Danish Committees on Scientific Dishonestry (DCSD/UVVU)
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Ministry of Science, Technology and Innovation

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Comments on professor Bente Klarlund Pedersen´s (BKP) response to my report of 18.07.2011 concerning "the Penkowa fraud case", sags-nr 11-114338, dok nr 2041626.

Introductory remarks.

Because of an unforeseeable disaster (disease and subsequent death), which has developed within my family over the past four weeks, I am not able before the deadline to examine the enclosures of BKP´s response, nor to produce a comprehensive and detailed rebuttal. Instead I will make some general comments followed by comments on selected issues. However, I believe these comments, together with my original report, easily justify the conclusions in my original report.

1. General comments.

I still fully stand by my original report.

Concerning BKP, the most crucial point in that report, was the demonstration of scientific fraud related to immunohistochemical analyses in some of the papers, she had written together with Milena Penkowa, and the fact that suspicion was raised, that also most of their other common papers included false histochemical analyses. In her response BKP essentially accepts these premises by referring to retraction of Papers 1, 3, 4 and 5, and by expression uncertainty about the validity of

immunohistochemical data also in Papers 2 and 8-11. Four possibilities then exist: 1. BKP deliberately participated in the fraud (which may also have included the studies, she does not express uncertainty about). 2. She did not read the papers including the flawed findings before submission for publication. 3. Her intellectual and professional skills were so limited that she, despite having been warned, was unable to see through the glaring weaknesses inherent in the histochemical data (e.g. use of the same muscle section to illustrate two different time points within one figure). 4. She had a suspicion that the immunohistochemical analyses might be flawed, but profited from them and chose to close her yes. A few obvious questions about the histochemical analyses would have revealed/prevented the fraud.

No matter which of the listed possibilities is true, BKP, being in charge of 11 of the 12 studies coauthored by Penkowa, had a clear responsibility for publication of the fraudulent material. This responsibility is, of course, not annulled , as BKP claims, by referring to the role of Penkowa, to the fact that some of the papers have now been "retracted", or to results of later studies. Others share this view as it is apparent from the fact that BKP was asked to resign as an editor of one of the involved journals in order to avoid bringing the journal into disrepute.

Another main focus in my original report was the use of mRNA to confirm the existence of the corresponding protein in muscle cells, the central theme of the studies. My view was that mRNA data in the reviewed studies were generally presented in such a way that the actual level of expression and its asserted correspondence with histochemical and other data cannot be properly evaluated by the reader, who, accordingly, may potentially be mislead, e.g. to believe that a given mRNA is expressed in myocytes rather than in other cells in muscle. In the present context absolute measures (e.g. CT values) should have been reported in order for the reader to evaluate how big a cell population might contribute to the mRNA measurements (very few or many cells? In the latter case probably myocytes). Instead of responding to this criticism, BKP defends her use of fold changes to illustrate mRNA findings by saying that fold changes have often been used, e.g. by me, to illustrate an effect of an intervention (p.4 in her response). However, she ignores the fact that in her studies, documentation of the location of the mRNA was essential, whereas in studies of metabolism of proteins, which are well established components of myocytes, this is not the case. In other words, the "defense" misses

the point.

The rest of my report illustrated an extensive lenient practice concerning study populations, measurements, and analyses and interpretation of data in general, indicating lack of qualified leadership. In such a milieu proper scientific fraud would be supposed to, and did, thrive.

BKP wants to be "cleared". If this will be the outcome, the Danish Committees on Scientific Dishonestry will accept a standard for scientific conduct, which will be detrimental to the international reputation of Danish biomedical research. Rather, the Committees should bear in mind the disrepute, which Danish biomedical science has already suffered, and act so as to ensure that it will not be repeated.

2. Comments on selected issues in BKP´s response, among these corrections of some of the incorrect statements, and examples of her peculiar way of arguing. Page numbers refer to BKP´s response.

2.1. Histochemistry.

2.1a. The involvement of Penkowa is not clear. On p.1 it is stated that in three of the studies (probably 6, 7 and 12) the immunoblots (probably it should be the immunohistochemistry) were performed by people from BKP´s laboratory, Penkowa did not have "hands on", and BKP had no reason to believe that produced data were fake. Nevertheless, in her comments p. 31 to paper 6, BKP in response to a question about histochemistry answers "This part of the study was performed by Penkowa". Furthermore, in comments on p.52 about Paper 12, it is stated that "Penkowa was involved in supervising the IHC technique and in the composition and description of Fig.1d" (the quality of which was questioned by me). Anyhow, it should be remembered that the quality of the histochemistry and other aspects of the work can be disputed also in the papers for which BKP repudiates a negative impact of Penkowa (see my original report). Finally, on the first page of her accompanying letter BKP writes that she has prepared the report in agreement with the co-authors of the 12 publications. Does this really mean that also Penkowa was consulted?

2.1b. Illustrating my claim that the attitude in the dealing with data was to promote own hypotheses, on pp.52 and 54 BKP writes about Fig.1d in Paper 12 “we show the IHC image that best supported the notion that the increased BDNF expression 24 h post-exercise was indeed intramyocellular”.

2.1c. I asked for an explanation for the discrepancy between Papers 1 and 6 regarding absence and presence, respectively, of IL-6 in muscle fibers at rest. This is highly relevant, because both papers focused on, whether IL-6 is located in myocytes, and because the studies were carried out by use of the same techniques in the same laboratory. Obviously, the authors themselves should have asked the question. Nevertheless, BKP on p.29 states that this is not an obvious issue for discussion, and she refers to the fact that a qualitative method was used. However, a qualitative method should be able to distinguish between absence and presence of a substance.

2.1d. On p.12 BKP writes that she cannot remember, if she was present at the CMRC scientific meeting, at which I pointed out that her immunohistochemistry data were not in agreement with what should be expected from endocrine physiology. However, her participation is apparent from the correspondence I have mentioned, and also from the program from the meeting, according to which she gave the presentation “IL-6-immunohistochemical detection, effect on liver glucose out-put, lipolysis and insulin resistance”.

2.1e. On p.4 BKP blames me for believing that immunohistochemistry is a quantitative technique. In the studies, histochemical findings were expressed in terms, which I think oblige to presentation of numerical evidence including all muscle specimen, which can be evaluated by the reader. Examples of the expression of data: in Paper 1 about IL-6: “increased significantly” vs “had clearly decreased again by 24h” “but were still higher than those of resting muscle”; in Paper 2: “type 1 fibres showed the highest increases”; in Paper 8 about the IL-8 receptor: “low or absent before exercise” vs “increased at 3 hours” and “peaked 6 hours after”; in Paper 9 about IL-6 protein: “very low in controls” vs “reduced below the levels of controls”. The fact that I do not believe that immunohistochemistry is a technique, which immediately yields data that are genuinely quantitative, is apparent e.g. from my comment to Paper 5: “attempts to quantify findings (e.g. simply: per cent of type 1

and 2 fibers, respectively, positive for a given cytokine) were not made". Another simple approach would be semiquantitative grading as described below (2.1g).

2.1f. On p.1 BKP writes that she informed the involved scientific journals on the 04.04.2011 about 4 papers with manipulated histochemistry data. If this is true, it is surprising that two of the journals, Experimental Physiology and J. Physiology, did not publish an "Expression of Concern" until the 24th of May.

2.1g. On p.7 BKP blames me that in my report I did not include a pathophysiological human muscle study from 2005 made in collaboration by a former student of mine, professor Flemming Dela, and Milena Penkowa. Frankly speaking, I was not aware of the study. However, if I had known the study, I would have been disqualified due to my close relationship with Dr. Dela. Still, it may now be mentioned that he exerted exactly the caution regarding the histochemical data provided by Penkowa, which one would wish that BKP had exerted. Thus, the slides showing the key variables and prepared by Penkowa were analysed blindfolded by two researchers from Dela´s lab independent of Penkowa. Furthermore, the histochemical stains were subjected to blindfolded semiquantitative evaluation (by visually grading staining intensity).

2.2. mRNA.

In the BKP/Penkowa papers measurements of mRNA were used to support the existence, as judged from histochemistry, of various corresponding proteins, which had not been extensively studied earlier, in muscle cells. This, of course, implies an obligation to render probable that the measured mRNA itself originates in muscle cells. That is the reason that, in the absence of in situ hybridization, CT-values were warranted as described in my report and above (1. General comments). Co-variation between mRNA and histochemical findings may also support the latter, because this is the immediately expected pattern. If, then, the occurrence of mRNA in muscle tissue is sparse, indicating no mRNA in myocytes, or mRNA and corresponding histochemically determined protein do not show co-variation, you must consider the possible causes, and one is that the histochemical findings are wrong. I certainly do

not fail to appreciate, as alleged by BKP (e.g. p.3) that other explanations may be true. However, as regards co-variation its absence or inconsistencies were often overlooked, even though being so remarkable that it is surprising that the authors did not question the histochemical data. As regards the existence of mRNA in muscle, some – but far from all - of the CT-values asked for are now provided by BKP (averages without measures of dispersion). Those given are not impressive, indicating an at most modest occurrence of the mRNA in myocytes. So, the suspicion remains that readers were deliberately mislead, data not supporting the authors´ hypotheses being neglected.

It is directly stated in the papers that IL-8 mRNA (Paper 3) and Metallothionein mRNA (Paper 4) were located within muscle cells, while CXCR2 mRNA was located in vascular endothelial cells of the muscle fibers (Paper 8). I objected against this because of lack of evidence (pp.19, 23 and 35). BKP now responds as regards IL-8 mRNA that "We made the assumption in the discussion that the increase in muscular IL-8 mRNA corresponded to the IHC (HG: immunohistochemistry) image demonstrating an increase in muscular IL-8 protein". If so, this assumption was "tacit", as it was not apparent to the reader, who, accordingly, was mislead by the text. However, the response shows that the description of the location of IL-8 mRNA was based on the assumption that it corresponded with that of IL-8 protein determined by IHC. The same reasoning most likely applied to the description of Metallothionein mRNA and CXCR2 mRNA, although BKP does not respond to my critic regarding these, and also do not inform of their CT-values. It appears that in the papers support for the existence of the mentioned proteins in specific cell types as determined by IHC was provided by mentioning the existence of the corresponding mRNA in exactly the same cells, but this was evidently misleading, because the mRNA location was based on the IHC measurements. The view that the authors were aware that mRNA expression in muscle cells might be doubted is in accordance with the fact that BKP explains the absence of IL-8 protein in the presence of the corresponding mRNA at rest by referring to high CT-levels (p.19, bottom).

2.3. Subject populations.

As indicated in the Conclusion in my original report, which is not reproduced in BKP´s response, the tacit reuse of subjects must be judged from the fact that it was extensive (occurred in 58-75% of the 12 papers taken by spot test) and practiced in the context of other lenient conduct. Furthermore, the reuse was often not very transparent, and description of subject populations even differing within individual papers. In her response BKP now also reports supplementation of previously used populations with new subjects or later repetitions of finished experiments, practices which of course imply problems because of the time lapse. Problems, which the reader cannot evaluate, if he is not informed. Finally, BKP does not mention, whether she substituted appropriate referencing by informing editors in submission letters, as some of my coworkers have done.

2.4. Examples of unsatisfactory argumentation.

2.4.a. No answer given.

In her accompanying letter BKP states that she will respond “in a point by point fashion”. Nevertheless, you will find that numerous concerns presented in my report are not commented on. BKP divides my text into pieces, but her response often only covers a part of the corresponding piece of text (e.g. P. 56, middle. I found data dispersions surprisingly small and differing between similar experiments, which might reflect manipulations. However, this part of a short piece of my text was not commented on). Furthermore, over long continuous stretches the text is not commented on at all (e.g. most of p.35, where essential conclusions of Paper 8 were challenged. Among other shortcomings, my report here points out that the authors´ interpretation of the histochemical data in Fig.2 is contrary to what the reader can

actually see).

2.4.b. The response does not relate directly to the posed question/deals with something else/uses irrelevant or not fully true arguments.

2.4.b1. P.11 and 28. IL-6 was found in muscle fibers at rest in Paper 6, but not in Paper 1. The reader (and the authors) obviously needs an explanation to know which of these essential findings, he should trust. Instead of addressing this need, BKP gives the surprising information that the IHC essentially is unreliable.

2.4.b2. P.11. It was concluded that IL-6 was secreted by muscle cells, even though an accumulation, and not a depletion, of IL-6 was found in myocytes. I wondered, why the authors at that time could draw such a conclusion rather than being startled of the apparently disagreeing findings. If they had thought about the discrepancy they might have revealed that the immunohistochemistry was faked. The fact that they did´nt, raises the possibility that they were involved in the fraud. In her response BKP refers to later observations, which of course were not relevant at the time (and which also are more questionable than alledged).

2.4.b3. P. 16-17. I pointed out that after exercise relationships between IL-6 mRNA and protein levels, respectively, differed between Papers 1 and 2, a fact calling for an explanation. If no obvious explanation is available data must be questioned. BKP answers that differences in IL-6 between studies were discussed in Paper 2. However, it is the difference in relationships between mRNA and protein, which is remarkable, and that was not discussed.

2.4.b4. P.23, l. 2-4. My objection was that it would not be possible to calculate fold changes in Metallothionein mRNA from values at rest, when the latter as stated were not quantifiable. BKP responds that the mentioned mRNA was expressed relative to another mRNA. However, this of course cannot compensate for the fact that the former was hardly detectable. She also answers that the reader can evaluate the fold changes from a figure showing the ratios, but this is not correct, because the reader cannot see from the figure that basal values were based on unquantifiable

measurements.

2.4.b5. P. 25, middle. The objection was that some IL-6 measurements were mentioned in the Discussion of Paper 5, which had not been presented earlier in the paper. BKP answers that it should be apparent from a given "proper" reference that measurements originated from a former publication (Paper 1). However, the reference is not given in connection with the mentioning of the measurements.

2.4.b6. P. 25, bottom. The objection was that 4 papers probably were based on the same study, while this was not apparent from citations. In her response BKP indicates that the mutual origin should be apparent from reporting in Paper 5 of IL-6 data from Paper 1 and inclusion of a reference to that paper. However, as mentioned in 2.4.b5 it is not at all clear from Paper 5 that the data derived from Paper 1. Furthermore, the citation of Paper 1 did not mention an intimate relationship between the material of the two papers, and Papers 3 and 4 were not quoted.

2.4.b7. P. 26, top. Because I found it surprising that IL-6 or saline were infused intraarterially in Paper 5, I wondered if the study was part of another study, in which an arterial catheterization would be justified by measurement of FFA turnover. BKP admits that my suspicion was right but argues that no double publication of data took place and that reference was given in Paper 5 to the original study. However, IL-6 plasma values were reported in both papers. Furthermore, it is not apparent from the quotation in Paper 5 of the original study that the two studies are basically one. Because I state that for the purpose in Paper 5 arterial catheterization would be unethical, BKP indicates that I have overlooked the fact that the study has been approved by the ethical committee. However, I still think that the arterial catheterization was approved for another purpose than that of Paper 5.

2.4.b8. P. 32, bottom. I wondered why data from one muscle was not included in the correlation analyses. BKP does not give an answer to this. Instead she responds that all individual data can be seen from the figures, and that the authors accordingly did not hide anything. Still, the reader has to be very careful to reveal that data from one muscle have been excluded without direct mentioning.

2.4.b9. P. 37, bottom. Indicating slovenliness, RNA extraction from adipose tissue was described in the Methods section of Paper 9, although the paper dealt with

muscle and not adipose tissue. BKP´s response is not informative: “we chose to include this information”.

2.4.b10. P. 38, top. I wondered why results from IL-8 stainings of muscle were not reported. Exclusion of undesired results must be suspected. However, BKP chooses to completely misunderstand my concern by answering: “We agree that the information about IL-8 staining is irrelevant”.

2.4.b11. P. 41, bottom. It is stated that neighbouring muscle sections were compared, and to facilitate this one given fiber was marked by an asterisk in each of two sections claimed to be adjacent. I pointed out that the sections as well as the fibers marked by asterisks were apparently not identical. BKP answers that “the muscle fibers in Fig 2C are slightly out of position” but does not comment on the fact that the fiber used to guide the reader is not the same in the two panels to be compared.

2.4.b12. P. 41, lower half. I was concerned about the lack of parallelism between IL-15 mRNA and protein measurements in response to exercise, and questioned the tentative explanation that transcription occurred without translation. In her response BKP now instead emphasizes later studies (which of course cannot justify the explanation given earlier) and claims that the finding in Paper 10 of increased mRNA levels with no change in protein after a single bout of exercise corresponds with the later finding that IL-15 protein levels may be increased at rest in muscle of trained subjects. However, effects seen upon training are the accumulated result of the single bouts of exercise together constituting the training program. So, if repeated exercise (training) results in an increase in basal IL-15 protein, an increase in IL-15 mRNA upon a single exercise bout would be supposed to be accompanied by an increase in IL-15 protein in relation to that particular bout.

2.4.b13. P. 45. The conclusion from Paper 11 was that in type 2 diabetics TNF-alpha is increased in an – undefined – subgroup of type 2 muscle fibers. To me an obvious question would have been to determine the size of this putative subgroup. However, by rearranging my original text in her response (p. 44, the last three lines in the Critique paragraph has been moved up from the subsequent paragraph in my report) BKP makes it difficult for the reader to follow this idea, and her response deals with subgroups of subjects instead of subgroups of fibers.

2.4.b14. P. 47, upper half. I found data dispersion for several variables surprisingly small (suggesting manipulations) based on my calculation of SD values from reported confidence intervals (Table 1). BKP responds that I am confused, because data are described as means and SEM. However, this was not the case regarding the variables I pointed out.

2.4.b15. P. 51. In my comment I compared the relationship between increases in BDNF mRNA and protein, respectively, in human muscle in Paper 12 with that in a previous study of rat muscle. However, in her answer BKP instead discusses, why increases in mRNA levels may differ from increases in protein levels, a completely different subject. Also, although I did not question her finding of an increase in BDNF mRNA, she uses 9 lines arguing that such an increase occurred.

2.4.b16. P. 56. It is claimed in Paper 12 that BDNF phosphorylated AMPK, which then phosphorylated ACC resulting in enhancement of fat oxidation. I questioned this sequence of events, because in two model systems, upon treatment with BDNF an increase in ACC phosphorylation could be seen without any increase in AMPK phosphorylation. The response by BKP "that the kinetics of the response in two very different model systems is somewhat different should not be surprising" does not at all correspond with my query.

2.4.c. The response is incomplete, incorrect, not understandable, and/or demonstrates poor acquaintance with the paper in question.

2.4.c1. P. 9, lower part. I pointed out that the legend to the key Fig.1 indicates that the material shown was derived from more than one exercising subject, which would not be correct. BKP answers that "it is stated that we show a representative subject". This is not correct. The legend mentions "resting subjects" and "exercising subjects", not "a representative subject". In the Results section the phrase "representative data" from "one subject before exercise" is used, but it is not told, if sections illustrating events during exercise were derived from this subject. So, the possibility remains that the authors here just as admitted for Paper 12 (see 2.1b) picked those images, which fitted their hypotheses best.

2.4.c2. P. 14 – 15. I compared the presented immunohistochemistry data on content of IL-6 in muscle cells with data on leg release of IL-6 and reached the conclusion that it would not be possible to reconcile the various findings within the frames of the overall conclusion by the authors. In other words, the apparent inconsistencies should have made the authors skeptical towards the validity of their data. BKP responds (p. 15, upper half) that "it makes little sense to try to make direct comparisons" between immunohistochemistry data and IL-6 net release data. However, this view contrasts with the indisputable fact that comparisons between changes in pool size of a substance and flux of the substance from that pool, respectively, are absolutely essential in physiological and biochemical kinetic analysis.

2.4.c3. P. 20. I doubted a main finding in Paper 3 that IL-8 was released from an exercising leg only at one measurement in the middle of a 3h exercise period, and not either before or after that time point. This unusual pattern and the fact that at all other time points at rest, during exercise and recovery, IL-8 tended to be taken up rather than released from the leg should have made the authors skeptical towards the validity of the single measurement, on which they base their conclusion. However, without commenting on the odd secretion pattern, BKP maintains the conclusion that they "demonstrate that IL-8 is released from an exercing limb" (p. 21), a fact which "only supports local production, since no systemic increases in plasma IL-8 were seen" (p. 20). She does not realize either that the lack of an increase in systemic (arterial) IL-8 concentration should have made the authors even more skeptical towards the claimed release from the leg, because this lack requires an explanation, as to where the released IL-8 disappeared.

2.4.c4. P. 28. I questioned the conclusion presented in the final paragraph of Paper 5 that "contractions induce expression of IL-6 receptor possibly to sensitize muscle to the decreasing IL-6 levels elicited by exercise". My reason was that exercise does not elicit a decrease in IL-6 below basal levels. BKP responds by repeating another paragraph from the Discussion section, which, however, has a nearly identical wording.

2.4.c5. P. 37, upper part. In Paper 9 patients with chronic obstructive pulmonary disease (COPD) were compared with healthy control subjects. I wondered how

controls with a high BMI could be excluded a priori as described, because it was also stated that controls were matched with patients according to BMI. BKP gives the non-satisfactory response that “It is obvious we chose to exclude patients with obesity”. Furthermore, she states “we decided to match the groups for BMI in an attempt to exclude patients with severe end-stage COPD”. However, it is not clear, how you can avoid patients with end-stage COPD by matching for BMI. Also, because people with end-stage COPD are unlikely to be obese, an explanation for the exclusion a priori of obese controls is still needed. Finally, recruitment of patients was apparently not successful, since six patients did suffer from end-stage COPD as judged from the fact that they were awaiting pulmonary transplantation. Another concern of mine was that while patients at the time of study were non-smokers, half of the controls were smokers, and, nevertheless, the impact of on-going smoking was not discussed. BKP gives the not very instructive response that “We find it rather obvious that ongoing smoking is an issue in COPD pathophysiology”.

2.4.c6. P.38, lower half. I pointed out remarkable inconsistencies in Paper 9 between histochemical findings and also in relationships between mRNA and corresponding histochemically determined protein. Inconsistencies which might reflect poor quality of the histochemical analyses, and accordingly should have made the authors cautious. The response does not deal with histochemistry, but just briefly refers to general comments on lack of correspondence between mRNA and protein presented earlier in the response. Although it is correct that mRNA and protein concentrations do not always change in parallel, this does not excuse from considering explanations for remarkable deviations regarding co-variation.

2.4.c7. P. 46, middle. I questioned the main conclusion in Paper 11 by referring to a non-significant correlation in control subjects and a low correlation coefficient in diabetics, which, furthermore, as judged from p-values would be even lower, when adjusted for confounders. BKP responds that “This is not correct”. However, the correlation coefficients, I referred to, can be found in Table 2, and the p-values in Table 3 of the paper.

2.4.c8. P. 45, lower half. Discrepancies within Fig. 2 and between parts of this and the text, respectively, are pointed out. Nevertheless, BKP just responds that “Fig. 2 provides the reader with a clear overview”.

2.5. My professional competence.

Throughout her response BKP questions my professional competence. Examples can be found above, and more are given below. Her view is interesting considering the fact that my formal professional background in physiology, biochemistry and pathophysiology as well as in clinical medicine might indicate a biomedical insight second to none. Including that of BKP, who has never been employed at a "theoretical" University Institute, a fact corresponding with the following:

2.5.1. P. 3, top: "cell biology and cell signaling are not areas of his expertise", and p.3, middle, and p.54, top: "Again, it appears that Dr. Galbo is confused". I had pointed out that the conclusion in Paper 11 that BDNF "works in an autocrine and/or paracrine manner" was in conflict with the finding of no release of BDNF in contraction-treated myotubes. BKP responds by defining autocrine and paracrine signaling, whereupon she explains that "the fact that we found no increase in BDNF in either the medium of the cells or in the circulation of the animals, is precisely why we concluded that the effects was either paracrine or autocrine". Apparently, she does not realize that a substance has to be secreted from a cell in order to exert an autocrine effect on that cell or a paracrine effect on cells located in the neighborhood, and that the secretion evidently will be accompanied by spill-over to the medium/interstitel fluid, because receptor binding cannot be 100%.

2.5.2. P. 20. "Dr. Galbo is confused" and "even considering Dr. Galbo´s confusion". I wrote that in Paper 3 the calculation of IL-8 release from a leg was wrong as it was done by multiplying veno-arterial plasma concentration differences with leg blood flow, instead of with plasma flow. However, BKP insists that the applied procedure was correct, because "IL-8 is known to interact intimately with the red blood cells". What that implies is not clear, but the fact is that use of blood flow rather than plasma flow in the mentioned calculation will only be correct, if the concentration of IL-8 in whole blood is identical to that of plasma (which is very unlikely). One has to use the flow for which the measured concentration is valid, and if blood flow is used,

the concentration of IL-8 should have been determined in whole blood, not in plasma.

2.5.3. P.1 in BKP´s accompanying letter and elsewhere: My comments on relationships between mRNA and protein levels are said to illustrate that my "criticism is based on an outdated and wrong perception of molecular biology". This is not the case as it will appear from 2.2., 2.4.b3, 2.4.b12, 2.4.b15 and 2.4.c6 above.

On P.4 BKP mentions the role of miRNA and quotes a paper of which she herself is an author (Genome Med. 2,9,2010) for showing "no change in mRNA using the microarray, but the differences in miRNA are predicted to result in a difference in protein. In fact, BDNF was shown to be changed in the proliferating cells." However, this is misleading, because mRNA was not measured in the proliferating cells, and thus both mRNA and protein may well have changed in the cell culture. Apparently, BKP has not studied or understood her own publication.

2.5.4. P.4.: "Dr. Galbo appears to be confused with regard to the IHC technique" "he believes IHC is a quantitative technique". I do not, see 2.1e above.

2.6. Jamie Timmons.

BKP postulates a "positive relationship" between me and professor Jamie Timmons (p.2 of her accompanying letter), and think that my report has been "inspired by the report submitted to UVVU by him" (p.2). This issue would seem to be of no relevance in the assessment of BKP´s work. The facts, however, are that while I in the spring of 2011 was preparing my report, I was told that he, too, was working on a report. Until that point of time I was not aware of his existence, and I have not met him until once in late august 2011. The primary focus of my report was, whether only Milena Penkowa was responsible for the possible dishonest work, she is accused of, and, consequently, the report was originally sent to Rector at the University of Copenhagen. In contrast, Timmons´report, as far as I know, deals with his professional relationship with BKP. Because I did not want my efforts to be mixed up with his, and because I prefer to work independently, I did not give him my report.

Recently, however, when it became clear that BKP had widely spread her response to my report, I mailed him a copy.

2.7. The enzyme Hormone Sensitive Lipase, HSL.

Although this is essentially irrelevant in the present context, BKP on p.12 brings up a dispute, we have had about HSL. Because it may serve to illustrate her way of working and arguing, I will comment on it. My view was that because I was recognized in the research center, we were both parts of ,CMRC, as well as in the rest of the world, as the one who first studied the role of HSL in muscle metabolism, it would have been natural, if she, who had worked in other areas, had told me about her interest in HSL, before she presented a study on HSL, she had carried out with collaborators outside CMRC. She now states that her collaborators were more experienced regarding HSL than me, but that is not true as regards role in muscle, and also irrelevant in the context of what is decent behavior within a research co-operative as CMRC. Furthermore, if our collaborators are of interest, it is easy to document that the one, who helped me with the HSL analysis, was far more experienced with this enzyme than her collaborators.

In line with the HSL story, it can also be documented that BKP wrongfully has claimed to be the discoverer of IL-6 and the originator of the idea that muscle is an endocrine organ. These matters deserve to be counts of indictment in a new case at the UVVU.

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Because BKP has send her response to the University of Copenhagen, The Faculty of Health, Rigshospitalet, and the Danish National Research Foundation, these institutions will also receive the above comments.

In addition, I expect that BKP will forward the present comments as well as the Conclusion from my original report to the many other people I know she has informed about my response.