

STATEMENT
6 September 2016

Ref. no. O 1-2016

University that requested the statement

Karolinska Institutet
SE-171 77 Stockholm

Background

In a petition received on 29 February 2016, Karolinska Institutet has requested a statement from the Expert Group for Misconduct in Research at the Central Ethical Review Board. The petition includes a reference to a letter of allegation from C

. According to the petition the authors are, by publishing the scientific article "Experimental orthotopic transplantation of a tissue-engineered oesophagus in rats", included in Nature Communications (2014;5:3562) journal, guilty of scientific misconduct. The authors of the scientific article are S

. The Expert Group has been asked to provide a statement on whether the contents of the documents in the case constitute misconduct in research. The Expert Group is thereby requested particularly to comment on whether the descriptions of the results in the article come across as distorted and if the co-authors are responsible for the content of the article both before and after publication.

On 18 March the Expert Group appointed Professor Eva Ekblad, Department of Experimental Medical Science at Lund University as external reviewer. Eva Ekblad's report was received by the Expert Group on 9 July. Both those accusing and those who are accused of misconduct have had an opportunity to reply, of which the following have submitted replies; Y

The Expert Group has made several requests for supplementary documents from Karolinska Institutet, e.g. animal log records and ethical research permits for the animals included in the article. The case was supplemented by replies from Karolinska Institutet which partly answered the above-mentioned requests, two letters from and one letter from two of the co-authors,

Postal address	Street address	Telephone	Fax
Central Ethical Review Board c/o Swedish Research Council Box 1035 SE-101 38 Stockholm	Västra Järnväggsgatan 3	+46 8 546 77 610 exchange.	+46 8 546 441 80

Ref, no. O 1-2016

A further letter arrived on 23 August 2016 in which I mainly commented on [redacted] reply. In the Expert Group's view, however, this letter does not contribute information of any importance for the assessment of the misconduct case in question.

The Expert Group's assessment

In the assessment of whether misconduct in research is the case, the Expert Group has used the reported article in its entirety and therefore not specifically focused on the four points raised by the complainers. This was also Eva Ekblad's starting point.

Eva Ekblad concludes that the main authors of the reported article are guilty of scientific misconduct for refusing or being unable to present the raw data for the results presented in the article; for refusing or being unable to present experiment records for the animals that were used in the article; misleading presentation, interpretation and description of the results; serious deviation from the animal ethics permit and for misleading the regional ethical committee on animal research.

Firstly, as regards the refusal or inability to present the raw data for the results presented in the article and log records for the animals that were used, the Expert Group agrees with Eva Ekblad's assessment. In his reply to Eva Ekblad's report, [redacted] maintains that he at all times helped in providing the Expert Group with the requested data. Despite repeated and clearly defined requests, however, the Expert Group was largely given access to incomplete and sporadically incorrect data. The Expert Group is unable to comment on whether this was due to a refusal or inability. Irrespective of this, in the Expert Group's view, the inadequate and incomplete documentation is a sufficiently serious deviation from good scientific practice to constitute misconduct in research. It is noted that this lack of order in the research results and cooperation also places responsibility on the head of the department and, ultimately, on Karolinska Institutet as a public research university.

Secondly, as regards whether the content of the article is consistent with the research that was conducted or if the article is misleading, the Expert Group's assessment is as follows. In the article, the authors have claimed, via successful experiments on rats, to have developed an artificial oesophagus which could be used as a model of well-functioning oesophagus transplant on humans. They argue that, inter alia, the rats that were operated with the artificial oesophagus survived 14 days while they were examined. The reported article therefore clearly suggests to the reader that the presented research demonstrates that the transplanting of oesophagus on rats was successful. In the investigation it transpired that the aspects that were reported as being successful were not successful. The rats which were part of the experiment, for example, contrary to what the article maintains, showed very significant weight loss, which would not have been the case if the experiment had been a success. In addition, the rats lost so much weight and deteriorated so much in condition that the experiment should have been stopped. The article also contains a number of references which have resulted in incorrect interpretations, thereby misleading the ethical committee on animal research. The pictures and figures that reportedly demonstrate the success of the experiment are also incorrect and misleading in several places. The raw data that the Expert Group has had access to is not always consistent with the figures in the article, which leads to incorrect conclusions. The methodology is briefly described in the article; it is not possible to extract original data

Ref, no. O 1-2016

from the material submitted in the case; there are no systematic records or summaries, inter alia, of which analyses and how many were performed, and how the data has been processed and analysed statistically. In addition, there is no indication of which animals or how many were included or excluded in individual analyses. It is therefore, in the Expert Group's view, conclusively established that the presentation of the results in the article is inconsistent with the outcome of the research that was conducted, which is scientific misconduct.

Eva Ekblad has also pointed out that deviations from animal ethics permits and misleading the regional ethical committee on animal research constitutes scientific misconduct. Research without the necessary permit – in this case ethical laboratory animal permit – is a serious breach of ethical research standards and could also constitute a violation of the Swedish Animal Welfare Act (1988:534). The question about whether research conducted without the required permit, or violations of them, constitutes misconduct in research varies between a number of different definitions in use. The investigation revealed that the rats that were included in the research showed significant weight loss, although details about how much weight was lost varies. In the Expert Group's view it is therefore not possible in this case to establish that the deviation from the ethical permit for animals constituted misconduct in research.

The question regarding who can be held responsible for the scientific misconduct also arises. There is no doubt that the article's main author, _____, has the main responsibility for the content of the article and that he is therefore guilty of misconduct in research.

As regards the responsibility of the other co-authors, the Expert Group's assessment is as follows. In accordance with good scientific practice all co-authors must approve the latest version of the script and thereby assume responsibility for the same. The scientific and co-authors' contributions should be identifiable, which is largely not the case in the article which is by itself reprehensible. A scientific article with several co-authors is a joint endeavour with collective responsibility. If one scientific article is deemed to be marred by serious shortcomings grave enough to constitute scientific misconduct, the responsibility therefore falls on all the co-authors. This also applies, as in this case, where the majority of the co-authors' specific contributions to the article are not specified and where it's one person's word against the other on key points. Some of the authors of the article, except for _____, have had a more prominent role than others. Amongst them it is clear that _____ have had key roles in the research process.

The Expert Group has some degree of understanding for the more junior researchers who have been in a position of dependency on _____ and other leaders of the research group, which at the time of the research in question, also had significant support from the management of Karolinska Institutet. This does not free them from responsibility but it should be seen as an extenuating circumstance.

The processing of case is thereby concluded on the part of the Expert Group.

Ref, no. O 1-2016

This Statement is decided by Lena Berke (chair), Holger Luthman, Elisabeth Rachlew, Ann-Charlotte Smedler and Elin Wihlborg. At the concluding processing of the case, substitutes Jerry Eriksson, Aleksander Giwerzman and Christina Moberg, Head of Administration Jörgen Svidén and Administrative Secretary Eva Kaaman Modig were also present.

On behalf of the Expert Group for Misconduct in Research

Lena Berke