

Udvalgene vedr. Videnskabelig Uredelighed  
Ministeriet for Videnskab, Teknologi og Udvikling  
Forsknings- og Innovationsstyrelsen  
Bredgade 40  
1260 Copenhagen K

Copenhagen, November 18, 2011

Dear Anders Rømer Kania

I acknowledge receipt of your letter of consultation of November 9, 2011, including e-mail correspondences between UVVU and Prof. James A. Timmons (JT).

I take the liberty to start my response with a chronological overview of this case.

*April 18, 2011:*

I receive JT's report by e-mail from my Dean at 14:37 and from JT at 18:15. The same day Poul Pilgaard Johnsen from Weekendavisen informs me by telephone that UVVU has received a report about me from JT.

Shortly after (I do not remember the date), Lene Kløcker Knüppel confirms by telephone that UVVU has received a report from JT.

*May 23, 2011:*

I, BKP, submit a report to UVVU in which I ask to be cleared with regard to the accusations put forward against me and my research group by JT.

*August 15, 2011:*

I am for the first time formally approached by UVVU with a request to respond to the report submitted by JT on April 18 as well as to all additional reports/material submitted by JT to UVVU from April to June 2011. I am given a response time of three weeks.

*August 22, 2011:*

I forward my response to UVVU on behalf of myself, Camilla Scheele, Søren Nielsen and Matthew Laye.

*September 1, 2011:*

UVVU asks JT for his comments. He is given a response time of three weeks.

*September 2, 2011:*

I am informed by UVVU in an e-mail from Béatrice Lamberget Sloth that JT has asked for and been granted an extended deadline for his "replik" which is now due on October 6, 2011.

*October 10, 2011:*

We receive the comments (replik) by JT first from JT at 00:03 and later at 10:38 from UVVU. It appears from the attached e-mail correspondence that on September 24, UVVU decided to grant JT yet another extension of his deadline from October 6 to October 10. I am given a response time of three weeks.

*October 10, 2011:*

I am informed by Beatrice Lamberget Sloth that our "duplik" will be sent to JT, but only for his information.

*October 28, 2011:*

We forward our "duplik" to UVVU.

*November 1, 2011:*

In an e-mail to UVVU (with cc to us) JT comments on our "duplik".

*November 4, 2011:*

JT submits additional material to UVVU. Later the same day, Beatrice Lamberget Sloth informs me by telephone that I shall not respond to the forwarded by JT on November 4.

*November 9, 2011:*

UVVU, now represented by Anders Rømer Kania, asks by e-mail for my comments to the material forwarded by JT on November 4.

Thus, enclosed, please find our response to the latest documents forwarded to UVVU by JT.

The present response to UVVU will be submitted also for information to our authorities at the University of Copenhagen and Rigshospitalet as well as to the Danish National Research Foundation.

Sincerely



Bente Klarlund Pedersen MD DMSc  
Professor of Integrative Medicine  
Director of Centre of Inflammation and Metabolism (CIM)  
Rigshospitalet 7641  
University of Copenhagen, Faculty of Health Sciences  
DK-2100 Copenhagen, Denmark  
Phone: + 45 35 45 77 97 ; + 45 26 17 05 24 (mobile)  
bkp@rh.dk  
<http://www.inflammation-metabolism.dk>

**JT:**

**BKP S1** – in support of my statement that it was common knowledge among CIM staff that the myokine immunoblots were “unsound” is demonstrated by this email from Soren Nielsen. Mr Nielsen is a 35yr old person who has worked at CIM for project work and PhD since before 2007. He you can see him ‘ridiculing’ a ‘myokine’ blot from fun, in an email to me. This type of communication was common place verbally among CIM (ex)students from 2005 – few ever put such comments in writing.

**BKP:**

To say that “it was common knowledge among CIM staff that the myokine immunoblots were unsound” is indeed a very serious accusation. It is therefore surprising that this statement is backed by a document in which Søren Nielsen has inserted a picture of himself wearing a silver wig into a figure from one of our articles.

Søren Nielsen, Camilla Scheele and JT were close friends at that time. JT stayed in the apartment of SN and CS and SN and CS visited JT on a daily basis while he was in hospital for a long period. It is obvious that the BKP S1 document represents a joke among close friends who have a relaxed and humorous tone.

Please, also see the statement by SN. I\_1\_1 and I\_1\_2.

**JT:**

**BKP S2, BKP S3 and BKP S4** – in support of my statement that productivity was so great from students it had to mean they were gaining publications for nothing OR that supervision was absent and data was being published unchecked by BKP. We now know that the Diabetologia BDNF article was shambolic and unchecked – but here are some specific examples of lack of supervision stated by the student themselves in 2006.

For example, as a collaborator from Sweden (as I was at the time) I found that the clinical data sheet, worked on by several MD PhD students from CIM, had not been peer-reviewed by BKP and contained very basic ‘unsound’ data.

The student responses are attached – where among other things they state lack of guidance and supervision from their mistakes.

**BKP:**

With regard to JT’s statement: “in support of my statement that productivity was so great from students it had to mean they were gaining publications for nothing”, I assume that JT primarily refers to ARN. Please see the comments in our first report (May 23), page 35:

*“Anders Rinnov Nielsen started in CIM in 2004:*

<http://www.inflammation-metabolism.dk/index.php?pageid=111&username=rinnov>

*He has been a PhD student/research assistant since 2004 and he has spent much of his free time, including weekends within CIM. He was responsible for establishing the so-called diabetes cohort, including approx. 200 individuals, who underwent clinical examination and muscle- and adipose tissue biopsies. He has also been involved in several other demanding clinical studies. ARN has since 2004 gained 21 publications, including 5 first author publications. I (BKP) can guarantee that ARN has made a substantial contribution to these publications and deserves every single credit as author. For your information, JT recently published an article (BMC Endocr Disord. 2011 Mar 22;11:7) including adipose biopsies from the before-mentioned CIM diabetes cohort without giving any authorship credit to CIM. We acknowledge that we are facing different cultures with regard to authorship. “*

JT states: “I found that the clinical data sheet, worked on by several MD PhD students from CIM, had not been peer-reviewed by BKP and contained very basic ‘unsound’ data”.

This is again an undocumented and very serious accusation. The so-called diabetes cohort, which was established by Dr. Anders Rinnov Nielsen (ARN), consists of more than 200 patients and controls from which ARN and other researchers within CIM have obtained muscle and fat biopsies. In total, there are approximately 100 clinical and paraclinical parameters. These data have been checked both by me and by an experienced MD, PhD Christian P. Fischer.

1. Subject no. 16762:

The VO<sub>2</sub>max of 108,3 represents a “missing value”, which was removed from the data-sheet and was never included in any publication.

2. Subject no. 15496:

This subject (15496) demonstrated an increase in plasma-insulin during the OGTT: 2108 pM one hour into the OGTT test. Although a high value, other subjects showed similar increases (e.g. 15528: 3121 pM at 1h, and 15610: 2701 at 1h). The high insulin levels found in some of the diabetic subjects could not be excluded as erroneous values, but fitted into a normal distribution (after log transformation). Rather, the high insulin values seemed to simply indicate that some of the subjects in the diabetes group were indeed very insulin resistant; hence we found no reason to exclude these data in the final analysis. Of note, the insulin measurements were performed by personnel at the Department of Clinical Biochemistry (Rigshospitalet).

We are surprised that JT uses the e-mail correspondence, presented in BKP S2, S3, and S4, in his accusations against us. Obviously, he must have confidence in our ways of handling scientific data as he has used these same data and our biological material in his own publications:

- Gene-chip studies of adipogenesis-regulated microRNAs in mouse primary adipocytes and human obesity. Keller P, Gburcik V, Petrovic N, Gallagher IJ, Nedergaard J, Cannon B, Timmons JA. BMC Endocr Disord. 2011 Mar 22;11:7.
- Integration of microRNA changes in vivo identifies novel molecular features of muscle insulin resistance in type 2 diabetes. Gallagher IJ, Scheele C, Keller P, Nielsen AR, Remenyi J, Fischer CP, Roder K, Babraj J, Wahlestedt C, Hutvagner G, Pedersen BK, Timmons JA. Genome Med. 2010 Feb 1;2(2):9.

- The importance of brown adipose tissue. Timmons JA, Pedersen BK. *N Engl J Med*. 2009 Jul 23;361(4):415-6; author reply 418-21. No abstract available.
- Genomic variants at the PINK1 locus are associated with transcript abundance and plasma nonesterified fatty acid concentrations in European whites. Franks PW, Scheele C, Loos RJ, Nielsen AR, Finucane FM, Wahlestedt C, Pedersen BK, Wareham NJ, Timmons JA. *FASEB J*. 2008 Sep;22(9):3135-45. Epub 2008 May 21.
- Altered regulation of the PINK1 locus: a link between type 2 diabetes and neurodegeneration? Scheele C, Nielsen AR, Walden TB, Sewell DA, Fischer CP, Brogan RJ, Petrovic N, Larsson O, Tesch PA, Wennmalm K, Hutchinson DS, Cannon B, Wahlestedt C, Pedersen BK, Timmons JA. *FASEB J*. 2007 Nov;21(13):3653-65. Epub 2007 Jun 12.

With regard to “lack of supervision”, please see the attached statement by ARN, which illustrates the nature of the relationship between ARN and JT and how it developed during ARN’s wasted sojourn in Edinburgh in the spring of 2007, I\_2.

In my opinion, there is no doubt that ARN was initially very impressed by JT. I interpret ARN’s phrase regarding “lack of supervision” as a means by which ARN tries to protect himself against the criticism, raised by JT. This interpretation is based on the fact that since 2004 and up to now ARN has continuously chosen the CIM environment as the basis for his own research.

***Finally, we take the liberty to add some new information, showing that JT’s accusations with regard to “the BDNF story” are completely unsubstantial:***

BDNF is expressed by human muscle

Over and over again JT has stated that our data, showing that muscle expresses BDNF, are fraudulent and that we were aware of this seeing that he had warned us on several occasions; e.g. in his report forwarded to us on October 10, 2011, he states:

*“In Jan 2009 I write to BKP “mature muscle does not really express bdnf unless damaged” – I can’t think of a more direct warning that her “BDNF expressed everywhere data” was problematic. I have also reported my concerns to Diabetologia who now await the outcome of the UVVU investigation.”*

On October 31, 2011, Camilla Scheele attended the NordForsk Meeting and Conference on Systems Biology of Metabolism in Hørsholm, at which Prof. Mathias Uhlén from Royal Institute of Technology, Sweden gave a presentation about his protein atlas. This is a very impressive project in which all human proteins are being mapped in human tissues and cells. In support of our findings with regard to BDNF, he finds that BDNF is highly expressed in skeletal muscle at the protein level:

*“Staining summary: Weak to moderate cytoplasmic and occasional membranous or nuclear positivity was observed in most normal tissues. Neuronal cells, appendix and skeletal muscle (normal) displayed strong positivity.”*

<http://www.proteinatlas.org/ENSG00000176697/normal/skeletal+muscle>

BDNF article in Diabetologia

As regards Diabetologia, we have now received confirmation from the Journal's editorial office that they have accepted to print our Erratum in regard to the fact that we by mistake had omitted to mention a group of subjects involved in the study. Please see, I\_3\_1 and I\_3\_2.

We trust that this information will put an end to the accusations against us for trusting data demonstrating that normal human skeletal muscle has the capacity to express BDNF.