

December 15th, 2017
National University Corporation Tottori University

Results of investigation into wrongdoings in research activities at Tottori University

Wrongdoings have been found regarding research activities for four papers published by a former associate professor, so we are publicly announcing the results of our investigation.

1. Summary

(1) Content and timeline of discussions

On February 7th, 2017 there was a discussion related to wrongdoing with research activities. On February 10th, 2017 following a complaint based on “the guidelines regarding research activity impropriety at Tottori University” not being met, a preliminary investigation into this matter was opened.

The contents of this discussion were as follows.

1) Discussion contents:

Four papers on which the accused (*) was a corresponding author contained image data that fell under suspicion of being altered.

(*) Because this is being handled following a complaint, we use the word “accused” here.

2) The accused:

Former Tottori University Medical Sciences Associate Professor Miura Norimasa

3) Papers under suspicion of wrongdoing:

| Paper Number | Journal Name Volume / Edition: Page, Publication Year |
|--------------|---|
| | Title of Paper |
| 1 | BMC Cancer 16: 415, 2016 |
| | Tumor-suppressive effects of atelocollagen-conjugated hsa-miR-520d-5p on undifferentiated cancer cells in a mouse xenograft model |
| 2 | Scientific Reports 4: 3852, 2014 |
| | Hsa- miR-520d induces hepatoma cells to form normal liver tissues via a stemness-mediated process |
| 3 | Nucleic Acid Therapeutics 23: 332, 2013 |
| | Human RGM249-Derived Small RNAs Potentially Regulate Tumor Malignancy |
| 4 | BMC Molecular Biology 10: 5, 2009 |
| | A noncoding RNA gene on chromosome 10p15.3 may function upstream of hTERT |

(2) Results of investigation

It has been found that research activities by the accused above did include wrongdoings of “falsification” and “alteration.”

2. Investigation

(1) Structure of investigation

- This Investigation (Research Activity Wrongdoing Investigation Committee): 9 persons (4 persons internal to the university, 5 persons external to the university)

(2) Composition of the Research Activity Wrongdoing Investigation Committee

| | | | |
|------------------|---|-----------------------------------|--------------------|
| Committee Chair | Tottori University | Director (in charge of education) | Nakajima Hiromitsu |
| Committee Member | Tottori University | Director (in charge of research) | Matsumi Yoshiharu |
| Committee Member | Tottori University - Postgraduate engineering research division | Head of postgraduate research | Kawata Yasushi |
| Committee Member | Tottori University - Medical sciences | Professor | Ninomiya Haruaki |
| Committee Member | Tottori University - Medical sciences | Professor | Urano Takeshi |
| Committee Member | Asai Total Law Office | Representing attorney | Asai Kouji |
| Committee Member | Shinshu University Medical sciences | Specially appointed professor | Ichikawa lekuni |
| Committee Member | LPixel Inc. | Representing board member | Shimahara Yuki |
| Committee Member | LPixel Inc. | Sales manager | Nakao Yuki |

(3) Timeline, details, and methods of investigation

The preliminary investigation and main investigation were carried out in accordance with “the guidelines regarding research activity impropriety at Tottori University.”

1) Details

Around the end of January 2017, a suspicious issue with some of the image data in the scientific paper (BMC Cancer 16: 415, 2016) (Paper 1) was pointed out internally by a professor at this university.

On this paper the first author was (at the time) Associate Professor Miura Norimasa, and the professor looked at other papers in which Miura Norimasa was the first author or corresponding author to determine if alterations or falsifications had been made to image data. As a result image data in four papers was deemed to be under suspicion of impropriety, and this was brought up in a discussion with the head of the medical sciences department on February 10th, 2017.

The head of the medical sciences department discussed this with the person responsible for supervising research ethics. Based on that discussion, on February 10th, 2017 the person responsible for supervising research ethics decided that an investigation was in order.

2) Investigation timeline

This investigation: April 3rd, 2017 to October 31st, 2017 (12 committee meetings)

3) Papers under investigation

The four papers published between 2009 and 2016 specified as being under suspicion, in addition to 35 papers with which the accused was associated, for a total of 39 papers.

4) Method of investigation

- Investigation of related documents and materials: Confirmation of papers, research notebooks, electrophoresis images, recording media (CD, USB) related to the papers involved in this research.
- Investigation questioning the accused: The accused was questioned via documentation and interviewed. From this a selection of the image data was confirmed, and this was compared against the original data.
- Investigation questioning related parties: Joint authors of Papers 1-4 were questioned via documentation or interviewed.
- Image analysis: The PDF data of the papers and the original image data was analyzed and compared by an image analysis company to determine if any alterations or inappropriate image processing had taken place

3. Investigation results (content of specified wrongdoing)

(1) Type of specified wrongdoing found

Falsification, alteration

(2) Researchers determined to be involved in the specified wrongdoing

Miura Norimasa (Former Tottori University Associate Professor)

(3) Specific details of specified wrongdoing

- Falsification: Reusing images (Reusing an individual image as a separate research result either as-is or after mirroring, flipping, rotating, shrinking / stretching, etc.)
- Alteration: Altering images (Using cut and paste to take images of electrophoresis and combine them with a series of experimental results.)

- Details provided in the accompanying documents (Specific details regarding the specified wrongdoings, reference data 1-12)

(4) Reason for decision

1) Result of analysis by image analysis company

- Regarding the reuse of image data for separate experimental results, there was a very good match at an over 96% image concordance rate. (For one part of an image, with an image concordance rate of 84.16%, taking into account the ROI value (*) for the image, this was determined to be high.)

(*) ROI value: Region of Interest (Area of observation / measurement)

- Regarding the alteration of image data, in regions that necessitated work being done in sequence, unnatural gaps and straight line artifacts (discontinuous noise patterns) were detected. Also, because only some portions of an image showed unnaturally fixed brightness levels, it was determined that in only those portions image data had been deleted.

2) Testimony of the accused and related parties

- The accused acknowledged that he acted alone in altering the images for use in papers to be published.
- Related parties gave testimony that altering the images was done by the accused.

3) Original images

- There are original images from the accused that were not submitted.
- The images submitted as being originals have a low image concordance rating with these originals, so it is believed the submitted images were not the originals.
- The submitted images are in a completely different form, so it is not possible to determine whether or not they are originals.

4) Due to considerable problems with the preservation of the research notes including original images and image data, it was not possible to provide objective proof to clear the accused of the suspicion of falsifying and altering the images.

(5) Appeal overview, results of follow-up investigation

Regarding the results of the investigation, there was an appeal from the accused on November 13th, 2017, but because no new objective and scientific evidence was tangibly presented, and because the claims espoused during questioning, etc. were repeated with no new rational claims made, the appeal was denied.

(6) Directly related expenses to the specified wrongdoing

Three of the four papers specified for falsification or alteration had expenses under the following.

- Grants-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (KAKENHI Series of Single-year Grants)
¥42,683 (English proofreading fee)
- Adaptable and Seamless Technology Transfer Program through Target-driven R&D (A-STEP) from the Japan Science and Technology Agency

¥47,627 (English proofreading fee)

- Operating expense grant from the Ministry of Education, Culture, Sports, Science and Technology

¥487,228 (Paper proofreading fee, paper submission / printing / processing fees, open access publication fee)

- Research grant-in-aid from public utility foundation corporations

¥341,525 (Paper proofreading fee, paper publication fee)

The following was not directly related to expenses for the papers with the specified wrongdoing.

- Grants-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (KAKENHI Multi-year Fund)

4. Details of the measures the investigation committee has taken thus far

(1) Regarding measures to stop competitive funding

Starting May 31st, 2017, the budget of the accused (Grants-in-Aid for Scientific Research for fiscal year 2017 and individually allotted research funds) was stopped. Furthermore, regarding the research tasks related to receiving the 2017 Grants-in-Aid for Scientific Research, as of September 30th, 2017 following the resignation of the accused, the notification of discontinuance of the research topics and the notification of change regarding the reallocation of research responsibilities were submitted to the distribution system and acceptance was acknowledged.

(2) Treatment of related parties

On September 30th, 2017 the accused resigned, and the school is internally considering what needs to be done moving forward.

(3) Regarding the withdrawal of papers

The accused was advised to withdraw the four papers involved in the specified wrongdoing and to notify any authors who had cited the papers in question.

5. Primary causes of the specified wrongdoing and measures to prevent future occurrence

(1) Causes

The primary causes of this problem are thought to be the lack of research integrity and improper preservation of research data by the accused (disposal of original image data, failure to indicate where images had been cut and pasted, reusing previous data without performing new experiments), as well as his immaturity as a researcher and inability to maintain accuracy (lack of understanding of experiment principles / meanings, lack of understanding about the importance of experiment notes, lack of detail in records regarding sample names, antibody names, experiment dates, etc.).

Also, due to a lack of awareness of his role as a guide for other researchers (situations where students acted in his stead, failure to provide guidance to students to summarize and publish their research), and despite there being numerous other persons involved in the research, the failure to construct a system or mechanism for confirming multilateral and

objective study, and the failure to prevent impropriety on the part of the accused also contributed to the cause.

(2) Preventing future occurrence

In order to prevent an issue such as this from occurring again, this university is taking the following measures.

1) Raising the awareness of research ethics to prevent research impropriety

Centering on the Research Impropriety Prevention Promotion Committee, there are plans to disseminate information regarding rules related to preventing research impropriety, standards of conduct, and guidelines.

Regarding research ethics training, at this university since 2014 we have invited in external lecturers and held research ethics seminars, and since 2015 all professors have been required to take part in an e-Learning course with materials provided by CITI-Japan.

Moving forward the research ethics seminars will be made to be mandatory, and we will disseminate information on the important points of the seminars with “Duties and responsibilities of research advisors,” “Duties and responsibilities of researchers toward society,” and “Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals as put forth by the International Committee of Medical Journal Editors (ICMJE).”

2) Strengthening the system that provides research guidance to graduate students

Research fundamentals education will be part of course credit. We will investigate specific countermeasures for each separate research department.

For each postgraduate student in medical sciences, in addition to their advisor other professors will be put in place to help provide guidance, and we will strengthen the research system so that the research environment promotes “healthy and open communication.”