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Ministeriet for Forskning, Innovation og Videregående Uddannelser

Ministry of Science, Innovation and Higher Education

DRAFT – Draft ruling by the Danish Committee on Scientific Dishonesty for Research in Health and Medical Science (USF)

25 June 2013

Danish Committees on Scientific Dishonesty
c/o
Danish Agency for Science, Technology and Innovation
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1 Introduction

On 18 April 2011, Professor James Timmons of the Royal Veterinary College, University of London (hereinafter referred to as the Complainant), submitted a complaint by e-mail to the Secretariat of the Danish Committees on Scientific Dishonesty (DCSD) against you (Defendant 1) and Matthew Laye, Camilla Scheele and Søren Nielsen (defendants 2-4), all of whom work at the Centre of Inflammation and Metabolism (CIM), alleging that all four defendants had acted in a scientifically dishonest manner when drawing up and reporting on research results in four articles.

The Complainant alleges that a series of actions by Defendant 1 in conjunction with an application for funding from the UNIK pool (the UNIK application) for a research project in Defendant 1's laboratory at CIM also fall under the definition of scientific misconduct.

In addition, the Complainant highlights a number of other areas, particularly regarding Defendant 1, in which the Complainant considers aspects of behaviour to have been unacceptable.

Defendants 1-4 submitted a joint response.

The case has been considered by the Danish Committee on Scientific Dishonesty for Research in Health and Medical Science (USF) The USF draft ruling is reproduced below.

Please submit any response you may have to the draft within 15 August 2013.

The draft has also been sent to the Complainant for any additional comments.

[DRAFT RULING – START]

2 Ruling

The Committee finds that Defendant 1 did act in a scientifically dishonest manner when writing an article published in Diabetologia (see Note 1). The Committee finds that significant information about the test subjects was omitted from the original methodology section in the article, and that this omission corresponds to 'undisclosed construction of data' as per section 2, 1 of executive order no. 306 of 20 April 2009 and executive order of amendment no. 144 of 20 February 2012 on Danish Committees on Scientific Dishonesty. The Committee also finds that Defendant 1 did act in a grossly negligent manner as it was her responsibility as the lead author to ensure that the information in the methodology section was accurate.

The Committee has informed the Defendant's employers, the University of Copenhagen and Copenhagen University Hospital, by sending a copy of this ruling as per 15 (1) of the DCSD order.

Due to the fact that an erratum has been printed correcting the article's methodology section, the Committee has decided to take no further action.

This unanimous decision was reached by Lise Wogensen Bach, Ulla Feldt-Rasmussen, Palle Holmstrup, Kirsten Ohm Kyvik, Ole Haagen Nielsen and Jens Overgaard and Henrik Gunst Andersen (chairperson).

3 Brief summary

In April 2011, a professor from a university outside Denmark (the Complainant) submitted a complaint to the DCSD alleging scientific misconduct in research conducted by four researchers affiliated to a Danish research centre (Defendants 1-4).

The Complainant alleges that Defendants 1-4 acted in a scientifically dishonest manner during the drafting and reporting of research results in four articles, citing plagiarism of the Complainant's work, failure to accredit data from an article for which the Complainant was as the lead author, unjustified claims of authorship, failure to cite the Complainant as a co-author, improper use of statistical methods and skewed presentation of both literature and the Defendants' own research results. The Complainant also alleges plagiarism and failure to credit the Complainant when applying for UNIK funding, and complains about a number of other areas, particularly regarding Defendant 1, in which the Complainant considers aspects of behaviour to have been unacceptable.

DCSD has reviewed the case papers, including the four articles and the UNIK application, the parties' consultation responses and e-mail correspondence. The following is a summary of the DCSD's conclusions concerning the four articles, the UNIK application and the other aspects of the complaint.

Regarding the four articles, DCSD concludes that:

- They do not constitute plagiarism as significant differences exist between the work of the Complainant and of Defendants 1-4.
- The Defendants did not act dishonestly in relation to citing the Complainant's data because:
    1) the data was presented in an e-mail from the Complainant to Defendant 1 and referred to in such vague terms that the e-mail cannot be consider to constitute a request by the Complainant to have it mentioned in a potential joint article. At that point in time, it was only a matter of days before the deadline for final submission of the joint article to the journal in which it was published.
    2) The data was published about six months after the aforementioned article and is only mentioned in one sentence followed by *Data not shown*. Basic information such as age and gender of the test subjects was not included in the article concerned.
- Defendants 1-4 did not improperly accredit authorship, since they were able to account satisfactorily for their share of the work.
- The Defendants did not neglect to cite the Complainant as an author to one of the articles, as the available e-mail correspondence does not indicate a form of collaboration that would justify co-authorship. In the correspondence concerned, the Complainant was only asked to evaluate the article by Defendants 1-4 in order to ensure that there was not too much

overlap with his own, which the Complainant confirmed was not the case.

- The article that was the subject of the complaint about the use of the wrong statistical methods contained an inadequate methodology section as significant information about the test subjects was omitted, which in the opinion of the Committee corresponds to 'undisclosed construction of data' as per 2 (1) of the DCSD order. The Committee also finds that Defendant 1 did act in a grossly negligent manner because it was her responsibility as the lead author to notice the significant omissions from the methodology section. DCSD therefore finds that Defendant 1 did act in a scientifically dishonest manner with regard to this part of the complaint.
- The literature cited, as well as the mentions by Defendants 1-4 of their own work in the four articles, fall within the parameters for discussion among authors given the restrictions placed by academic journals on the scope of articles and bibliographies.

Regarding the application for UNIK funding, DCSD finds that:

- Defendant 1 was a co-author of the work that the Complainant claimed had been plagiarised.
- The application was to an internal pool and Defendant 1 was already a member of the group that had received the funds after responding to a government call for applications. The Complainant was informed that this internal application had been submitted, and even received a copy of it, many months before the Complainant submitted the complaint to the DCSD.
- Plagiarism software did not detect plagiarism of the Complainant's article, as alleged by the Complainant.

DCSD also finds that a number of other aspects of the complaint that the Complainant alleges are unacceptable do not fall under the jurisdiction of the DCSD.

Overall, the DCSD finds that Defendant 1 did act in a scientifically dishonest manner and has informed Defendant 1's employers of this ruling.

As the DCSD rejects the other charges brought by the Complainant, it finds that Defendants 2-4 did not act in a scientifically dishonest manner.

4 Process, background and subject matter for the case

4.1 Process

On 18 April 2011, the Complainant submitted a complaint by e-mail to the DCSD Secretariat, alleging that Defendants 1-4 acted in a scientifically dishonest manner when drawing up and reporting on research results in four articles.

The Complainant also alleges that a series of actions by Defendant 1 in conjunction with the planning of research results and applying for funding from the UNIK pool (the UNIK application) also fall under the definition of scientific misconduct.

In addition, the Complainant highlights a number of other areas, particularly regarding Defendant 1, in which the Complainant considers aspects of behaviour to have been unacceptable.

In a further e-mail to the DCSD Secretariat, dated 18 May 2011, the Complainant submitted additional comments to his complaint of 18 April 2011.

On 23 May 2011, Defendants 1-4 submitted an unsolicited provisional report and appendices concerning the allegations to the Secretariat. This was occasioned by the Complainant sending them a copy of his complaint.

In an e-mail to the DCSD Secretariat, dated 12 June 2011, the Complainant submitted a supplementary report with appendices to the complaint of 18 April 2011.

In an e-mail to the DCSD Secretariat, dated 14 June 2011, the Complainant submitted new comments concerning editing errors in the complaint of 18 April 2011 and also attached a missing appendix to the complaint.

In an e-mail to the Complainant, dated 23 June 2011, the DCSD Secretariat attempted to summarise and specify the Complainant's allegations of scientific misconduct on the basis of the material received to date.

In an e-mail to the DCSD Secretariat, dated 28 June 2011, the Complainant responded to the e-mail of 23 June 2011 by making comments and providing clarifications.

On 15 August 2011, the DCSD Secretariat sent the case papers to Defendants 1-4 for consultation.

On 22 August 2011, the DCSD Secretariat received a response and appendices from Defendants 1-4.

On 1 September 2011, the DCSD Secretariat sent the Defendants' response of 22 August 2011 to the Complainant for consultation.

The Complainant asked the DCSD Secretariat several times to extend the deadline until 10 October 2011, when the Complainant submitted his response and appendices.

On 10 October 2011, the DCSD Secretariat sent the Complainant's response of 10 October 20112 to Defendants 1-4 for consultation.

On 28 October 2011, the DCSD Secretariat received a second response and appendices from Defendants 1-4.

On 31 October 2011, the DCSD Secretariat sent the Defendants' response of 28 October 2011 to the Complainant for information.

On 4 November 2011, the DCSD Secretariat received an e-mail from the Complainant containing supplementary comments to his response of 10 October 2011.

On 9 November 2011, the DCSD Secretariat sent the Complainant's supplementary comments of 4 November 2011 to Defendants 1-4 for consultation.

On 18 November 2011, the DCSD Secretariat received supplementary comments in an e-mail with appendices from Defendants 1-4 concerning the Complainant's supplementary comments of 4 November 2011.

On 21 November 2011, the DCSD Secretariat sent Defendants 1-4's supplementary comments with appendices of 18 November 2011 to the Complainant for information.

On 26 November 2011, the DCSD Secretariat received an e-mail from Defendants 1-4 containing a supplementary appendix to the response of 28 October 2011.

On 8 December 2011, the DCSD Secretariat sent the Defendants' supplementary appendix of 26 November 2011 to the Complainant for consultation.

On 8 and 9 December 2011, the DCSC Secretariat received e-mails with further comments from the Complainant concerning the supplementary appendix of 26 November 2011.

4.2 Background and subject matter

The parties to the case agree that the Complainant, in his capacity as group leader at the Center for Genomics and Bioinformatics (CGB) at Karolinska Institutet, and Defendant 1 in her capacity as head of CIM, collaborated on research from 2005 onwards.

As shown below, the Complainant alleges that Defendants 1-4 acted in a scientifically dishonest manner when drawing up and reporting on research results in four articles submitted in the period after the research collaboration with the Complainant commenced.

- Article in Diabetologia[1] (concerns Defendant 1)
- Article in Experimental[2] Psychology (concerns Defendant 1)
- Article 1 in the Journal of Physiology[3] (concerns Defendants 1-4)
- Article 2 in the Journal of Physiology[4] (concerns Defendant 1)

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[1] Matthews VB, Aström MB, Chan MH, Bruce CR, Krabbe KS, Prelovsek O, Akerström T, Yfanti C, Broholm C, Mortensen OH, Penkowa M, Hojman P, Zankari A, Watt MJ, Bruunsgaard H, Pedersen BK, Febbraio MA, 'Brain derived neurotrophic factor is produced by skeletal muscle cells in response to contraction and enhances fat oxidation via activation of AMP-activated protein kinase', Diabetologia, 52 (7), 2009, p. 1409-1418

[2] Pedersen BK, Pedersen M, Krabbe KS, Bruunsgaard H, Matthews VB, Febbraio MA, 'Role of exercise-induced brain-derived neurotrophic factor production in the regulation of energy homeostasis in mammals', Experimental Physiology, 94 (12), 2009, p. 1153-60

[3] Nielsen S, Scheele C, Yfanti C, Akerström T, Nielsen AR, Pedersen BK, Laye MJ, 'Muscle specific microRNAs are regulated by endurance exercise in human skeletal muscle', Journal of Physiology, 588 (20), 2010, p. 4029-4037

The Complainant also alleges that a series of actions by Defendant 1 in conjunction with an application for funding from the UNIK pool (the UNIK application)[5] for a research project also fall under the definition of scientific misconduct.

In addition, the Complainant highlights a number of other areas, particularly regarding Defendant 1, in which the Complainant considers aspects of behaviour to have been unacceptable.

Defendants 1-4 contend that they are innocent of all charges of scientific misconduct and other allegations of unacceptable behaviour.

In the section below, the parties' claims, responses and contentions have been sub-divided into the categories of the above-mentioned four articles, the UNIK application and other unacceptable conditions.

A number of scientific works are also referred to in the parties' claims, responses and contentions – in particular an article in Genome Medicine[6] and early manuscripts for this article.

In addition, a number of individuals with links to the parties are mentioned.

5 The parties' claims, responses and contentions

5.1 Article in Diabetologia

5.1.1 The Complainant's claims and contentions

The Complainant alleges that Defendant 1 acted in a scientifically dishonest manner when drawing up and reporting on research results for an article in the journal Diabetologia (see Note 1).

5.1.1.1 Warning about unsound data

In support of his allegation, the Complainant asserts that he sent e-mails on 4 January 2009 and 20 February 2009, i.e. before the article was submitted to Diabetologia on 25 February 2009, in which he warned Defendant 1 that the data in the article was unsound and directly contradicted comparable quantitative Polymerase Chain Reaction data (qPCR) data from an analysis conducted in the Complainant's laboratory (the analysis was attached to the Complainant's e- mail of 20 February 2009).

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[4] Akerstrom T, Steensberg A, Keller P, Keller C, Penkowa M, Pedersen BK, 'Exercise induces interleukin-8 expression in human skeletal muscle', J Physiol, 563.2, 2005, p. 507-516

[5] Application for funding from a UNIK pool (Universitetsforskningens InvesteringsKapital - University Research Investment Capital) under the project name 'Regulation of myo-miR in humans'

[6] Gallagher IJ, Scheele C, Keller P, Nielsen AR, Remenyi J, Fischer CP, Roder K, Babraj J, Wahlestedt C, Hutvagner G, Pedersen BK, Timmons JA, 'Integration of microRNA changes in vivo identifies novel molecular features of muscle insulin resistance in type 2 diabetes', Genome Medicine, 1;2(2), 2010, p. 9.

In his e-mail of 4 January 2009, the Complainant refers to results from a study of elderly diabetics and healthy test subjects.

According to the Complainant's e-mail of 20 February 2009, the qPCR analysis conducted in the Complainant's laboratory for a partner showed that *brain-derived neurotrophic factor-* mRNA (BDNF-mRNA) is virtually undetectable in complete muscle tissue (biopsy) both at rest and after 24 hours of endurance training by 24 young male test subjects. According to the Complainant, the data shows that the signal for BDNF-mRNA-expression does not occur until after 37 cycles of signal amplification, which according to the Complainant would be consistent with expression in <3% of the cells in the muscle tissue. According to the Complainant, this conclusion is consistent with the known biology concerning BDNF and the article in Genome Medicine of which Defendant 1 was a co-author.

The Complainant also asserts that Defendant 1's argument concerning *splice variants* (see below under Defendant 1's responses and contentions) is not valid because the PCR primers used were directed towards a common sequence in an exon.

The Complainant also asserts that the cDNA he used to conduct a BDNF plot was correct (see below under Defendant 1's responses and contentions), because at the same time, he was measuring a second gene (asBDNF), which is expressed slightly higher than BDNF and demonstrates a beautiful, dense and non-variable frequency profile.

5.1.1.2 Presentation of relative data normalised to 1

The Complainant also asserts that the article posits that BDNF-mRNA is regulated by the training done by the young male test subjects (n=8) but the article does not present the *actual* level of BDNF-mRNA. Instead, it presents 'relative' data normalised to 1, and according to the Complainant, this conceals the true incidence of BDNF-mRNA.

5.1.1.3 Use of unconventional and invalid statistical methods

According to the Complainant, the article's authors use an *area under the curve* analysis (AUC analysis) and a single unpaired t-test, instead of an *analysis of variance* (ANOVA) for repeated measurements. According to the Complainant, this method is neither conventional nor sound. The Complainant thus asserts that Figure 1a in the article presents the normalised mRNA levels over time and that the data in the article is analysed by means of an AUC analysis, which conceals the fact that BDNF is almost unquantifiable. In addition, the Complainant asserts that the reader is not presented with a model for adjusting the points in time, nor with data for the AUC calculations. This means that information about the mean value and spread of the AUC data is omitted, making it impossible to verify the data.

The Complainant also asserts that the choice of statistical analysis used on the AUC data was the wrong one. According to the Complainant, an unpaired t-test was used, but according to the description of the test subjects in the original material and methodology section, it should have been a paired t-test.

5.1.1.4 Publication despite the lack of biological relevance of the results or invalid findings

According to the Complainant, the ~1.25-fold increase in mRNA expression cited by Defendant 1, compared with the comparative control samples five hours after the training, corresponds with the expression of an mRNA molecule in ~5% of the cells (which could reflect a contamination of the blood in the biopsy taken after training) or is actually an expression of *technical noise* and a non-significant data set.

5.1.1.5 Ignoring data from the research collaboration with the Complainant, including the article in Genome Medicine

Further, the Complainant asserts that in the article, Defendant 1 chose to ignore data generated in collaboration with the Complainant's laboratory. The data shows that BDNF was not higher in mature muscle cells, but 'only' in a few selected cells characterised by immature skeletal muscle cells. According to the Complainant, Defendant 1 chose instead to focus on the more positive data from the collaboration with another partner, Mark Febbraio (hereinafter referred to as Co-author 1). According to the Complainant, Defendant 1 also chose to ignore two decades of literature showing that BDNF plays a role in neuromuscular regeneration, in which BDNF is expressed in muscle damage to support the repair of the neuromuscular junctions.

The Complainant also asserts that the data in the article contradicts data in the work published in Genome Medicine (see note 6) and co-authored by Defendant 1.

The Complainant also states that the redrafting of the discussion section of the article in Genome Medicine (see below under Defendant 1's responses and contentions) was sent to Defendant 3, since all communication was to be with her according to an agreement with Defendant 1.

Furthermore, the Complainant asserts that the redrafting of the discussion section of the article in Genome Medicine merely clarifies the existing wording.

5.1.1.6 Immunoblot with changed/manipulated contrast/image preferences

According to the Complainant, the article contains a particularly important immunoblot from another co-author of the article, Milena Penkowa (hereinafter referred to as Co-author 2), which shows a universal and markedly increased expression of whole-muscle BDNF protein in all muscle fibres in young men 24 hours after endurance training, but not in the time-control biopsy. According to the Complainant, the time-control biopsy data in the article rules out any possibility that the BDNF is caused by unintentional damage to the biopsy.

The Complainant asserts that Defendant 1 chose to ignore that the positive 24-hour protein-blot was compared – with changed/manipulated contrast/image preferences – with the control samples ('pre-ex' and 'O'). According to the Complainant, the image contrast is not consistent across the image.

5.1.1.7 Significant Western blot

The Complainant also asserts that a former postdoc at CIM in late 2008 and in 2009 told the Complainant that the original Western blot in the article had been

repeated several times at CIM, and in early drafts of the manuscript, it was not significant. However, at an early point the manuscript was sent to Co-author 1, and when it came back, the figure that showed the aforementioned Western blot, was now suddenly given a 'star', which described the change as significant.

Finally, the Complainant alleges that the increase of BDNF protein in muscle fibres is impossible, since there is no mRNA template in most muscle cells – and without mRNA it is not possible to synthesise BDNF protein.

5.1.1.8 Misquotations of three articles

The Complainant also asserts that in the article, Defendant 1 misquoted the following three articles (references 22, 23 and 24 in the article):

- Dupontversteegden et al.[7]
- Gómez-Pinilla et al.[8]
- Avila et al.[9]

According to the Complainant, Defendant 1 mistakenly states that the article by Dupont-Versteegden et al. and the article by Gómez-Pinilla et al. demonstrate that muscle contraction increases BDNF mRNA.

According to the Complainant, Defendant 1 also mistakenly states that the article by Avila et al. demonstrates that BDNF increases when *histone deacetylase* (HDAC) is inhibited but that Defendant 1 fails to mention protein data in this context.

In this light, the Complainant asserts that Defendant 1 seriously misinterpreted the literature to make it fit the data in the article.

5.1.1.9 Incorrect presentation of clinical trials

The Complainant also asserts that the clinical trials in the article are presented incorrectly. To support this assertion, the Complainant states that the critical *time-course immunoblot* shown in the article is only from the 'best' test subject (n=1).

5.1.1.10 Improper accreditation of co-author

The Complainant asserts that if Co-author 2, as stated by Defendant 1 (see below under Defendant 1's responses and contentions), did not produce the immunoblots shown in Figure 1, then Co-author 2 has been wrongly listed as an author of the article.

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[7] Dupont-Versteegden EE, Houlé JD, Dennis RA, Zhang J, Knox M, Wagoner G, Peterson CA, 'Exercise-induced gene expression in soleus muscle is dependent on time after spinal cord injury in rats', Muscle Nerve, 29 (1), 2004, p. 73-81

[8] Gómez-Pinilla F, Ying Z, Opazo P, Roy RR, Edgerton VR, 'Differential regulation by exercise of BDNF and NT-3 in rat spinal cord and skeletal muscle', Eur J Neurosci, 13 (6), 2001, p. 1078-84.

[9] Avila AM, Burnett BG, Taye AA, Gabanella F, Knight MA, Hartenstein P, Cizman Z, Di Prospero NA, Pellizzoni L, Fischbeck KH, Sumner CJ, 'Trichostatin A increases SMN expression and survival in a mouse model of spinal muscular atrophy' J Clin Invest 117 (3), 2007, p. 659-71

5.1.2 Defendant 1's responses and contentions

Defendant 1 contends that she is innocent of all charges of scientific misconduct.

5.1.2.1 Not a warning, but an exchange of scientific points of view

Defendant 1 contends that the Complainant's e-mails of 4 January and 20 February 2009 do not constitute warnings, nor is there any indication that the Complainant directed Defendant 1's attention to any misconduct in 2009. Defendant 1 considered the e-mail correspondence solely to be an exchange of scientific points of view.

5.1.2.2 No contradiction with data from the research collaboration with the Complainant, including the article in Genome Medicine

Defendant 1 also contends that the Complainant's argument that BDNF mRNA is virtually undetectable in whole muscle tissue (biopsy), is partly based on a qPCR analysis carried out in the Complainant's laboratory and not on peer-reviewed published data.

According to Defendant 1, one of the problems with handling BDNF at mRNA level is the presence of an unusually high number of variants of BDNF-mRNA, and for this reason, Defendant 1 chose to use an already developed and optimised assay from Applied Biosystems. Defendant 1 states that if you direct primers towards a particular variant with lower expression, you arrive at a lower signal from the qPCR analysis. According to Defendant 1, the Complainant did not stipulate the sequence of his primers nor did he specify which variant he directed his primers towards.

According to Defendant 1, the Complainant asserts that BDNF is not expressed in muscles but there is no evidence to support this. As Defendant 1's data showed a different result, Defendant 1 chose to proceed with the publication of the article.

According to Defendant 1, a Western blot is presented as an appendix, which clearly shows the BDNF protein expression in healthy control individuals and patients with type 2 diabetes.

Defendant 1 also contends that a correct adjustment of the Ct threshold in the Complainant's qPCR analysis could lead to a measured Ct value on the same level as in the article.

According to Defendant 1, the Complainant's samples exhibit major variations, possibly indicating that the cDNA is in poor condition, and thus exerting a negative influence on the quality and results. In support of this, Defendant 1 contends that the samples the Complainant used stem from mRNA that Defendant 3 isolated during her studies under the Complainant at Karolinska Institutet in 2006. According to Defendant 1, the cDNA was therefore two years old and had been thawed and frozen repeatedly.

Defendant 1 contends that the Complainant's data is an analysis of mRNA expressions after six weeks of endurance training, whereas the article studies mRNA differences in acute exercise. As a result, according to Defendant 1, the

Complainant's samples can only be compared with the resting-time samples in the article, where they have a Ct value of 33.

Defendant 1 also contends that there may be several reasons for this discrepancy between the article and the article in Genome Medicine. Defendant 1 contends for example that the article in Genome Medicine focuses primarily on microRNA (miRNA)[10] and that BDNF was included as one of six proteins in order to validate the analytical prognosis. Defendant 1 also states that the samples for evaluation of BDNF expression in the article in Genome Medicine are from test subjects aged approx. 60, whereas the test subjects in this article consist of healthy males aged 20-30. In this light, according to Defendant 1, the data in the two articles is not comparable.

Defendant 1 contends that the Complainant changed the wording of the discussion section of the article in Genome Medicine without informing or obtaining the permission of Defendant 1.

5.1.2.3 Literature not ignored

As far as the literature is concerned, Defendant 1 contends that there are several ways in which proteins can change without a (major) change in messengerMRNA levels (mRNA levels).

Defendant 1 also states that the article did not ignore the literature or data cited by the Complainant. In this context, Defendant 1 refers to the fact that a reviewer at the journal FASEB (to which the article was initially submitted) found that the data in the article was not innovative. According to Defendant 1, the reviewer's reference to the literature indicates that it is widely accepted that contracting skeletal muscles express BDNF.

5.1.2.4 The AUC analysis was conducted on the advice of statisticians

According to Defendant 1, the AUC analysis was conducted on the advice of the authors' statisticians. According to Defendant 1, this method of statistical analysis was not questioned during the peer-review process.

Defendant 1 also contends that the data in the article shows a low to moderate, but consistent, expression of BDNF-mRNA in human skeletal muscle. According to Defendant 1, the data in the article is described as it is, without over-interpretation on the part of the authors.

5.1.2.5 False accusation of significant Western blot

Defendant 1 contends that the Complainant's accusation that a Western blot in the article was repeated several times in order to achieve significance is false. According to Defendant 1, it was due to an error that the Western blot concerned was at one point marked as significant. The error was discovered and the significance symbol removed. Defendant 1 also states that this sequence of events has been confirmed by a PhD student at CIM, who was responsible for the Western blots concerned.

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[10] In the ruling, only the term miRNA is used, although it is noted that the parties use both miRNA and microRNAs.

5.1.2.6 The background to the presentation chosen for the clinical studies
Defendant 1 claims that the immunohistochemistry (IHC) was used in the article (Figure 1d) to indicate whether the expression of BDNF had possibly increased inside the muscle fibres (intramyocellular). In the article, according to Defendant 1, the authors chose to show the IHC image of the test person with the highest expression of BDNF-mRNA. According to Defendant 1, this individual apparently also had the most pronounced expression of BDNF protein. Defendant 1 states that the authors thus chose to show the IHC image that best supported the idea that increased BDNF-expression after 24 hours after training took place inside the muscle cells.

5.1.2.7 No improper accreditation of co-author
According to Defendant 1, the IHC in the article was not performed personally by Co-author 2, but by Maj Brit Åstrøm (hereinafter referred to as Co-author 3) and a student at Co-author 2's laboratory. According to Defendant 1, Co-author 2 was involved in the supervision of the IHC technique and the description of Figure 1d and is, therefore, properly listed as a co-author of the article.

5.1.2.8 Printing of an erratum due to errors in the methodology section
Defendant 1 states that the methodology section of the article does not contain a description of the control group used in the study because of an error. At the request of Defendant 1, Diabetologia has published an erratum to the article.

5.2 Article in Experimental Physiology

5.2.1 The Complainant's claims and contentions
The Complainant alleges that a series of actions by Defendant 1 could be characterised as scientifically dishonest when reporting on the research results in an article in the journal Experimental Physiology (see Note 2).

5.2.1.1 The results in the article are not substantiated, and they contradict the articles in Diabetologia and Genome Medicine
The Complainant asserts that Defendant 1 makes wild and unsubstantiated claims in the article that BDNF, to some extent or another, plays a role in the regulation of muscular fat burning.

Specifically, the Complainant quotes the following from the article: "*By demonstrating that BDNF is expressed in muscle and has an impact on fat oxidation, we add a new dimension to the pleiotrophic nature of BDNF, which can now be identified as playing a role in neurobiology as well as in both central and peripheral metabolism*".

The Complainant also asserts that the statement quoted above from the article directly contradicts the article in Diabetologia (of which Defendant 1 is the author). According to the Complainant, the Diabetologia article says that an effect of BDNF was only found if it was artificially up-regulated, and that the BDNF's mechanism of action in vivo was unclear.

According to the Complainant, the statement in the article claiming that it has been proven that BDNF plays an important role in regulation of the human metabolism is pure fabrication and an example of dishonest scientific writing.

In support of this claim, the Complainant also asserts that in the conclusions to the article, Defendant 1 ignored the body of existing literature, as well as an article by both the Complainant and Defendant 1 that had already been published (the article in Genome Medicine). According to the Complainant, the article in Genome Medicine proves that BDNF is not always expressed in human muscles, nor can it always be induced by hard physical training.

5.2.2 Defendant 1's responses and contentions

Defendant 1 contends that she is innocent of the complaint alleging scientific misconduct.

5.2.2.1 The results in the article are substantiated and do not contradict the article in Diabetologia

Defendant 1 contends that the authors of the article presented their data in a balanced manner. Defendant 1 states, however, that the use of the word "markedly" to describe the increase in BDNF-mRNA and protein-expression may be viewed as an over-interpretation of the results presented in the article as BDNF's increased protein expression was approximately 50%.

With reference to Figures 3, 4, 5 and 6 in the article in Diabetologia, Defendant 1 states that the article and existing literature provide a strong basis for assuming that the statement in the article that is contested by the Complainant is, in fact, correct.

Defendant 1 contends that it is incorrect of the Complainant to claim that the article in Diabetologia only found a BDNF effect when it was artificially up-regulated.

Defendant 1 also refutes the Complainant's suggestion that the claim put forward in the article that BDNF plays an important role in the regulation of the human metabolism is a pure fabrication. In other words, Defendant 1 stands by the conclusion contained in the article.

5.3 Article 1 in the Journal of Physiology

5.3.1 The Complainant's claims and contentions

The Complainant alleges that Defendants 1-4 acted in a scientifically dishonest manner when drawing up and reporting on research in an article in Journal of Physiology (see Note 3).

5.3.1.1 Reproduction of the Complainant's observations

The Complainant asserts that Defendants 1-4, via access to confidential data and advice from the Complainant's laboratory, have reproduced the Complainant's observations and published them in the article.

According to the Complainant, he sent a draft of a major manuscript, which was being considered for publication by Nature, to Defendants 1-4 in September

2008. The Complainant asserts that in doing so, he presented to Defendants 1-4 data from his laboratory, which indicates that miRNAs (also known as "myo-mirs") are regulated by endurance training. At that point in time, according to the Complainant, no other studies had been published of human muscle response in relation to these molecules.

The Complainant asserts that Defendants 1-4 submitted duplicate endurance-training miRNA data to the Journal of Physiology with the article.

5.3.1.2 Improper not to list the Complainant as co-author/plagiarism
The Complainant asserts that he was asked for help to edit the manuscript for the article and that the Complainant therefore assumed that he would be listed as a co-author of the article. The Complainant also states that he recommended a number of changes to the article at this juncture.

In addition, the Complainant asserts that on a general level, it was he who started the work that led to the article and that it was the Complainant's laboratory that first identified "myomirs" as a new research area.

Furthermore, the Complainant asserts that he mentored Defendant 4. According to the Complainant, the fact that he is not listed as a co-author of the article constitutes plagiarism of his data.

5.3.1.3 Defendant 2 is wrongly listed as lead author
The Complainant asserts that Defendant 2 is falsely listed as the lead author of the article. The Complainant asserts that Defendant 2 neither started, was responsible for, nor wrote the article. In support of this claim, the Complainant refers to the section of the article under the heading "author contributions". According to the Complainant, this section shows that Defendant 2 had nothing to do with the experiments, the design or the conducting of the study.

5.3.1.4 Defendant 3 has wrongly been listed as author no. 2
The Complainant also questions the validity of listing Defendant 3 as author no. 2 of the article. According to the Complainant, her contribution does not merit second billing. According to the Complainant, Defendant 3 neither conducted the physiological studies, nor the miRNA measurements, nor did she write the article.

5.3.2 Defendants 1-4's responses and contentions
Defendants 1-4 contend that they are innocent of all charges of scientific misconduct.

5.3.2.1 No reproduction of the Complainant's observations
Defendants 1-4 contend that at no time did they use data in the article that was obtained from, analysed in or initiated by the Complainant's laboratory.

Defendants 1-4 also contend that the choice of the four miRNAs in the article was based on the article in Genome Medicine, of which Defendants 1 and 3 are co-authors.

Irrespective of when the Complainant showed his data to people from Defendant 1's laboratory, Defendants 1-4 contend that on the basis of the literature available at the time when the miRNA measurements concerned started to be taken, it cannot be considered a major intellectual leap in the dark to assume that muscle-specific miRNAs possibly play a role in adaptation to training.

In addition, according to Defendants 1-4, the Complainant had himself, in a conversation with Defendant 4, given his consent to Defendants 1-4 submitting the article.

Furthermore, Defendants 1-4 contend that when they became aware that the Complainant's group was working on a similar project, they asked the Complainant to read the manuscript to ensure that there was as little overlap in the data as possible. According to Defendants 1-4, after reading the manuscript the Complainant concluded that the data overlap was minimal and that Defendants 1-4 should submit the manuscript.

Defendants 1-4 contend that data and training in the two studies (the one by the Complainant and the one by Defendants 1-4) were different. In support of this contention, Defendants 1-4 state that while they observed a deregulation of four different miRNAs (miR-133a, miR-133b, miR-206, miR-1) after endurance training, the Complainant only observed a difference in two of the miRNAs (miRNA-133a and miR-1).

According to Defendants 1-4, the Complainant's training protocols are very different from Defendants 1-4's training protocols. According to Defendants 1-4, their study involved high-intensity intervals, whereas the Complainant's study involved lower intensity, lower frequency and shorter time periods.

In addition, Defendants 1-4 contend that they conducted analyses during acute exercise, as well as insulin *clamps*, and that they measured miRNAs two weeks after training stopped, which necessitated inclusion immediately after endurance training. According to Defendants 1-4, in his study the Complainant measured mRNA levels in high-and low-responding individuals during physical activity. In this light, Defendants 1-4 are convinced that the Complainant's manuscript was very different from Defendants 1-4's article.

5.3.2.2 Not improper to omit the Complainant from the list of co-authors

In support of their contention that there was no need to list the Complainant as a co-author, Defendants 1-4 contend that at no point during the writing process did the Complainant express any concerns about plagiarism, nor did he ask to be listed as an author. Defendants 1-4 adjudged that the Complainant had spent minimal time reading the manuscript, and as a result the Complainant's contribution was listed under *Acknowledgements.*

Further, Defendants 1-4 also contend that the Complainant was not involved in the studies conducted, nor was the Complainant a key factor in determining which studies were selected to perform tests in.

5.3.2.3 Listing Defendant 2 as lead author was proper

In support of their contention that listing Defendant 2 as lead author was proper, Defendants 1-4 contend that the Complainant did not have first-hand knowledge of the extent to which Defendant 2 contributed to the study discussed in the article, nor of how much time Defendant 2 spent working on the manuscript in all of its forms.

Defendants 1-4 also contend that Defendant 2, in the role of Defendant 4's supervisor, oversaw all data processing, including the collation of raw data.

In addition, Defendants 1-4 state that Defendant 2 was involved in the statistical tests and the intensive discussions concerning the interpretation of the data. According to Defendants 1-4, it was at the behest of Defendant 2 that measurements were initiated before and after insulin *clamps* and after a two-week break from training.

According to Defendants 1-4, Defendant 2's contribution is listed in the "contributions section" as limited to manuscript preparation and editing because they were convinced that the concept and design described in the *contributions section* referred exclusively to the original experiment, which was conducted with different purposes in mind than just to analyse miRNAs.

Defendants 1-4 also contend that it was Defendant 2 who discovered the value of the design in relation to taking measurements two weeks after the training and that Defendant 2 was responsible for the choice of the target proteins to be analysed as part of the response to the reviewers. Defendants 1-4 also state that Defendants 2 and 4 spent many hours writing and editing the article.

5.3.2.4 Listing Defendant 3 as an author was proper

Finally, Defendants 1-4 also contend that Defendant 3, in addition to preparation and editing of the manuscript, was also involved in the analysis of the Western blot and miRNA data. In particular, Defendant 3 contributed expertise concerning *non-coding RNA regulation in human skeletal muscle*, which was the main focus of Defendant 3's PhD work and mainly concerning technical issues related to the qPCR-miRNA analysis of skeletal muscle tissue.

5.4 Article 2 in the Journal of Physiology

5.4.1 The Complainant's claims and contentions

The Complainant alleges that Defendant 1 acted in a scientifically dishonest manner in a number of ways when drawing up and reporting on research results in the article in Journal of Physiology (see Note 4).

The Complainant asserts that the raw data from the study, which was conducted at CIM, in connection with the article (to which the Complainant had access via Defendant 4), shows that IL-8 occurs at about 38-40 cycles when performing qPCR.

The Complainant asserts that the authors present this data as normalised to 1, so it is impossible to know that the real levels were extraordinarily low, unless – like the Complainant – you have seen the raw data at CIM.

The Complainant alleges that another researcher demonstrates a striking protein induction at six hours, and that she, according to the Complainant, visualises this with an image of an immunoblot (Figure 2d)[11] that looks so unusual and artificial that it is unlikely that three researchers at CIM and Defendant 1 would not have found this immunoblot suspect.

5.4.2 Defendants 1's responses and contentions

Defendant 1 contends that she is innocent of all charges of scientific misconduct.

In relation to the Complainant's claims concerning raw data in the article, Defendants 1 contends that the raw data to which the Complainant refers is confidential and has never been published.

Defendant 1 also contends that the raw data relates to IL-18 (i.e. another cytokine) but that because of a typo, the name of the file containing the data is IL-8 instead of IL-18.

Defendant 1 also contends that it is common practice to normalise to 1, as was done in the article, which is about IL-8.

According to Defendant 1, the data set to which the Complainant had improper access, and which has never been published, was analysed one year after publication of the article on IL-8, and in reality represents an IL-18 measurement.

5.5 The UNIK application

5.5.1 The Complainant's claims and contentions

The Complainant alleges that a series of actions by Defendant 1 when reporting on the research results as part of the application process for funding from the UNIK pool (see Note 5) could be characterised as scientifically dishonest.

5.5.1.1 Plagiarism of the article in Genome Medicine in the UNIK application

The Complainant alleges that Defendant 1 plagiarised an article on miRNA written by the Complainant in the journal Genome Medicine when the Defendant was applying to UNIK for funding (see Note 6).

According to the Complainant, Defendant 1 used the Complainant's article in the UNIK application, in which – according to the Complainant – Defendant 1 stated that all of the work on miRNAs was done at CIM. The Complainant also states that neither the complainant nor his laboratory was mentioned in the UNIK application.

The Complainant adds that the UNIK application paints a picture suggesting that all of the miRNA work was conducted at CIM, which the Complainant claims is untrue since – according to the Complainant – this work was done in the Com-

[11] The Committee bases its decision on the fact that figure 2d illustrates immunohistochemical staining of a tissue section and not, as stated by the Complainant, an immunoblot.

plainant's laboratory in Scotland. In addition, the Complainant asserts that the UNIK application mentions "miRNA changes in relation to exercise", which refers to the data from the Complainant's laboratory, which he sent to staff at CIM in September 2008.

Furthermore, the Complainant asserts that large parts of the UNIK application consist of a "cut and paste" job from the article in Genome Medicine written by the Complainant. According to the Complainant, Defendant 1 did not write any of the article in Genome Medicine.

5.5.2 Defendant 1's responses and contentions

Defendant 1 contends that she is innocent of all charges of scientific misconduct.

5.5.2.1 No plagiarism of the article in Genome Medicine in the UNIK application

In support of her contention, Defendant 1 contends that this was an internal application to the UNIK pool rather than a competing application, and that she sent an e-mail to the Complainant with the UNIK application attached. According to Defendant 1, the Complainant did not respond at the time, and she finds it strange that the Complainant now accuses her of plagiarism.

In addition, Defendant 1 claims that in the background section to the UNIK application she incorporated a few lines from the article in Genome Medicine, of which Defendant 3 was joint lead author, a number of individuals from CIM were co-authors, Defendant 1 was the second last author and the Complainant was the last author.

According to Defendant 1 she stated the following in the UNIK application: *"Researchers within CIM have demonstrated robust changes in miRNA in muscle biopsies from patients with insulin resistance when compared to carefully matched controls"*.

Defendant 1 thus contends that all clinical trials and clinical characterisation of diabetics and controllers covered by the article in Genome Medicine were conducted in her laboratory.

Furthermore, Defendant 1 also contends that a large part of the molecular work was carried out by Defendant 3 at CIM and that the miRNA analyses were conducted by the Complainant, who was affiliated to CIM when the study was initiated.

5.6 Other factors

5.6.1 The Complainant's claims and contentions

The Complainant also highlights a number of other areas, particularly regarding Defendant 1, in which the Complainant considers aspects of behaviour unacceptable.

5.6.1.1 Improper and incompetent supervision of PhD students at CIM

The Complainant alleges that Defendant 1's supervision of PhD students at CIM was improper and incompetent.

5.6.1.2 Unauthorised disclosure of the miRNA work at an international congress

The Complainant asserts that Defendant 1 presented miRNA data from the article in Genome Medicine on an inappropriate basis, as if it originated from CIM. Defendant 1 is thus alleged to have encouraged Defendant 3 to give a "keynote" lecture at an international conference in Miami, USA; in 2010. According to the Complainant this was tantamount to an abuse of power by Defendant 1.

5.6.1.3 False CVs as a result of irregular mass publishing among students at CIM

The Complainant alleges irregular 'mass publishing' at CIM at the behest of Defendant 1, thus, according to the Complainant, producing false CVs for her students.

In this context, the Complainant asserts that he personally was forced to grant authorship to a student at CIM, even though the student had not contributed to the analysis, interpretation or writing process, but had simply conducted a muscle biopsy/blood test.

The Complainant alleges a "salami-slicing" of studies in 38 instances where authorship was accredited to researchers at CIM in collaboration with Defendant 1, and in 37 articles by two other researchers at CIM.

The Complainant asserts that all of the work with myokines at CIM from 2000-2011 should be investigated because – according to the Complainant – it would not have received substantial attention without the extremely important muscle-protein immunoblot data set from 12 articles by another researcher.

5.6.1.4 Improperly accrediting authorship to students affiliated with CIM

The Complainant also asserts that a student affiliated with CIM was improperly accredited with co-authorship of a series of unnamed articles, despite the fact that the individual concerned provided no intellectual input into the article and only took biopsies or blood samples.

5.6.1.5 Changed perception of IL-6's role in human skeletal musculature

The Complainant asserts that it is suspicious that Defendant 1 apparently changed her perception of interleukin-6's (IL-6) role in human skeletal muscle over a number of years. According to the Complainant, in an article in 1998[12] Defendant 1 wrote that IL-6 is undetectable prior to training and only occurs in five out of eight samples after two hours of exhausting workouts.

[12] Ostrowski K, Rohde T, Zacho M, Asp S, Pedersen BK, 'Evidence that interleukin-6 is produced in human skeletal muscle during prolonged running', J Physiol, 508.3, 1998, p. 949-953

According to the Complainant, Defendant 1 contradicts this view in an article[13] 10 years later, proclaiming that IL-6 is an extremely important factor in human skeletal muscle and exercise metabolism.

The Complainant asserts that Defendant 1's contention that the new measurement technique for RNA (qPCR) can lead to different results in relation to expression (see below under Defendant 1's responses and contentions) is not valid. The Complainant asserts that the sensitivity of the measurement (detection sensitivity) is irrelevant to the question of physiological relevance. The Complainant also states that if a gene is barely detectable, it means that the gene exists only in a minority of cells from the biopsy, no matter what 'numbers' you register.

5.6.1.6 Inconsistency between mRNA measurements and systematic misinterpretation

The Complainant also asserts that mRNA measurements made by two researchers at CIM from 2001-2005 were incompatible with protein data produced by another researcher. Further, the Complainant asserts that the alleged inconsistency in mRNA measurements was systematically misinterpreted by three researchers affiliated with CIM during the years 2001-2007, such that the lack of any correlation between mRNA and the other researcher's protein data was not apparent to the reviewers.

5.6.1.7 Defendant's relation to the editor of Diabetologia

The Complainant also criticises Defendant 1's relationship with an editor of Diabetologia.

5.6.1.8 One of Defendant 1's research collaborators conducted the peer review of Article 1 in the Journal of Physiology

The Complainant alleges that one of Defendant 1's research collaborators conducted the peer review of Article 1 in Journal of Physiology (see Note 3).

5.6.1.9 Defendant 1 misled DCSD during the consultation process

The Complainant also alleges that Defendant 1 is misleading the DCSD by claiming that the statement by the FASEB reviewer about the literature suggests that it is widely accepted that skeletal muscle that contracts expresses BDNF (see below under Defendant 1's responses and contentions). According to the Complainant, some of the articles mentioned by the reviewer do not mention skeletal muscle at all.

5.6.2 Defendant 1's responses and contentions

Defendant 1 contends that she is innocent of all charges of unacceptable behaviour.

5.6.2.1 Supervision of PhD students at CIM is proper

Defendant 1 contends that the Complainant's allegation that Defendant 1's supervision of PhD students at CIM was improper and incompetent is incorrect. In this

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[13] Pedersen BK, Febbraio MA, 'Muscle as an endocrine organ: focus on muscle-derived interleukin-6', Physiol Rev., 88 (4), 2008, p. 1379-1406

context, Defendant 1 refers to the CIM laboratory manuals and instructions for the supervision of PhD students.

Furthermore, Defendant 1 contends that PhD students at the CIM laboratory are deeply involved in the scientific writing process. According to Defendants 1-4, CIM puts considerable effort into the supervision of PhD students and teaching students how to write scientific articles.

5.6.2.2 Unauthorised disclosure of the miRNA work at an international congress

Defendant 1 contends that she suggested that Defendant 3 should give a key-note lecture at the international congress in Miami in 2010, as Defendant 1 had been asked to give another speech at the congress and considered it inappropriate to make two speeches at the same conference. According to Defendant 1, the Complainant was present at the congress in Miami, and Defendant 3 credited him as lead author for the study in her key note. According to Defendant 1, it was also made clear to the audience that the Complainant had played a leading role in the study.

Defendant 3 also states that the Complainant personally asked her to present the article in Genome Medicine in Miami because the Complainant thought it would be a good opportunity to promote this article to a wide audience.

5.6.2.3 No mass publishing

Defendant 1 refutes the assertion of *salami-slicing* of studies at CIM in the incidences mentioned by the Complainant. According to Defendant 1, the three researchers at CIM conducted a large number of experiments in Defendant 1's laboratory.

Defendant 1 contends that muscle and fat samples from an experiment have been used in various publications with different scientific objectives. The Defendant also contends that this is common practice when you have conducted a large, complex and intrusive human study, and that Defendant 1 does not consider this *salami slicing* because different scientific questions were studied, including different hypotheses, and because different molecular analyses were also used.

Defendant 1 guarantees that the student affiliated to CIM made a substantial contribution to the publications for which he is listed as an author and deserves all the credit he has earned as an author.

5.6.2.4 The changes to results concerning. IL-6's role in human skeletal muscle are due to scientific developments in measurement technology

As regards the Complainant's assertion that Defendant 1 has changed her perception of IL-6's role in human skeletal muscle over a 10-year period, Defendant 1 states that during the period in question a new technique emerged for measuring mRNA. According to Defendant 1, this technique makes it is possible to measure cytokine levels before training.

5.6.2.5 No inconsistency between mRNA measurements and no systematic misinterpretation

Defendant 1 contends that the Complainant's claim of lack of any correlation between the mRNA measurements conducted at CIM and another researcher's protein data are false and highly speculative.

Defendant 1 contends that she had no reason to be suspicious of the other researcher's data before the case was covered by the media. In addition, Defendant 1 states that in April 2011 she became aware of possible manipulation with immunoblots[14] in four of the 12 articles of which the other researcher was a co-author. Defendant 1 immediately reported these four articles to DCSD and contacted the respective journals.

5.6.2.6 No knowledge of who performed the peer review of the article

Defendant 1 contends that at no point in time has she known who performed the peer review of article 1 in the Journal of Physiology (see Note 3).

6 Rules and regulations

This case has been processed under the Danish act on research advisory system, etc., cf. consolidated act no. 1064 of 6 September 2010 and the related executive order no. 306 of 20 April 2009 on the Committees on Scientific Dishonesty, as amended by executive order no. 144 of 20 February 2012 (the DCSD order).

Scientific misconduct is defined in section 2, no. 3 of the act and in section 2 of the DCSD order:

"Section 2. Scientific dishonesty shall mean: Falsification, fabrication, plagiarism and other serious violation of good scientific practice committed wilfully or grossly negligent on planning, performance or reporting of research results. Included hereunder are:
1) Undisclosed fabrication and construction of data or substitution with fictitious data.
2) Undisclosed selective or surreptitious discarding of a person s own undesired results.
3) Undisclosed unusual and misleading use of statistical methods.
4) Undisclosed biased or distorted interpretation of a person s own results and conclusions.
5) Plagiarisation of other persons results or publications.
6) A false credit given to the author or authors, misrepresentation of title or workplace.
7) Submission of incorrect information about scientific qualifications^."

DCSD's remit is described in the DCSD order sections 3 and 6:

[14] The Committee bases its decision on the fact that this refers to micro photos of an immunohistochemical stained tissue section and not, as stated by Defendant 1, an immunoblot.

"Section 3. The Committees shall not be entitled to consider cases involving the validity or truth ofscientific theories or cases involving the research quality of a scientific product.

"Section 6. The Committees on Scientific Dishonesty may consider cases involving complaints about a written scientific product after the defendant s voluntary handing over thereof, cf. section 1(4).
(2) The Committees may also consider cases involving complaints about an application filed with a view to applying for a grant from public research funds.

7 The DCSD ruling

7.1 Basis and subject matter for the case

DCSD has based its ruling on the documents
cited above under item 4 – Proceedings.

The following articles and an application for funding from a UNIK pool (the UNIK application) play a particularly key role in the parties' claims, responses and contentions:

- Article in Diabetologia (concerns Defendant 1)
- Article in Experimental Psychology (concerns Defendant 1)
- Article 1 in the Journal of Physiology (concerns Defendants 1-4)
- Article 2 in the Journal of Physiology (concerns Defendants 1-4)
- UNIK application (concerns Defendant 1)

The DCSD has also reviewed the article in Genome Medicine, which is related to the above articles and the UNIK application in a number of ways. The article in Genome Medicine stipulates that the manuscript was submitted on 13 September 2009, a revised version was submitted on 27 October 2009 and the manuscript was approved and published on 1 February 2010. The case documents also show that prior to submission to Genome Medicine, an attempt had been made to have the article published in the Journal of Clinical Investigation (JCI).

In sections 7.2-7.5 below, the DCSD rules on the extent to which Defendants 1-4 acted in a scientifically dishonest manner while drawing up and reporting on their research results in the four articles in Diabetologia, Experimental Physiology and Journal of Physiology.

In section 7.6, the DCSD rules on whether the funding application to the UNIK pool constitutes scientific misconduct.

Finally, in section 7.7 "Other matters", the DCSD rules on the Complainant's other claims and contentions about matters not related to the above four articles or UNIK application.

7.2 Article in Diabetologia

This section accounts for the DCSD's assessment of the parties' claims, responses and contentions concerning the article in Diabetologia.

The article stipulates that the manuscript was submitted to the journal on 17 December 2008, resubmitted on 25 February 2009, accepted 16 March 2009 and published online on 22 April 2009. An erratum to the article was published online on 10 January 2012.

7.2.1 Warning about unsound data

The Committee notes a discrepancy between the Complainant and Defendant 1 about the Ct values found in the qPCR analyses, which were performed on muscle tissue in order to obtain a measurement for the expression of BDNF-mRNA. The Committee notes that the Complainant did not find BDNF-mRNA in muscle tissue from a given group of test subjects, while Defendant 1 describes the presence of BDNF-mRNA in the article in the group of test subjects selected by Defendant 1. The Committee notes that there are differences in the results obtained in the Complainant's and Defendant 1's laboratories, and that this is a matter of scientific methods and quality, and falls outside the remit of the Committee, cf. section 3 of the DCSD order.

The Committee finds that there is a discrepancy between the Complainant and Defendant 1 about the choice of primers, and whether or not primers detect splice variants. The Committee notes that a range of primers were used, which ought to detect the maximum number of BDNF variants. In this specific instance, the Committee considers that this discrepancy is a matter of scientific methods and quality, and falls outside the remit of the Committee, cf. section 3 of the DCSD order, because it refers to concerns selecting methods, their applicability and limitations.

The Committee finds that there is a discrepancy between the Complainant and Defendant 1 about the stability of mRNA. It is correct that the different mRNA transcripts have varying stability, depending on the sequence, in particular in the three prime non-translated region (3'UTR). However, it is also correct that cDNA has a limited shelf life, so long-term storage and/or repeated thawing/freezing can destroy the sample material. In this specific case, the Committee finds that this is a matter of scientific quality and the validity of scientific theories, and falls outside the remit of the Committee, cf. section 3 of the DCSD order.

7.2.2 Presentation of relative data normalised to 1

In relation to the Complainant's claim that the article presented 'relative' data normalised to 1, and that this conceals the true incidence of BDNF-mRNA, Defendant 1 refers to her general comments on standard practice concerning the presentation of mRNA expressions.

The Committee finds that when an article presents relative values, it is desirable that the original data and variation are also presented in order to provide the reader with the opportunity to assess the actual biological variation. The Committee is of the opinion that citing the original data and variations helps avoid any obscuration of the actual data.

The Committee finds that Defendant 1 did not account for the calculation of the mRNA data presented in the article in the methodology section. The Committee notes that the article cites reference # 34 (Chan et al 2004), an article that also omits a description of its calculations, and one other reference.

The Committee also notes that Figure 1a presents the variation of data in all of the observations ('0 ', 2, 3, 5, 8, 24, 48 and 72 h).

The Committee finds that due to the lack of a description of how the data underlying the Figures 1a was arrived at, readers are unable fully to assess the validity of the data presented.

The Committee therefore finds that although the approach used in the article is not consistent with good scientific practice, it cannot be characterised as a serious breach of good scientific practice and thus as an example of scientific misconduct because, in the opinion of the Committee, the failure to specify the calculations of mRNA data is more a matter of the research quality in the scientific product concerned.

7.2.3 Use of non-conventional and non-valid statistical methods

The Committee is of the opinion that the criticisms raised about the statistical methodology arose because the original article contains an incomplete description of the test subjects.

The Committee notes that the original wording of the methodology section was as follows:

"*Human in vivo experiments Eight healthy, physically active but untrained men (mean±SD age: 25±4 years, weight: 82± 8 kg, height: 181±1 cm, BMI: 25±2 kg/m^2) were recruited to participate in the study, which was approved by the Ethics Committee of the University of Copenhagen. On the day of the experiment, the volunteers arrived at about 07:00 hours after an overnight fast. The participants performed 120 min of bicycle exercise at 60% of their predetermined VO_{2max} followed by a 24 h recovery period. Muscle biopsy samples were obtained from vastus lateralis before exercise, immediately after exercise, and 3, 5, 8, 24, 48 and 72 h into recovery using a percutaneous needle biopsy technique with suction. Samples were snap frozen before being analysed for BDNF mRNA and protein expression. Serum was obtained at the above mentioned time-points. Serum levels of BDNF were measured by ELISA (R&D Systems, Wiesbaden-Nordenstadt, Germany). Platelet counts were determined by standard laboratory procedures.*"

The Committee further notes that on 10 January 2012, an erratum was published pertaining to the article's methodology section, from which the following extract is taken:

"*The first paragraph of the Methods should have read as follows (new material shown in [bold]):*

Human in vivo experiments ***Twenty healthy, physically active but untrained men (age 25.6±3.5 years, weight 78.9±9 kg, height 185±6.5 cm, BMI 21.3±2.11 kg/m^2 [mean±SD]) were randomised to either an exercise (n = 10) or control (n= 10) group. There was no difference between the two groups with regard to age, weight, height or $V0_{2max}$. Subjects either performed 120 min of bicycle exercise at 60% $V0_{2max}$ followed by a 6 h recovery period (exercise) or rested in bed for 8 h (control). Subjects also reported to the laboratory after an overnight***

fast at 24, 48 and 72 h after the commencement of the experimental trial. Blood was obtained at the following time points: O, 2, 3, 5 8, 24, 48 and 72 h. *Muscle biopsy samples were obtained from vastus lateralis at time points O, 2, 3, 5, 8, 24, 48 and 72 h using a percutaneous needle biopsy technique with suction. 0Samples were snap-frozen before being analysed. Serum levels were measured by ELISA (R&D Systems, Wiesbaden-Nordenstadt, Germany). Platelet counts were determined by standard laboratory procedures.* ***Data from this study are included in Figs 1 a,b,d and 2a,b. Because of a lack of material, we included another*** *eight healthy men (age 25±4 years, weight 82±8 kg, height 181±1 cm, BMI 25±2 kg/m2 [mean±SD]).* ***They had muscle biopsies taken immediately pre and post exercise and at 3 and 24 h after exercise. The data from these subjects are used only in Fig. 1c.*** *[...]"*

The Committee notes that a full description of the test subjects has been added to the methodology section in the erratum. It has now been made clear that the control group and the active group consist of different people and it is therefore correct to use an un-paired analysis instead of a paired one.

In the case at hand, the Committee is of the opinion that the time sequence and the pattern are the same for the whole group. With this in mind, the Committee considers the use of an AUC calculation to be acceptable.

It is correct that the assumptions on which the AUC is calculated are not specified, and thus the reader of the article is not aware of the mean value and spread for AUC for the two groups.

The Committee is of the view that it would have been preferable to have specified the assumptions for the AUC calculations. However, it does not consider that this omission constitutes a serious breach of good scientific practice because it is not critical to the reader's assessment of the article's content and findings.

The Committee notes that the choice of statistical method was wrong in relation to the original description in the article of the test subjects, as this was inadequate.

In addition, the Committee finds that the information in the article concerning the number of persons/control population (n-values) is unclear. The original methodology section indicates n = 8. Figure 1 also stipulates n = 8, but the Committee does not think it is entirely clear whether there are four people in each group (2 x 4 = 8) or eight people in each group. No control group is specified in the original methodology, and it appears therefore as if all eight test subjects were involved in the cycling experiment. Figure 2 specifies n = 10, but the Committee finds that it is not clear whether this means ten people (2 x 5 = 10) or 20 people (2 x 10 = 20).

In this light, the Committee finds that the original methodology section does not make it clear that the article is referring to two test groups nor how many test subjects there are/how big the control population is in the groups. In other words, the Committee does not think that it is entirely clear from the article that two different groups were involved. The Committee notes in this context that it would have been natural to mention this in, for example, the results section, where fig-

ures 1b and 1c are contained in the same parenthesis, or in the legend for Figure 1, as well as in the methodology section

The Committee therefore finds it impossible to assess the relevance of the effect shown in figures 1b and 1c because the original article does not mention that the two figures contain data pertaining to different test subjects, and that these subjects participated in the experiment at different times. It was not until the erratum was published that it became clear that two different groups were referred to in these two figures.

The Committee also finds that in the erratum to the test methodology some sentences from the original methodology description have been moved around, such that the erratum inserts new text at various parts of the original text in the methodology description.

Defendant 1 contends that due to space limitations the authors mistakenly omitted the description of one group in the original methodology description.

In the eyes of the Committee, the fact that the authors felt compelled to edit the text in the methodology section so heavily implies that it was not just a minor oversight that led to a section being omitted from the original methodology description by mistake.

One of the most important requirements on scientific work of the type concerned is transparency in the choice of methodology and the description of the methodology, because this facilitates reproduction and relevant interpretations of the results presented as well as assessments of their credibility.

The Committee finds that the omission of significant information about the test subjects from the original methodology description constitutes a serious breach of good scientific practice. As described above, the inadequate description of the subjects in the methodology section has consequences for the interpretation of results contained in the article.

The Committee does not find that the erratum containing a revised description of the methodology justifies any change to its findings, as the complaint was about the article in its original form and the erratum was published after the complaint had been submitted.

The Committee notes that Defendant 1 is credited as co-director of the study on which the article is based, and that Defendant 1 is also 'corresponding author' of the article along with the last author. In addition, Defendant 1 was head of CIM, where parts of the research on which the article is based, was conducted.

In this light, the Committee finds that Defendant 1 must be regarded as one of the leading senior authors of the article.

The Committee is of the opinion that a leading senior author of a scientific article has overall responsibility for all of the article's content, including reading the final manuscript carefully before submitting it to a journal. Senior authors' overall

responsibility is part of good scientific practice and is stipulated, for example, in DCSD's own guidelines for good scientific practice.[15]

In the light of the above, the Committee finds that Defendant 1 had a particular responsibility for the overall content of the article due to her role as a leading senior author of the article.

The Committee finds that the inadequate description constitutes an act of gross negligence by Defendant 1, as a close reading of the article by Defendant 1 would have brought the inadequacies in the methodology description to light provided sufficient care was taken.

In this light, the Committee finds that Defendant 1 did act in a scientifically dishonest manner by signing off an article with such glaring deficiencies in the methodology description that they have consequences for the interpretation of the results in the article, and that this corresponds to 'undisclosed construction of data' as per Section 2, no. 1 of the DCSD order.

7.2.4 Publication despite the lack of biological relevance of the results or non-valid findings

The Complainant gives the impression that the amount of mRNA per cell is a direct measure of the amount of protein produced subsequently, and thus that the functional significance of the observed increase of the expression of mRNA (without simultaneous protein expression) after physical activity is not biologically relevant.

A number of other factors are important, e.g. mRNA stability.

The duration of the experimental design also affects whether you can expect to detect mRNA expression and protein simultaneously or separately. It is thus a well-known phenomenon in scientific articles that a correlation between mRNA- and protein expressions cannot readily be shown, if specimens are only collected at an early stage, where only an mRNA expression can be expected, or at a later date, where only protein is present.

The Committee therefore finds that the increase in mRNA expression may well have biological relevance.

The Committee finds that the alleged lack of biological relevance of results, or non-valid findings, is a question of the scientific theories' validity and the quality of the research, and falls outside the remit of the Committee, cf. section 3 of the DCSD order.

[15] http://fivu.dk/en/publications/2009/files-2009/guidelines-for-good-scientific-practice.pdf, p. 33.

7.2.5 Ignoring data from the research collaboration with the Complainant, including about the article in Genome Medicine

The Complainant alleges that there is a contradiction between the data from the Complainant's laboratory (published in Genome Medicine) and data in the article in Diabetologia.

Defendant 1 accounts for the differences in the data used in the article in Genome Medicine and the article in Diabetologia. The immediate explanation for the divergence of the data in the two articles is that there are different test subjects and two different age groups.

In the light of the evidence presented in the case, the Committee finds that it has been documented that the article in Diabetologia (with the positive findings) was submitted, accepted and published in a period from December 2008 until April 2009, during which time the draft for the article that ended up being published in Genome Medicine was revised with a view to resubmission to the Journal of Clinical Investigation (JCI).

Defendant 3 conducted three analyses of BDNF in diabetics and the control population (older people) for the article in Genome Medicine as a result of the discussions held after Defendant 1 sent the revised article intended for Diabetologia to the Complainant on 19 February 2009. In the e-mail correspondence, the Complainant mentioned some of the findings that are reported in Genome Medicine, and presented the results of BDNF measurements he had taken of 24 people who were not described in any detail. In this light, Defendant 1 offered that Defendant 3 could perform the analyses of BDNF in the diabetics and control population (older persons) on whom the Complainant had based his Genome Medicine article and who had been studied in Defendant 1's laboratory.

The Committee notes that it is good scientific practice to refer to articles or own unpublished findings that do not support the findings you are seeking to have published.

In addition, the Committee notes, however, that when the article was submitted, BDNF data for the above-mentioned cohorts was not available from Defendant 1's laboratory. In addition, the BDNF data cited by the Complainant in his e-mail of 20 February 2009 is mentioned in very vague terms.

In the light of the above, the Committee finds that Defendant 1 did not act in a scientifically dishonest manner by not referring to the data to which the Complainant refers. The Committee finds that the lack of reference to this data in this specific case does not constitute a breach of good scientific practice because at the time of the submission of the article to Diabetologia it was unpublished data that had not been adequately described and the data referred to a different group of subjects than those covered by the article in Diabetologia.

The Complainant also claims that Defendant 1 ignores two decades of literature reporting that BDNF is involved in neuromuscular regeneration.

The Committee notes that the choice of references should always reflect the state of knowledge in the research field, whether that is contradictory or identical to

the results to be discussed in the article concerned. It is an author's right to prioritise the choice of references with regard to species, model and methodology, but this should never lead to a deliberate omission of significant conflicting references. The Committee notes in this connection that the number of references can also be affected by restrictions on the scope of the article, as set by the journal concerned.

The topic of the article in Diabetologia is muscle activity. The Committee therefore conducted a PubMed search of the literature from 1989-2009 with the following keywords: "BDNF exercise muscles". It identified 11 articles, including the three articles that Defendant 1 – according to the Complainant – has misquoted, cf. the section below 7.2.8.

In this light, the Committee finds that Defendant 1's choice of references does not constitute a breach of good scientific practice, but rather an expression of the author's right to prioritise references.

7.2.6 Immunoblot with changed/manipulated contrast/image preferences

The Committee finds that the biopsies for Western blot in the article were conducted in a different series of experiments with a different design than the experiment that generated the material for the mRNA analyses, and it is not clear whether all of the biopsies from test subjects in the supplementary experiments were analysed for BDNF protein.

The Committee notes that it is correct that the background around each band rises across the immunoblot. As this may be a case of a knock-on effect from the rising signal, and as the immunoblot has been plucked out of a wider context, the Committee finds that the actual background is difficult to assess. On this basis, the Committee finds that there is no basis for considering the immunoblot to be a falsification.

The Committee finds that the question of inadequacies during the performance of the BDNF immunoblot concerned is a question of the quality of the scientific work, and falls outside the remit of the Committee, cf. section 3 of the DCSD order.

7.2.7 Significant Western blot

The Complainant alleges that results from an important Western blot in the article were manipulated and that he was told this by a former postdoc at CIM.

Both the former postdoctoral student and another researcher affiliated with CIM, who performed the immunoblot, contend that this is not the case. Furthermore, they explain that a mark on the blot suggesting that it was significant was placed there by mistake and was removed once the mistake was discovered, which happened before the article was submitted.

The Committee finds that this is not an example of scientifically dishonest behaviour, but rather a mistake during the preparatory work for the article. The Committee finds no basis to reject Defendant 1's explanation in the light of the statements from the individuals mentioned above.

The Complainant alleges that the finding of BDNF protein is incompatible with the lack of BDNF-mRNA expression in muscle tissue.

The Committee finds that the Complainant is in part referring to his own observations on muscle tissue, in which the Complainant did not observe expressions of BDNF-mRNA, while the Defendant – unlike the Complainant – observes BDNF-mRNA expression in all of the groups of tests subjects studied.

It is the opinion of the Committee that the Complainant's assertion is a matter of scientific methods and quality, and falls outside the remit of the Committee, cf. section 3 of the DCSD order.

7.2.8 Misquotations of three articles

The Committee has reviewed the three articles that the Complainant alleges were misquoted. According to the Complainant, Defendant 1 misquoted

- Dupontversteegden et al. (see Note 7) and Gómez-Pinilla et al. (see note 8) by stating that BDNF-mRNA rises in the two articles, and
- Avila et al. (See note 9) by stating that BDNF increased with inhibitor of HDAC but failed to mention protein.

The Committee finds that Defendant 1 did not misquote the three articles as far as the increase in BDNF-mRNA and protein is concerned. The Committee finds that Defendant 1 used the references to substantiate her findings about a rise in BDNF-mRNA in muscle tissue. As such, the Committee finds that no breach of good scientific practice occurred in this context.

7.2.9 Incorrect presentation of clinical trials

This allegation relates to the presentation of the IHC results in Figure 1d. The Complainant asserts that a single sample was selected (highest mRNA content) to locate protein using IHC.

The Committee notes that the article does not make it clear whether all of the test subjects' biopsies were analysed using IHC. In her responses to the consultation process, Defendant 1 notes that several biopsies were stained. She also notes that a decision was taken only to show the IHC image of the biopsy from the person with the highest mRNA expression in muscle tissue, who also had a high protein level.

The Committee affirms that scientific journals have restrictions on the number of images that can be published in an article, and it is therefore usual that the authors of an article select one or a very few images that they consider representative of their findings. In this light, the Committee finds that the above does not constitute a breach of good scientific practice.

7.2.10 Improper accreditation of co-author

The Complainant alleges that Co-author 2 is improperly credited as a co-author of an article for which it was not Co-author 2 but Co-author 3 and a student who supplied an immunoblot. The Committee notes that according to the information it has received Co-author 2 conducted pilot experiments to establish the method and supervised the technique.

The Committee finds that the co-author was not improperly accredited as the co-author's contribution was sufficient to warrant billing as a co-author.

7.3 Article in Experimental Physiology

The article in the journal Experimental Physiology (see Note 2) is a review article *(Hot Topic Review)* that refers to the original articles and gives interested readers the opportunity to find further original data.

The article focuses on BDNF protein and describes how the protein can be triggered by physical exertion, and that this is important for the regulation of human energy homeostasis.

The article concludes that BDNF is a protein that is produced in skeletal muscle, and that it increases lipid oxidation, probably by means of an autocrine/paracrine mechanism in the skeletal muscle. BDNF is thus characterised as a new contraction-induced protein with beneficial health effects in conjunction with physical exertion – possibly through an increase in fat oxidation in skeletal muscle.

The authors believe that BDNF plays a neurobiological role as well as roles in both the central and peripheral metabolism. The text for Figure 5 in the article describes that BDNF-mRNA and protein expression are markedly increased in skeletal muscle after exertion, and this is repeated in the main body of the text under the heading *Brain-derived neurotrophic factor and the role of exercise* on the penultimate line (p.1158), which refers to the article in Diabetologia.

After a close reading of the article in Diabetologia, the Committee notes that Figure 1 shows that there is an approx. 50% increase in BDNF in conjunction with physical exertion *versus* rest – and that it is a question of interpretation whether such an increase can be termed *marked*. The Committee finds that this interpretation does not constitute a breach of good scientific practice as the data in the article supports the conclusion.

The Committee finds that the review article does not break with the norm for generally acceptable scientific presentations. The contention that the conclusion in the article deviates from the general literature is a matter of the validity of scientific theories and scientific quality, and falls outside the remit of the Committee, cf. section 3 of the DCSD order.

7.4 Article 1 in the Journal of Physiology

This section accounts for the DCSD's assessment of the parties' claims, responses and contentions concerning the article in the Journal of Physiology (see Note 3).

7.4.1 Reproduction of the Complainant's observations

The Committee notes that the article in Genome Medicine is based on a cohort of diabetic patients (n = 71) and a control population (n = 47), whose miRNA (the so-called myomiRs) and several proteins, including BDNF, are studied.

The article specifies that the test subjects have an average age of over 50 and an average BMI of over 30. The article compares the findings from these groups. The discussion section of the article also refers to findings concerning BDNF-mRNA after endurance training by 24 test subjects. This data is not disclosed and

the methodology not described. In other words, the Complainant's contention that the test subjects are all young males is not specified in the published article.

In his complaint, the Complainant describes how this data stems from Defendant 1-4's laboratory, but in the e-mail correspondence of 22 February 2009 it is specified that the data stems from analyses conducted by the Complainant himself for a research collaborator called Claes.

The Committee also notes that the article in the Journal of Physiology is about the study of myomiRs before and after acute endurance training and insulin *clamps* in 10 young healthy men.

In the e-mail correspondence of 11 March 2010 between Defendant 4 and the Complainant, it is explicitly stated by the Complainant that there is no significant overlap between the two articles. The Complainant also states that since his own article is only approx. 80% complete, he thinks that Defendant 4 should go ahead and submit the article.

In this light, the DCSD finds that the data from the Complainant's laboratory is not reproduced in the article in the Journal of Physiology, as the article refers to a different group of test subjects and a different design.

7.4.2 The question of whether the Complainant should have been listed as co-author

Regarding the Complainant's assertion that he should have been credited as a co-author of the article, the Committee finds that in the correspondence between the Complainant and Defendants1-4, the Complainant does not express a wish to be listed as a co-author.

The Committee also finds that it is clear from the correspondence that the article from Journal of Physiology was sent to the Complainant in order to ascertain whether there was any overlap between this article and the similar article on which the Complainant was working at the time. The Committee does not consider that forwarding the article to the Complainant implies compliance with a request to be credited as a co-author of the article.

The Committee therefore finds that it was proper of Defendants 1-4 not to credit the Complainant as a co-author of the article in the Journal of Physiology. The Committee notes in this regard that the Complainant is thanked in the article's 'Acknowledgements' section for scientific discussions and advice, which in the view of the Committee is consistent with the contribution evident from the e-mail correspondence.

7.4.3 Improper crediting of Defendant 2 as an author

The Complainant asserts that Defendant 2 was not entitled to be credited as a senior author of this article.

The Committee finds that Defendants 1-4 have accounted in detail for Defendant 2's contribution to the article.

In assessing Defendant 2's contribution, the Committee finds no basis for rejecting Defendants 1-4's account, as Defendants 1-4 were the most closely involved parties in the study and in the preparation of the article, and must, therefore, be deemed to be the most appropriate judges of the individual authors' contributions. The Complainant's comments on Defendant 2's lack of input do not change this.

In the light of the evidence presented in the case, the Committee finds that it has been amply demonstrated that Defendant 2's contribution to the article entitles Defendant 2 to be credited as senior author.

7.4.4 Defendant 3's co-authorship

The Complainant asserts that Defendant 3 was not entitled to be credited as a co-author of the article.

The Committee finds that Defendants 1-4 have accounted in detail for Defendant 3's input to the article.

In assessing Defendant 3's contribution, the Committee finds no basis for rejecting Defendants 1-4's account, as Defendants 1-4 were the most closely involved parties in the study and in the preparation of the article, and must, therefore, be deemed to be the most appropriate judges of the individual authors' contributions. The Complainant's comments on Defendant 3's lack of input do not change this.

In the light of the evidence presented in the case, the Committee finds that it has been amply demonstrated that Defendant 3's contribution to the article entitles Defendant 3 to be credited as a co-author of the article.

7.5 Article 2 in the Journal of Physiology

The Complainant asserts that data is incorrectly presented in the article, including the fact the data is normalised to 1, which obscures the real values. In support of this, the Complainant states that he has seen the original data concerned.

The Committee finds that the Defendants have explained that the original data seen by the Complainant at CIM stemmed from the analysis of another cytokine (IL-18) and not the IL-8 data, which was included in Article 2

The Committee notes that Defendant 1 contends that it is standard practice to normalise data to 1.

The Committee finds that when an article presents relative values, it is desirable to specify the original data and any variations of it in order to be able to assess the actual biological variation and, in doing so, avoid obscuring the actual data.

The Committee finds that in the methodology section of the article, the authors have accounted in detail for the calculations of the mRNA data presented in Figure 1. The Committee also finds that Figure 1 does not specify variation for data to the time '0', but that the variation is set for data from the other observation times. The Committee also comments that the IL-8 expression is low at time '0'.

The Committee finds that despite the lack of variation for data at time '0', the reader is provided with a sufficient basis upon which to assess the validity and biological relevance of the data presented.

The Committee therefore finds that this does not constitute a breach of good scientific practice.

The Complainant also alleges that Figure 2d in the article looks unusual, artificial and suspect.

The Committee finds that the nature of Figure 2d[16] does not provide any basis for establishing that it has been manipulated. The Committee stresses that a range of factors may influence the appearance of a reproduced image of an immunohistochemical staining, including the preparation and fixation of cells and tissues, performing antigen retrieval, the type of the antibodies used and their dilution, the colouring agent and incubation time, the exposure time and filtering conditions in the microscope. The appearance also depends on the subsequent image processing in conjunction with the printing of the article. In this light, and based on the Complainant's assertions, the Committee finds that the figure does not give rise to concerns that warrant further investigation.

7.6 Application for UNIK funding

The Danish Agency for Research and Innovation called for applications from UNIK (Universitetsforskningens Investerings Kapital/University Research Investment Capital) in 2008/2009. UNIK targets major research groups which are evaluated by international experts as part of the application procedure.

Defendant 1 is part of a consortium that received a major grant from UNIK in 2009. According to Defendant 1, the consortium allocates the UNIK funding by means of an internal application procedure. It is in one such internal application that the Complainant alleges that Defendant 1 committed plagiarism.

The Committee notes that UNIK funding was no longer publicly available at the time of the application, and the application by Defendant 1 can, therefore, be considered internal and not anti-competitive in relation to the Complainant.

7.6.1 Plagiarism of the article in Genome Medicine in the UNIK application

The Committee fed the UNIK application though SafeAssign, a programme that checks online publications for signs of plagiarism. The results show that there is a certain overlap between the application and published resources but that this overlap is exclusively in the references. References aside, when the application is compared with the Complainant's article in Genomic Medicine, two sentences feature in both.

Sentence no. 1:

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[16] As stated above, the Committee bases its decision on the fact that figure 2d illustrates immunohistochemical staining of a tissue section and not an immunoblot.

"The molecular rules governing the targeting of a miRNA to individual genes have been documented and help identify which protein coding genes are targeted when a single miRNA is modulated in a cell."

Sentence no. 2:
"MicroRNA detection shall be carried out using the miRCURY™ v10.0 LNA microRNA array from Exiqon (Vedbæk, Denmark)."

The Committee notes that it is common and accepted practice to re-use the wording of methodology descriptions to a certain extent. In this context, the Committee notes that methodology descriptions are often not included in searches by plagiarism programmes.

The Committee therefore finds that sentence no. 2 does not constitute plagiarism in a form of sufficient substance to constitute a breach of good scientific practice.

The Committee also finds that sentence no. 1 constitutes a small section of the total and does not have sufficient substance to constitute a serious breach of good scientific practice. The re-use of the sentence is considered below the trivial level for scientific misconduct.

In its ruling above, the Committee has stressed that Defendant 1 is co-author of the article in Genome Medicine, cf. below, which according to the Complainant was plagiarised in the UNIK application. The Committee has also emphasised that this was an internal funding application and not anti-competitive, which means that greater scope is allowed for the reuse of the Defendant's own previously published wording.

The Complainant asserts that Defendant 1 did not write the article. The Committee finds that it is beyond all reasonable doubt that Defendant 1 is entitled to be credited as an author of the article. The case papers demonstrate that Defendant 1 obtained the clinical material on which the Complainant based the article, and that Defendant 1 read and commented on the manuscript before submission, as witnessed by the copies of correspondence submitted by Defendants 1-4.

7.6.2 Failure to credit the Complainant in the UNIK application

As described above, the application for UNIK funding was an internal application and not, therefore, anti-competitive in relation to the Complainant.

The Committee notes that the Complainant and Defendants 1-4 were research collaborators at the time the internal application was submitted, and that the Complainant was informed of the submission of the application.

The Committee finds that Defendant 1's failure to credit the Complainant in the internal application does not constitute a serious breach of good scientific practice.

In this context, the Committee stresses that the same requirements for credits or co-authorships do not apply to articles and to internal applications. The application concerned was for funding that Defendant 1 has already helped to generate

with the original UNIK application and for which the Complainant was not eligible to apply.

7.7 Other aspects of the complaint

The Committee finds that the following contentions by the Complainant do not fall under the remit of the DCSD as they do not refer to a specific written scientific product, cf. section 6 of the DCSD order, i.e. that:

- Defendant 1's supervision of PhD students at CIM was improper and incompetent,
- Defendant 1 presented the miRNA work in the article in Genome Medicine as stemming from the CIM by getting Defendant 3 to give a keynote lecture at an international congress in Miami, USA, in 2010,
- irregular 'mass publishing' occurred at CIM at the behest of Defendant 1 who, according to the Complainant, produces false CVs for her students,
- "salami-slicing" of studies took place in connection with Defendant 1's 38 credits as author along with one researcher at CIM and in 37 articles along with two other researchers at CIM,
- all of the work with myokines at CIM from 2000-2011 should be investigated because – according to the Complainant – it would not have received substantial attention without the extremely important muscle-protein immunoblot data set from 12 articles by another researcher,
- mRNA measurements taken by two researchers at CIM in the period 2001-2005 were incompatible with protein data produced by another researcher, and that the mRNA measurements were systematically misinterpreted by three researchers at CIM in the period 2001-2007,
- a student affiliated with CIM was improperly credited with co-authorship of a series of unnamed articles, despite the fact that the individual concerned provided no intellectual input into the article and only took biopsies or blood samples.
- Defendant 1's relationship with an editor of Diabetologia is open to criticism, and
- Defendant 1 misled the DCSD during the consultation process.

The Committee finds that the contention that Defendant 1 apparently changed her view of IL-6's role in human skeletal muscle over the years falls outside the remit of the DCSD, as this part of the complaint is a matter of the validity or truth of scientific theories, cf. section 3 of the DCSD order. The Committee therefore considers the apparent change of mind to represent a development in scientific knowledge.

The Committee finds that the Complainant's contention that it was improper for Defendant 1's research collaborator to perform the peer review of article 1 in the Journal of Physiology (see Note 3) falls outside the remit of the Committee, as this part of the complaint is not a matter of scientific misconduct, cf. section 2 of the DCSD order.

8 Summary

Taking the complaint as a whole, the Committee concludes that only the article in Diabetologia constitutes a serious breach of good scientific practice. There were significant deficiencies in the methodology description in the article, which had consequences for the interpretation of the results in the article, and this corresponds to 'undisclosed construction of data' as per section 2, no. 1 of the DCSD order.

The Committee does not find that the erratum containing a revised description of the methodology justifies any change to its findings, as the complaint was about the article in its original form and the erratum was published after the complaint had been submitted.

The Committee also concludes that Defendant 1 acted in a grossly negligent manner as a close reading of the article by Defendant 1 would have brought the inadequacies in the methodology description to light if Defendant 1 had taken the necessary care when drawing up and editing the article.

The Committee stresses that Defendant 1 was co-director of the study that led to the article, and was also the corresponding author of the article, so Defendant 1 can reasonably be considered to be one of the leading senior authors of the article.

The Committee therefore considers that overall Defendant 1 did act in a scientifically dishonest manner with regard to this part of the complaint, cf. no. 2 (1) of the DCSD order.

The DCSD rejects the other charges brought by the Complainant, and finds that Defendants 2-4 did not in any way act in a scientifically dishonest manner.

9 Appeals procedure

This decision cannot be appealed to any other administrative authority, cf. section 34 of consolidated act no. 1064 of 6 September 2010 on research advisory system, etc.

[DRAFT RULING – END]

Yours sincerely,

Henrik Gunst Andersen
Chair of the Danish Committees on
Scientific Dishonesty