

Report from the ad hoc investigative panel concerning the
JBC paper (Kimura et al. 275(23):17233-17236, 2000)

(November 8 - 15, 2002)

Investigators:

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1. Assignment of an ad hoc investigative panel

Following receipt of a notice from the Editor of the JBC, Dr. Herbert Tabor, indicating the possibility of data fabrication in part of a figure of a paper published by the Narumiya laboratory, Shuh Narumiya immediately informed the dean of the Faculty of Medicine, Kyoto University about the matter. Upon direction of the Dean, an independent panel consisting of the three faculty-investigators mentioned above was appointed. All three were selected on the ground that they were members of the Department of Pharmacology, but had access to independent funding and laboratory spaces. None of the three was directly linked with the work in question, but all were with relatively good knowledge about the area of research conducted in the Narumiya laboratory.

2. Investigative aim of this panel

The panel examined one major issue: Was there a scientific misconduct in Figure 4 as alleged in the e-mail from the Editor of JBC ?

3. Results from the panel's investigation

The panel conducted multiple hearings from the authors of the Kimura et al. paper, and examined the raw images, datafiles, notebooks related to the paper.

3.1 Determination of the role of each author in the paper:

First we examined the respective role of each author associated with this paper. It was found that the contribution of the second author, Takahiro Tsuji was mainly to assist the first author, Kazuhiro Kimura, in a number of experiments under Kimura's direct supervision. It was also found that the contribution of the third author, Yuka Takada was to optimize Western blot protocol for Rho A detection. The role of the fourth author, Tohru Miki was to supply with various Ect2 constructs and Ect2 antibodies. The last author, Shuh Narumiya, had no part in the wet work, but did most of the manuscript writing. Thus, it was found that the first author Kazuhiro Kimura essentially conducted all experiments reported in this paper. Concerning the figure assemblage, both Kimura and Narumiya contributed to it, although most, if not all, of the assembly of the figures (either at the printout or computer screen level) seemed to have been carried out by Kimura, under close supervision from Narumiya, however.

Because it became immediately clear that Tsuji, Takada and Miki had little role in the execution of the experiments / figure assemblage pointed out by the Editor of JBC, the hearing of this panel has essentially been limited to Kimura and Narumiya.

3.2 Examination of the possibility of scientific misconduct in Figure 4 of the Kimura paper.

In the original notice by the JBC Editor, a physical duplication of lanes was pointed out in Figure 4 by an anonymous reader. We confirmed that such duplication occurred indeed in the figure 4 of the original manuscript submitted to JBC (Evidence 1: original Figure 4 as submitted by the authors, at the original magnification). Clearly, the third lane from the left in either the left or the right figure panels are identical, based on the background dots and lines of the image, exactly as pointed out by the anonymous reader. Such duplication of the band including the background noise cannot be explained experimentally, and therefore indicates an improper post hoc misrepresentation of the data.

We next examined whether this misrepresentation was explicit and intentional. Narumiya and Kimura testified that during the making of Figure 4, Kimura essentially cropped image data out of an original blot image and carried out an re-assembly of lanes on a lane-to-lane basis, to better separate data from non-transfected (-) vs transfected (+) cells. (Evidence 2: original blot data for Figure 4). Blow-up examination clearly showed that all lanes in the submitted Figure 4 indeed originated from this data (Evidence 3: assembly process reconstructed by this panel). We however also noted that we found no sign of intent or attempt to conceal the fact that this figure consisted of an assemblage of lanes: the artificial boundary of the lanes were clearly noticeable in the submitted figure, when examined under the original magnification (see arrowheads in Evidence 1 for an example of boundary). Furthermore, Kimura submitted independent blot showing that the data in Figure 4 was in essence reproducible (Evidence 4: independent blot supporting findings in Figure 4).

Taken together, this panel finds that there was little benefit, either scientific or cosmetic, to intentionally duplicate the lanes in the way the authors of this paper did. As the re-assembly of the different lanes was rather complex (see Evidence 3), this panel cannot rule out the possibility that the first author Kimura who conducted this manual cropping on Photoshop may have miscreated such duplication by an unintentional error, without himself and the other authors to be able to detect and correct the error until submission.

3.3 Examination of other possible concerns with the paper.

During the hearings, this panel also examined raw data and notebooks related with Figures 1 to 3 as well. So far, the panel has not found indices that definitively discredit any of the data shown in these figures. It should be mentioned, however, that the search for potential flaws in the paper was limited because of lack of time.

4. Conclusions and recommendations by the panel

During the period of November 8th to 11th 2002, this panel conducted hearings and examination of experimental data with a view to investigating the existence of possible scientific misconduct in the JBC paper by Kimura et al (2000).

Conclusion 1:

It is this panel's opinion that it could not find indisputable evidence for scientific misconduct with regards to Figure 4, unlike the original claim by the anonymous reader. Importantly, the data reported in this figure were found to be reproducible in the authors' hand, making it unlikely for the authors to gain substantial benefit by data fabrication. However, it also determined that the authors were responsible for carrying out a complex assembly of photographic data using computer software, and that it was most likely that they were unable to prevent an erroneous insertion of inappropriate data during the preparation of the submitted manuscript.

Recommendation 1:

The panel finds that at this stage of the investigation, the claim for scientific misconduct in Figure 4 is not solid enough to warrant retraction of this paper per se. While this panel thinks that the misrepresentation created in the Kimura paper may not be a misconduct per se, it remains at the discretion of the Editor of JBC to decide how such an error should be corrected.

Conclusion 2:

As the statute of this panel was to mainly determine the validity of the claim of misconduct, as alleged in the e-mail from the Editor of JBC, and because of the limitation of the time, we have not been able to definitively examine whether all other experiments described in the paper has been carried out flawlessly.

Recommendation 2:

To dissipate any doubt, we recommend Kazuhiro Kimura, Shuh Narumiya and co-workers to conduct an internal re-validation process of the reagents, protocols etc. used in the study, and to make its results known to the Editor of JBC. The verification process shall be closely monitored by this panel, if necessary, and the conclusions of this process shall be reported to the Dean and to the Editor of JBC, in due time.

Explanation for Evidence

The following explanations are based on Kimura's experiment record submitted by the authors.

Evidence 1

The figure 4 of the original manuscript submitted to JBC. The panel has created this image by re-scanning one of the printed copies used for the submitted manuscript.

Evidence 2

The original blot of figure 4. Control samples (M phase, G2 phase, and S phase) were prepared from HeLa cell lysates collected at the indicated cell cycle in a different experiment. HeLa cell lysates either from cells without transfection ((-)) or from cells transfected with the ECT2-N1 construct ((+)) were collected at S phase (S), or at 0 (0), 45 (45), 90 (90) minutes after cells were released from the nocodazole arrest (dated 1/25/2000). The samples were analyzed by Western blot using an anti-ECT2 antibody.

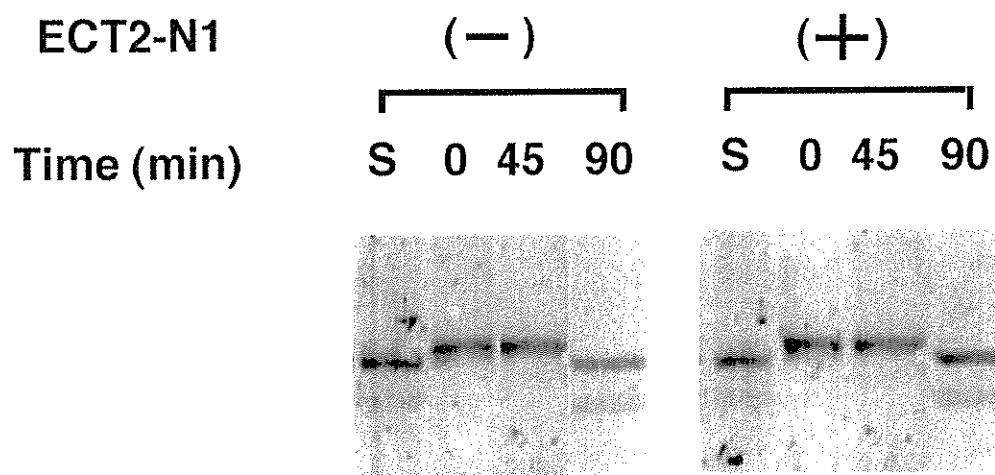
Evidence 3

Assembly process reconstructed by this panel. As shown, the lane marked with "(+)" and "45" was duplicated on the lower image. The asterisk indicates the lane that was lost during the assembly process. In addition to the lane duplication pointed out by the anonymous reader, the panel has found that the lanes (+) and (-) at the time point 0 were switched with each other.

Evidence 4

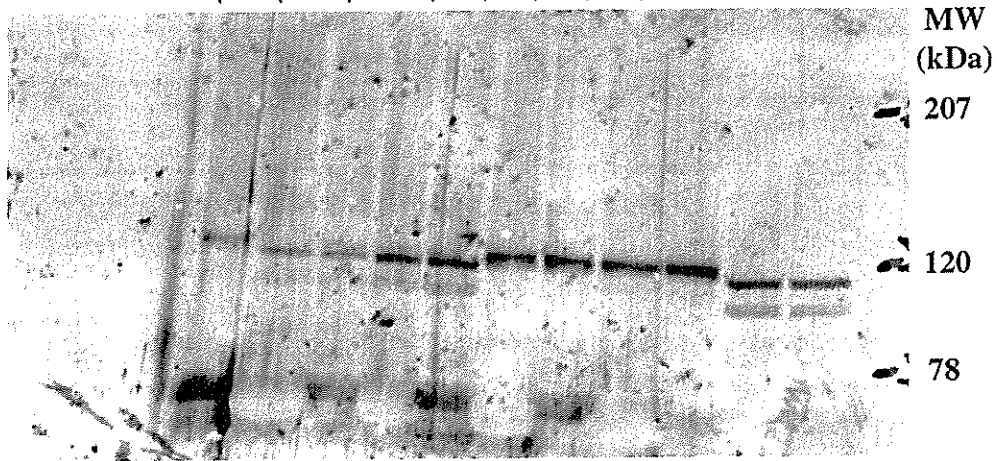
Independent blot supporting findings in figure 4. The samples were prepared and analyzed as in Evidence 2 except that samples from S phase arrested cells were absent in this experiment (dated 2/5/2000). The control sample was made by mixing HeLa cell lysates collected at M phase and at S phase.

Evidence 1



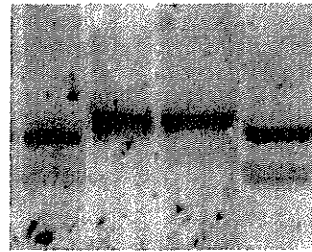
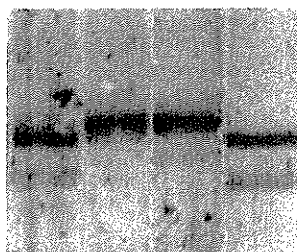
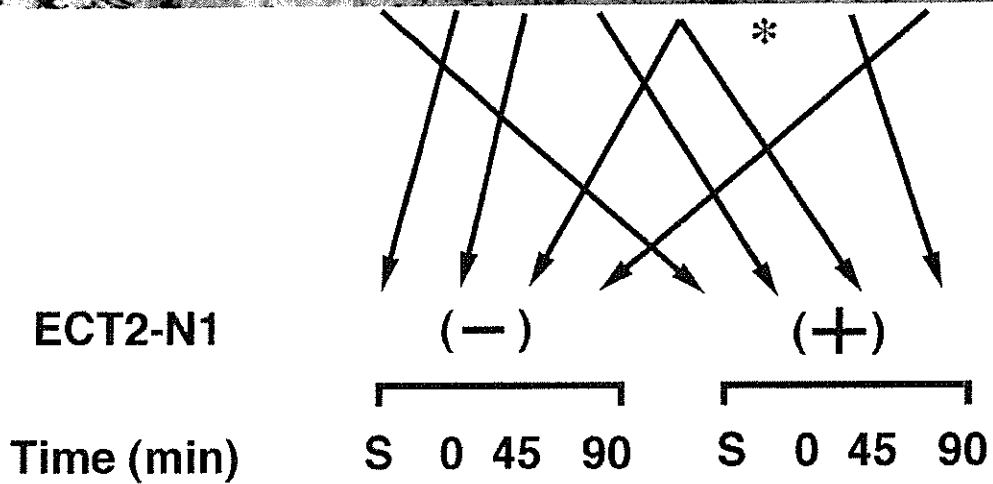
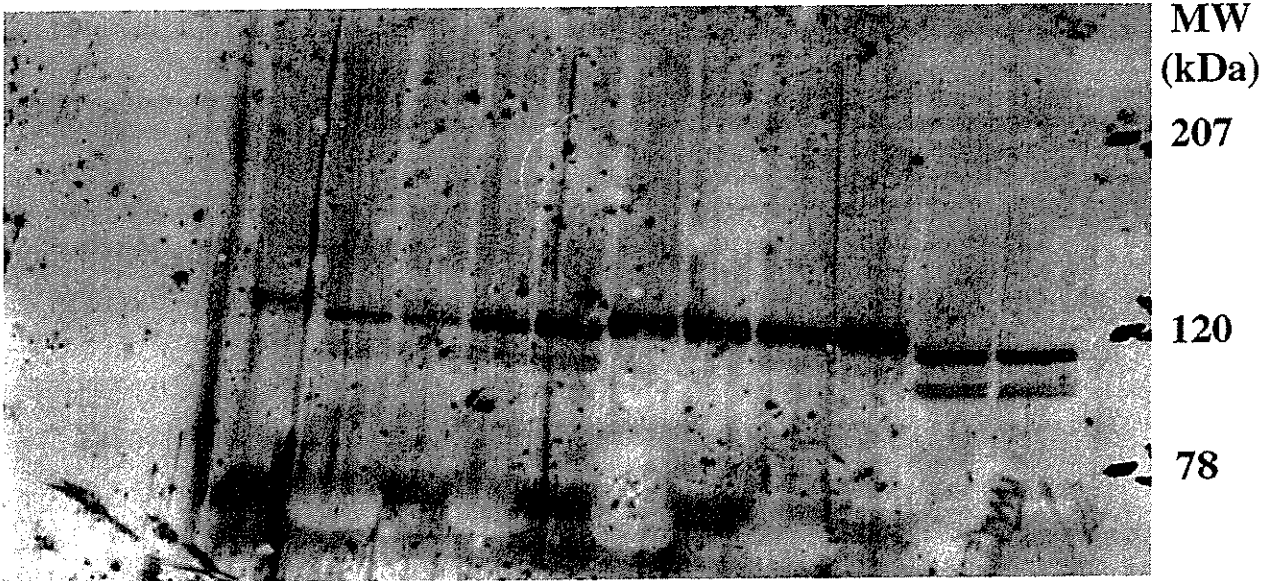
Evidence 2

control		ECT2-N1 transfection							
M phase	G2 phase	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)
	S phase	S	S	0	0	45	45	90	90

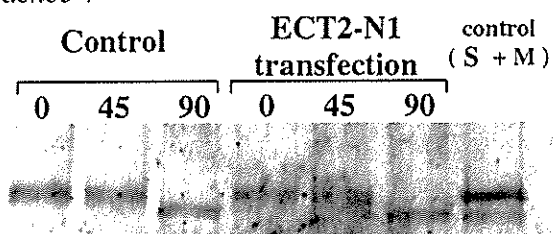


Evidence 3

control		ECT2-N1 transfection							
M phase	G2 phase	(+)	(-)	(+)	(-)	(+)	(-)	(+)	(-)
	S phase	S	S	0	0	45	45	90	90
		/	/	/	/	/	/	/	/



Evidence 4



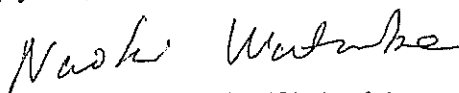
Professor Tasuku Honjo, M.D., Ph.D.
Dean
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Sakyo-ku, Kyoto
Japan

November 19, 2002

Dear Sir:

After being assigned for this task on November 8th 2002, we have conducted an investigation on the JBC paper (275(23):17233-17236, 2000) by Kimura et al.. The report of this investigation has been attached. All three members of this panel concur on the conclusions and the recommendations of this report. Should you have further questions concerning this report, please feel free to contact either one of us.

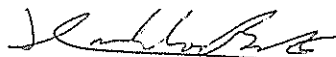
Sincerely yours,



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Dr. Herbert Tabor
Editor in Chief
The Journal of Biological Chemistry
Bethesda, Maryland
USA

November 19, 2002

To follow up on allegation of possible misconduct in the JBC paper (275(23):17233-17236, 2000) by Kimura et al., a departmental panel consisting of three independent faculty members has been appointed on November 8, 2002 under the auspices of the Dean of Kyoto University Faculty of Medicine. Based on our investigation, we have submitted the following report to the Dean, Dr. Tasuku Honjo. While we feel that our immediate task has been accomplished, please feel free to address further inquiries to us if you deem it to be necessary under the circumstances.

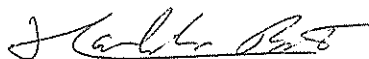
Sincerely yours,



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