

DECISION
Date: 4 September 2020
Ref.: 3.1-20/0022

Decision concerning research misconduct

Decision

Owing to statutory limitation, the National Board for Assessment of Research Misconduct (“the Board”) is not investigating the question of whether [REDACTED] [REDACTED] is guilty of research misconduct with respect to the following articles:

- [REDACTED] The genome landscape of ERalpha- and ERbeta-binding DNA regions. *Proc Natl Acad Sci USA*. 2008;105(7):2604–2609. (Article 5)
- [REDACTED]
- [REDACTED] The estrogen receptor α-selective agonist propyl pyrazole triol improves glucose tolerance in ob/ob mice: potential molecular mechanisms. *J Endocrinol*. 2008;199(2):X1. (Article 7)
- [REDACTED]
- [REDACTED] Estrogen receptor specificity for the effects of estrogen in ovariectomized mice. *J Endocrinol*. 2002;174(2):167–178. (Article 8).

The Board has examined seven articles in total.

The Board has decided that [REDACTED], as the corresponding author, is guilty of research misconduct with respect to the following articles:

- [REDACTED]
- [REDACTED] Estrogen signalling and the metabolic syndrome: targeting the hepatic estrogen receptor alpha action. *PLoS One*. 2013;8(2):e57458. (Article 1)
- [REDACTED] AP-1-mediated chromatin looping regulates ZEB2 transcription: new insights into TNF α-induced epithelial-mesenchymal transition in triple-negative breast cancer. *Oncotarget*. 2015;6(10):7804–7814. (Article 2)
- [REDACTED] Estrogen receptor α promotes breast cancer by reprogramming choline metabolism. *Cancer Res*. 2016;76(19):5634–5646. (Article 3).

- [REDACTED] The atypical ubiquitin ligase RNF31 stabilizes estrogen receptor α and modulates estrogen stimulated breast cancer cell proliferation. *Oncogene*. 2014;33(34):4340–4351. (Article 4)

The Board has decided that [REDACTED] is not guilty of research misconduct with respect to the following articles:

- [REDACTED] Estrogen receptor beta as a novel target of androgen receptor action in breast cancer cell lines. *Breast Cancer Res.* 2014;16(1):R21. Published 2014 Feb 19. (Article 6)
- [REDACTED] Induction of USP17 by combining BET and HDAC inhibitors in breast cancer cells. *Oncotarget*. 2015;6(32):33623–33635. (Article 9)
- [REDACTED] AP-1 Is a Key Regulator of Proinflammatory Cytokine TNF α -mediated Triple-negative Breast Cancer Progression. *J Biol Chem.* 2016;291(10):5068–5079. (Article 10).

In this case, the Board examined only [REDACTED] responsibility for the misconduct. The other co-authors' responsibility was not investigated.

Background

On 29 January 2020, pursuant to the transitional provisions for the Swedish Act (2019:504) on responsibility for good research practice and the examination of research misconduct, Karolinska Institute (KI) submitted a case to the Board.

The case is based on three reported allegations of research misconduct concerning Professor [REDACTED], all of which were received by KI in July 2018. The allegations relate to image manipulation in ten specified publications (Articles 1–10) in which [REDACTED] was either the corresponding author or a co-author. Three of the publications reported are more than ten years old.

KI engaged the University of Gothenburg (GU) to investigate whether [REDACTED] was guilty of research misconduct. GU assigned the task to an internal body, its committee that investigates cases of suspected misconduct in research or in artistic research or development. This committee engaged an external expert¹ in its investigative work and requested an opinion from the expert group for misconduct in research at the Ethics Appeal Review Board (ÖNEP), which in turn hired an external expert² to issue the opinion requested.

¹ Sven Pählman, senior professor of molecular medicine, Lund University.

² Nils Billestrup, professor of endocrinology and metabolism, University of Copenhagen.

On 5 September 2019, the “Statement for Karolinska Institute” was adopted, and this concluded GU’s investigative mission. The Statement was then communicated to the researchers concerned, who were given the opportunity to comment on it. A number of opinions were received by KI in the autumn of the same year. Subsequently, [REDACTED] spoke to the committee.

[REDACTED] contests the allegation that she has been guilty of research misconduct and her statement included the following points. First, one of the ten articles reported (Article 3) includes a figure that was modified ahead of the final proofreading by the researcher responsible. Neither [REDACTED] herself nor any of the other co-authors noticed this. According to [REDACTED], the modification does not mean that the article conveyed false or distorted research results, or information that is fabricated or plagiarised. Moreover, she states that failing to draw attention to the fact that the figure has been modified is not, in any case, a serious deviation from good research practice, nor can any intent or gross negligence be considered to have been demonstrated.

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 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.

Under Section 8, investigation of research misconduct may not be based on circumstances predating the initiation of the case by more than ten years, unless there are special reasons for such investigation.

Statutory limitation

One of the articles reported (Article 8) was published in 2002 and two (Articles 5 and 7) were published in 2008. As stated above, the Board may not investigate research misconduct based on circumstances predating the initiation of the case by more than ten years, unless special reasons exist. In the absence of special reasons, given that the case commenced at the Board on 29 January 2020, the Board is not allowed to examine the three articles.

The reasons for the legislation make it clear that special considerations might be that the alleged misconduct has had, or poses a risk of having, major or severe repercussions on the research or society as a whole. For example, it might affect people’s health or the ways in which processes, methods or products are designed.³ The Board considers that nothing has emerged to support the view that the alleged misconduct has had, or risks having, such effects. The Board therefore reaches the

³ Government Bill 2018/19:58, p. 72.

assessment that there are no special reasons for investigating the three articles that were published more than ten years ago.

Accordingly, owing to statutory limitation, these articles are not to be examined by the Board.

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 they are described in codes (codices) and guidelines on research ethics, such as *The European Code of Conduct for Research Integrity*.⁴ They are also explained in the Swedish Research Council's publication *Good Research Practice*.⁵

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 unjustified alteration, omission or suppression of information or results. Lastly, plagiarism is defined as a researcher's use of other people's texts, ideas or work without duly acknowledging the original source.

The Board finds it clear from the expert reports in the investigations preceding the case submission to the Board that the published images in four of the articles in question (Articles 1–4) may be regarded as manipulations. In this matter, the incorrectness of the published images in question is not disputed; for example, images have been used that do not show the results described. It may therefore be deemed evident that what has been done in this respect constitutes falsification in the legal sense.

The Board's assessment is that, for three of the articles (Articles 6, 9 and 10), nothing has emerged showing that the image content in these three has been manipulated. Accordingly, there is no question of falsification in these articles and, therefore, no further investigation relating to them is required by the Act.

Serious breach

Only serious breaches of good research practice constitute research misconduct and are subject to investigation by the Board. The entities responsible for the research must themselves, according to the preparatory work for the Act, deal with breaches that are not serious.⁶

According to the preparatory work, fabrication and falsification are, as a main rule, serious breaches of good research practice, while there may be cases of plagiarism that are less serious.⁷

The premise for the Board's investigation in this respect is therefore that falsification is, in principle, a serious breach of good research practice. The fact that image

⁴ *The European Code of Conduct for Research Integrity*, revised edition, 2018. All European Academies (ALLEA), section 3.1.

⁵ *Good Research Practice*, Swedish Research Council 2017, Chapter 8.

⁶ Government Bill 2018/19:58, p. 43.

⁷ Government Bill 2018/19:58, p. 100.

manipulation has not at all, or only to a small extent, affected the research result lacks importance, according to the Board, in its assessment of seriousness. No reason for deviating from the premise stated in the preparatory work has emerged in the case. The Board's conclusion is therefore that the breaches 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 that the researcher must have understood what (s)he has done, while "negligence" means that the researcher, in any case, should have understood this. "Gross negligence" requires the negligence not to have arisen solely as a result of oversights, carelessness or misunderstanding.⁸

That a researcher is responsible for conducting research in accordance with good research practice is an obligation that has long been clear in codes (codices) and guidelines on research ethics. Since 1 January 2020, researchers' responsibility to follow good research practice in their work has been subject to statutory regulation under Section 4. It must be examined in every individual case how far-reaching this kind of responsibility may or should be. The fact that a research environment has inadequate routines, for example, cannot release a researcher from the responsibility for doing what is right. As a main rule, moreover, responsibility for the person who manages a research project or is in charge of a research environment should be relatively extensive.

According to recommendations for publishing ethics, every author of an article has obligations in the pre-publication submission and scrutiny process unless otherwise stated, and the corresponding author is primarily responsible for communicating with the journal regarding these processes.^{9,10} In the research area concerned, moreover, the first and last authors bear special responsibility.

[REDACTED] has long experience of research and has participated in a large number of publications. She has been the last author in most of the publications in question, and has also led the research groups that planned, implemented and reported on the research. The investigation in the case shows that [REDACTED] has, on repeated occasions, been responsible for reviewing the material for publication and approved material containing incorrect images.

Regarding [REDACTED] experience and position in the research groups concerned, the Board's view is that the fact that she repeatedly reviewed and approved incorrect images cannot be seen solely as a result of excusable ignorance or a temporary oversight. The Board's assessment is therefore that she acted with gross negligence.

⁸ Government Bill 2018/19:58, pp. 50–51.

⁹ *The European Code of Conduct for Research Integrity*, revised edition, 2018, All European Academies (ALLEA), section 2.7.

¹⁰ *Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals*, updated in 2019. International Committee of Medical Journal Editors.

The material investigated shows that at least one of the image manipulations took place at a late stage in the review; that several researchers reviewed the images; and that it was not entirely easy to detect that the images were incorrect. In view of the fact that [REDACTED] bears clear responsibility for having repeatedly approved material containing manipulated image, however, these circumstances do not alter the Board's assessment.

In summary, the committee therefore finds [REDACTED] guilty of research misconduct.

The Board has made a decision in this matter following a presentation by Miriam Matsson, caseworker. Karin Nylén also participated in the final administrative session.

Thomas Bull
Chair

Miriam Matsson
Caseworker