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REPORT

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University requesting the report

Uppsala University
Box 256
751 05 Uppsala

Background

In an official letter submitted on 22 January, Uppsala University has requested a report from the Expert Group for Scientific Misconduct at the Central Ethical Review Board. The letter refers to a report from Professor Olof Leimar at Stockholm University, in which unlawful image manipulations in ten research publications are pointed out. The report states that the responsible parties for the publications are lecturer Irene Söderhäll and senior professor Kenneth Söderhäll, at the Institution for Organism Biology.

On 12 January 2015, Uppsala University decided to open a preliminary investigation.

In an official letter submitted to the Expert Group on 16 February 2015, Irene and Kenneth Söderhäll dispute the accusations of misconduct by stating that they are baseless. According to Irene and Kenneth Söderhäll, irregularities have occurred in some of the reported projects. However, a scientist who was previously employed by them, Dr. Apiruck Watthanasurorot, is responsible for the projects and has assumed responsibility for the irregularities.

Investigation

On 6 February 2015, the Expert Group decided to assign Professor Björn Dahlbäck at Lund University, Skåne University Hospital in Malmö, as an expert in the matter.

The conclusions in the preliminary investigation from Uppsala University dated 16 March 2015 point out that mistakes have been made during the publications of certain figures and that a certain degree of negligence has occurred. The university does not, however, find that any malicious intent has been present and that the conclusions in the essays are not affected, thus Irene and Kenneth Söderhäll are not guilty of scientific misconduct.

In an official letter submitted to the Expert Group on 8 May 2015, Björn Dahlbäck made a preliminary assessment of the publications in question. He states that image manipulation has occurred in a number of the reviewed projects, three of which Apiruck Watthanasurorot was not the co-author.

Postal address

Central Ethical Review Board
C/O Science Council
Box 1035
101 38 Stockholm

Address

Västra Järnvägsgatan 3

Telephone

+46 8 546 77 610

Fax

+46 8 546 441 80

In an official letter dated 19 May 2015, Irene and Kenneth Söderhäll reject Björn Dahlbäck's conclusions and primarily state that since Professor Dahlbäck has not had access to the original files, he is not in a position to determine whether or not image manipulation has occurred.

In an official letter submitted on 20 May 2015, Björn Dahlbäck subsequently reviewed new material that was submitted by Irene and Kenneth Söderhäll with the purpose of proving that Björn Dahlbäck's analysis is not reliable. Professor Dahlbäck's conclusion is that this material is directly misleading and he maintains his position based on the previous analysis.

During the Expert Group's meeting on 29 May 2015, both Björn Dahlbäck and Irene and Kenneth Söderhäll participated. After Björn Dahlbäck had presented the reported articles orally and via a slideshow, Irene and Kenneth Söderhäll agreed that image manipulation had taken place in some of the articles, although in their opinion, they were not responsible for it. They maintained that someone else must have been responsible. Irene and Kenneth Söderhäll believed they had submitted the original images to the Expert Group, which was not the case. Most of the original images have not been possible to acquire either because the researchers who were employed at the Institution for Organism Biology the time of publication are no longer employed there, or because the images have simply not been found.

On 30 July 2015, the Expert Group, represented by professors Elisabeth Haggård and Lars Gustafsson, visited Irene and Kenneth Söderhäll's workplace with the purpose of inspecting the original material. During this meeting, additional image material and excerpts from the institution's scanner were acquired.

In an official letter dated 19 August 2015, Irene and Kenneth Söderhäll subsequently maintained that Apiruck Watthanasurorot is solely responsible for manipulating images and creating original files and that they are not responsible for this or any other misconduct.

All image material from the 10 reported published projects and all available original images in laboratory notebooks or scanners have been analysed with the Photoshop-based computer applications Forensic Gradient Map and Enhance Weak Features, developed by the national Office of Research Integrity, USA. Image computer files from the scanner software Quantity One and PDQuest (.lsc and .gsc files; Bio Rad, USA) have been studied in the original software and the header sections have been read with a text editor.

Analysing the image material in the reported projects has been a very extensive process and has led to numerous inquiries with the Office of Research Integrity in the US, as well as with the software manufacturer of the scanner software. It can be established that image compression effects and artefacts in the original material are important to take into consideration in this type of investigation, which is why quick and secured access to original material is paramount. It can be noted that the Expert Group has contacted Uppsala University on three occasions with the purpose of securing primary data, however the university has failed to comply and has not been able to secure primary data within the boundaries of its own investigation into the matter. This has delayed the Expert Group's investigation significantly. However, it has been possible to complete via direct collaboration with the reported researchers.

It is also worth noting that the hard drive to the scanner in question has not been secured by Uppsala University. It should have been analysed in order to determine if files had been erased and, if so, when such activity took place.

A presentation of the conclusions for each individual publications are available in Appendix 1. Appendix 2 contains the material for the conclusions of the image analyses. The publication numbering is the same as in the report.

The Expert Group's Assessment

For a detailed description of the individual projects, please find Appendix 1 and 2.

The Expert Group has not found any image manipulations in three of the reported publications.

- Dev. and Comp. Immun.2011, H. Liu, C- Wu, Y. Matsuda, S.-i. Kawabata, B.L. Lee, K. Söderhäll, I. Söderhäll, project 3.
- Plos One 2010, C. Noonin, P. Jiravanichpaisal, L Söderhäll, S. Merino, J.M. Tomás, K. Söderhäll, project 4.
- Plos One 2013, N. Saelee, C. Noonin, B. Nupan, K. Junkunlo, A. Phongdara, X. Lin, K. Söderhäll, L Söderhäll, project 5.

Two of the reported publications contain image manipulations where corrections should be submitted to the journals with correct images.

- Plos Pathogen 2014.M. Jearaphunt, C. Noonin, P, Jiravanichpaisal, S. Nakamura, A.Tassanakajon, I. Söderhäll, K. Söderhäll, project 1.
- BMC Immunology, 2008. X. Lin, K. Söderhäll, I. Söderhäll, project 2.

The other publications contain deliberate image manipulations. Original images are not available at Uppsala University, thus the following publications should be withdrawn.

- J. Virol. 2010, A. Watthanasurorot P. Jiravanichpaisal, L Söderhäll, K. Söderhäll, project 7.
- Plos Pathogen 2010. A. Watthanasurorot, P. Jiravanichpaisal, H. Liu,I. Söderhäll, K. Söderhäll, project 6.
- J. Mol. Cell Biol.2013. A. Watthanasurorot, P. Jiravanichpaisal, K. Söderhäll, I. Söderhäll, project 8.
- Plos Genetics 2013. A. Watthanasurorot, N. Saelee, A. Phongdara, S. Roytrakul, P. Jiravanichpaisal, K. Söderhäll, I Söderhäll. Irene and Kenneth Söderhäll decided to retract this publication on 18 January 2015, which was published on 27 April 2015 in Plos Genetics, project 9.
- J. Virol. 201. A. Watthanasurorot, E. Guo, S. Tharntada, C.-F. Lo, K. Söderhäll, I. Söderhäll, project 10.

In a number of cases, the verification images have been manipulated. These should be included in every experiment since they represent an internal verification of the execution of the experiment. Without verification, the result cannot be evaluated.

It has not been possible to reach Apiruck Watthanasurorot. Therefore, his opinion of the accusations have not been possible to acquire. He has however, assumed responsibility for figures 1, 2, 3, 4 and 6 in project 8 (J. Mol. Cell Biolg.2013) and for figures 2, 3, 4, 5, 6, 7 and 8 in project 9 (Plos Genetics 2013).

In some instances, the image manipulations have been easy to demonstrate, however in most cases, they have been very advanced and difficult to detect. All co-authors are responsible for the content of the published articles. Since Irene and Kenneth Söderhäll have respectively been the main and secondary supervisor and since Irene Söderhäll has also been the head of the department, they also have more overall responsibility for what has happened.

The Expert Group shares the Scientific Council's definition of scientific misconduct, which, in addition to intent, also encompasses negligence. According to Uppsala University's definition, intent is a prerequisite for misconduct. In this matter, extensive image manipulations have been proven in a number of articles. It is therefore difficult to understand how some of said manipulations have not been detected. The Expert Group cannot, however, determine if Irene and Kenneth Söderhäll have acted with intent. Based on the extent of the image manipulations, it is however apparent that those ultimately responsible for the articles, who also happen to be researchers with great experience, must be considered to have failed in their roles as supervisors and department head and have thus acted negligently. As such, they have acted dishonestly according to the Scientific Council's definition and internationally accepted practice.

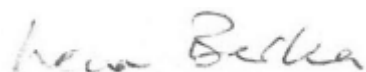
Four of the five articles in Apiruck Watthanasurorot's dissertation contains manipulated images. He has withheld original images and in response from journals, he has sent manipulated "original images" to Irene and Kenneth Söderhäll. Uppsala University should consider revoking his PhD.

In general, the university is responsible for handling and archiving the original data and for research ethics training. In this matter, Uppsala University has failed to comply with established scientific routines and standards. This should be rectified.

This matter has thereby been concluded as far as the Expert Group is concerned.

This report has been established by Lena Berke, Chairman, Jan-Otto Carlsson, Lars E Gustafsson, Elisabeth Haggard and Ulrik Ringborg. During the case review, Göran Collste and substitutes Jerry Eriksson and Elisabeth Rachlew, as well as Chief Secretary Jörgen Svidén have also participated.

The Expert Group for Scientific Misconduct



Lena Berke

Appendix 1

A presentation of the conclusions of the individual publications, based on the external and internal investigation. Explanatory image material is available in Appendix 2.

Project 1

Plos Pathog.2014, M. Jearaphunt C. Noonin, P. Jiravanichpaisal., S. Nakamura A. Tassanakaj, I. Söderhäll and K. Söderhäll (communicating authors).

The report concerns Figure 5 B.

The images in figure 5B, Tris-HCl (control) and ProPO-casp1 (bacteria treated with the N terminal of proPO) are identical/duplicated. As pointed out by Irene and Kenneth Söderhäll, the images are quantified in figure 5A, which makes it evident that a mistake has been made. A correction with the right image should be submitted.

It is worth noting that this image publication has not been detected by either author since the images are located closely too each other.

Project 2

BMC Immunology 2008, X. Lin, K. Söderhäll (communicating author) and I. Söderhäll.

The report concerns figure 4 A and 6.

Identical bands have been used for TGase in figure 4A (left side) and twice in figure 6 (with and without Astakin treatment). The bands are also identical for 40S in figure 4A (left side) and in figure 6, both with and without Astakin treatment.

The original images do not exist, however the quality is good enough to determine that the bands have been copied. Irene and Kenneth Söderhäll have stated that the experiment has been repeated numerous times with the same result. Nevertheless, the published work contains copied images, hence they should be replaced in a correction.

Project 3

Dev Comp Immun 2011, H. Liu, C. Wu, T. Matsuda, S.-i. Kawabata, B.L. Lee, K. Söderhäll and I. Söderhäll (communicating authors).

The report concerns figure 6 A and B.

The P1-SPH1 band in figure 6 A is identical with the GSP band in figure 6 B. The same image has been used in the two figures, and although not stated, it is related to the same control. The band labelling should therefore have been identical to avoid confusing the reader.

Project 4

Plos One 2010, C. Noonin P. Jiravanichpaisal, I. Söderjäll, S. Merino, J.M. Tomás and K. Söderhäll (communicating author).

The report concerns figure 4 and figure 7.

The original images for figure 4 and figure 7 is in C. Noonin's laboratory journal. They are RT-PCR images that have been photographed in a UV table and printed directly on a Polaroid film. Original images for Hepatopancreas 40S and Hemocyte Crustin 2 (figure 4) exist but are not the same. Original images for Hepatopancreas ALF (figure 4) and Pacifastin light chain (figure 7) exist but are not the same. Original images for Hemocyte LGBP (figure 4) and proPO (figure 7) exist but are not the same.

Therefore, this work does not contain any duplicated images.

Project 5

Plos One 2013, N. Saelee, C. Noonin, B. Nupan, K. Junkunlo, A. Phongdara, X. Lin, K. Söderhäll and I. Söderhäll (communicating author).

The report concerns figure 2A and 6A.

Figure 2A, the right panel, shown in a "Pull-Down Assay", has a patchwork-like background and it looks like bands have been removed. The original was available and has not been manipulated, however the bands are quite weak. The strange background is a consequence of image compression during computer processing.

The three .1sc files that have been acquired from the scanner during the visit to Uppsala were correct.

This work does not contain any manipulated images.

Project 6. J. Virol 2010, A, Watthanasurorot, P. Jiravanischpaisal, I. Söderhäll, K. Söderhäll (communicating author).

The report concerns the 40S controls in figure 5, 6, 7 and 8.

The initial analysis with a Forensic Gradient Map showed that the 40S controls in figure 5B, 6B, 7A and 8A were manipulated. On 19 May, three .1sc files were received from Irene Söderhäll. Two originate from figure 5B and 6B. One is labelled "40Sribosomalinvitro.1sc", which is correct (scanned on 14 January 2010) and the other is labelled "40S ribosomal in vivo", which is a converted TIFF file that was scanned on 4 October 2014 (user Adobe Photoshop). The original file labelled "In vitro and in vivo dsgCIqr and protein treatments.1sc" (figure 7A and 8A) was a converted TIFF file with the name "Kant test 2" which was scanned on 4 October 2014 (user Adobe Photoshop). Thus, the two latter .1sc files were not original images.

There is a strong suspicion that figure 6B contains three bands (1, 2, and 3) that are duplicated (band 7, 8 and 9) since Forensic Gradient Map showed identical pixels. One .1sc file labelled "in vivo silencing.1sc", which was acquired by Irene Söderhäll on 19 May, and which corresponds to figure 6B P1gCIqR, was a converted TIFF file that was scanned on 4 October 2014 (user Photo Shop), i.e. this was not the original image.

As such, severe image manipulations are present, both in the published images and in the material that was submitted to the Expert Group, where it has been established that so-called original files have been created by reimporting TIFF images in scanner software.

According to correspondence between Irene and Kenneth Söderhäll and Editor in chief of J. Virol on 11 August 2015, this article will be retracted as soon as they have been able to contact all authors involved.

Project 7.

J. Plos Pathogen 2011, A, Watthanasurorot, P. Jiravanischpaisal, H. Liu, I. Söderhäll, K. Söderhäll (communicating author).

The report concerns figure 5A and 7B.

Analysis of figure 5A showed that two bands were duplicated in the submitted image. On 10 August, .lsc files were acquired which Apiruk Watthanasurorot had sent to Kenneth Söderhäll. One corresponds to figure 5A and is labelled “Long gene isoforms whole” and the header shows that it was “converted from TIFF” with the same name and before the image reading, it says “user Adobe Photoshop” on 21 October 2014.

An initial analysis indicated a strong suspicion of duplication of bands in figure 7B, but that the resolution was too low for a reliable analysis. Upon a renewed analysis, it was not possible to establish that the bands in figure 7B P2 Dscam are not identical since the background for the bands differ, and that the area to the right looks very strange.

An analysis of the TIF file used in the publication of figure 7B (labelled GSP Dscam primer WSSV) and that Irene and Kenneth Söderhäll made available to us on 10 August indicates that the three leftmost bands in PIDScann have been duplicated once and that the three last missing bands look airbrushed. Irene and Kenneth Söderhäll also made the TIF file available that was used for publication of figure 7B WWSV VP28, which was labelled “7B_wssv Dscam.tif”. Analyses show that the image has been merged, a marker that was located in the middle has been removed and the three rightmost lanes are located to the left in the publication. Also, the background of the three first bands in the publication (the three last in the TIF file) appear airbrushed. The upper bands have different widths and their placement does not correspond with the three lower bands.

On 10 August, three .lsc files were made available that Apiruk Watthanasurorot had sent to Kenneth Söderhäll for figure 7B, labelled “GSP Dscam primer WSSV” (from 14 October 2010), “wssvDscam” (14 October 2010) and Dscam 40s (13 January 2010) which all appeared to be “converted from TIFF” with the same name and before the image reading, it says 21 October 2014, with the note “user Adobe Photoshop”.

As such, severe image manipulations exist in both the published images and in the material submitted to the Expert Group, where it has been established that so called original files have been created by reimporting TIFF images in scanner software.

Irene and Kenneth Söderhäll intend to contact journals regarding the images in question, however they would first like to repeat the experiment to verify the results.

Project 8.

J. Mol. Cell Biol 2013, A, Watthanasurorot, P. Jiravanischpaisal, K. Söderhäll, I. Söderhäll (communicating author).

In this project, a correction of the image material has been submitted (figure 3E and F were duplicated, and figure 4C was merged (which was not indicated). Nevertheless, an image manipulation is still present. Two of the actin bands in figure 4B are identical with bands labelled gC1qR under the “Membrane” heading.

As such, image manipulations are present and no original images are available. According to correspondence between Irene and Kenneth Söderhäll and Editor in chief of J. Mol Cell Biol. dated 29 May 2015, they wish to retract the publication.

Project 9.

Plos Genetics 2013, A. Watthanasurorot, N. Saelee, A. Phongdara, S. Roytrakul, P. Jiravanischpaisal, K. Söderhäll, I. Söderhäll (communicating author).

A dozen reports exist. Forensic Gradient Map analyses indicated image manipulations, however, Irene and Kenneth Söderhäll decided to retract said work in their official letter dated 18 January 2015, which is why it has not been further processed.

Project 10.

J. Virol. 2014, A. Watthanasurorot, E. Guo, S. Tharntada, C.-F. Lo, K. Söderhäll, I. Söderhäll (communicating author).

Reports regarding figure 2, 5 and 6.

Figure 2E. Normal HPT. A number of cells appear to have been copied numerous times. Initially, clear evidence of image manipulation was established in two cases. Two bands in figure 5D (purified WSSV and dsGFP) are identical with the actin bands in figure 6D. The bands in figure 6B labelled “TUN treated cells” are identical with the actin bands in figure 6E. Irene and Kenneth Söderhäll have submitted two .lsc files labelled “Tunica CRT down” (28 August 2013) and “Actine something” (26 August 2013), which both proved to be “converted from TIFF” and scanned on 5 October 2014 with the note “User Adobe Photo Shop”.

Moreover, images have been copied from two other publications: one from project 6, J. Virol 2010 (figure 9A). Identically coloured protein gel is present in figure 2A despite originating from two different protein “pull down” trials with virus envelope proteins. In one case, the protein PlgC1qR, which is 256 aa, in the other case, the CRT protein is 404 aa. Also, the GST controls in Far Western Overlay Assay are identical in the two publications.

The other is contained in project 8, JMCB 2013, where the actin control in figure 1G is identical with the actin control in figure 1D.

As such, severe image manipulations are present, both in the published images and in the material submitted to the Expert Group, where it has been established that so called original files have been created by reimporting TIFF images in scanner software. According to the correspondence between Irene and Kenneth Söderhäll and the Editor in chief of J. Virol on 11 August 2015, this article will be retracted as soon as they have been able to contact all authors involved.