Global Loss of Set1-mediated H3 Lys\(^4\) Trimethylation Is Associated with Silencing Defects in \textit{Saccharomyces cerevisiae}*

Received for publication, March 7, 2005, and in revised form, June 13, 2005
Published, JBC Papers in Press, June 16, 2005, DOI 10.1074/jbc.C500097200

Ian M. Fingerman\\*, Chia-Ling Wu\\†, Bradley D. Wilson\\‡, and Scott D. Briggs\\§

From the\\†Department of Biochemistry and the Cancer Center, Purdue University, West Lafayette, Indiana 47907 and the\\§Walther Cancer Institute, Indianapolis, Indiana 46202

The existence of histone methylation has been known for over 30 years (1) and recently site specific histone methylation and the corresponding methyltransferases have been identified (2, 3). The catalytic core for most histone lysine methyltransferases resides in the SET domain (2, 4). The SET domain is an evolutionarily conserved motif, with homologues present in organisms ranging from yeast to humans (5). In \textit{Saccharomyces cerevisiae}, Set1 is the sole methyltransferase responsible for histone H3 lysine 4 (H3 Lys\(^4\)) methylation and catalyzes the addition of up to three methyl groups to its substrate resulting in mono-, di-, or tri-methylation (6–10). Cells that do not express Set1 have several apparent phenotypes, including slow growth and defects in telomere, HML, and rDNA silencing. However, the mechanism by which the Set1 methyltransferase mediates differential histone H3 methylation (mono-, di-, and tri-) is still not understood, and the involvement of domains or regions in Set1 contributing to H3 Lys\(^4\) methylation has not been well characterized. In this study, the N terminus of Set1 was shown to be important for global and gene specific histone H3 trimethylation. We show that Set1 trimethyl-defective mutants can rescue a \textit{set1\(\Delta\)} slow growth defect. In contrast, Set1 trimethyl mutants were defective in telomere, rDNA, HML, and HMR silencing. Taken together, these data suggest that histone H3 Lys\(^4\) trimethylation is required for proper silencing, while mono- and/or dimethylation is sufficient for cell growth.

Post-translational histone modifications, such as acetylation, phosphorylation, ubiquitination, and methylation, have been correlated with regulation of gene expression. In \textit{Saccharomyces cerevisiae}, Set1 has been identified as the sole histone methyltransferase required for histone H3 lysine 4 (Lys\(^4\)) methylation. Yeast cells that do not express Set1 have several apparent phenotypes, including slow growth and defects in telomere, HML, and rDNA silencing. However, the mechanism by which the Set1 methyltransferase mediates differential histone H3 methylation (mono-, di-, and tri-) is still not understood, and the involvement of domains or regions in Set1 contributing to H3 Lys\(^4\) methylation has not been well characterized. In this study, the N terminus of Set1 was shown to be important for global and gene specific histone H3 trimethylation. We show that Set1 trimethyl-defective mutants can rescue a \textit{set1\(\Delta\)} slow growth defect. In contrast, Set1 trimethyl mutants were defective in telomere, rDNA, HML, and HMR silencing. Taken together, these data suggest that histone H3 Lys\(^4\) trimethylation is required for proper silencing, while mono- and/or dimethylation is sufficient for cell growth.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

A Sidney Kimmel Scholar. To whom correspondence should be addressed: Dept. of Biochemistry, Purdue University, 175 S. University, West Lafayette, IN 47907. Tel.: 765-494-0112; Fax: 765-494-7897; E-mail: sdbriggs@purdue.edu.

This paper is available on line at http://www.jbc.org

---

**MATERIALS AND METHODS**

Yeast Plasmids and Strains—Construction of the plasmid expressing FLAG-tagged full-length Set1 (1–1080) and Set1 (780–1080) has been
described previously (6). The N-terminal truncation of Set1 (1–1080) was made by PCR amplification of the desired region of Set1 using the full-length SET1 plasmid as template. All constructs were engineered with a single FLAG epitope at the N terminus and subcloned into yeast expression plasmids under the control of the ADH1 promoter and containing a URA3 or TRP1 selectable marker. The RRM deletion mutant (1–1080 ΔRRM) was made via site-directed deletion using the Stratagene Quikchange site-directed mutagenesis kit. Briefly, complementary oligonucleotides were designed that had homology both to the regions immediately upstream and downstream of the region to be deleted to PCR amplification of the template (Set1 1–1080) and subsequent steps were performed as described by the manufacturer. The following strains were used: MBY1198 (MATa hisΔ300 ade2::his3 G leu2Δ200 ura3Δ2 met15Δ0 trp1Δ63 Thylis3-316, Ytiade2A151, MYB217 (MATa hisΔ300 ade2::his3 G leu2Δ200 ura3Δ2 met15Δ0 trp1Δ63 Thylis3-316, Ytiade2A151 set1-1::TRP1) (6), MBY21 (MATa his3-52 leu2–3,112 trp1 his3::ΔHHT1-HHF1 Δ[HHT2-HHF2] pMS329 copy I (URA3, HHT1-HHF1-1) (23), MYB157 (MATa ura3–52 leu2–3,112 trp1 his3::Δ[HHT1-HHF1] Δ[HHT2-HHF2] pMS329 copy I (URA3, HHT1-HHF1-1) set1A::KanMX4) (6), UCC506 (MATa ade2–101 his3Δ200 leu2–Δ1 lys2–801 trp1 Δ1 ura3–52 URA3::TEL-V-R) (24) UCC506 set1Δ (isoogenic to UCC506, containing set1A::KanMX4; this study). UCC7262 (MATa ade2 his3 leu2 lys2 ura3 hhf1-hht1::LEU2 hhf2-hht2-TAE2-TEL-VR hml::URA3::pMP9) (25), UCC7262 set1Δ (isogenic to UCC7262, containing set1A::KanMX4; this study). UCC7266 (MATa ade2 his3 leu2 lys2 ura3 hhf1-hht1::LEU2 hhf2-hht2::MET15 ADE2-TEL-VR hml::URA3::pMP9) (25), UCC7266 set1Δ (isogenic to UCC7262, containing set1A::KanMX4; this study). UCC1188 (MATa ade2::Δ1 leu2–801 trp1 ura3 hhf1-hht1::LEU2 hhf2-hht2::HIS3 RDN1::URA3::pMP9) (25), UCC1188 set1Δ (isogenic to UCC7262, containing set1A::KanMX4; this study).

Preparation of Yeast Whole Cell Extracts and Immunoprecipitations—For analysis of yeast histones, yeast whole cell extracts were prepared as follows: 3–5 ml cultures of yeast were grown to mid-log phase (OD600 = 1.0). Cells were harvested, washed with water and resuspended in 250 μl of 2 M NaOH with 8% β-mercaptoethanol. Cells were incubated on ice for 5 min and then pelleted at 13,000 rpm for 2 min at 4 °C. Cell pellets were resuspended gently in 250 μl of Buffer A (40 mM HEPES-KOH, pH 7.5, 350 mM NaCl, 0.1% Tween 20, 10% glycerol, 1 μg/ml leupeptin, aprotinin, and pepstatin A, 1 mM phenylmethylsulfonyl fluoride) and pelleted as described above. Cell pellets were resuspended in 180 μl of 2× SDS-sample buffer. Five μl or 10 μl of each sample were loaded per lane for Western blotting. For immunoprecipitation of yeast Set1, 50–200 ml cultures of MBY1198 and MBY1217 expressing blank vector or the indicated FLAG-Set1 (1–1080) or FLAG-tagged Set1 mutants (1–1080 ΔRRM, 780–1080 and 829–1080) were grown in SC media (0.67% (w/v) yeast nitrogen base supplemented with 2% glucose and 0.5% uracil) and 5-fluoroorotic acid; RRM, RNA recognition motif.

Chromatin immunoprecipitations were performed as described previously using H3 Lys4 dimethyl- and H3 Lys4 trimethyl-specific antibodies (Upstate Biotechnology) (27). Immunoprecipitated DNA was analyzed by PAGE and gel images were quantified using ImageQuant software. For analysis of RNA, yeast total RNA was isolated using TRIzol reagent (Invitrogen) and RNA migration was determined on a 6% polyacrylamide gel.

RESULTS AND DISCUSSION

To investigate the importance of the N terminus of Set1 in regulating H3 Lys4 methylation, two FLAG-tagged N-terminal deletion mutants were constructed (1–1080 and 780–1080) and were generated (Fig. 1A) and expressed in a yeast strain in which the endogenous SET1 was deleted (set1Δ). To determine the histone H3 Lys4 methylation status in these cells, yeast set1Δ strains were transformed with plasmids containing blank plasmid (Vector) and the two N-terminal set1 deletion constructs (780–1080 and 829–1080) were grown to an OD600 = 1.0 and extracted with 2× SDS-Laemmli sample buffer. Clarified supernatants were run on SDS-polyacrylamide gels, transferred to a PVDF membrane, and probed with methyl-specific antibodies (Upstate Biotechnology) to mono-, di-, and trimethylated forms of histone H3 Lys4. As shown in Fig. 1B, H3 Lys4 trimethylation was nearly abolished in set1Δ strains expressing N-terminal set1 deletion constructs (780–1080 and 829–1080). Trace amounts of H3 Lys4 trimethylation were detected after longer exposure time to film (Fig. 1B).

Surprisingly, H3 Lys4 mono- and dimethylation were restored to similar levels to that of a wild-type isogenic strain, indicating that the N terminus of Set1 is specifically required for H3 Lys4 trimethylation. To confirm that the Set1 N-terminal deletion mutants (780–1080 and 829–1080) were expressed, mutant yeast strains were grown to an OD600 = 1.0 and lysed using glass beads. Clarified supernatants were immunoprecipitated with an anti-FLAG affinity resin (M2 resin, Sigma). Immunoprecipitates were run on SDS-polyacrylamide gels, transferred to a PVDF membrane, and probed with anti-FLAG monoclonal antibodies (M2, Sigma). Western blots indicated equal expression of the two N-terminal set1 deletion constructs (780–1080 and 829–1080) (Fig. 1B). No FLAG-Set1 deletion mutants were detected in the unbound fraction (data not shown).

Besides the n-SET, SET, and post-SET domains of Set1, which are required for methyltransferase activity, the only other known domain found in Set1 is its putative RRM. The RRM is a domain commonly found in RNA-binding proteins and has been implicated in binding RNA, single-stranded DNA, as well as proteins (28). To test whether the putative RRM domain might be the
region in the N terminus of Set1 that regulates H3 Lys⁴ trimethylation, we constructed a FLAG-tagged Set1 expression construct that lacked this domain (Fig. 1A). This deletion construct was expressed in the set1Δ strain and examined for H3 Lys⁴ methylation status. As shown in Fig. 1C, the Set1 ΔRRM (1–1080 ΔRRM) mutant restored H3 Lys⁴ mono- and dimethylation levels similar to wild-type cells and full-length Set1 (1–1080). Similar to the N-terminal Set1 deletion mutants (780–1080 and 829–1080), H3 Lys⁴ trimethylation was nearly abolished in the Set1 ΔRRM (1–1080 ΔRRM) mutant strain (Fig. 1C). Again, longer exposure time to film indicated the presence of trace amounts of H3 Lys⁴ trimethylation (Fig. 1C). Together these data suggest the RRM domain is at least one domain within the N terminus of Set1 that is needed for trimethylation. In further support of our data, Schlichter and Cairns (29) recently published a similar result showing that the RRM domain of Set1 is required for H3 Lys⁴ trimethylation. To determine the levels of protein expression, full-length FLAG-Set1 (1–1080) and FLAG-Set1 ΔRRM (1–1080 ΔRRM) were immunoprecipitated from whole cell extracts and immunoblotted with anti-FLAG antibodies (Fig. 1A). Our results showed expression of both full-length Set1 (1–1080) and Set1 ΔRRM (1–1080 ΔRRM). However, lower levels of Set1 ΔRRM (1–1080 ΔRRM) mutant protein were detected when compared with full-length Set1 (1–1080) (Fig. 1C). Again, no FLAG-Set1 (1–1080) or Set1 ΔRRM (1–1080 ΔRRM) was detected in the unbound fraction (data not shown). Together these data may indicate that the Set1 ΔRRM (1–1080 ΔRRM) mutant protein is less stable. Interestingly, Swd2, a Set1-associated protein, has been implicated in the protein stability of Set1 suggesting the possibility that Swd2 or other Set1-associated proteins (Swd1, Swd3, Spp1, Bre2, Sdc1, or Shg1) interact with the RRM domain to stabilize the protein levels of Set1 (30).

To examine the effects Set1 trimethyl-deficient mutants at the gene level, chromatin immunoprecipitations were performed using H3 Lys⁴ di- and trimethyl-specific antibodies. The GAL10 and PYK1 loci, which are known targets of Set1 and H3 Lys⁴ methylation, were examined (19, 31, 32). A complete loss of H3 Lys⁴ trimethylation was observed at these loci in our set1Δ strain expressing Set1 829–1080 under conditions in which GAL10 and PYK1 were either induced (Fig. 2) or uninduced (data not shown). Importantly, the level of H3 Lys⁴ trimethylation was similar to that of wild type cells (Fig. 2). Together these data suggest that our Set1 trimethyl-deficient mutants are still targeted to chromatin and are competent to dimethylate chromatin templates.

With the establishment of Set1 mutants that are defective for H3 Lys⁴ trimethylation but not mono- or dimethylation, we wanted to determine whether differential methylation of H3 Lys⁴ played a distinct biological function. Deletion of SET1 in S. cerevisiae leads to the loss of telomere, HML, and rDNA silencing (6, 8, 10–13). In addition, some yeast strains deleted for SET1 also demonstrate a slow growth phenotype (6). To examine the extent of H3 Lys⁴ methylation (mono-, di-, or trimethylation) associated with these known set1Δ phenotypes, we expressed full-length Set1 (1–1080), Set1 ΔRRM (1–1080 ΔRRM), and both N-terminal Set1 deletions (780–1080 and 829–1080) in set1Δ strains that either have growth or silencing defects (6, 8, 10, 11).

To determine whether slow growth is the result of a loss in H3 Lys⁴ mono- or trimethylation, the yeast strain background, MSY421, was used. This strain was previously shown to have a significant growth defect when SET1 was deleted (6). Both full-length Set1 (1–1080), Set1 ΔRRM (1–1080 ΔRRM), and the two N-terminal Set1 deletion mutants (780–1080 and 829–1080) were expressed in the MSY421 set1Δ strain. All cells were grown to A600 = 1.0, and 5-fold serial dilutions were spotted on plates containing synthetic complete media lacking uracil (SC-Ura, Bio 101, Inc.) and incubated at 30 °C. Interestingly, set1Δ strains expressing Set1 trimethylation mutants (1–1080 ΔRRM, 780–1080, and 829–1080) rescued the slow growth phenotype similar to that of full-length Set1 (Fig. 3).

Furthermore, these data would suggest that mono- or dimethylation of H3 Lys⁴ or a combination of both is sufficient for proper cell growth.

To determine whether the observed loss of telomere silencing in a set1Δ strain is the result of losing H3 Lys⁴ mono- or trimethylation, SET1 was deleted in a strain where a URA3 gene has been integrated at a subtelomere locus (24). Surprisingly, we...
Set1-mediated Lys⁴ Trimethylation Is Required for Silencing

observed that the set1Δ cells expressing Set1 ΔRRM (1–1080 ΔRRM) or N-terminal Set1 deletions (780–1080 and 529–1080) showed a dramatic sensitivity to 5-FOA (Bio 101, Inc.) as compared with both wild-type cells transformed with blank plasmid (Vector) or set1Δ cells expressing full-length Set1 (1–1080) (Fig. 4). Interestingly, cells expressing Set1 trimethylation mutants (1–1080 ΔRRM, 780–1080, and 529–1080) will eventually grow on 5-FOA plates, albeit in a diminished capacity, upon longer incubation periods at 30 °C (data not shown). This is consistent with our data indicating trace amount of H3 Lys⁴ trimethylation in cells expressing trimethyl-defective mutants (Fig. 1, A and B). Since these cells contain proper H3 Lys⁴ mono- and dimethylation, our data suggest that H3 Lys⁴ trimethylation is needed for proper telomere silencing.

To determine whether silencing at rDNA, HML, and HMR loci is dependent upon H3 Lys⁴ trimethylation, similar assays, as described above, were performed in strains lacking Set1 and containing a URA3 gene integrated at the rDNA locus and the HMR and HML silent mating type loci (24, 25). In all instances, cells that expressed Set1 mutants that are deficient for H3 Lys⁴ trimethylation exhibit sensitivity to 5-FOA as compared with both wild-type cells transformed with blank plasmid (Vector) or set1Δ cells expressing full-length Set1 (1–1080) (Fig. 4). This data again suggests that H3 Lys⁴ trimethylation is also needed for proper silencing at the rDNA, HML, and HMR loci.

Interestingly, at the different silent loci, silencing seems to be compromised at varying degrees when SET1 is deleted or when expressing the Set1 trimethyl-deficient mutants in a set1Δ. Although the reason for this difference is not known, this has been commonly observed among other protein factors that disrupt silencing. However, various explanations could account for our observed differences. For example, the differences between HML and HMR silencing could be a consequence on how the URA3 gene was previously integrated in these strains. It has been shown previously that the URA3 gene is silenced better at the HML than HMR locus due to the way the gene was inserted (33). Therefore, HMR silencing in this strain has been shown to be more sensitive to silencing defects than HML (33). Another strain difference is that HMR, HML, and rDNA strains contain one gene copy of histones H3 and H4, therefore histone amounts may also contribute to these silencing differences. Although we speculate that some of these differences are due to subtle strain differences, it is also possible these differences are due to the type or amount of protein factors (e.g. Sir proteins) that are required for silencing at each of these distinct loci (34).

Our results demonstrate a strong correlation between H3 Lys⁴ trimethylation and silencing. Although, the mechanism by which H3 Lys⁴ trimethylation regulates silencing is still unclear, it has been proposed that loss of histone methylation at H3 Lys⁴ and/or H3 Lys⁷⁹ methylation allows promiscuous binding of Sir proteins to euchromatic regions, which results in titrating away Sir proteins from silent loci (35). In support of this model, it has recently been shown that Sir3 localization is disrupted in a yeast strain expressing a catalytically inactive mutant of Set1 and that Sir3 can bind to unmodified histone peptides but not peptides trimethylated at H3 Lys⁴ (12). It will now be interesting to determine whether similar results are observed using yeast strains lacking only H3 Lys⁴ trimethylation. However, other possibilities could still exist. For example, protein-protein interactions at the N terminus of Set1 may be needed for proper gene silencing, or Set1-mediated trimethylation may regulate expression of a known or unknown silencing factor(s).

It has been indicated by several groups that H3 Lys⁴ trimethylation plays a role in transcriptional activation and/or elongation (7, 19–21, 36). To determine the role of Set1 trimethyl-deficient mutants in transcription, mRNA levels of known Set1 target genes GAL1, GAL10, and PYK1 (19, 31, 32, 37) were examined under uninduced and induced conditions. Surprisingly, reverse transcription-PCR and quantitative real time PCR analysis revealed no significant changes in GAL1, GAL10, and PYK1 steady state mRNA levels under uninduced or induced conditions in either set1Δ cells or set1Δ cells expressing Set1 trimethyl-deficient mutants (data not shown). These data suggest that specific loss of H3 Lys⁴ trimethylation is not sufficient to disrupt transcription of these Set1 targeted genes. In addition, set1Δ and Set1 trimethyl-deficient mutant strains do not show a hypersensitive phenotype when plated on media containing 6-azauracil, suggesting they are not defective in transcriptional elongation. Further investigation will be needed to assess the precise role of Set1-mediated Lys⁴ trimethylation in transcriptional activation and elongation.

In summary, this study demonstrates that a region outside the SET domain (i.e. the RRM domain or other domains in the N terminus of Set1) is required for regulation of Set1-mediated trimethylation. This is in contrast to Set7/9 and Dim5 histone methyltransferases in which a conserved tyrosine or phenylalanine residue within the SET domain mediates the degree of

— I. M. Fingerman and S. D. Briggs, unpublished observation.
and UCC1188 were transduced into MBY1198, MBY1217 and MBY1587 yeast strains; and Peter Cheung and Mary Bryk (TEL). We thank Ann Kirchmaier, Joe Ogas, and Harry Charbonneau for helpful discussions; Dan Gottschling for the UCC506, UCC7266, UCC7262, and UCC1188 yeast silencing strains; Mary Bryk for the MBY1198, 1217 and 1587 yeast strains; and Peter Cheung and Doug Mersman for critical review of the manuscript.

Acknowledgments—We thank Ann Kirchmaier, Joe Ogas, and Harry Charbonneau for helpful discussions; Dan Gottschling for the UCC506, UCC7266, UCC7262, and UCC1188 yeast silencing strains; Mary Bryk for the MBY1198, 1217 and 1587 yeast strains; and Peter Cheung and Doug Mersman for critical review of the manuscript.

REFERENCES

1. Murray, K. (1964) Biochemistry 127, 10–15
2. Lachner, M., O’Sullivan, R. J., and Jenuwein, T. (2003) J. Cell Sci. 116, 2117–2124
3. Peterson, C. L., and Laniel, M. A. (2004) Curr. Biol. 14, R546–R551
4. Rea, S., Eisenhaber, F., O’Carroll, D., Strahl, B. D., Sun, Z. W., Schmid, M., Opravil, S., Mechtler, K., Ponting, C. P., Allis, C. D., and Jenuwein, T. (2006) Nature 445, 593–599
5. Jenuwein, T., Laible, G., Dorn, R., and Reuter, G. (1998) Cell. Mol. Life Sci. 54, 80–93
6. Briggs, S. D., Bryk, M., Strahl, B. D., Cheung, W. L., Davie, J. K., Dent, S. Y. R., Winston, F., and Allis, C. D. (2001) Genetics 155, 3286–3295
7. Santos-Rosa, H., Schneider, R., Bannister, A. J., Sherriff, J., Bernstein, B. E., Emre, N. C. T., Schreiber, S. L., Meller, J., and Kouzarides, T. (2002) Nature 418, 407–411
8. Nagy, P. L., Griesenbeck, J., Kornberg, R. D., and Cleary, M. L. (2002) Proc. Natl. Acad. Sci. U. S. A. 99, 90–94
9. Rogger, A., Schaff, D., Shcherchenko, A., Pijnappel, W. W. M. P., Wilm, M., Aasland, R., and Stewart, A. F. (2003) EMBO J. 22, 1731–1748
10. Krogan, N. J., Dover, J., Schürr, S., Greenblatt, J. F., Schneider, J., John-
11. 12902–12907
12. Wysocka, J., Myers, M. P., Laherty, C. D., Eisenman, R. N., and Herr, W. (2004) Genes Dev. 18, 7137–7148
13. Bryk, M., Briggs, S. D., Strahl, B. D., Curcio, M. J., Allis, C. D., and Winston, F. (2002) Curr. Biol. 12, 165–170
14. Miller, T., Krogan, N. J., Dover, J., Erdjument-Bromage, H., Tempst, P., Johnston, M., Greenblatt, J. F., and Shilatifard, A. (2001) Proc. Natl. Acad. Sci. U. S. A. 98, 12902–12907
15. Milne, T. A., Briggs, S. D., Brock, H. W., Martin, M. E., Gibson, D. A., Allis, C. D., and Hess, J. L. (2002) Mol. Cell. 10, 1107–1117
16. Yokoyama, A., Wang, Z., Wysocka, J., Sanyal, M., Anfuso, D. J., Kitabayashi, I., Herr, W., and Cleary, M. L. (2004) Mol. Cell. Biol. 24, 5639–5649
17. Wysocka, J., Myers, M. P., Laibert, C. D., Eisenman, R. N., and Herr, W. (2003) Genes Dev. 17, 896–911
18. Hughes, C. M., Rozenblatt-Rosen, O., Milne, T. A., Copeland, T. D., Levine, S. S., Lee, J. C., Hayes, D. N., Shannagam, K. S., Bhattacharjee, A., Biondi, C. A., Kay, G. F., Hayward, N. K., Hess, J. L., and Meyerowitz, E. M. (2004) Mol. Cell 13, 587–597
19. Ng, H. H. R., Young, R. A., and Struhl, K. (2003) Mol. Cell. Biol. 23, 799–819
20. Bernstein, B. E., Humphrey, E. L., Erlich, R. L., Schneider, R., Bouman, P., Liu, J. S., Kouzarides, T., and Schreiber, S. L. (2002) Proc. Natl. Acad. Sci. U. S. A. 99, 8700–8705
21. Krogan, N. J., Dover, J., Wood, A., Schneider, J., Heidt, J., Boettger, M. A., Dean, K., R. O., Ghralhi, A., Johnston, M., Greenblatt, J. F., and Shilatifard, A. (2003) Mol. Cell. 11, 721–729
22. Xiao, T., Kao, C. F., Krogan, N. J., Sun, Z. W., Greenblatt, J. F., Osley, M. A., and Struhl, B. D. (2005) Mol. Cell. Biol. 25, 635–651
23. Morgan, B. A., Mittman, B. A., and Smith, M. M. (1990) Cell. 63, 571–576
24. van Leeuwen, F., Gafken, P. R., and Gottschling, D. E. (2002) Cell 109, 745–756
25. Carvin, C. D., and Kladde, M. P. (2004) J. Biol. Chem. 279, 33057–33062
26. Kao, M. H., and Allis, C. D. (1999) Methods 19, 425–433
27. Stefl, R., Skrisciouka, L., and Allain, P. H. (2005) EMBO Rep. 6, 33–38
28. Dichtl, B., Aasland, R., and Keller, W. (2005) DNA (N. Y.) 10, 965–977
29. Ezhkova, E., and Tansey, W. P. (2004) Mol. Cell. Biol. 24, 435–442
30. Daniel, J. A., Torok, M. S., Sun, Z. W., Schult, D., Allis, C. D., Yates, J. R., III, and Grant, P. A. (2004) J. Biol. Chem. 279, 1867–1871
31. Singer, M. S., Kahana, A., Wolf, A. J., Meisinger, L. L., Peterson, S. E., Goggin, C., Mahowald, M., and Gottschling, D. E. (1998) Genes Dev. 12, 613–622
32. Rutsche, L. N., Kirchmaier, A. L., and Rine, J. (2003) Annu. Rev. Biochem. 72, 481–516
33. van Leeuwen, F., Gafken, P. R., and Gottschling, D. E. (2002) Cell 109, 756–762
34. Hampsey, M., and Reindberg, D. (2003) Cell 113, 429–432
35. Henry, K. W., Wyce, A., Lo, W. S., Duggan, L. J., Emre, N. C., Kao, C. F., Pills, L., Shilatifard, A., Osley, M. A., and Berger, S. L. (2003) Genetics 17, 2849–2803
36. Zhang, X., Yang, Z., Khan, S. I., Horton, J. R., Tamaru, H., Selker, E. U., and Cheng, X. (2003) Mol. Cell 12, 177–185
37. Collins, R. E., Tachibana, M., Tamura, H., Smith, K. M., Jia, D., Zhang, X., Selker, E. U., Shinkai, Y., and Cheng, X. (2005) J. Biol. Chem. 280, 5563–5570
Global Loss of Set1-mediated H3 Lys$^4$ Trimethylation Is Associated with Silencing Defects in *Saccharomyces cerevisiae*

Ian M. Fingerman, Chia-Ling Wu, Bradley D. Wilson and Scott D. Briggs

*J. Biol. Chem.* 2005, 280:28761-28765.
doi: 10.1074/jbc.C500097200 originally published online June 16, 2005

Access the most updated version of this article at doi: 10.1074/jbc.C500097200

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 39 references, 20 of which can be accessed free at http://www.jbc.org/content/280/31/28761.full.html#ref-list-1