with the exception that ChIP assays were performed on cells harvested 72 h following a single transfection with dsRNA. *dRing* dsRNA including exonic sequences extending from 167 to 1,154 base pairs (bp) downstream of the ATG was synthesized by bi-directional transcription of RT–PCR products containing T7 promoter sequences at both ends. Isolation of wing imaginal discs and ChIP assays were performed as previously described[22].

Information for purification and identification of histone H2A ubiquitin ligase complex, for generation and characterization of Ring2 knock-down cell lines, as well as for the specificity of the uH2A antibody, is available in Supplementary Methods and Supplementary Data.

Received 29 June; accepted 2 September 2004; doi:10.1038/nature02985.

1. Jenuwein, T. & Allis, C. D. Translating the histone code. *Science* **293,** 1074–1080 (2001).
2. Zhang, Y. & Reinberg, D. Transcription regulation by histone methylation: interplay between different covalent modifications of the core histone tails. *Genes Dev.* **15,** 2343–2360 (2001).
3. Zhang, Y. Transcriptional regulation by histone ubiquitination and deubiquitination. *Genes Dev.* **17,** 2733–2740 (2003).
4. Robzyk, K., Recht, J. & Osley, M. A. Rad6-dependent ubiquitination of histone H2B in yeast. *Science* **287,** 501–504 (2000).
5. Hwang, W. W. *et al.* A conserved RING finger protein required for histone H2B monoubiquitination and cell size control. *Mol. Cell* **11,** 261–266 (2003).
6. Wood, A. *et al.* Bre1, an E3 ubiquitin ligase required for recruitment and substrate selection of Rad6 at a promoter. *Mol. Cell* **11,** 267–274 (2003).
7. Sun, Z. W. & Allis, C. D. Ubiquitination of histone H2B regulates H3 methylation and gene silencing in yeast. *Nature* **418,** 104–108 (2002).
8. Dover, J. *et al.* Methylation of histone H3 by COMPASS requires ubiquitination of histone H2B by Rad6. *J. Biol. Chem.* **277,** 28368–28371 (2002).
9. Nickel, B. E. & Davie, J. R. Structure of polyubiquitinated histone H2A. *Biochemistry* **28,** 964–968 (1989).
10. Lee, S. J. *et al.* E3 ligase activity of RING finger proteins that interact with Hip-2, a human ubiquitin-conjugating enzyme. *FEBS Lett.* **503,** 61–64 (2001).
11. Satijn, D. P. *et al.* RING1 is associated with the polycomb group protein complex and acts as a transcriptional repressor. *Mol. Cell. Biol.* **17,** 4105–4113 (1997).
12. Fritsch, C., Beuchle, D. & Muller, J. Molecular and genetic analysis of the Polycomb group gene Sex combs extra/Ring in *Drosophila*. *Mech. Dev.* **120,** 949–954 (2003).
13. Gorfinkiel, N. *et al.* The *Drosophila* Polycomb group gene Sex combs extra encodes the ortholog of mammalian Ring1 proteins. *Mech. Dev.* **121,** 449–462 (2004).
14. Francis, N. J., Saurin, A. J., Shao, Z. & Kingston, R. E. Reconstitution of a functional core polycomb repressive complex. *Mol. Cell* **8,** 545–556 (2001).
15. Levine, S. S. *et al.* The core of the polycomb repressive complex is compositionally and functionally conserved in flies and humans. *Mol. Cell. Biol.* **22,** 6070–6078 (2002).
16. Joazeiro, C. A. & Weissman, A. M. RING finger proteins: mediators of ubiquitin ligase activity. *Cell* **102,** 549–552 (2000).
17. Wang, H. *et al.* mAM facilitates conversion by ESET of dimethyl to trimethyl lysine 9 of histone H3 to cause transcriptional repression. *Mol. Cell* **12,** 475–487 (2003).
18. Vassilev, A. P., Rasmussen, H. H., Christensen, E. I., Nielsen, S. & Celis, J. E. The levels of ubiquitinated histone H2A are highly upregulated in transformed human cells: partial colocalization of uH2A clusters and PCNA/cyclin foci in a fraction of cells in S-phase. *J. Cell Sci.* **108,** 1205–1215 (1995).
19. Cao, R. & Zhang, Y. SUZ12 is required for both the histone methyltransferase activity and the silencing function of the EED-EZH2 complex. *Mol. Cell* **15,** 57–67 (2004).
20. Voncken, J. W. *et al.* Rnf2 (Ring1b) deficiency causes gastrulation arrest and cell cycle inhibition. *Proc. Natl Acad. Sci. USA* **100,** 2468–2473 (2003).
21. Cao, R. *et al.* Role of histone H3 lysine 27 methylation in Polycomb-group silencing. *Science* **298,** 1039–1043 (2002).
22. Wang, L. *et al.* Hierarchical recruitment of polycomb group silencing complexes. *Mol. Cell* **14,** 637–646 (2004).
23. Henry, K. W. *et al.* Transcriptional activation via sequential histone H2B ubiquitylation and deubiquitylation, mediated by SAGA-associated Ubp8. *Genes Dev.* **17,** 2648–2663 (2003).
24. Kao, C. F. *et al.* Rad6 plays a role in transcriptional activation through ubiquitylation of histone H2B. *Genes Dev.* **18,** 184–195 (2004).
25. Ng, H. H., Xu, R. M., Zhang, Y. & Struhl, K. Ubiquitination of histone H2B by Rad6 is required for efficient Dot1-mediated methylation of histone H3 lysine 79. *J. Biol. Chem.* **277,** 34655–34657 (2002).
26. Briggs, S. D. *et al.* Gene silencing: trans-histone regulatory pathway in chromatin. *Nature* **418,** 498 (2002).
27. Devroe, E., Erdjument-Bromage, H., Tempst, P. & Silver, P. A. Human Mob proteins regulate the NDR1 and NDR2 serine-threonine kinases. *J. Biol. Chem.* **279,** 24444–24451 (2004).
28. Plath, K. *et al.* Role of histone H3 lysine 27 methylation in X inactivation. *Science* **300,** 131–135 (2003).
29. Schoorlemmer, J. *et al.* Ring1A is a transcriptional repressor that interacts with the Polycomb-M33 protein and is expressed at rhombomere boundaries in the mouse hindbrain. *EMBO J.* **16,** 5930–5942 (1997).

Supplementary Information accompanies the paper on **www.nature.com/nature**.

Acknowledgements We thank J. Kim for help with mass spectrometry. This work was supported by NIH grants to Y.Z., R.S.J. and P.T.

Competing interests statement The authors declare that they have no competing financial interests.

Correspondence and requests for materials should be addressed to Y.Z. (yi_zhang@med.unc.edu).

corrigenda

The lipid phosphatase SHIP2 controls insulin sensitivity

S. Clément, U. Krause, F. Desmedt, J.-F. Tanti, J. Behrends, X. Pesesse, T. Sasaki, J. Penninger, M. Doherty, W. Malaisse, J. E. Dumont, Y. Le Marchand-Brustel, C. Erneux, L. Hue & S. Schurmans

Nature **409,** 92–96 (2001).

In this Letter, we investigated the production and the phenotypic characterization of a SHIP2 (SH2 domain containing inositol phosphate 5-phosphatase type 2, or *Inppl1*) knockout mice. Total or partial loss of SHIP2 enzyme in these mice resulted in an increased insulin sensitivity. From these experiments, we concluded that SHIP2 is a potent negative regulator of insulin signalling and insulin sensitivity *in vivo*. However, we have recently realized that the 7.3-kilobase genomic DNA fragment deleted in these mice includes, in addition to exons 19–29 of the *SHIP2* gene, the third (and last) exon of the *Phox2a* gene. The deletion of this exon results in the absence of the 124 carboxy-terminal amino acids from a total of 280, including part of the homeodomain, and should give rise to a completely non-functional Phox2a protein if expressed. As a consequence, the mice we described have both *SHIP2* and *Phox2a* genes inactivated. It is currently unknown whether the increased insulin sensitivity we observed in our mice results from the inactivation of the *SHIP2* gene alone, of the *Phox2a* gene alone, or of both genes. □

Induction of DNA methylation and gene silencing by short interfering RNAs in human cells

Hiroaki Kawasaki & Kazunari Taira

Nature **431,** 211–217 (2004).

In the Methods section of this Letter, the published primer sequences used to amplify the E-cadherin and *erbB2* promoters for bisulphite sequencing were incorrect. We used two primer sets, one for unconverted DNAs and the other for converted DNAs. Primers for unconverted DNAs were: for the E-cadherin promoter, the forward primer was 5′-TCTAGAAAAATTTTTTAAAAA-3′ and the reverse primer was 5′-CAGCGCCGAGAGGCTGCGGCT-3′; for the *erbB2* promoter, the forward primer was 5′-CCTGGAAGCCA-CAAGGTAAAC-3′ and reverse primer was 5′-TTTCTCCGG TCCCAATGGAGG-3′. Primers for converted DNAs were: for the E-cadherin promoter, the forward primer was 5′-TTTA-GAAAAATTTTTTAAAAA-3′ and the reverse primer was 5′-CAA-CACCAAAAAACTACAACT-3′; for the *erbB2* promoter, the forward primer was 5′-TTTGGAAGTTATAAGGTAAAT-3′ and the reverse primer was 5′-TTTCTCCAATCCCAATAAAAA-3′. □