

Dated: 03-02-2014

Dear Mr. de Bok,

Thank you for your mail of 27-01-2014. First, I will mention the background including sequence of events and then I will provide my reply.

The original complaint was only against Nature 2013 paper [as communicated to me by Utrecht University Committee for Scientific Integrity (UU CWI) on 03-05-2013] and hence, the UU CWI should have taken up this issue only. However, this did not happen. Surprisingly, the issues related to Cell 2012 paper and Nature 2008 paper were also taken up by the UU CWI - (i) they were sent by UU CWI to the experts together with the issues of Nature 2013 without letting the accused (me) know about them and without providing me an opportunity to respond to them, (ii) they were not properly discussed with me during my hearing with UU CWI, (iii) they were included in the advice of UU CWI, and (iv) they were included in the decision of the Executive Boards of UU/WUR. As mentioned in the decision of Executive Boards of UU/WUR (communicated to me on 13-09-2013) and as written therein *'If you are not satisfied with (aspects of) the Committee's advice and/or our decision, you can appeal to the National Board for Research Integrity (LOWI).'* Accordingly, I conveyed my concerns related to inclusion of articles other than Nature 2013 paper in UU CWI's investigation and in the decision of the Executive Boards of UU/WUR to LOWI. I am waiting for LOWI's decision related to this.

I had been thoroughly cooperating with UU investigation process in a good faith and trust from the very beginning since May, 2013. However, as mentioned to you earlier, I lost my trust in the UU procedures based on - (i) above non transparent events, (ii) the issues in Cell 2012 were evaluated and advised by UU CWI to correct through a 'corrigendum' (on 13-09-2013) but they were later on changed to 'retraction' (on 02-10-2013) by Executive Board of UU without letting me and other co-authors know the reasons for this change when we requested it by our letter to UU Rector (on 26-09-2013) and (iii) post Cell retraction intentional media coverage individually targeting me with posting of subjective comments and confidential documents from the UU CWI investigation process by involved parties on the internet.

After getting mail from you on 25-11-2013, I requested the information on technical committee and its evaluation in relation to the composition of committee, its reference points and the manuscripts that will be looked at. Apart from the list of the manuscripts, I did not get complete information from you on the other two points. Therefore, as communicated to you in December 2013 - (i) non-availability of LOWI's advice, (ii) loss of my faith and trust in UU procedures and (iii) non-transparency of UU regarding the technical committee and its evaluation forced me unable to comply with UU investigation of my papers other than Nature 2013.

UU went on with the technical committee evaluation whereby it again received information from Prof. Scheres who is a co-author of most manuscripts. This questions the objectivity, and the time regime of inclusion of the points when LOWI remains busy with evaluating the decision of UU including the technical evaluation of all manuscripts and has not yet conveyed its verdict.

In the course of your mail of 27-01-2014 referring to the UU's report on the technical investigation of other papers, I have no option provided than to reply. Please find below my reply for the three areas of issues reported by UU technical committee and my brief comments in a tabular list (page 4) of all issues from manuscripts co-authored by me during my stay at UU.

1. Gel band issue:

'Cutting and pasting of gel bands' mistakes have occurred due to lack of my and other author's knowledge of representation of gel data. The gel band issues of Nature 2013 have been addressed extensively in our

rebuttal provided to UU CWI (on 30-05-2013). I and other author helped reconstructing the gel band images of Cell 2012 that Prof. Scheres communicated to UU CWI on 24-05-2013 (without letting us know). My comments on gel band issues of Cell 2012 have also been communicated to UU Rector (on 26-09-2013 and on 15-10-2013). Furthermore, our original raw data (as evident from gel reconstructions for Nature 2013 shown in our rebuttal of 30-05-2013 and for Cell 2012 shown in my communication to Cell and CCed to UU Rector on 15-10-2013) and the independent verifications (as in the rebuttal of 30-05-2013) underline the validity of our experiments, results and conclusions related to gel band images.

Development 2010 paper was a joint venture between Offringa group from Leiden University and Scheres group from UU with equal contributions. This is also reflected by a shared first authorship between two members of Offringa group and me from Scheres group. The new gel image issue (Fig. 3C) from Development 2010, in which gel bands were cut and pasted, is not from my work. These data are from the Offringa group and they have been used in the figures of Development 2010. These data have been provided by Dr. Offringa to the Scheres group (via e-mail on 30-11-2009). The same cut and paste band gel image that we received from Dr. Offringa was also used in the manuscript version which was submitted to Nature Cell Biology on 28-12-2009 where I was not a coauthor but Prof. Scheres was. This shows that 'cutting and pasting of gel bands' mistakes have also occurred with other researchers.

As pointed out in the report of technical committee of UU Fig. 3D of Cruz-Ramirez et al. Cell 2012 (where Prof. Scheres is the corresponding author) also shows cut and paste of bands. These data are also not from my work and this raises the very same concerns and questions those have been raised on other papers where I am a first or last author. This shows that the senior corresponding author also missed this when the junior authors proceeded with manuscript versions by considering his checking as a quality control of the manuscript. This also raises the questions that why this paper was not reported before by Prof. Scheres to Cell and to UU CWI when similar mistakes in Dhonukshe et al. Cell 2012 had been specifically targeted up to its retraction.

In addition, the Journals 'Plant Cell' and 'Plant Physiology' jointly published a notice in *Plant Cell Vol 25:3147-3148, September 2013* with rules for publishing gel bands (much later than our publications). From this notice it can be concluded that more scientists must not be aware of the rules related to presentation of gel bands.

2. Microscopy image issue:

The issue of Fig. 1A and Fig. S2A of Nature 2008 paper was communicated by Prof. Wasteneys to UU CWI on 13-05-2013 but this was never discussed with me by UU CWI. Therefore, I am unable to agree with UU technical committee's reporting that Fig S2A of Nature 2008 was not previously brought to the light. The issue of Nature 2008 was later on communicated to me by Prof. Friml (a senior corresponding author of Nature 2008) on 17-12-2013 after he received it from Prof. Wasteneys. I provided my reply to Prof. Friml and other coauthors the same day on 17-12-2013. In my reply I attached the last image file submitted to Nature prior to the publication of the article by Nature. Due to the evident difference in last submitted image version to Nature and the published Nature PDF this issue is related to PDF conversion. This was confirmed by analysis of another coauthor of Nature 2008. As indicated before by Prof. Scheres, most of the work for Nature 2008 (including Fig. 1A and Fig. S2A) was performed more than 6 years ago before my joining to UU. My UU affiliation for Nature 2008 was mentioned based on the agreement between Prof. Scheres, Prof. Friml and myself considering a very unusual situation whereby neither Prof. Friml nor I was affiliated anymore to our previous work place (where most of the work in Nature 2008 was done) when we submitted the manuscript. The figure panels for Nature 2008 were assembled (including contrast adjustments) by UU image processing personnel as also mentioned in the acknowledgements section. Furthermore, our conclusions related to these images are based on results from more than one approach as also seen in Fig. 1 and Fig. S2.

The issue in Fig. 4J in Cruz-Ramirez et al. Cell 2012 appears not a background intensity shift but rather a selective background blackening by inconsistent processing. In the raw data that I provided for this manuscript the background is not as black as that in the publication; moreover the processing of this figure has not been done by me. This raises questions of inconsistent processing on manuscripts where I am not a first or a last author.

3. Duplicated image issue:

As already conveyed earlier to the UU CWI and as mentioned in the report of UU CWI, the duplicated image panels D, E and G, I in Fig. 4 of Nature 2013 are due to mistakes caused by sloppiness (during multistep and multipersonal assembly of the figure panels in a time constrained situation).

I am unable to agree with two panels in Fig 7D of Development 2010 paper to be a 'duplication' as green background noise in both panels is not identical (based on non-matching distinct parts) and in a duplication everything should be identical.

Further, I am also unable to see the relation of my being first and last author to the issues when - (i) all authors (including the cases where someone else is a last author when I am a first author and where someone else is a first author when I am a last author with respective responsibilities) have worked on all manuscript versions and jointly agreed for publication by taking the responsibility to publish the content and (ii) very same image processing personnel from UU composing figure panels for other papers have also assembled the figure panels where I am a first or last author. On the contrary, I am left with the feeling that it seems to be the intention of the UU procedures to technically rate the mistakes (ranging to <5 % of all presented data and which do not influence the main findings) as manipulations for putting the blame on me. I have already expressed my regret for those mistakes which occurred due to lack of knowledge and sloppiness in intense and competitive time course of manuscript preparations with multistep and multipersonal assembly of hundreds of figure panels from thousands of raw images involving years of work. The processing generally referred as 'bewerken' in Dutch language (in English it is 'worked on') cannot be referred as 'manipulations' as otherwise every single published article whereby the raw images have been touched (worked on) to assemble the figure panels falls into the so called 'manipulation' category. Further, many questionable events have occurred in UU's investigation and my job is taken away from me during UU investigation. I have been out of job and without salary for over five months now. However, it has been a fulltime job for me over these months to fight false accusations and allegations. I hope that UU investigation of my work is without a tunnel vision in order to allow me going on with my (professional) life on a short term notice.

In conclusion, the issues from Nature 2013, Cell 2012, and Nature 2008 have already been investigated by UU CWI along with their expert evaluations and their incorporation in UU CWI report. The newly identified issues from Development 2010 and issues from my coauthored papers do not stand as: i) many of the identified figure panels with issues (in Dhonukshe et al. Development 2010, Robert et al. Cell 2010, Nagawa et al. PLOS Biology 2012, Cruz-Ramirez et al. Cell 2012) are not my data and thus come from different authors and ii) Fig. 7D from Development 2010 is not a duplication.

As the above matter also relates to LOWI's evaluation, I am CCing this mail to LOWI.

Best regards,
Pankaj Dhonukshe

Annex on page 4: A tabular list of all issues from all manuscripts coauthored by me during my stay at UU along with my brief comments on them.

Annex to all issues from all manuscripts coauthored by Dhonukshe during stay at UU along with brief comments.

Paper	Fig.	UU Technical Committee's conclusion	Scheres, intern investigation	Dhonukshe conclusion and comment
Dhonukshe as first or last author				
Dhonukshe et al. Nature 2008	1A	inconsistent image acquisition or processing		No, because submitted Figure to Nature publication is a PDF conversion issue, central (mostly bleached) part cropped for clarity and due to space limitations
	S2A	inconsistent image acquisition or processing		No, because of PDF conversion issue, central (mostly bleached) part cropped for clarity and due to space limitations
Dhonukshe et al. Development 2010	3C	cut-and-paste		Not my data, data published as provided by collaborators
	7D	figure duplication		No, unable to call it 'duplication' due to presence of non-matching parts
Dhonukshe et al. Cell 2012 (retracted)	4N	possible cut and paste		Gel reconstruction from raw data provided to UU CWI validating published data
	S5G	possible cut and paste		Gel reconstruction from raw data provided to UU CWI validating published data
	S6E	possible cut and paste		Gel reconstruction from raw data provided to UU CWI validating published data
Kakar et al. Nature 2013	1B	possible cut and paste		Gel reconstruction from raw data and independent confirmation by experimental repetition validating published data provided to UU CWI
	4D-E	figure duplication		Conveyed to UU CWI, experimental repetition validating published data provided to UU CWI
	4G-I	figure duplication		Conveyed to UU CWI, experimental repetition validating published data provided to UU CWI
	S4G	possible cut and paste		Gel reconstruction from raw data and independent confirmation by experimental repetition validating published data provided to UU CWI
	S5J	cut and paste		Gel reconstruction from raw data and independent confirmation by experimental repetition validating published data provided to UU CWI
	S8K	cut and paste		Gel reconstruction from raw data and independent confirmation by experimental repetition validating published data provided to UU CWI
	S9H	cut and paste		Gel reconstruction from raw data and independent confirmation by experimental repetition validating published data provided to UU CWI
	S10K	cut and paste		Gel reconstruction from raw data and independent confirmation by experimental repetition validating published data provided to UU CWI
Dhonukshe as coauthor				
Robert et al. Cell 2010	S5	awkward presentation of non-existing phenotype, but no sign of manipulations.		Not my data
Li et al. Cell Research 2011		no signs of manipulations		-
Prasad et al. Curr Biol, 2011		no signs of manipulations	No data of PD included in final version of the paper	-
Cruz-Ramirez et al. Cell 2012	3D	signs of cut and paste	PD only responsible for 4J	3D is not my data
	4J	no signs of manipulations	confirmed background intensity shift, but independent experiments have shown that data are reproducible	In my provided raw data the background is not as black as that in publication. It appears not a background intensity shift but rather a selective background blackening by inconsistent processing which was not done by me.
Nagawa et al. PLOS Biology 2012	S2, S7, S8	suboptimal imaging but no signs of manipulations		Not my data
Lin et al. Current Biology 2012		no signs of manipulations		-
Sassi et al. Development 2012		no signs of manipulations		-
Zamioudis et al. Plant Phys 2013		no signs of manipulations		-

Note: The issues from Nature 2013, Cell 2012, Nature 2008 have already been investigated by UU CWI along with their expert evaluations and their incorporation in UU CWI report. The newly identified issues from Development 2010 and issues from my coauthored papers do not stand as above.