For instance, since transcriptional induction is often correlated with increases in histone acetylation, it seems likely that constitutive acetylation observed in a *sin3*-mutant might de-regulate transcription. Consistent with this view, mutations in *SIN3* allow transcription of several genes in the absence of a transcriptional activator or in the absence of the Gcn5p histone acetyltransferase. For instance, *SIN3* was first identified as a mutation that allowed expression of the *HO* gene in the absence of the Swi5p activator [Sternberg et al., 1986]. Subsequent studies showed that a *sin3* mutation also alleviates the requirement for *GCN5* in *HO* expression [Perez-Martin and Johnson, 1997]. Thus, Sin3p behaves formally as a repressor of transcription, and several studies have focussed on identifying the cis- and trans-acting elements involved in targeting Sin3p to specific genes (including *HO*). However, we propose that the regulatory role of Sin3p at *HO* (and probably at many other genes) is accomplished in a nontargeted fashion during S/G2 when the Sin3p/Rpd3p deacetylase complex facilitates the erasure of replication-associated histone acetylation events.

CONCLUSIONS

Studies over the past few years have emphasized the dominant role of chromatin remodeling enzymes in the regulation of transcription. In many cases, it is clear that the primary purpose of transcriptional activators is to recruit enzymes that modulate the accessibility of the chromatin template for RNA polymerase II. Chromatin remodeling enzymes can also exert global effects by acting on chromatin structure during DNA replication or during the mitotic chromosome condensation/decondensation cycle (Fig. 1). The absence of such nontargeted activities (e.g., in certain mutants) may lead to gene-specific changes in transcriptional regulation.

One focus of this review has been the active targeting of chromatin remodeling enzymes by direct interactions with transcriptional activators. But is this the only means to recruit remodeling enzymes to a target promoter? In the case of the *HO* gene, recruitment of a Gcn5p HAT complex during late anaphase of the cell cycle requires SWI/SNF remodeling activity [Krebs et al., 1999; Cosma et al., 1999] (Krebs and Peterson, unpublished observations). How SWI/SNF activity might influence Gcn5p recruitment is unclear. This observation is especially puzzling since SWI/SNF and Gcn5p HAT

complexes do not appear to directly associate, and SWI/SNF remodeling activity does not enhance *GCN5*-dependent HAT activity in vitro. It is possible that the SWI/SNF-dependent recruitment of Gcn5p is a general feature of *SWI/SNF* and *GCN5*-dependent genes, or, alternatively, it may be peculiar to genes that are expressed in late mitosis. Clearly one of the advantages of yeast as an experimental system is that these ideas can be easily addressed in vivo by a combination of yeast genetics and chromatin immunoprecipitation methods.

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REFERENCES

Biggar SR, Crabtree GR. 1999. Continuous and widespread roles for the SwiSnf complex in transcription. EMBO J 18:2254–2264.

Brown SA, Imbalzano AN, Kingston RE. 1996. Activator-dependent regulation of transcriptional pausing on nucleosomal templates. Genes Dev 10:1479–1490.

Brownell JE, Zhou J, Ranalli T, Kobayashi R, Edmondson DG, Roth SY, Allis CD. 1996. Tetrahymena histone acetyltransferase A: a homolog to yeast Gcn5p linking histone acetylation to gene activation. Cell 84:843–51.

Burns L, Peterson CL. 1997. Yeast SWI/SNF complex facilitates the binding of a transcriptional activator to nucleosomal sites in vivo. Mol Cell Biol 17:4811–4819.

Cairns BR, Lorch Y, Li Y, Zhang M, Lacomis L, Erdjument-Bromage H, Tempst P, Du J, Laurent B, Kornberg RD. 1996. RSC, an essential, abundant chromatin-remodeling complex. Cell 87:1249–1260.

Candau R, Moore PA, Wang L, Barlev N, Ying CY, Rosen CA, Berger SL. 1996. Identification of human proteins functionally conserved with the yeast human putative adaptors ADA2 and GCN5. Mol Cell Biol 16:593–602.

Cho HG, Orphanides X, Sun XJ, Yang V, Ogryzko E, Lees Y, Nakatani Y, Reinberg D. 1998. A human RNA polymerase II complex containing factors that modify chromatin structure. Mol Cell Biol 18:5355–5363.

Cosma MP, Tanaka T, Nasmyth K. 1999. Ordered recruitment of transcription and chromatin remodeling factors to a cell cycle-and developmentally regulated promoter. Cell 97:299–311.

Côté J, Quinn J, Workman JL, Peterson CL. 1994. Stimulation of GAL4 derivative binding to nucleosomal DNA by the yeast SWI/SNF protein complex. Science 265:53–60.

Fletcher TM, Hansen JC. 1996. The nucleosomal array: structure/function relationships. Crit Rev Eukaryotic Gene Express 6:149–88.

Fryer CJ, Archer TK. 1998. Chromatin remodeling by the glucocorticoid receptor requires the BRG1 complex. Nature 393:88–91.

Gavin IM, Simpson RT. 1997. Interplay of yeast global transcriptional regulators Ssn6p-Tup1p and Swi-Snf and their effect on chromatin structure. EMBO J 16: 6263–6271.

Georgakopoulos T, Thireos G. 1992. Two distinct yeast transcriptional activators require the function of the GCN5 protein to promote normal levels of transcription. EMBO J 11:4145–4152.

Grant PA, Duggan L, Cote J, Roberts SM, Brownell JE, Candau R, Ohba R, Owen-Hughes T, Allis CD, Winston F, Berger SL, Workman JL. 1997. Yeast Gcn5 functions in two multisubunit complexes to acetylate nucleosomal histones: characterization of an Ada complex and the SAGA (Spt/Ada) complex. Genes Dev 11:1640–1650.

Holstege FC, Jennings EG, Wyrick JJ, Lee IT, Hengartner CJ, Green MR, Golub TR, Lander ES, Young RA. 1998. Dissecting the regulatory circuitry of a eukaryotic genome. Cell 95:717–728.

Ikeda K, Steger DJ, Eberharter A, Workman JL. 1999. Activation domain-specific and general transcription stimulation by native histone acetyltransferase complexes. Mol Cell Biol 19:855–63.

Ito T, Bulger M, Pazin MJ, Kobayashi R, Kadonaga JT. 1997. ACF, an ISWI-containing and ATP-utilizing chromatin assembly and remodeling factor. Cell 90:145–155.

Kingston RE, Narlikar GJ. 1999. ATP-dependent remodeling and acetylation as regulators of chromatin fluidity. Genes Dev 13:2339–2252.

Kowenz-Leutz E, Leutz A. 1999. A C/EBP Isoform Recruits the SWI/SNF Complex to Activate Myeloid Genes. Mol Cell 4:735–743.

Krebs JE, Kuo MH, Allis CD, Peterson CL. 1999. Cell cycle-regulated histone acetylation required for expression of the yeast HO gene. Genes Dev 13:1412–1421.

Kuo M-H, Zhou J, Jambeck P, Churchill MEA, Allis CD. 1998. Histone acetyltransferase activity of yeast Gcn5p is required for the activation of target genes in vivo. Genes Dev 12:627–639.

Kwon H, Imbalzano AN, Khavari PA, Kingston RE, Green MR. 1994. Nucleosome disruption and enhancement of activator binding by a human SWI/SNF complex. Nature 370:477–481.

Lee CH, Murphy MR, Lee JS, Chung JH. 1999. Targeting a SWI/SNF-related chromatin remodeling complex to the beta-globin promoter in erythroid cells. Proc Natl Acad Sci USA 96:12311–12315.

LeRoy G, Orphanides G, Lane WS, and Reinberg D. 1998. Requirement of RSF and FACT for transcription of chromatin templates in vitro. Science 282:1900–1904.

Logie C, Peterson CL. 1997. Catalytic nucleosome remodeling by the yeast SWI/SNF complex on nucleosome arrays. EMBO J 16:6772–6782.

Logie C, Tse C, Hansen J, Peterson CL. 1999. The core histone N-terminal domains are required for multiple rounds of catalytic chromatin remodeling by the SWI/SNF and RSC complexes. Biochemistry 38:2514–2522.

Marcus GA, Silverman N, Berger S, Horiuchi J, Guarente L. 1994. Functional similarity and physical association between GCN5 and ADA2: putative transcriptional adaptors. EMBO J 13:4807–4815.

Myers LC, Gustafsson CM, Bushnell DA, Lui M, Erdjument-Bromage H, Tempst P, Kornberg RD. 1998. The Med proteins of yeast and their function through the RNA polymerase II carboxy-terminal domain. Genes Dev 12:45–54.

Natarajan K, Jackson BM, Zhou H, Winston F, Hinnebusch AG. 1999. Transcriptional activation by Gcn4p involves independent interactions with SWI/SNF complex and SRB/Mediator. Mol Cell 4:657–664.

Neely KE, Hassan AH, Wallberg AE, Steger DJ, Cairns BR, Wright APH, Workman JL. 1999. Activation domain-mediated targeting of the SWI/SNF complex to promoters stimulates transcription from nucleosome arrays. Mol Cell 4:649–55.

Neish AS, Anderson SF, Schlegel BP, Wei W, Parvin JD. 1998. Factors associated with the mammalian RNA polymerase II holoenzyme. Nucleic Acids Res 26:847–853.

Ogryzko VV, Kotani T, Zhang X, Schlitz R, Howard T, Yang XJ, Howard BH, Qin J, Nakatani Y. 1998. Histone-like TAFs within the PCAF histone acetylase complex. Cell 94:35–44.

Owen-Hughes TA, Utley RT, Cote J, Peterson C, Workman JL. 1996. Persistent site-specific remodeling of a nucleosome array by transient action of the SWI/SNF complex. Science 273:513–516.

Papoulas O, Beek SJ, Moseley S, McCallum CM, Sarte M, Shearn A, Tamkun JW. 1998. The Drosophila trithorax group proteins BRM, ASH1 and ASH2 are subunits of distinct protein complexes. Development 125:3955–3966.

Perez-Martin J, Johnson AD. 1998. Mutations in Chromatin Components Suppress a Defect of Gcn5 Protein in Saccharomyces cerevisiae. Mol Cell Biol 18:1049–1054.

Pollard KJ, Peterson CL. 1997. Role for ADA/GCN5 products in antagonizing chromatin-mediated transcriptional repression. Mol Cell Biol 17:6212–6222.

Roberts SM, Winston F. 1997. Essential functional interactions of SAGA, a Saccharomyces cerevisiae complex of Spt, Ada, and Gcn5 proteins, with the Snf/Swi and Srb/mediator complexes. Genetics 147:451–65.

Saleh A, Lang V, Cook R, Brandl CJ. 1997. Identification of native complexes containing the yeast coactivator/repressor proteins NGG1/ADA3 and ADA2. J Biol Chem 272:5571–8.

Sternberg PW, Stern MJ, Clark I, Herskowitz I. 1987. Activation of the yeast HO gene by release from multiple negative controls. Cell 48:567–577.

Sudarsanam P, Cao Y, Wu L, Laurent BC, Winston F. 1999. The nucleosome remodeling complex, Snf/Swi, is required for the maintenance of transcription in vivo and is partially redundant with the histone acetyltransferase, Gcn5. EMBO J 18:3101–3106.

Tong JK, Hassig CA, Schnitzler GR, Kingston RE, Schreiber SL. 1998. Chromatin deacetylation by an ATP-dependent nucleosome remodeling complex. Nature 395: 917–921.

Tsukiyama T, Wu C. 1995. Purification and properties of an ATP-dependent nucleosome remodeling factor. Cell 83:1011–1020.

Tsukiyama T, Palmer J, Landel CC, Shiloach J, Wu C. 1999. Characterization of the imitation switch subfamily of ATP-dependent chromatin-remodeling factors in Saccharomyces cerevisiae. Genes Dev 13:686–697.

Utley RT, Ikeda K, Grant PA, Cote J, Steger DJ, Eberharter A, John S, Workman JL. 1998. Transcriptional activators direct histone acetyltransferase complexes to nucleosomes. Nature 394:498–502.

Varga-Weisz PD, Wilm M, Bonte E, Dumas K, Mann M, Becker PB. 1997. Chromatin-remodelling factor CHRAC contains the ATPases ISWI and topoisomerase II. Nature 388:598–602.

Wade PA, Jones PL, Vermaak D, Wolffe AP. 1998. A multiple subunit Mi-2 histone deacetylase from Xenopus laevis cofractionates with an associated Snf2 superfamily ATPase. Curr Biol 8:843–846.

Wallberg AE, Neely KE, Gustafsson JA, Workman JL, Wright AP, Grant PA. 1999. Histone acetyltransferase complexes can mediate transcriptional activation by the major glucocorticoid receptor activation domain. Mol Cell Biol 19:5952–5959.

Wilson CJ, Chao DM, Imbalzano AN, Schnitzler GR, Kingston RE, Young RA. 1996. RNA polymerase II holoenzyme contains SWI/SNF regulators involved in chromatin remodeling. Cell 84:235–244.

Winston F, Carlson M. 1992. Yeast SNF/SWI transcriptional activators and the SPT/SIN chromatin connection. TIG 8:387–391.

Wu L, Winston F. 1997. Evidence that Snf-Swi controls chromatin structure over both the TATA and UAS regions of the SUC2 promoter in Saccharomyces cerevisiae. Nucleic Acids Res 25:4230–4234.

Xu W, Edmondson DG, Roth SY. 1998. Mammalian GCN5 and P/CAF acetyltransferases have homologous amino-terminal domains important for recognition of nucleosomal substrates. Mol Cell Biol 1998 18:5659–69.

Xue Y, Wong J, Moreno GT, Young MK, Cote J, Wang W. 1998. NURD, a novel complex with both ATP-dependent chromatin-remodeling and histone deacetylase activities. Mol Cell 2:851–861.

Yang X-J, Ogryzko VV, Nishikawa J, Howard BH, Nakatani Y. 1996. A p300/CBP-associated factor that competes with the adenoviral oncoprotein E1A. Nature 382: 319–324.

Yudkovky N, Logie C, Hahn S, Peterson CL. 1999. Recruitment of the SWI/SNF chromatin remodeling complex by transcriptional activators. Genes Dev 13:2369–2374.

Zhang Y, LeRoy G, Seelig HP, Lane WS, Reinberg D. 1998. The dermatomyositis-specific autoantigen Mi-2 is a component of a complex containing histone deacetylase and nucleosome remodeling activities. Cell 95:279–289.