Npof.

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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 18 May 2021, Karolinska Institute (KI) submitted a case concerning research misconduct to the Board. This submission took place in accordance with Section 6 of the Swedish Act (2019:504) on responsibility for good research practice and the examination of research misconduct.

It emerges from the submission that the original complainant first reported the following article published in *Cancer Cell* to KI in 2009:

[redacted]

After KI had replied to the complainant that, as the main rule, investigation of research misconduct may not be based on circumstances predating initiation of the case by more than ten years, the complainant sent a report concerning the following article:

[redacted]

The suspicion regarding misconduct in this 2013 article relates to falsification or fabrication, consisting in reuse of data from western blot analyses. In Figure 3D in the

2013 article, western blot panels are alleged to show that a cell line has been duplicated and reused in order to represent results from another cell line as well.
On 12 October 2021, a report was received by the Board from the original complainant with respect to suspicion of manipulated results regarding analyses published in *PubPeer* in October 2021 by [redacted], the last author of the above-mentioned articles. The analyses published in *PubPeer* refer to a replication of results from the 2009 article from 2009 that was first reported to KI (see above).

All the authors of the 2013 article reject the allegations of research misconduct in this article and state that they believe the duplication took place by mistake. They regret that the error occurred and that they did not notice it at the time of publication. The last author, [redacted], states that she was alerted to the mistake in the 2013 article in connection with KI's submission to the Board, and that she was then able to ascertain that western blot panels had been mixed up in the article.

Figure 3D shows protein levels for a number of target genes for the tumour suppressor gene p53, and how these are affected by treatment with the RITA molecule. [redacted] (the last author) states that the same western blot panels that serve to show p21 and Noxa levels in SKN-DZ cells were used to show PUMA and Noxa levels in SKN-BE(2) cells. During a late stage of work on the article, she says, the decision was taken to add western blot data for the SKN-BE(2) cell line, and the duplication must then have taken place in error when the panel concerned was composed. She states that she attempted to find the images used to generate Figure 3D, but that they were not possible to find. She asserts that she found analyses performed in 2013 by the second author, [redacted] who obtained similar results in an independent experiment in the same cell line, SKN-BE(2). Further, she states that she asked the first author, [redacted] who was the one who performed the analyses investigated in the article, to repeat these analyses for SKN-BE(2), and that the same results were obtained.

The journal was contacted, and an Editor's Note was published on 1 September 2021. The first author, [redacted], states his belief that he must have mistakenly and inadvertently inserted the wrong panel in the article, and did not notice the error when the article was submitted for publication. The fourth author, [redacted] describes his role in the project and states that his main contribution was the clinical perspective, and that he did not take part in the laboratory work. Moreover, he asserts that the mixing of individual western blot results that took place cannot be deemed to entail fabrication or falsification of results or to have affected the conclusions drawn in the article.

Regarding the suspicions associated with the analyses published in October 2021 by the last author, [redacted] in *PubPeer* — suspicions relating to the 2009 article — she states that the analyses are correct and that she had added more images that the complainant had not noticed. The last author asserts that she also contacted the journal regarding the errors in this article that had come to light.

The Board has obtained an expert statement in the case.

Concerning the 2013 article, the expert states[1] that two western blot panels in Figure 3D are clearly duplicated and reused in the same figure to represent results from different cell lines: SKN-DZ vs. SKN-BE(2) and other proteins, p21/Noxa, vs.

[1] Professor Mikael Nilsson of the Sahlgrenska Comprehensive Cancer Centre.

Noxa/PUMA. The expert's assessment is that the duplication thus constitutes falsification. The expert states that he is leaving it open whether the falsification was unintended and a result of carelessness or whether it resulted from active manipulation.

Regarding the suspicion relating to falsification or fabrication of the results entered by the last author in *PubPeer* in October 2021, the expert's assessment is based on the replies given and the additional images of the analyses that were uploaded. He finds nothing that indicates manipulation of the analyses in *PubPeer*.

The respondents have issued statements concerning the expert's statement.

With respect to the 2013 article, all the authors regret the duplication and maintain that it occurred through an unintentional error when the manuscript was completed and data for the SKN-BE(2) cell line were added.

Regarding the allegation of manipulated results published in *PubPeer* in October 2021, the last author [redacted] states that she agrees with the expert's assessment that the images are correct.

Grounds for decision

Legal regulation

Under the Swedish 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.

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 legislative work on 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 on society at large, affecting people's health, for example, or how processes, methods or products are designed.[2]

The documentation from KI makes it clear that the original complainant first reported the 2009 article referred to above. The Board's assessment is that there are no exceptional reasons to deviate from the prescribed limitation period, and the Board is thus not examining the allegations relating to the article from 2009.

According to the above reasoning, the 2013 article is not subject to statutory limitation and must therefore be investigated.

The Board is also examining the allegations regarding the analyses published in

[2] Government Bill 2018/19:58, p.72.

PubPeer in October 2021.

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*.[3] [4] They are also explained in the Swedish Research Council's publication *Good Research Practice*.[5]

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 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.[6]

In Figure 3 in the 2013 article, two western blot panels in Figure 3D are reused in the same figure to represent results from other proteins in another cell lines. This reuse constitutes falsification according to the above definitions.

The analyses published in *PubPeer* 2021 are judged by the expert to be manipulated. The Board has reached the same assessment, and thus finds that it is not a matter of falsification or fabrication. This part of the case therefore does not need to examined further.

Serious breach

Under Section 2 of the Act, only serious breaches of good research practice constitute research misconduct and are thus subject to 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 research themselves. The preparatory work for the Act states that fabrication and falsification are, in principle, always serious breaches of good research practice. In certain cases, plagiarism should not be considered a serious breach of good research practice, for example if it is a minor infraction on a single occasion.[7]

The premise for the Board's investigation in this part of the case is that falsification is, in principle, a severe breach of good research practice. The fact that a reuse of images has not affected 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. No reason to deviate from the premise stated in the preparatory work on the Act has emerged in the case. The Board's conclusion is therefore that the breaches are serious.

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[3] *The European Code of Conduct for Research Integrity*, revised edition. Berlin: All European Academies (ALLEA); 2018, section 3.1.
[4] Government Bill 2018/19:58, pp. 45, 100.
[5] *Good Research Practice*, Swedish Research Council; 2017, Chapter 8.
[6] Government Bill 2018/19:58, pp. 45, 100.
[7] Government Bill 2018/19:58, p. 100.

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.[8]

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 claim that the mistake took place unintentionally. In light of the expert’s statement, the Board’s assessment is that nothing has emerged in the case to indicate that the reuse of images in the 2013 article took place with intent. Nor, since only a single error took place, does the Board find that there are reasons to deem that the authors have acted with gross negligence.

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

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The Board has made a decision in this matter, following a presentation by caseworker Dorota Green.

Thomas Bull	Dorota Green
Chair	Caseworker

[8] Government Bill 2018/19:58, pp. 50–51, 100.