

## Decision regarding research misconduct

### Decision

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

[REDACTED] and [REDACTED] not guilty of research misconduct.

### Background

On 25 May 2021, the Board received an anonymous report containing allegations of research misconduct. The allegations concern six articles in which image duplication is suspected. On 6 June 2021, Karolinska Institutet (KI) submitted a case of alleged research misconduct to the Board. The submission took place pursuant to Section 6 of the Swedish Act on responsibility for good research practice and the examination of research misconduct (2019:504). The submission comprises five articles in which image duplication is suspected. The same articles are contained in the allegation report and the submission, with the difference that the report contains an additional article. These cases are being assessed collectively. The following articles are included in the allegation report and submission:

1. [REDACTED] Cancer-Specific Synthetic Lethality between ATR and CHK1 Kinase Activities. *Cell Rep.* 2016 Jan 12;14(2):298-309. doi: 10.1016/j.celrep.2015.12.032. Epub 2015 Dec 31. Erratum in: *Cell Rep.* 2016 Dec 20;17(12):3407-3416. PMID: 26748709; PMCID: PMC4713868.
2. [REDACTED] Castration therapy results in decreased Ku70 levels in prostate cancer. *Clin Cancer Res.* 2013 Mar 15;19(6):1547-56. doi: 10.1158/1078-0432.CCR-12-2795. Epub 2013 Jan 24. PMID: 23349316.
3. [REDACTED] PARP-3 Is a Mono-ADP-ribosylase That Activates PARP-1 in the Absence of DNA\*, *Journal of Biological Chemistry*, Volume 285, Issue 11, 2010.
4. [REDACTED] Methyl methanesulfonate (MMS) produces heat-labile DNA damage but no detectable *in vivo* DNA double-strand breaks. *Nucleic Acids Res.* 2005 Jul 11;33(12):3799-811. doi: 10.1093/nar/gki681. Erratum in: *Nucleic Acids Res.* 2012 Jul;40(12):5794. PMID: 16009812; PMCID: PMC1174933.

5. [REDACTED] ATM is required for the cellular response to thymidine induced replication fork stress. *Hum Mol Genet.* 2004 Dec 1; 13(23):2937-45. doi: 10.1093/hmg/ddh316. Epub 2004 Sep 30. PMID: 15459181.
6. [REDACTED] A tumour-derived mutant allele of XRCC2 preferentially suppresses homologous recombination at DNA replication forks. *Hum Mol Genet.* 2004 Jan 15;13(2):203-12. doi: 10.1093/hmg/ddh022. Epub 2003 Nov 25. PMID: 14645207.

Article 1 was previously the subject of an allegation report at KI, where the matter was rejected on 17 March 2017. However, it is included in the material now examined by the Board, as is Article 2. Articles 3–6 were all published more than ten years ago and are thus subject to statutory limitation and exempt from the Board’s investigation. The co-authors of Articles 1 and 2 who were affiliated with Swedish higher education institutions at the time of publication were considered to have been reported to the Board and given the opportunity to comment on the matter.

For Article 1, the authors sent the journal an erratum, which was published in December 2016. They also submitted an erratum for Article 2, but this time the editor of the Journal decided to publish an editor’s note concerning the erratum, which was done in November 2021.

[REDACTED] submitted a statement to the Board. As a co-author of Article 1, he says there was no falsification or fabrication and the errors were corrected according to generally accepted practice. He states that he personally did not contribute to the erroneous parts of the work, but thinks that the “main authors” managed the whole project transparently and correctly. He neither collaborated in nor co-authored Article 2.

[REDACTED], the last author of Articles 1 and 2, has submitted a statement to the Board. In both articles, he thinks the errors arose inadvertently and did not change the conclusions. He also points out that errata for both articles were published.

[REDACTED] submitted a statement to the Board. As a co-author of Article 1, he denies contributing directly to the parts of the article where the errors were made. His view is that the errors were inadvertent and that they did not change the interpretation of the results. He neither took part in the work on, nor co-authored, Article 2.

[REDACTED] submitted a statement to the Board. He claims that he was not involved in the work that led to the incorrect images and, accordingly, not in the suspected falsification or fabrication either. He points out that the article’s conclusions were not changed because of the errors and that the mistakes were corrected in errata. He neither participated in the work on, nor co-authored, Article 2.

[REDACTED] submitted a statement. He refers to the existence of an erratum and confirms that he was involved only in work on Article 1.

[REDACTED], the first author of Article 1, submitted a statement to the Board in which he refers to the handling of the case at KI. He neither participated in work on, nor

co-authored, Article 2.

[REDACTED]  
[REDACTED] and [REDACTED] did not submit any statements to the Board.

The Board has obtained an expert's statement on the case. The expert<sup>1</sup> has reviewed the alleged articles and the corrections and believes that there is no reason to suspect that falsification, fabrication or plagiarism have occurred. Based on the respondents' statements, her assessment is that the errors in both articles were made inadvertently during the compilation of the manuscripts and that they do not constitute research misconduct. She also emphasises that the authors have corrected their mistakes in the journals in which the articles were published.

All the respondents were given the opportunity to comment further on the expert's statement, but declined.

## Grounds for decision

### Legal regulation

Under the Act (2019:504) on responsibility for good research practice and the examination of research misconduct ("the Act"), the Board is tasked to investigate issues of research misconduct. Section 2 of the Act defines research misconduct as a serious breach of 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.

Research carried out abroad or at private companies is not covered by the Act. [REDACTED] stated that they were employed by Vertex Pharmaceuticals Ltd in Oxfordshire, UK, when Article 1 was written and are therefore not subject to investigation by the Board.

### Statutory limitation

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

The allegation report and submission refer to four articles (Articles 3–6 above) that were more than ten years old when the case was initiated. The Board's assessment is that there are no exceptional reasons for waiving the limitation period, that it will thus not investigate the allegations relating to these articles.

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<sup>1</sup> Professor Maréne Landström, Department of Medical Biosciences, Umeå University.

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

The articles from 2013 and 2016 (Articles 1 and 2) are not subject to statutory limitation as set out above, and must therefore be examined.

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

The Board's remit is to investigate three forms of research misconduct: fabrication, falsification and plagiarism. These terms are not defined by law, but the preparatory work for the Act 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> Fabrication is often described, according to the preparatory work for the Act, as inventing results and documenting them as if they were genuine. Falsification refers to manipulation of research material, equipment or processes or unjustified alteration, omission or suppression of data or results.

In the article from 2013 (Article 2), the same image appears twice in figure 2A, although the different images are supposed to show different sections of the same prostate biopsy.

In the article from 2016 (Article 1), the image intended to show the control measurement (far left) in 1B reappears, representing the control measurement, in S2A. Moreover, another image from 1B reappears in two other figures, 6A and S2A. The image in Figure 6A purports to show something different from what the image from 1B shows. In Figure S2A, the image represents the same type of measurement as that shown in the image from 1B.

Furthermore, two images from Figure 1E have been duplicated in Figure S2C. The leftmost image in S2C should show a different measurement from the one in the duplicate image from 1E. The third image from the left in S2C is supposed to show the same type of measurement as the duplicate image from 1E.

In total, there are thus two different images in two different figures (6A and S2C) that do not show what they are claimed to show. The images that do not show what they purport to show are instances of falsification, as defined above.

The Board therefore finds that falsification has taken place.

### **Serious breach**

Only serious breaches of good research practice constitute research misconduct and undergo investigation by the Board. Chapter 1, Section 17 of the Swedish Higher Education Ordinance (1993:100) prescribes that other breaches should, instead, be dealt with by the entities responsible for the research. The preparatory work for the Act states that fabrication and falsification are, in principle, always serious breaches of good research practice.

The premise for the Board's investigation is that falsification is, in principle, always a

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

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

serious breach of good research practice. Whether or not the falsification changed the final results reported in the articles does not, in the opinion of the Board, affect the assessment of its seriousness. No reason to deviate from the premise, stated in the preparatory work, has emerged in the case. Accordingly, the Board's conclusion is that the breaches are serious.

### **Intent or gross negligence**

Under Section 2 of the Act, for research misconduct to be found, the serious breach of good research practice must have been committed with intent or through gross negligence. "Intent" means, according to the preparatory work, that the researcher must have understood what (s)he did, while "negligence" means that the researcher, in any case, should have understood this. "Gross negligence" requires the conduct to stand out as particularly serious or reprehensible. According to the preparatory work, oversights, carelessness or misunderstanding should not, as a rule, be regarded as gross negligence.<sup>6</sup>

Since 1 January 2020, researchers' responsibility to follow good research practice in their work has been subject to statutory regulation under Section 4. The potential or requisite extent of such responsibility must be examined and assessed in each individual case.

The authors state that the mistakes were made unintentionally. Their data and other documents indicate that it was a matter of mixing up images, rather than of wilfully distorting them. The expert witness consulted drew the conclusion that the errors occurred in the final stage of work on the article, and that this happened by mistake and inadvertently. The Board's assessment is that nothing has emerged in the case that would suggest that reuse of the images in the articles had taken place intentionally. Since there are only occasional errors in individual articles and they probably arose in the final stage of the work on the articles, the Board's assessment is that there is no reason to consider that the authors' conduct has been grossly negligent.

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

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The Board has made a decision on this matter following a presentation by case officer Sofia Ramstedt. The case officer Dorota Green also participated in the proceedings.

Thomas Bull  
Chair

Sofia Ramstedt  
Case officer

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<sup>6</sup> Government Bill 2018/19:58. pp. 50–51, 100.