

## Decision on research misconduct

### Decision

The Swedish National Board for Assessment of Research Misconduct (“the Board”) finds

not guilty of research misconduct.

### Background

On 10 August 2021 an anonymous allegation of research misconduct was received by the Board. The complainant refers to PubPeer and states that two articles, Articles 1 and 2 below, contain duplicated images. The complainant states that reuse of illustrations occurs in more of the authors’ publications and lists another four articles, Articles 3–6 below.

1. [REDACTED] APR-246/PRIMA-IMET inhibits thioredoxin reductase 1 and converts the enzyme to a dedicated NADPH oxidase. *Cell Death & Disease* 2013 Oct 24;4(10):e881. doi: 10.1038/cddis.2013.417. Erratum in: *Cell Death & Disease* 2017 Apr 13;8(4):e2751. PMID: 24157875; PMCID: PMC3920950.
2. [REDACTED] Dual targeting of wild-type and mutant p53 by small molecule RITA results in the inhibition of N-Myc and key survival oncogenes and kills neuroblastoma cells in vivo and in vitro. *Clinical Cancer Research* 2013 Sep 15;19(18):5092-103. doi: 10.1158/1078-0432.CCR-12-2211. Epub 2013 Jul 17. Erratum in: *Clinical Cancer Research* 2021 Sep 1;27(17):4943. PMID: 23864164.
3. [REDACTED] Reactivation of mutant p53 and induction of apoptosis in human tumor cells by maleimide analogs. *Journal of Biological Chemistry*. 2005 August 26;280(34):30384-91. doi: 10.1074/jbc.M501664200. Epub 2005 Jul 1. Erratum in: *Journal of Biological Chemistry* 2017 Dec 1;292(48):19607. PMID: 15998635.
4. [REDACTED] Restoration of the tumor suppressor function to mutant p53 by a low-molecular-weight compound. *Nature Medicine*

2002 Mar;8(3):282-8. doi: 10.1038/nm0302-282. PMID: 11875500.

5. [REDACTED] Ablation of Key Oncogenic Pathways by RITA-Reactivated p53 Is Required for Efficient Apoptosis. *Cancer Cell*. 2009 May 5;15(5):441-53. doi: 10.1016/j.ccr.2009.03.021. Erratum in: *Cancer Cell*. 2017 May 8;31(5):724-726. PMID: 19411072.
6. [REDACTED] Rescue of p53 function by small-molecule RITA in cervical carcinoma by blocking E6-mediated degradation. *Cancer Research* 2010 Apr 15;70(8):3372-81. doi: 10.1158/0008-5472.CAN-09-2787. Erratum in: *Cancer Research* 2017 Jul 1;77(13):3719. PMID: 20395210.

For Article 1, the complainant states that duplication may be found in Figure 3A. The suspicion concerns the use of the same western blot panel in Figure 3A to show the expression of the control protein on three separate occasions. Articles 2–6 are not being investigated; see below in this Decision for details, under the heading Prescription.

All the authors of Article 1 deny allegations of research misconduct. The last author, [REDACTED] describes how in their western blot analysis, to confirm that the same quantity of cell lysate had been used for all samples of the gel, they had analysed a control protein, beta-actin. He writes that, by mistake, when the figure was compiled, they had used the same beta-actin control on three different occasions, after 48, 72 and 96 hours respectively. He states that they were made aware of the mistake through PubPeer in March 2016. They discussed the comment within the authors' group and realised it was the same image that had been used for the three occasions. The co-author [REDACTED], then a PhD student, is said to be the person who had prepared the images, and had retained the raw data from the experiment. [REDACTED] states that they replied to the comments in PubPeer in April 2016 and that they also sent a correction to the journal. When the mistake was discovered, [REDACTED] attaches correspondence with [REDACTED], the co-author, and [REDACTED], which in his view shows that it is not a matter of manipulation or fabrication of data. In the correspondence, [REDACTED] describes how she happened to take the same image when she put the figure together the first time. She also describes how she would usually transfer the images from the western blot analysis by email, saying that she still has the images from all three occasions in her email correspondence, and that she sees that she forwarded them to [REDACTED] and [REDACTED].

[REDACTED] writes in her statement that the authors, when the error came to their attention through PubPeer, took it seriously and realised that the beta-actin images were extremely similar in one experiment. She states that she realised that she had made a major editing mistake when she compiled the figure. She states that she used to transfer original data from the western blot equipment by email, and that she was able to find data there for all three occasions. Like [REDACTED], she writes that original data and old emails show that it was a matter of an unintentional error in editing. She also states that the authors, as soon as they became aware of the error, published a corrected figure.

██████████ say in their statements that they think the image duplication in Figure 3A occurred by mistake when the figure was compiled; that the author group discussed the error when they became aware of it; and that a correction was sent to the journal. ██████████ replies that she was mainly involved in the project at an early stage.

The Board obtained an expert statement on the subject. Regarding Article 1, the expert<sup>1</sup> states that it is clear that the article contains duplicated results in Figure 3A, consisting in reuse of beta-actin control panels. The expert writes that he sees no signs of similar duplications in Figure 3A or in other figures in the article. He states that he had not read the raw data files, but that he considers that the panels have clearly not affected the conclusions from the results in the article. He thinks the documented email correspondence among the authors regarding the comments in PubPeer in 2016 supports the authors' statements that the duplication was an unintentional error, and that he finds no indication of deliberate falsification of data in Article 1. He also states that the authors, long before the allegation in question was reported to the Board, became aware of the error, and that the journal has published a corrected figure with an appropriate explanation.

## **Grounds for decision**

### **Legal regulation**

The Board's remit is to examine issues of research misconduct under the Swedish Act (2019:504) on responsibility for good research practice and the examination of research misconduct ("the Act"). Section 2 of the Act defines research misconduct as a serious deviation from good research practice in the form of fabrication, falsification or plagiarism, committed with intent or through gross negligence, in the planning, conduct or reporting of research.

### **Statutory limitation**

Section 8 of the Act states that investigation of research misconduct may not be based on circumstances predating the beginning of the case by more than ten years. The provision in the first paragraph does not apply if there are special reasons for such investigation. The preparatory legislative work on the Act shows that special reasons may be that the alleged misconduct has had, or risks having, major or serious repercussions on the research or the wider society, such as on people's health, or on how processes, methods or products are designed.<sup>2</sup>

The allegation concerns four articles, Articles 3–6, that were more than ten years old when the case commenced. The Board's assessment is that there are no special reasons to depart from the period of statutory limitation, and has therefore not examined the suspicions relating to these articles.

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<sup>1</sup> Mikael Nilsson, Professor, Sahlgrenska Center for Cancer Research.

<sup>2</sup> Swedish Government Bill 2018/19:58, p. 72.

Articles 1 and 2 were both published in 2013 and, accordingly, are not subject to statutory limitation. Article 2 is part of a case that was previously examined by the Board (reference number 3.1-21/0076). The assessment in that case was that the authors were not guilty of research misconduct. The article that is to be investigated is therefore Article 1.

### **Fabrication, falsification or plagiarism**

The forms of misconduct the Board is tasked to examine are fabrication, falsification and plagiarism. These concepts are not defined by the Act, but the preparatory legislative work on it refers to the fact that they are described in codes (codices) and guidelines on research ethics, such as *The European Code of Conduct for Research Integrity*.<sup>3,4</sup> They are also explained in the Swedish Research Council's publication *Good Research Practice*.<sup>5</sup> According to the preparatory legislative work, "fabrication" is often described as inventing results and documenting them as if they were genuine. "Falsification" refers to manipulation of research material, equipment or processes, or alteration, omission or suppression of data or results without justification. Finally, the description of plagiarism is a researcher's use of other people's texts, ideas or work without due acknowledgement of the original source.<sup>6</sup>

The investigation shows that the same beta-actin control was used to show results on three different occasions in Figure 3A in Article 1. This reuse constitutes falsification according to the definitions above.

### **Serious breach**

Only serious breaches of good research practice constitute research misconduct and fall within the scope of investigation by the Board. Other breaches are, instead, dealt with by the entities responsible for the research (the higher education institutions), pursuant to Chapter 1, Section 17 of the Swedish Higher Education Ordinance (1993:100). It is stated in the preparatory legislative work on the Act that fabrication and falsification are always, in principle, severe breaches of good research practice. In certain cases, for example concerning a minor infraction on a single occasion, plagiarism should not be considered a serious breach of good research practice.<sup>7</sup>

The premise for the Board's investigation of this aspect is that falsification is, in principle, a serious breach from good research practice. The fact that reuse of images has not influenced the research results, or has done so only to a small extent, does not in the Board's opinion affect its assessment of the seriousness of the offence. The Board's conclusion is therefore that the deviations are serious.

### **Intent or gross negligence**

Under Section 2 of the Act, the serious breach of good research practice must have been committed with intent or through gross negligence to be considered research misconduct. "Intent" means, according to the preparatory legislative work on the Act, that the

<sup>3</sup> *The European Code of Conduct for Research Integrity*, revised edition. Berlin: All European Academies (ALLEA); 2018, section 3.1.

<sup>4</sup> Swedish Government Bill 2018/19:58, pp. 45, 100.

<sup>5</sup> *Good Research Practice*. Stockholm: Swedish Research Council, 2017, Chapter 8.

<sup>6</sup> Swedish Government Bill 2018/19:58, pp. 45, 100.

<sup>7</sup> Swedish Government Bill 2018/19:58, p. 100.

researcher understands what (s)he has done, while “negligence” means that the researcher should have understood this in any case. “Gross negligence” requires the conduct to stand out as particularly serious or reprehensible. Oversights, carelessness or misunderstanding should not, as a rule, be regarded as gross negligence according to the preparatory legislative work.<sup>8</sup>

Since 1 January 2020, researchers’ responsibility to follow good research practice in their research has been subject to statutory regulation under Section 4. There must be investigation and assessment of how far-reaching this responsibility may or should be in each individual case.

The expert’s assessment is that there is every indication that the reuse of images in the article took place by mistake. The Board has reached the same assessment, and finds that no evidence has emerged in the case that would support the opinion that the reuse of images in Article 1 took place intentionally. Since the only error involved is a single, isolated one, the Board considers that there is no reason to consider that the authors acted with gross negligence either. It has emerged that the authors were alerted to the error through PubPeer and thereafter published an erratum in the journal. The Board, like the expert, notes that this erratum was published several years before the recent allegation to the Board.

The Board therefore finds that [REDACTED] are not guilty of research misconduct.

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The Board has decided in this case following its presentation by caseworker Dorota Green.

Catarina Barketorp  
Chair

Dorota Green  
Caseworker

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<sup>8</sup> Swedish Government Bill 2018/19:58, pp. 50–51, 100.