Corrections in our papers

コミュニティーの皆様へ　2017.6.17

このたび東京大学に対する匿名の論文不正の告発があり、私どもの研究室から出された7報の論文について全てのデータに渡る詳細な調査を受けることになり、研究室を上げて全面的に調査に協力してきました。8ヶ月に及ぶ調査の結果、5報の論文において、いくつかのデータの表示において不適切な操作およびミスがあったことが調査委員会により指摘されました。私は今回の調査結果を真摯に受け止め、これらの論文の責任著者として、論文に正確さに欠ける図表が載ってしまったことに大きな責任を感じております。指摘を受けたいずれの記載も、当該論文自体の科学的な結論に影響を与えるものではないと考えておりますが、論文の訂正あるいは取り下げに関しましては、掲載誌と相談した上で最も適切な処置を速やかにとらせて頂く所存です。私どもの論文疑惑が関連分野の研究者の皆様をいたずらに惑わすことのないように、委員会より不適切の指摘を受けた記載についての詳細な情報と、それに対する生データに基づいた修正を、以下に開示いたします。このたびの私どもの軽率な行いにより、研究者コミュニティーの皆様には大変なご迷惑をおかけしましたことを心より陳謝いたします。

東京大学分子細胞生物学研究所　染色体動態研究分野　渡邊嘉典

To whom it may concern,

After receiving anonymous allegations of research misconduct, the University of Tokyo conducted an investigation of seven articles published by my laboratory during 2005–2015. My colleagues and I have cooperated fully with the investigative committee, providing access to all raw data and participating in direct interviews. After an extensive investigation lasting eight months, the committee reported a number of errors in the handling of data in five of the seven papers in question. As the head of the laboratory, I take ultimate responsibility for these errors, and extend my sincerest apologies to the scientific community for any concern or inconvenience these may have caused. Although we believe that none of the errors affect the main conclusions of any of the reports, we are in contact with the journals in which they were published to determine the most appropriate action we should take for each of the articles (correction, retraction, etc.). In the interests of transparency and a speedy resolution to concerns about these articles, in the following slides I discloses the errors, steps now being taken to resolve them, and the implications for the conclusions of the respective publications. I provide both the originally published data and corrections (below). Again, I apologize deeply for any confusion that these errors may have caused.

Sincerely,

Yoshinori Watanabe, PhD
Laboratory of Chromosome Dynamics,
Institute of Molecular and Cellular Biosciences, The University of Tokyo

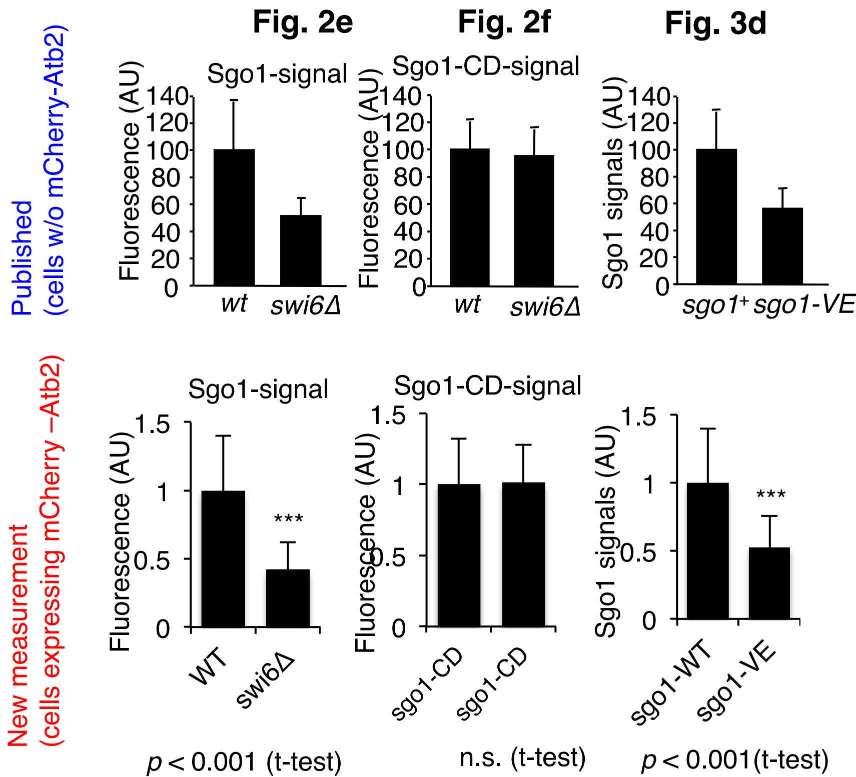
Anonymous allegations (and our responses):
https://www.dropbox.com/s/3zwoop33r8x0c7k/Accusation%20%28E%29.pdf?raw=1

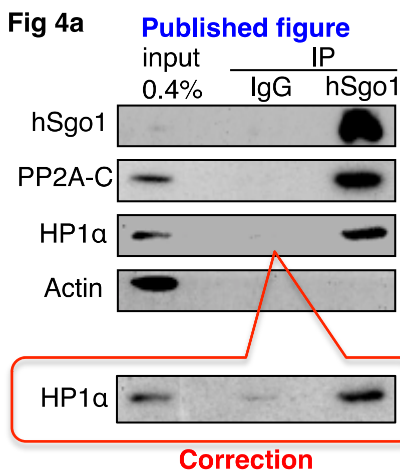
Two of the 23 allegations are raised in PubPeer: https://pubpeer.com/publications/16325576
https://pubpeer.com/publications/20383139

Yamagishi, Y., Sakuno, T., Shimura, M. & Watanabe, Y.
Heterochromatin links to centromeric protection by recruiting shugoshin.
***Nature* 455, 251-255 (2008)**

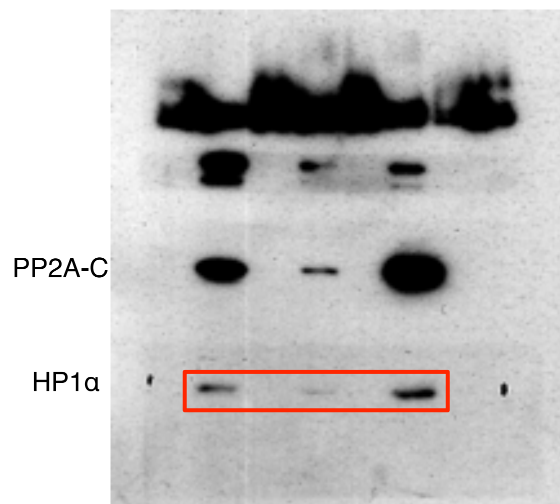
In Figs. 2e, 2f and 3d, the cells in the representative pictures expressed mCherry-Atb2 (tubulin), whereas the cells used in the quantification did not express mCherry-Atb2. During preparation of the manuscript, we mistakenly used a different population of cells during quantification, and due to this oversight we did not register the latter cells (i.e., those lacking mCherry-Atb2) in the published list of cell strains. However, because both of these cells are similarly arrested at metaphase I by inactivation of APC, the results of the quantification are closely similar and our conclusions are unaffected by this error. We have submitted a request to the journal for correction of the strain list. In Fig 4a, western blot panel of HP1α was improperly processed. We apologize for any confusion that these errors may have caused.

We confirmed that the quantitative intensities of Sgo1-GFP signal in mCherry-Atb2 expressing cells are nearly identical to those in cells lacking mCherry-Atb2. SD (n = 30 cells).





Uncropped image of blottings



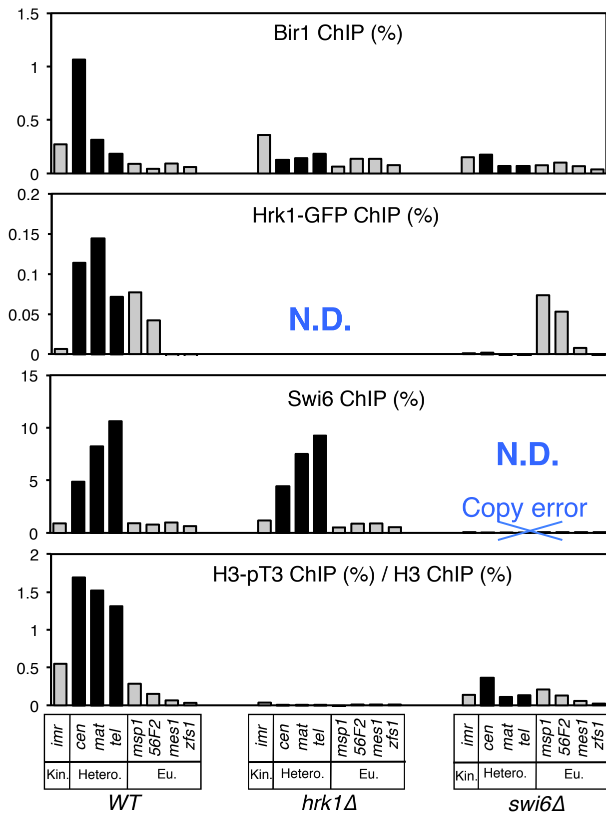
Yamagishi, Y., Honda, T., Tanno, Y. & Watanabe, Y.
Two histone marks establish the inner centromere and chromosome segregation.
Science **330, 239-243 (2010)**

In Fig. 3A, two ChIP datasets (ChIP1 and ChIP2) were improperly combined into a single graph. In the corrected Fig. 3A, ChIP1 and ChIP2 are presented separately. These corrections do not affect the description of the results of the specific experiment or the conclusions of the article as a whole. We apologize for any confusion that this error may have caused.

Errors

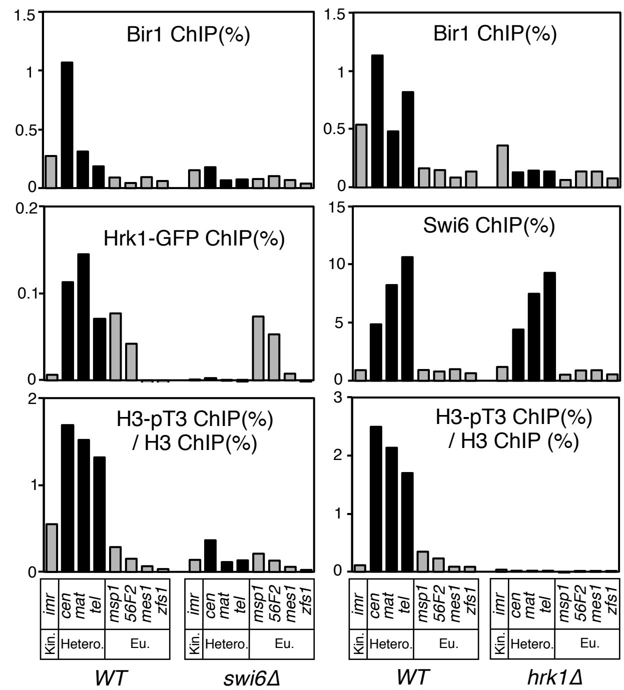
1) Bir1 *(WT)* and H3-pT3/H3 *(WT)* derive only from ChIP1 but not ChIP2.
2) Experiment has not been performed, and should have been indicated as N.D. (not determined).
3) There is a copy error in Swi6 *(swi6Δ)*.

Published Fig. 3A



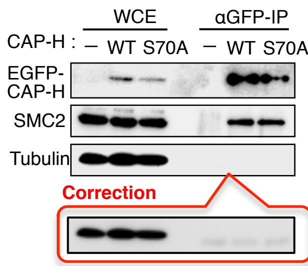
Corrected Fig. 3A

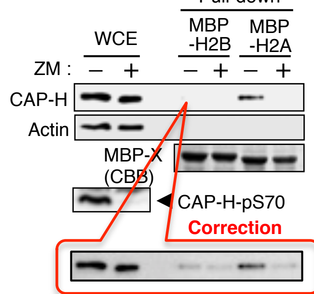
(ChIP1) (ChIP2)

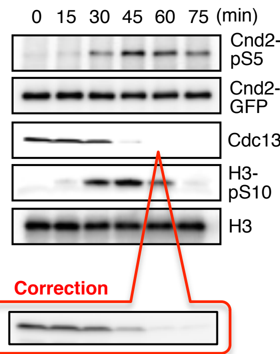


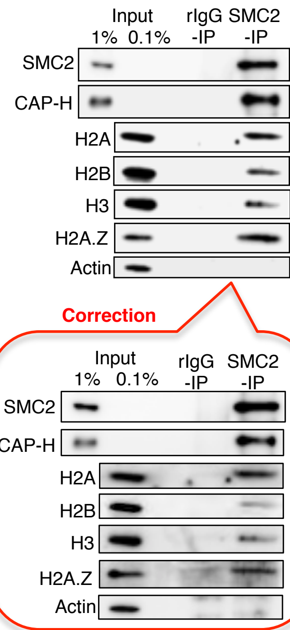
Tada, K., Susumu, H., Sakuno, T. & Watanabe, Y.
Condensin association with histone H2A shapes mitotic chromosomes.
***Nature* 474, 477-483 (2011)**

In Figs. 3e, 3g, 5a and S16, the western blot panels were not properly processed. We show the corrected panels, which have been reconstructed from the raw data files, are shown here. These corrections do not affect the description of the results of the specific experiment or the conclusions of the article as a whole. We apologize for any confusion that this error may have caused.



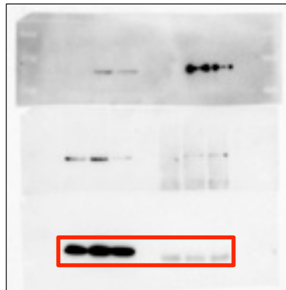


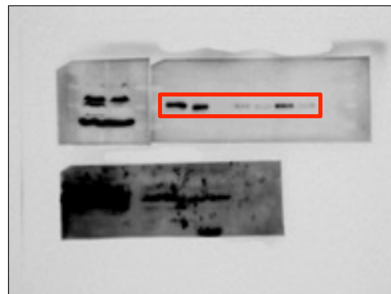


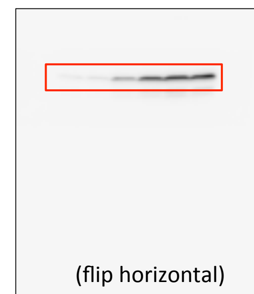


We have received an affirmative reply from Nature.

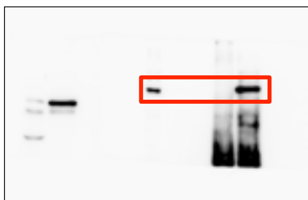
Uncropped images of blottings

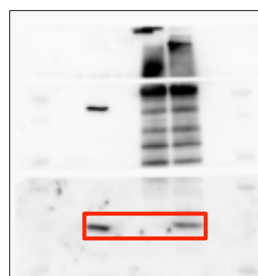


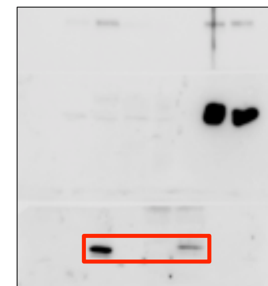


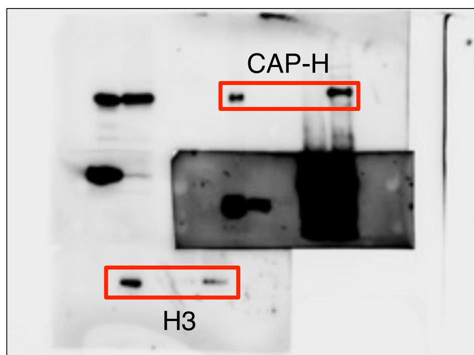


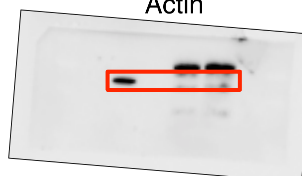
(Fig S16)

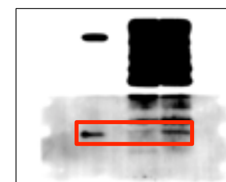






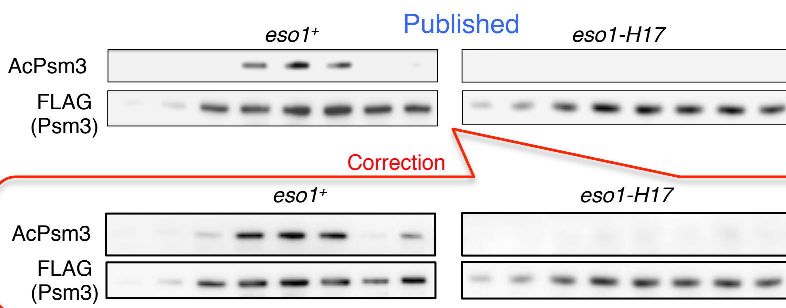




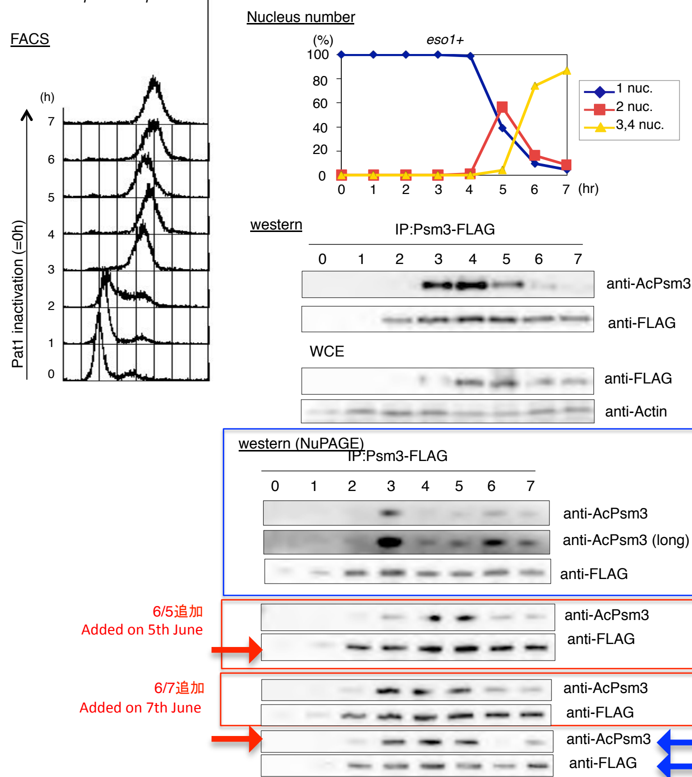


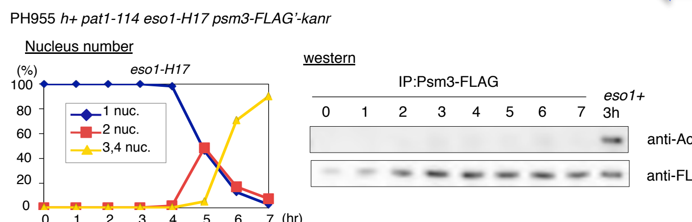
Kagami, A., Sakuno, T., Yamagishi, Y., Ishiguro, T., Tsukahara, T., Shirahige, K., Tanaka, K., Watanabe, Y. Acetylation regulates monopolar attachment at multiple levels during meiosis I in fission yeast.
***EMBO Rep.* 12, 1189-95 (2011)**

In Fig. 2A, western blot panels were misprocessed. Yoshinori Watanabe is responsible for this processing. The corrected figure is assembled from blots in the same experiment. This change does not affect the conclusion in the paper. We apologize for any confusion that this error may have caused.



This page is a copy of the progress report file by Dr. Kagami (June 10 2011).

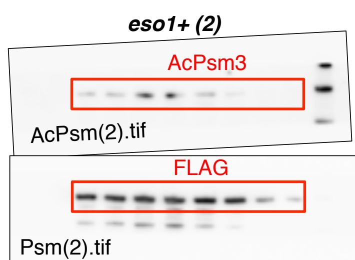


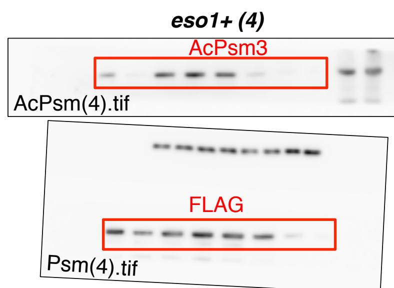


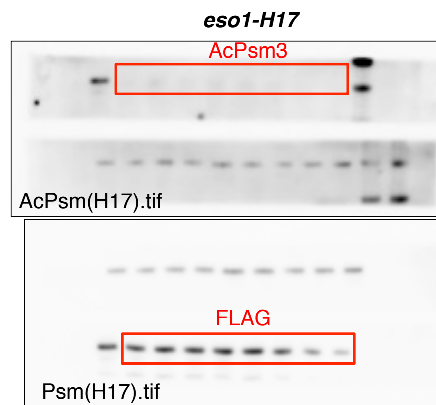
Explanation for the left panels:
The immunoprecipitation products prepared from *eso1+* cells were analyzed by NuSDS PAGE, and blots were probed first with anti-AcPsm3 and then with anti-FLAG. This experiment was repeated four times, loading the same samples, until the IP samples were exhausted. None of the blots was perfect in terms of band loading and/or transfer, although 2), 3) and 4) are consistent. The red arrows show the published WBs; however, these were inappropriately taken from different WBs, which was not noted in the published figures. Moreover, background signals in the anti-Psm3 WB disappeared because the image contrast was increased in the published panel. Here, we provide a corrected version based on the original data, in which the WBs are indicated by blue arrows. We note that this version also supports the previous conclusion that 'In meiosis, cohesin is acetylated depending on Eso1 also during late S phase and persists until prophase '.

Explanation for the left panels:
IP products prepared from *eso1-H17* cells were similarly analyzed and shown as a negative control (in both the previous and corrected versions).

Uncropped images of blottings
(please note that all gels are flip horizontal)







EUROPEAN MOLECULAR BIOLOGY ORGANIZATION

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Institute of Molecular and Cellular Biosciences, University of Tokyo,
Yayoi 1-1-1, Tokyo 113-0032, Japan

01.05.2017

Re.: EMBO Press assessment of potential image aberration in *EMBO Rep.* 2011;12(11):1189-95. doi: 10.1038/embor.2011.188 by Yoshinori Watanabe and colleagues

Dear Yoshinori,

I have written a formal letter to the Dr. Takeshita of the investigation committee that outlines our assessment of the issues in the 2011 paper. Given the lack of signal in one of the panels in particular, we would suggest to issue a short corrigendum that incudes the updated images from matched Western blots based on the original source data of figure 2Aa.
We would like to invite you to issue this text and we will aim to publish it as fast as possible as a corrigendum in the journal.

To summarize this case, you alerted us to apparent problems in fig 2A on March 29th 2017, apparently based on issues pointed out as part of the institutional investigation. We assessed all of the published images of the paper and found no other problems than those noted by you in fig 2A. Regarding fig 2A, we conclude that the contrast is overly accentuated in the Western blot panels in the left part of the figure, which leads to a loss of linear signal, limiting the quantitative information that can be derived from the images.
You also rightly noted that there is no apparent signal in the top right hand Western blot panel of fig 2A. This may be due either to the complete absence of experimental data or images that were over-contrasted to the point where all signal is lost at the resolution of the published image. Either way, panels with no detectable data are not informative. In this case, our view is that the problem is most likely either due to a mistake or to poor image processing, rather than intentional falsification.
You also provided a set of PowerPoint files including some Japanese language annotations that we could not decipher. These files appear to represent notes taken at the time by the postdoc who performed the experiments and you confirmed that these files were saved in 2011. You also supplied a set of digital image files that apparently represent unprocessed source data scans. We have assessed all of these files and conclude that they are consistent with your claim that you ran four sets of Western blots with the same set of samples in parallel and processed these blots in parallel (i.e. they all derived from a single experiment). The blots underlying the different panels were probably processed somewhat differently, resulting in the different contrast and background noted in the published figure. This clearly limits the quantitative comparisons possible between the panels, but nonetheless allows for qualitative comparisons. The conclusions in the paper derived from this figure are largely qualitative and we therefore see no compelling reason to doubt these conclusions. We do not have access to primary lab-book records or indeed the primary photographs of the Western blots, the Western blots themselves or remaining denatured protein samples, and as such we cannot run a full research investigation at EMBO Press. However, we see no reason to doubt your explanations.

We recommend issuing a corrigendum primarily to point to the fact that the top right panel lacks signal and to show the correct panels. As part of this corrigendum, we would also invite you to note that the Western blots in fig 2A were derived from the same samples, run at the same time, but that these were concatenated to assemble the published figure. This

resulted in differential contrast and exposures in the published figures, limiting the quantitative information content of the figure, but not *per se* the conclusions derived.

On the EMBO Press scale of image aberrations (see *The EMBO Journal* (2015) 34, 2483-2485), this would be a level 1, the lowest level on the scale we use to classify image and data aberrations (http://embor.embopress.org/classifying-image-aberrations). Thus, our view is that the basic conclusions of this figure, and therefore the paper as a whole, stand. To be clear, we do not regard it as best practice to mix and match Western blot panels to obtain the most 'compelling' figure. However, as long as it is true that the matched blots all derived from a single set of samples from the same experiment, we see no case of especially poor experimental rigour, or indeed to conclude formal wrongdoing.

Please note that we also assessed the figures of other papers that you kindly published in journals that belong to the *EMBO Press* group (listed below). We detected no other issues of image aberration or manipulation based on our standard screening process.

Yours sincerely,

Bernd Pulverer, Ph.D.

Head of Scientific Publications; Chief Editor, *The EMBO Journal*; Acting Chief Editor, *EMBO reports*

Other papers assessed by *EMBO Press* standard image forensic processes:

The cohesin REC8 prevents illegitimate inter-sister synaptonemal complex assembly.
Ishiguro K, Watanabe Y. EMBO Rep. 2016 Jun;17(6):783-4. doi: 10.15252/embr.201642544.

Acetylation regulates monopolar attachment at multiple levels during meiosis I in fission yeast.
Kagami A, Sakuno T, Yamagishi Y, Ishiguro T, Tsukahara T, Shirahige K, Tanaka K, Watanabe Y.
EMBO Rep. 2011 Oct 28;12(11):1189-95. doi: 10.1038/embor.2011.188.

A new meiosis-specific cohesin complex implicated in the cohesin code for homologous pairing.
Ishiguro K, Kim J, Fujiyama-Nakamura S, Kato S, Watanabe Y. EMBO Rep. 2011 Mar;12(3):267-75. doi: 10.1038/embor.2011.2

Aurora controls sister kinetochore mono-orientation and homolog bi-orientation in meiosis-I.
Hauf S, Biswas A, Langegger M, Kawashima SA, Tsukahara T, Watanabe Y. EMBO J. 2007 Oct 31;26(21):4475-86.

Rec8 cleavage by separase is required for meiotic nuclear divisions in fission yeast.
Kitajima TS, Miyazaki Y, Yamamoto M, Watanabe Y. EMBO J. 2003 Oct 15;22(20):5643-53.

Tanno, Y., Susumu, H., Kawamura, M., Sugimura, H., Honda, T., & Watanabe, Y.
The inner centromere-shugoshin network prevents chromosomal instability. ***Science*** **349, 1237-1240 (2015)**

In figs. 2C, S13C and S15A, the representative images for comparison were captured under different imaging conditions. In fig. S8B, S11F, S12B, the images used for compared were not adjusted using identical settings. In fig. S8A, the dot blots were mislabeled and not properly adjusted for contrast. We show corrected images or explanation here. Given that quantifications were performed using the original images, we believe that the changes in the representative images do not affect the conclusions of the paper. However, as this paper has a number of errors, we are contacting the journal to inquire whether extensive correction or retraction is more appropriate. We apologize for any confusion that these errors may have caused.

Fig 2C

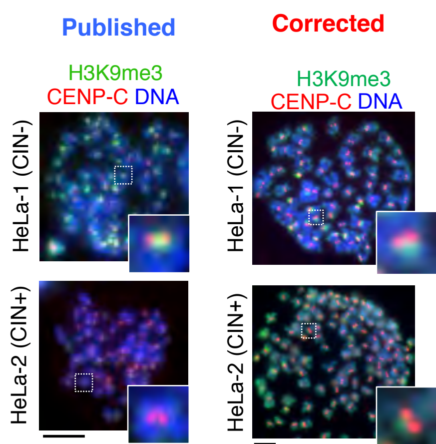
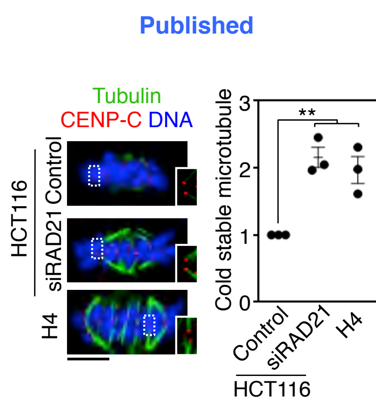


fig S13C



Explanation

Cold-treated and non-treated samples were prepared in parallel. The exposure conditions for filming tubulin signals are adjusted by the signal strength of each non-treated sample and applied to the cold-treated sample. Accordingly, the exposure time was different among samples. Quantification was done by the ratio between cold-treated and non-treated samples and normalized to that of control. The differences in exposure time compensate for differences in the intensity of staining between independent non-treated samples. Because imaging conditions were adjusted in a way that non-treated samples showed similar intensity, representative pictures of the cold-treated samples do reflect quantitative differences in the different conditions.

fig S15A

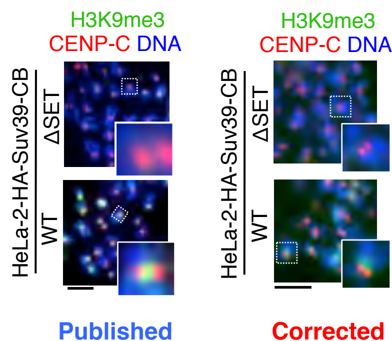


fig S11F

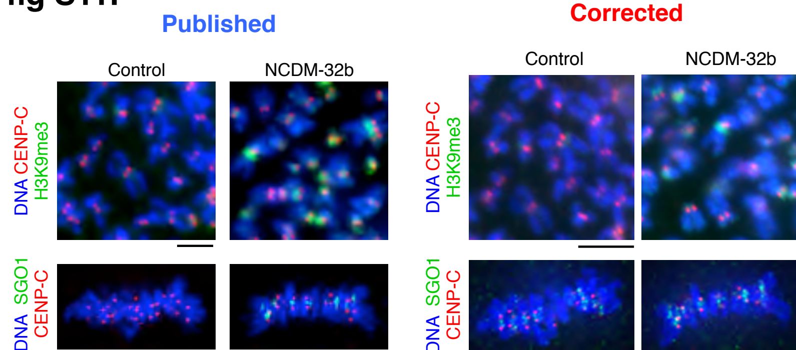


fig S8A

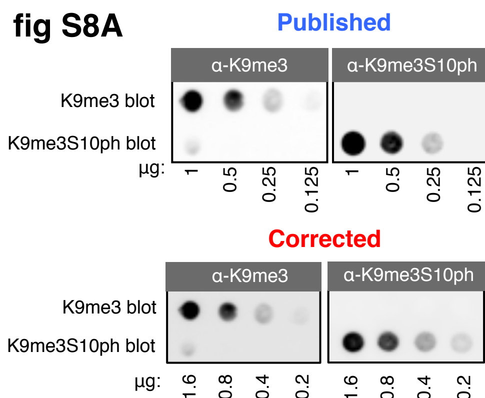
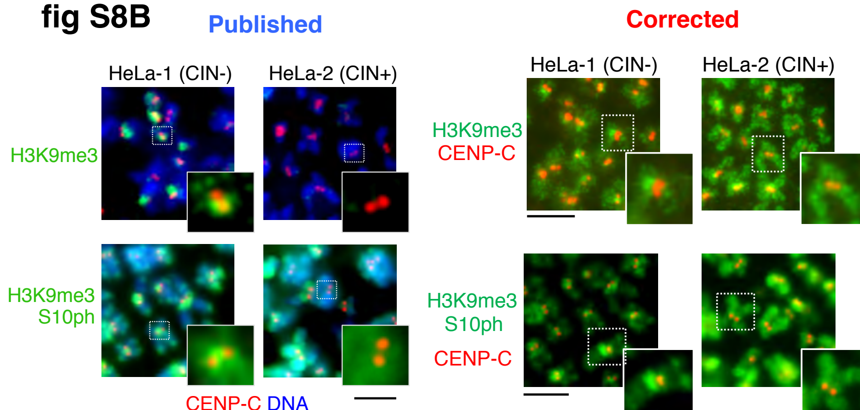


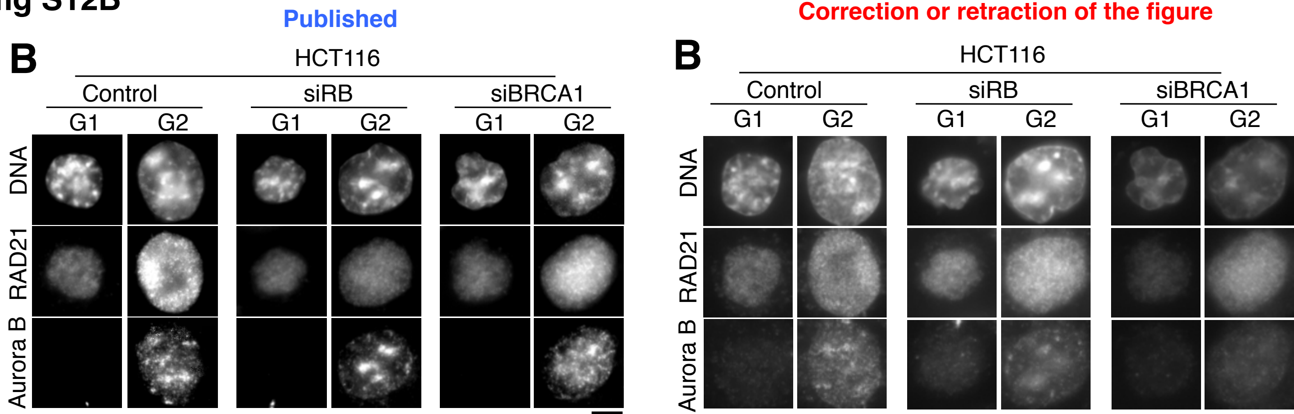
fig S8B



Science 349, 1237-1240 (2015)

fig S12B

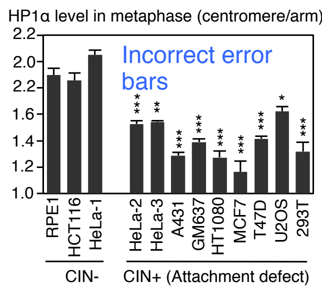
Published | Correction or retraction of the figure



We additionally made some inadvertent mistakes (due to a mistake in our use of the graph software) in adding error bars in Fig. 2A, 4A, S6 and S13D, while preparing or revising the manuscript. We have confirmed that the statistical analyses are all valid, as they were performed on the original data. The errors are corrected here. We apologize for any confusion that these errors may have caused.

Fig 2A

Published graph



Corrected graph

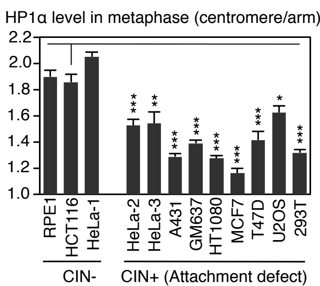
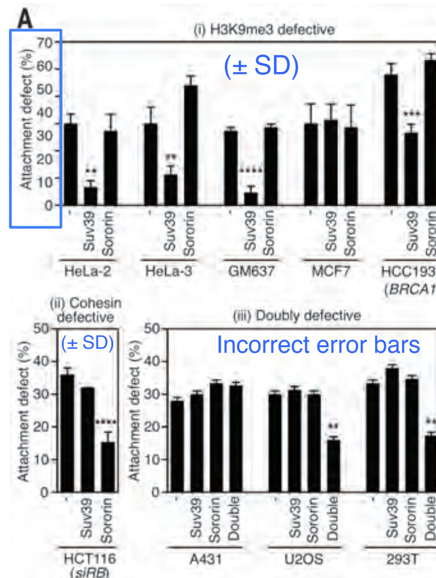


Fig 4A

Published graph



Corrected graph (all ± SEM)

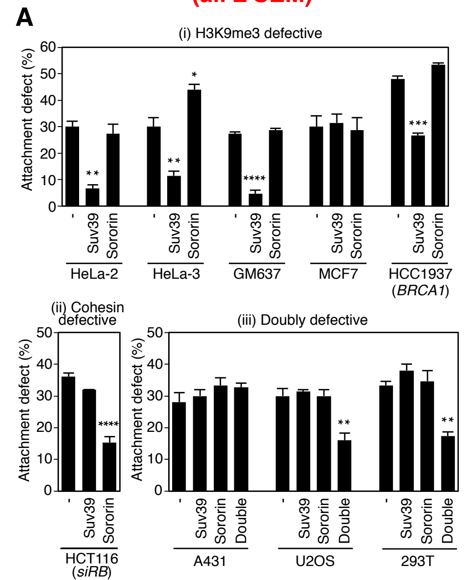
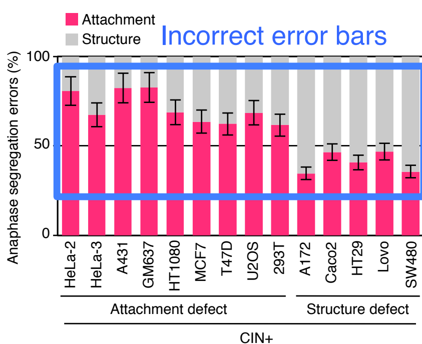


fig S6

Published graph



Corrected graph

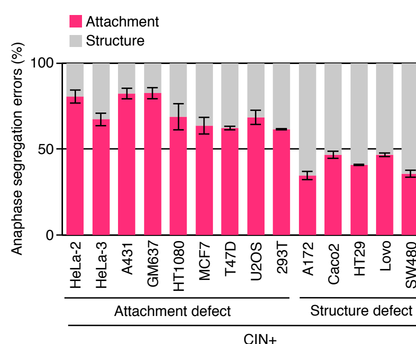
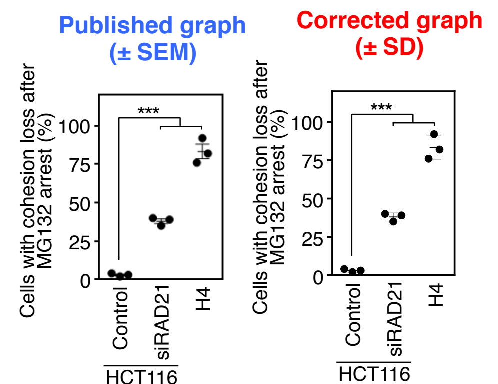


fig S13D

Published graph (± SEM)



Corrected graph (± SD)