UNIVERSITY OF TROMSØ UiT

FACULTY OF HEALTH SCIENCES
INSTITUTE OF MEDICAL BIOLOGY

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Rådet för utredning av misstänkt oredlighet

i forskning och utvecklingsarbete

ved Kristina Ullgren

Kristina Ullgren@gu.se

Your reference:
Our reference:
Date: July, 18th, 2013

Investigation scientific misconduct Dr. Pontus Boström

The University of Göteborg contacted me concerning an on-going investigation of scientific misconduct. In particular, I was asked by the University of Göteborg to express my opinion about following issues:

1) Our interpretation is that the original primary data are in the xls.files (bilaga 6). Is this correct?
2) Has a change occurred of the primary data when composing xls.files?
3) According to your opinion, are there some novel original data that can form the basis for the data provided in the xls.files and the corresponding ppt diagrams?
4) Have data from the xls.files been used in the ppt files that were e-mailed (bilaga 6, 2008-09-07) to Sven-Olof Olofsson?
5) Have data from the xls.files been used in the diagrams presented in the manuscript submitted to *Cell Metabolism* (respectively *Diabetes*)?
6) Do you find it reasonable to believe that scientific misconduct has occurred based on the guidelines outlined in the document "with reference number Dnr H 5 865/05 "Handläggningsordning för ärenden om misstänkt oredlighet I forskning och utvecklingsarbete"?
7) Are there any other comments that you wish to present in relation to this case?

The person under investigation is Dr. Pontus Boström. I declare that I have no scientific or any other relation with Dr. Pontus Boström and therefore that I act completely independent (no conflict of interest; "jäv"). After examining the provided information carefully, it is my conclusion according to the specific questions that:

Question 1: Our interpretation is that the original primary data are in the xls.files (bilaga 6). Is this correct?

I agree. I cannot find other primary data than the one presented in the xls.files in "bilaga 6".

Question 2: Has a change occurred of the primary data when composing xls.files?

It is beyond doubt that primary data have been changed when composing the xls.files. This is obvious for the data provided in the files called "090113 behandlingar blottar gjenomgång LA.xlsx; 090113 behandlingar blottar LA.xls; and Kvnat Stx5 Pontus värden från Multigauge.xlsx. (bilaga 2), and in the file entitled PCR Stx5 muskel biopsier LA.xls ("bilaga 3"). As pointed out in the e-mail to Pontus Boström (2012-04-26; 05:33) and the letter by prof. Jan Borén (2012-08-31), it is striking that usual the first or first two digits (higher number) have been changed.

Question 3: According to your opinion, are there some novel original data that can form the basis for the data provided in the xls.files and the corresponding ppt diagrams?

I have meticulously examined the information that was provided to me and I cannot detect additional information that could have formed the basis for novel original data provided in the xls.files or to generate the corresponding ppt diagrams.

Question 4: Have data from the xls.files been used in the ppt files that were e-mailed (bilaga 6, 2008-09-07) to Sven-Olof Olofsson?

Yes. The graph presenting Syntaxin 5 protein levels in diabetes, lean controls and obese controls is based on values that have been manipulated (some original a-tub and stx5 values have been adapted). Because a-tub values have been modified, the graph presenting relative SNAP23 protein levels (standardized against a-tub) may also partially be based on manipulated values. The same holds true for the graph showing no significant changes in total a-tubulin levels (control protein). Some original values for samples from diabetes and lean control group have been changed. Also the graph showing the effect of insulin stimulation on syntaxin 5 levels is based on manipulated data.

Question 5: Have data from the xls.files been used in the diagrams presented in the manuscript submitted to *Cell Metabolism* (respectively *Diabetes*)?

(a) Manuscript submitted to *Cell Metabolism* (bilaga 11):
Figure 4A (normalized syntaxin-5 mRNA levels):
Using data from "bilaga 7", Pontus kvantifiering and Kvantifiering med data från Pontus txt filer (LA), I calculated following relative syntaxin-5 mRNA values (with the value in lean controls arbitrary set as 100%):

	Figure 4A	Pontus kvantifisering	Kvant med data från Pontus txt filer
LC	100%	1,4259=100%	1,17=100%
CO	~80%	1,10212=77,3%	0,74=63%
D	~75%	1,06163=74,5%	1,15=98,3%

While the original data shown no difference between LC and D (100% versus 98,3%), the modified data show a significant difference between these two groups (100% versus 74,5%). The results in Figure 4A illustrate differences between LC and D. This strongly indicates that the modified data were used to construct Figure 4A.

Figure 4B (normalized syntaxin-5 protein levels in lean control, obese control and type 2 diabetes patients) shows a significant difference between type 2 diabetes and the other groups. This is in accordance with the manipulated data, but not with the original quantification data of the western blots.

Figure 2B (normalized SNAP23 protein). The original a-tub data for CL39 was 283644,23 but was changed into 83644,23. It is not clear whether the modified a-tub value was also used to normalize the corresponding SNAP23 value.

(b) Manuscript submitted to *Diabetes* (bilaga 12):
Figure 1A: again a significant difference in syntaxin-5 mRNA levels is presented between lean controls and diabetes. This indicates that the manipulated data were used.

Figure 1B: again a significant difference in syntaxin-5 levels is depicted between diabetes and lean controls. This is in contraction with the original data, but in agreement with the manipulated data. The p-value is p=0.016 (while in the corresponding figure in the Cell Metabolism manuscript p=0.003).

In conclusion: manipulated data were used to generate some of the figures in the manuscript submitted to *Cell Metabolism* and *Diabetes*.

Question 6: Do you find it reasonable to believe that scientific misconduct has occurred based on the guidelines outlined in the document "with reference number Dnr H 5 865/05 "Handläggningsordning för ärenden om misstänkt oredlighet i forskning och utvecklingsarbete"?

In my opinion, it reasonable to assume that scientific results have been systematically manipulated. The discrepancies cannot be attributed to sloppiness, but are the result of aimed falsification. Therefore, my conclusion is that scientific misconduct has occurred.

Question 7: Are there any other comments that you wish to present in relation to this case?

Several discrepancies are encountered in the statements of Dr. Pontus Boström when going through all the e-mails and additional inconsistency is observed between the data. Some examples are given.

(1) PB tries to minimalize his central role as a contributing author in this work. In his letter D2012/26 of 2012-09-19 he writes:

"Undetecknad var under perioden doktorand hos Sven-Olof Olofsson, men arbetade som AT-läkare heltid. Projektet i fråga drevs helt av professor Olofsson och en rad olika personer i hans dåavarande grupp, och undertecknad gjorde enstaka försök.

This is in contradiction with several statements mention in his e-mail correspondence with prof. Sven-Olof Olofsson. A few examples are:

-mail from 2009-01-14; 23:44:09: "EM-delen och lipiddroppsdelen flöt inte bra, men jeg har skrivit ett förslag til ändring".

-mail from 2008-10-17; 09:59:54 (bilaga 4): «Här är resultated av väldigt hart, ensamt jobb. Jeg vil vara med i alle diskussioner med ev samarbeten".

-mail from 2009-04-14; 15:06:09 (bilaga 5):

"*Jag kom med idén, satte själv upp alla piloter och visade att det fans något intressant"

"*Jag har varit den enda pådrivande kraften, och har faktiskt utfört en stor del av bulkarbetet/våtlabbandet".

-mail from 2008-09-07; 18:14 (bilaga 5): "I have run protein (WB on syntaxin5 and Munc18" and "I have had problems with RNA extractions – first trial yielded almost no RNA (with kit previously used on human muscle). A bit more in second test trial, but not enough for RT-PCR".

Moreover, Pontus Boström has on several occasions sent drafts of the manuscript and suggestions for corrections and improvements to prof. Sven-Olof Olofsson, indicating that he was highly involved in the writing process.

(2) PB changes his explanations for discrepancies in the values (Bilaga 2; quantitation by PB and by Linda Andersson). In his mail from 2012-04-26; 12:15 to Jan Borén, PB writes:

"Det jag kan tänka mig är att jeg gjorde upprepade western-kvantifieringar (vilket var väldigt vanligt), och istället för att göra om hela uträkningarna, så uppdaterade jag den gamle filen med det tusental som den nya kvantifieringen gav (och struntade i övr värdesiffror då de inte påverkar resultaten. Inte snyggt; jag vet).

In his letter D2012/26 of 2012-09-19 he writes: "mest sannolikt har jag inte analyserat dessa data".

Afterward he insinuates that somebody else may have changed the values because the files were on a computer that was accessible to everybody else in (and outside) the lab. According to the individual statements provided by the other co-workers in this project, nobody was involved in quantitation of the WB and q-RT-PCR experiments with syntaxin-5. According to the e-mail from Malin Celander to Kristina Ullgren, Björn Rydevik, Krstina Malmgren, Anders Blomberg, Anders Carlsson, Sally Boyd, and Philip Hwang sent 2013-01-18; 17:57), changes in the file with Western blot data occurred between 17:42 and 18:17 on 2008-09-07. For someone else to change Boström's data, he must have informed other persons about the results and then somebody must

have changed the data before Boström submitted the changed file to prof. Olofsson. All this must have occurred within this 35 min period.

(3) Inconsistency in the presentation that Boström had on one of the CMR lunch meetings: 2008-10-15 (bilaga 32). There is a discrepancy between the values in the diagram showing SNAP 23 protein levels in lean controls (LC), obese controls (=C) and diabetics (D) and the values presented in the diagram sent by e-mail to Olofsson on 2008-11-02 (skuggfigurer.ppt; Bostrom et al Figure 2; bilaga 29):

% of control (normalized to control=actin)	LC	OC	D
Diagram 2008-11-02:	100	~200	~350
Diagram 2008-10-15:	100	~125	~185

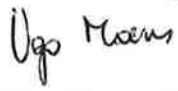
Data of the SNAP23 mRNA levels (standardized to actin) in LC, OC and D are also different in different graphs. E.g. Bilage 35 (e-mail to Olofsson on 2008-10-06; snap23 mRNA.ppt): in this graph SNAP mRNA levels in OC are lower than in the two other groups. This is not the case in the figures presented in "bilaga29", e-mail to Olofsson on 2008-11-02), Fig2A in manuscript submitted to Cell Metabolism (bilage 11).

(4) There exists also discrepancy between the data in "bilage 6" and Figure 2B in the manuscript submitted to *Cell Metabolism*. According to the figure legend in this manuscript represent these data the mean of 8 patients in each group. The table in "bilaga 6" mentions 9 CL patients: CL37,39,41,45,47,49,51,53 and 55. In the file with quantitation data in "bilaga 6", CL37 and 39 are on gel 1; CL41 and 45 on gel 2; CL47 and 49 on gel 3; CL51 and 53 and gel 4; CL55 on gel 5. The figure "SNAP23 levels – non insulin stimulated" also mentions that the data of the lean controls consist of 9 patients (n=9).

Finally, I just want to make a small remark. In the documents provided by professor Malin Calander, page 2, Table Western blot analyser, there is a little mistake. In this table, row Diabetes 17, column a-tub Gel nr a-tub.txt 2008-08-16: 34133 should be 24133 (24132,73) to be correct. This small mistake is not of relevance because this value was not manipulated in the files from Boström.

I hope that my contribution may be helpful in this case. I remain at your disposal if further information or advice is required.

Most sincerely,



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