Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Report of the ETH Commission of Inquiry set up to clarify allegations against Prof. Olivier Voinnet of ETH Zurich

Members of the commission were Prof. Matthias Peter (Chair of D-Biol), Prof. Yves Barral (Director of Studies of D-Biol), and two external experts, Prof. Edward Farmer (Plant Mol. Biol., Uni Lausanne) and Prof. Witold Filipowicz (Friedrich Miescher Institute, Basel), the latter acting as a Chair of the commission. In its duties, the commission was assisted by Dr. Raffael Iturrizaga, Office of Research, ETH Zurich.

The commission received a mandate from the Executive Board of ETH to:

1. Examine and provide clarifications and judgments regarding potential misconduct in publications as of January 27, 2015 listed in the document provided by Olivier Voinnet (henceforth OV) and further publications criticized on the *PubPeer* website.
2. Interview OV or any other persons who might provide help in reaching Commission's conclusions

The investigated problem, materials provided to the commission, and the commission's deliberations, conclusions, and recommendations will be summarized below in the following order:

1. The investigated problem
2. Initial material provided to Commission
3. Detailed analysis of the published papers containing errors and misrepresentation of the data accompanied by summaries of sessions with Respondent
4. Conclusions of the investigation
5. Recommendations

[redacted]

Detailed Part

1. The investigated problem

On December 20, 2014 a number of faculty members at ETH and other institutions, including two members of the commission, received anonymous emails pointing to the website *PubPeer*, where a number of posts provided evidence for irregularities in figures of papers co-signed by OV. Based on these accusations, a first ETH-internal commission viewed the criticized data, interviewed OV, and concluded that there was a need to establish an independent commission. Accordingly, this new commission was asked to further investigate allegations of research misconduct by OV concerning approximately 30 papers listed on *PubPeer*. These papers cover an approximately 15-year period spanning from OV's PhD thesis work (e.g. *Cell* 1998 95, 177-187) to recent papers on which he had sole or shared corresponding authorship (e.g. *PLoS Pathogens* 2013 9:e1003435). Clarifying the origins of the anonymous e-mails and their motivation was not part of the mandate of the commission, but the issue is part of the context in which the investigations took place.

The commission's work was conducted in compliance with the 'Procedure to address allegations of research misconduct at ETH Zurich (RSETHZ415)'. As all allegations pointed to manipulation in published figures, the duty of the commission was to determine whether OV and/or his coworkers committed any of the following research malpractice:

- Category 1: Publication of invented data. That is, the fraudulent production of results from unrealized or failed experiments, or manipulation of data in order to change the conclusions to be drawn from them.
- Category 2: Publication of “beautified” or idealized figures. That is, the willful modification, duplication or mislabeling of images in order to make them look cleaner or more convincing, without affecting the overall conclusion of the original experiment.
- Category 3: Publication of processed data including images without transparently announcing the nature of this processing (image splicing, contrast processing, etc). Awareness and journal requirements related to this

issue have evolved considerably since approximately 2006/2008 and more stringent requirements for transparency have been in place since then.

- Category 4: Unintended publication of erroneous images in place of the correct ones.

All levels of malpractice, except category 4, constitute cases of intentional misrepresentation of data and hence are misconduct, although their gravity and hence the consequences for the scientific enterprise decrease from category 1 to 3.

2. Initial materials provided to Commission

- Document produced by OV (dated 27.1.2015) “Report for the ETH commission in charge of investigation the various allegations regarding the scientific production of OV and his colleagues”. It summarizes all cases reported on *PubPeer* web site up to 25.1.2015, and also lists their explanations and possible actions to be taken.
- Procedure to address allegations of research misconduct at the ETH Zurich, dated March 30, 2005.
- Guidelines for Research Integrity and Good Scientific Practice at the ETH Zurich as of 25 October 2011.
- Additional materials requested in the course of investigation and provided by OV are listed in section 3 and also specified in the list of attachments at the end of report.

3. Detailed analysis of the published papers containing errors and misrepresentation of the data, including summary of sessions with the Respondent

Prior to its first meeting on 3.3.2015 the commission members examined commentaries related to OV's papers on the *PubPeer* website. In parallel, OV was asked to furnish a résumé of problems, their explanation, and possible actions to be taken. This document produced by OV is dated 27.1.2015 and covered *PubPeer* commentaries up to 25.1.2015. The document listed 19 papers that (according to OV) contained erroneous/manipulated figures. Also listed were 8 papers in which apparent anomalies could be due to inexplicable repeated background patterns in some blots,

or where the same blots were simply re-probed, explaining why the same loading controls were used for each image shown. The document listed a further 4 papers that were discussed on *PubPeer* but for which OV argues against the existence of actual problems. He interprets these posts as an attempt to inflate accusations against him. This document (OV27.1.2015) was examined by the commission prior to and during the 3.3.2015 meeting.

One by one the commission discussed each of the 31 papers listed in OV27.1.2015 with an emphasis on the 19 papers indicated by OV as containing problems. The picture to emerge confirmed that numerous publications contained obvious flaws of which one of the most common was the recurrent use of identical loading controls some of which appeared in figures in different publications (e.g. in *Nat. Genetics*, 2007 39:848; *Science* 2010 328: 912; EMBO J 2012 31: 2553). Additionally, and indicative of a more serious problem, Fig. 6 in *PLoS Pathogens* 2013 9:e1003435 had obviously been manipulated. Other papers contained figures in which bands were clearly duplicated (e.g. *Cell* 1998 95: 177 and *Plant Cell* 2004 16: 1235). For example, Fig. 7 in the 2004 *Plant Cell* paper contained examples of this in addition to loading controls being re-used between different experiments.

During its first meeting the commission found two papers: *PLoS Pathogens* 2013 9:e1003435 and *Plant Cell* 2004 16: 1235 to be most problematic since they appeared to contain images that could not have been made by error alone. The commission decided to focus particular attention on these two papers while not ignoring other publications. While looking into some of these other papers there were cases where the commission was unable to come to firm conclusions. This was the case for identical background patterns seen in different lanes on blots (e.g. in Fig 5F and 6A in *Nat. Genetics* 2013 45: 1029).

Based on the 3.3.2015 meeting the commission decided to investigate a number of specific cases that were considered to be particularly serious and to invite OV for an interview to discuss these particular cases and other broader issues. To prepare the interview OV was requested to address a number of concerns, the most important of them being listed below (the page numbers refer to numbers in the OV27.1.2015 document):

p. 21

PLoS Pathog. 2013

We asked for the original lab book in order to see:

1. Where the mistake originated?

2. The repeats of the experiments or correct gels from the experiments confirming that the results claimed in the paper are indeed correct.

3. In the light of serious problems with this paper what action is being planned?

p. 16/17

Nat. Genetics 2007; Science 2010; EMBO J 2012

Three papers (Nat. Gen, 2007; Science 2010; EMBO J 2012) used the same loading control. Can the authors provide convincing evidence that controls were carried out for these experiments?

p. 8

Plant Cell 2004

In the light of multiple errors (lane and loading control duplications) in this paper we would like to see better explanations for how tracks in Figs. 2A, 2B, 7C, 7D, 7E were duplicated. We would like to see original data providing convincing evidence that these experiments were actually carried out and that the results conformed to the conclusions.

p.9

Science 2006

In a number of cases mock figures were assembled. Why was this done and how did this finish up being published?

In several papers (e.g. EMBO J. 2002; p. 24) there are repeated background patterns from phosphorimages. Can you explain why this occurred and provide us with original files?

What measures are now in place in the Voinnet labs to prevent similar problems occurring in the future?

3a. Summary of the first session with the Respondent on 19.3.2015

The interview took place during the second commission meeting on 19.3.2015 in Zurich. In advance of the interview OV communicated the following items to the commission (these and other documents are attached to the report):

a) a newly annotated version of the OV27.1.2015 document (referred to as OV27.1.2015Bis; note that page numbers in this document differ from those in the original OV27.1.2015 document).
b) detailed notes on the *PLoS Pathogens* 2013 9:e1003435, *Plant Cell* 2004 16: 1235, *Science* 2006 313: 68; *Nat. Genetics* 2007 39:848; *Science* 2010 328: 912; *EMBO J* 2012 31: 2553 papers including scans of original data and scanned pages from a Master Thesis report that relate to the *PLoS Pathogens* 2013 9:e1003435 paper.
c) scans of original data and a 4-page document discussing repeated background patterns seen in blots presented in several papers.
d) a 3-page document addressing the issue of “mock” figures appearing in some papers despite apparently not being intended for publication.
e) a 3-page document on preventative measures that will be taken in the future.
The commission members made themselves familiar with these documents prior to the interview.

For the March 19 interview OV brought original laboratory notebooks pertaining to the papers in question, as well as the Master Thesis report. The commission noted that OV collaborated fully throughout the enquiries, providing original data (some over a decade old) and always answering questions even if they were of delicate nature. The first part of the March 19 interview involved addressing the above questions that had been previously communicated to OV.

Regarding the *PLoS Pathogens* 2013 9:e1003435 paper, OV admitted that Figure 6 was fabricated and that this was for him the 'worst case.' This faulty figure was retrieved from a Master's student report and was reused in the paper in response to a reviewer's comment, apparently without noticing that the student had fabricated these panels. OV was able to show, in the original lab notebooks, that experiments related

to the fabricated Figure 6 had indeed been performed and that a fully authentic figure could have been prepared at the time of publication. OV admitted responsibility for not having personally overseen preparation of the figure, neither for the Master's report nor for the final submission to *PLoS Pathogens*. OV added that the co-corresponding and last author on the paper had no responsibility for the figure in question.

The *Plant Cell* 2004 paper was then examined (note that additional concerns related to this paper are discussed further below). In question was the large composite Fig. 7 in which the same loading controls were used for different experiments and in which lane duplications appeared. In response to the commission's request to see original data guaranteeing that all experiments had indeed been performed, OV furnished lab notebooks produced by his collaborator [redacted]. The commission examined these books and specifically looked for elements related to Fig. 7. In the case of all panels, original replicated data were found by the commission. In many cases the same blot had been exposed multiple times and these carefully dated blots were stacked one on top of the other in the notebooks. Loading controls were also found in the appropriate places and had been annotated appropriately. When asked how so many errors could occur in the same figure, OV replied that the published Fig. 7 was almost certainly a 'mock' ('idealized') figure that had been cobbled together for a lab meeting, and that was then mistakenly used in the publication.

The *Science* 2006 315: 68 paper by Deleris et al. was then discussed. OV indicated that this paper did not contain "mock" idealised figures, as originally believed by the commission, but mistakes which occurred during mounting of composite figures from primary data contributed by two different graduate students. The errors included Northern blots mistakenly used in place of the intended originals, and also incorrect loading controls. OV stated that he is solely responsible for all errors in this paper (collaborative work with [redacted]) as he personally helped his students to mount the figures. Correct data have been recovered and corrected figures and explanations sent to *Science*. Since additional problems were subsequently found in this *Science* paper, the commission returned to its investigation in a second session with OV, also inspecting original data provided by OV.

Next, the interview examined the issue of the repeated use of the same loading controls for multiple experiments published within or between different publications over considerable periods (e.g. in one case between 2007-2012 in the three papers that OV was specifically asked to comment on). Inspection of lab notebooks for a limited number of experiments in the three papers (*Nat. Genetics* 2007 39:848; *Science* 2010 328: 912; *EMBO J* 2012 31: 2553) under scrutiny showed that appropriate loading controls had been performed for each experiment at the time. However, during the interview it emerged that an electronic library of RNA loading control data existed and that this library, rather than the cognate controls, was routinely used. OV admitted that this was bad practice.

Then the commission turned to the issue of repeated background patterns such as those that are seen in the *EMBO J* 2002 21: 4671 paper and other articles. OV referred to the data he had sent to the commission and to a 4-page document that he had prepared on this subject. This document discussed the 2002 *EMBO J* paper from OV's time as a doctoral student under [redacted], as well as a more recent *EMBO J* (2012 31: 2553) publication involving the researcher [redacted] who at the time was affiliated with both Strasbourg and Zürich. Neither the commission nor OV could provide an explanation of whether the duplication of entirely blank lanes had really occurred and, if so, what benefit would be gained by such an act. The commission and OV evoked a possible technical origin for repeated background patterns but the commission was unable to uncover any testable reasons for this. Inspection of lab books and comparison with published figures did not reveal that there was any reason to duplicate empty background lanes since the lanes in the primary data were already empty. The report will return to the issues of blank lanes and background duplications, as well as some issues associated with EMBO J (2012), below. Regarding the *EMBO J* 2002 paper, OV said that he would reproduce one of the experiments from his thesis time for which no primary blots are available to clarify the problem.

3b. Preparation for the second session with the Respondent

As a result of this discussion of individual papers the commission decided that it was necessary to request additional information from OV. In preparation for a third meeting of the commission, OV was asked to respond to the following points:

1. There are allegations of bands having been erased in one of the panels of Figure 2E of Moissiard et al. PNAS 2006 103: 19593, and Figure 2D of Moissiard et al. RNA 2007 13: 1268. The commission requested to see the original data for both of these figures.

2. The commission's prior discussion of Marí-Ordóñez et al., Nature Genetics 2013 45: 1029 had only focused on image compression issues. Regarding possibly duplicated lanes in Figures 5F and 6A the commission asked to see the primary data.

3. Concerning Gibbings et al., Nature Cell Biol. 2012 14: 1314. So far, on p. 20 of OV27.1.2015Bis, only flipping of the Coomassie stained bands between Fig. 5 panels C and E was discussed. But these two panels also contain the same tubulin blot. The commission asked to see evidence that panels C and E in Figure 5 indeed represented probing of the same blot with different antibodies.

Moreover, during the period following the 3.03.2015 meeting the commission was informed by OV that *EMBO J* had completed investigation of papers published in this journal and raised some new or sustained some old allegations regarding the following papers:

EMBO J 2010 29: 1699; for unmarked splicing, incorrect loading controls used, and duplications of background lanes. The published Fig. 4A looks better than the original data that show background clouding in all three @2039 panels.

EMBO J 2012 31:2553; for triplicated re-use of loading controls, repeat background patterns and unmarked splicing of lanes.

EMBO J 1998 17: 6739; in Fig. 6i there is apparent duplication of blank lanes. Primary data are unavailable for this paper.
In addition, the commission was informed of further developments. Firstly, a 1.4.2015 post on *PubPeer* by Prof. V. Vance (University of South Carolina) disclosed that she had reviewed what was later published as Dunoyer et al., *Plant Cell* 2004 16: 1235. V. Vance highlighted problems with some data, which were allegedly labelled

differently in submissions to different journals where she acted as a reviewer. V. Vance also raised other potential problems with the manuscript. *Plant Cell* editors and reviewers have accepted OV's rebuttal and a statement concerning this affair has been issued recently: (http://c.ymcdn.com/sites/my.aspb.org/resource/resmgr/publications/dunoyer_press_release_aspb.pdf).

On April 12th 2015 the commission received an email letter from V. Vance. This letter reiterated information in the *PubPeer* post made by V. Vance on April 1 but also stated: '*The practice of fabrication of data by the Voinnet lab has had serious negative impact on the field of RNA silencing. Many investigators are, in fact, not able to repeat some aspects of his reported results or have conflicting data*.' Related to this, a second article in *Le Monde* (9.4.2015) reported allegations that the group of Prof. A. Simon (University of Maryland) could not repeat some data published by OV and others in *Science* 2006 313: 69. A. Simon published results related to this in Manfre and Simon *Virology* 2008 379: 161. The commission returned to the points raised by A. Vance and A. Simon during its meeting with OV on 13.04.2015.

Prior to the third meeting of the commission on 13.4.2015, OV transmitted data related to the aforementioned points to the commission. [redacted] All the aforementioned issues were discussed with OV in the session on 13.4.2015.

3c. Summary of the second session with the Respondent on 13.4.2015

The second audition of OV started with an examination of specific issues concerning papers by Moissiard *et al*., *PNAS* 2006 103: 19593, and Moissiard *et al*., *RNA* 2007 13: 1268 (discussed jointly); and papers by Gibbings et al. *Nat. Genetics* 2013 45: 1029 and Marí-Ordóñez *et al*. *Nat. Cell Biol*. 2012 14: 1314. Each point was addressed in the three-point order as listed above.

1. Figure 2D of *RNA* 2007 13: 1268. In this figure the commission found evidence of unmarked lane splicing and erroneous representation of the WT band in the upper (GF probe) blot. Regarding potential bands erasure, this might have taken place to

beautify the picture by removing traces of degradation products seen at overexposure of lanes. OV provided an amended panel D, which will be issued to the journal for correction.

Figure 2E of *PNAS* 2006 103: 19593. OV confirmed that this figure contained a track that originated from a mock figure and also had a non-cognate loading control. The *dcl4* lane in the published figure originated from a slightly stronger *rdr6* lane from the same original membrane. In the bottom part of the figure the commission and OV found that one track (labelled *ago4* on the original film) had been spliced out without specification. On inspection of the original data the commission felt that these manipulations were unlikely to affect the conclusions of the paper. However, as indicated in the initial OV27.1.2015 document, the paper contained several other errors/misrepresentations. Indeed, during the discussion of this *PNAS* paper OV explained that 4 of 5 figures in the paper were problematic due to mounting 'mistakes' and lane duplications. OV stated that many of these errors apparently came from mock figures used in lab PowerPoint presentations, which OV used to assemble the paper. The commission learned from OV that although the scientific conclusions of *PNAS* 2006 103: 19593 do not appear to be affected, this paper is now retracted due to numerous mistakes and figure manipulations.

2. *Nature Genetics* 2013 45: 1029. Although original phosphorimages were lost when a room at the Strasbourg laboratory was flooded, the original membranes used to make Figs. 5F and 6A were found and reprobed (by first author A. Marí-Ordóñez). The reprobed blots fully support the published findings. In the specific case of Fig. 6A, the commission found evidence for blank lane duplication. However, after inspection of the reprobed blots the lanes corresponding to those in question were shown to contain no signal and fully support the published data. It was unclear to the commission why blank lanes were duplicated; these would not have altered conclusions. This provided an illustration of the types of problems encountered in numerous other publications where it was neither obvious to the commission nor explicable by OV why inserting blank lanes into images, made from blots where lanes were already blank, was done. Although not specifically requested by the commission, an original blot representing the upper panel of Fig. 2h (questioned on

PubPeer in the same *Nature Genetics* paper) was presented to the commission by OV. No evidence of manipulation was found for panel 2h.

3. *Nature Cell Biol*. 2012 14: 1314. OV provided images of original gels pertaining to Fig. 5C and E prior to the 13.04 meeting and justified why the same tubulin blot was used as a control in different panels representing gels and blots run in parallel in a single experiment. For the same reason, use of the same protein loading control for different blots is justified in this paper. The commission found no evidence of wrongdoing for this paper and was satisfied with explanations provided prior to and during the audition. The documented flipping of the loading control likely represents a genuine error.

The EMBO J papers

For the three *EMBO J* papers in question, experiments appear to have been done correctly but figures for publication were rearranged/spliced or some background removed in order to improve figure appearance.

Regarding Figure 6i in the *EMBO J* 1998 17: 6739 paper, the lower right 'GFP probe' panel in it shows that two lanes have the same repeated background pattern and the concern is that this hides bands observed in the original experiment. In the absence of the original data produced before 1998, OV has stated his wish to repeat, under institutional supervision, the key experiment shown in Fig. 6i. The commission supports this proposition, if EMBO J. allows publishing such a corrigendum.

Concerning *EMBO J* 2012 31:2553, OV first focussed on Fig. 5A where there is again a duplicated background region. The commission had previously seen original exposures of blots for these data and, again, the reason for the duplication remains unclear to the commission (and to OV): the duplicated background regions in question were blank on all provided blot exposures. No evidence of splicing was found in other parts of Fig.5A. However, Fig. 5B also contains inexplicable repeat patterns: the original film provided contains no signal in the suspected region. The mirrored duplicated loading controls in Fig. 5B that had been discussed in the first interview with OV were re-discussed as was evidence for other issues in this paper

that had been provided by OV to the commission prior to the 13.04 meeting. These included re-used loading controls in Figs S1 & S2 and spliced lanes in Fig. S3B. Regarding the unmarked spliced lanes in Fig. S3B, OV provided pictures of original blots arguing against any intentional manipulation. OV stated that, taken together, the *EMBO J* 2012 paper contains several 'mistakes' but none of them affects the conclusions of the paper.

EMBO J 2010 29: 1699. Data provided by OV prior to the 13.4.2015 meeting addressed problems in Figures 3C (duplicated and mirrored bands despite “correct” bands in the original data), 4A (duplicated loading controls, duplicated and rotated background patterns and removal of cloudy background) and S3 (two sets of duplicated loading controls). Regarding Fig. 3C, the original blot presented to the commission supports the validity of the data and leaves it unclear why the questioned band would have been duplicated. However, the bands in both panels of the figure have been spliced (upper panel) or moved in blocks from left to right to fit another panel (lower panel) without marking it; this movement of bands might underlie some apparent background duplications. The commission then focused on Fig. 4A and asked OV about the cloudy background patterns on original films for which OV had provided images; the background clouds (so usual in Westerns and Northerns) appear to be less intensive in the figure appearing in the paper. OV stated that in front of the facts he had to conclude, as did the commission, that in this case there must have been a deliberate attempt to 'clean the background' and to present an idealized/beautified figure.

Next, the commission asked OV for an update about what has been done to address journal editors concerns and what have editors done. OV first gave background on the *Plant Cell* 1998 10: 937 paper that had been mentioned in *PubPeer* (regarding Fig. 5B). It is possible that a corrigendum will be issued for this paper.

The *Science* 2006 313: 68 paper by Deleris et al., already discussed during the first interview, was then addressed again in detail. In Fig. 1D a lane that had no RNA was used as a mock instead of a lane containing RNA from a mock-infected plant. The loading controls were wrong. The commission asked OV about Fig. 1E containing a spliced lane where no splicing had been indicated on the figure or in the figure

legend. A lane labelled 'WT' in the figure came from a *dcl4* lane. Additionally, loading controls were not correct. OV admitted that it was himself who made the panel and underlined that none of the co-authors made these erroneous figures. In Fig. 2A the mock lane was moved from right to left, an *rdr2* lane was used as WT and the wrong loading control was used. The supplementary figures were also discussed.

The commission spent time discussing the review history of *Plant Cell* 2004 16: 1235 as recently revealed by Prof. V. Vance at *PubPeer* and her open letter to some members of the commission. Without covering this aspect in depth the commission noted potential breach of faith of both authors and reviewers making it difficult to concentrate only on one party. Moreover, it noted that publication of the paper was a sovereign decision of the *Plant Cell* editors and reviewers who at the time were all aware of V. Vance's accusations. Since this paper had already been treated in extensive detail by the commission (and retracted by OV on 27.03.2015 because of the documented figure manipulations) this discussion was not pursued. This part of interview was concluded with a brief discussion of the need for OV to make clear decisions concerning submission of corrigenda and possible retraction of some additional papers.

The final part of the 13.4.2015 interview with OV concerned the allegations of V. Vance, and *Le Monde*'s reported allegations from A. Simon that some of OV's results could not be repeated. Following questioning of OV on this, and inspection of Manfre & Simon *Virology* 2008 379: 161, the commission came to the conclusion that the *Virology* paper did not provide evidence that the experiments reported in *Science* 2006 313: 68 could not be repeated. A. Simon did not publish repetition of the experiments carried out in the *Science* paper. The conclusions in each paper were drawn from different types of assays.

3d. General discussion with OV regarding laboratory practice, origins of the problems, and future measures

During both meetings with OV the discussion also focused on analysis of the environment in OV's labs, with OV first being asked how a situation leading to so many manipulations and errors could have arisen. He responded by giving insights

into the way his lab was run with each individual researcher being subjected to considerable pressure and only having occasional chances (approx. once in six months) to present his/her data at lab meetings. The picture that emerged was one of an exciting but high-pressure environment at the forefront of science and where the lab was in strong competition with other laboratories. This, and the perceived need to publish quickly was fuelled by OV himself. OV admitted that many papers were assembled too quickly, with “no moment of reflection”, in a highly competitive environment.

Has there been an organized effort to discredit OV and inflate accusations against him? OV stated that a large number of emails targeting the RNA and plant biology community (in USA, France, and Switzerland) was sent out in late 2014/early 2015. Indeed, two members of the commission were themselves recipients of the anonymous alert email sent on 20.12.2014 by [redacted]. Additionally, OV mentioned that “although he has no proof of it, he has the strong suspicion that a colleague with whom he had a scientific conflict at *Cell Reports* (9: 795 and 9: 798) might have helped orchestrate the sudden dissection of all his scientific production”. This conflict is also mentioned in the article of *Le Monde* (31.3.2015).

OV was also asked 'What measures are now in place in his labs to prevent similar problems occurring in the future?' The commission had previously consulted a 4-page document 'Preventative measures' prepared by OV in which he detailed measures to be taken in the future. These included the following:
OV 'will issue a general document summarizing bad practices of scientific data manipulation to all lab members and newcomers' and will 'stop any personal involvement in the mounting of figures. OV 'will encourage lab members to conduct their lab meetings as much as they can with raw experimental material.' He will engage in 'an open discussion with the lab members regarding the level of pressure they experience.'

The commission then asked OV to reflect on the current size of his laboratories in Strasbourg and Zurich? OV answered 10 and 30 people respectively and then gave a detailed breakdown of the numbers and categories of researchers in each lab.

The commission concluded that big size of the groups and their different locations must make the proper supervision of collaborators difficult, likely explaining part of the problems.

4. Conclusions

The commission was set up on 5.02.2015 and has investigated the accusations against OV over the last 3 months. During these investigations, summarized on initial ~15 pages of this document, the commission scrutinized 32 papers (over half of the experimental papers published by OV) for possible misrepresentation and manipulation of data. Most of them were originally brought to light at *PubPeer*. A few additional publications that the commission investigated were identified by journal editors or by the authors themselves following their sensitization to the recurring problems. In the course of investigation the commission inspected approximately 65 documents, most of them provided by OV and representing primary data, files documenting origins of most serious manipulations (and also attempts to explain them), documents summarizing different types of errors, and also documents outlining future preventive measures. OV collaborated quickly and openly with the commission, providing all materials requested, including lab notebooks (sometimes originating from more than a decade ago) containing original gels and blots.

Different types of errors and manipulations were identified in figures of about 20 papers. These flawed figures spanned a spectrum of gravity, ranging from shifted sets of duplicated bands (*PLoS Pathogens* 2013 9:e1003435) and obvious whole-lane duplications (e.g. *Cell* 1998 95: 177), to the probable use of mock figures for publication (e.g. *Plant Cell* 2004 16: 1235), to papers in which images had been beautified by removal of background clouding (e.g. *EMBO J* 2010 29: 1699). There were a number of cases of splicing of 'ideal' lanes without transparent explanations, and some re-attribution of lane names (e.g. *Science* 2006 313: 68). Several papers either shared the same loading control images (*Nat. Genetics*, 2007 39:848; *Science* 2010 328: 912; *EMBO J* 2012 31: 2553) or used the same, sometimes mirrored control images in different figures within the same paper (e.g. *EMBO J* 2012 31:2553). For three papers flagged on *PubPeer* the accusations have not been substantiated by the commission; they were referring essentially to compression or

imaging artefacts, posterior to publication, or represented unsubstantiated accusations. In seven other *PubPeer*-flagged papers, the re-use of gel loading controls and control gel lanes was found fully justified (e.g., by re-probing of the same blot; examples of such papers published during the OV's tenure at ETH are listed in Addendum to the report). Different types of errors/manipulations confirmed or identified by the commission are discussed below.

4.1. Classification of the identified errors and misrepresentations

Inspection of lab books or raw images from lab books routinely revealed that the experiments reported in investigated publications had been conducted and recorded carefully. The commission did not find evidence of what it termed category 1 (see Section 1 of the report for definition of different categories) misconduct, corresponding to the invention of data in the place of experiments that were never conducted or manipulation of data with a purpose to change the conclusions. Several cases were classified as category 2, manifested by deliberate modification, duplication, or mislabeling of images in order to make them look nicer or more convincing, without however affecting the overall conclusion of the original experiment. Representative papers are PLoS Pathogens 2013 9:e1003435; Plant Cell 2004 16: 1235 (retracted); Science 2006 313: 68; PNAS 2006 103: 19593 (retracted) and EMBO J 2010 29: 1699. The majority of problematic papers contained clearly identified cases of misconduct that fell into category 3 that the commission designated as non-annotated processing of images. It is likely that some papers containing wrong or repeated loading control panels represent genuine errors (category 4) as might some image mislabellngs. In summary, about 20 papers representing approximately one third of OV's output of primary literature are affected.

Following types of manipulations and errors have been identified:

4.1a. *"Mock" idealized figures.*
Several papers (e.g. PLoS Pathogens 2013 9: e1003435; PNAS 2006 103: 19593; Plant Cell 1998 10:937) contain manipulated figures, which – according to OV – were not destined for publication but represented provisional figures used by lab members during internal lab meetings with the aim to facilitate presentation or sketching figures

for prepared manuscripts. These figures were then 'mistakenly' used in the publication. The commission considers the use of mock figures a serious issue. It points to a bad habit of using false idealized figures instead of primary raw data during lab discussions.

4.1b. *Duplicating of gel lanes or panels, associated in some cases with reattribution of lane names.*

Several of these types of actions appear intentional (e.g. PLoS Pathogen 2013 9: e1003435, and Cell 1998 95: 177) and together with those represented by “mock” figures, they confirm many *PubPeer* reports. It was not clear to the commission why these manipulations were done since inspected primary data looked similar and introduced changes generally had no effect on conclusions of the experiment.

4.1c. *Manipulations of background lanes.*

Manipulation of background in supposedly empty lanes was confirmed for some of the analyzed papers. Some of this might have resulted from a non-annotated reshuffling of bands from the same blot, but for 2-3 cases (e.g. *EMBO J* 2010 29: 1699) a deliberate attempt to clean the background in order to beautify the image was evident. Some cases raised on *PubPeer* concerned blank lane duplications (e.g. EMBO J 2012 31:2553). However, the commission could not find convincing explanation for why this would have been done, since the original blots, to which the commission had access, were empty in all suspicious regions.

4.1d. *Repeated use of the same loading controls for different experiments*.

An extreme case was represented by the use of the same loading control in three different papers (*Nat. Genetics* 2007 39:848; *Science* 2010 328: 912; *EMBO J* 2012 31: 2553). This issue was aggravated by the existence of an electronic library of loading controls originating from different experiments. Upon inspection of lab notebooks for the data appearing in some of the questioned papers the commission confirmed that appropriate loading controls had actually been properly performed for each experiment at the time.

4.1e. *Splicing of gel or blot lanes without marking the manipulation.*
This has been confirmed for many papers (including several published during last 5-7 years; e.g. PLoS Genet 2013 9: e1003791; EMBO J 2010 29:1699). Based on original data presented to the commission, the splicing events involved lanes from the same blot. This type of manipulation was acceptable until 2006-2008. Since then this must be clearly marked in papers.

4.2. General summary and an attempt to understand origins of the problem

The problems discussed in the report date back to OV's thesis period. As the years went by, the list of papers containing misrepresented data grew. Lane duplications, the re-use of loading control panels, and band shifting or band re-labelling spanned the entire 15 years period under investigation. With the seed of the problem carried to his own laboratories, OV may have permitted or even facilitated its use by some of his closest collaborators, and other lab members may have felt too junior to challenge this. Being at the cutting-edge of science, the OV laboratories were exciting, high-pressure and fast-working, and being fast was part of the problem as OV himself admitted. From the commission's perspective, many problems in data misrepresentation can be seen as speeding offences where experiments, once done, were rushed to submission using repeated short-cuts. Cumulatively, this has resulted in many flawed publications. Remarkably, this was not brought to full light until late 2014. In some part this may have been due to what was frequently considered acceptable: cutting and pasting of images - a procedure increasingly restricted by journals and reviewers over the last decade or so.

[redacted]. As OV has himself stated in one of the documents submitted to the commission: “It is almost as if, having generated the data and convinced ourselves of their robustness, the steps involving their representation under the form of figures (for publication or presentation) became somehow less important than the fact of having generated the data *per se* and answered a scientific question”. Caught-up in the race to explore radically new scientific terrain OV and some of his collaborators permitted and used image manipulation, sometimes small and seemingly benign, but sometimes very serious.

The damage to OV's reputation is already great, but the commission acknowledges the outstanding intellectual contributions of OV and his co-workers. OV's ideas and publications have had a large and positive impact in science and, we believe, will continue to do so. The tragedy is that the experiments that were (mis)reported in the papers investigated by the commission were actually conducted and, as based on the data inspection by the commission, executed with care. The original raw data (as seen by the commission) would have been sufficient to fully substantiate the authors conclusions. Moreover, with the exception of those that have not been retested yet, it appears that the conclusions of OV's papers have been reproduced by others and many have catalysed successful research directions in other laboratories.

4.3. What is to be learned from the OV case?

The wilful misrepresentation of data, as has occurred in this case, cannot be tolerated. However, such events are not easily controlled and the commission does not see fit to propose new laboratory rules that could potentially prevent similar situations from occurring. If any new rules are made, the freedom for scientists to make genuine mistakes must continue to exist - it sometimes leads to discovery.

PubPeer is a valuable forum for alerting the scientific community about potential malpractice, as witnessed in the OV case. However, the potential exists to exploit it in cases of scientific conflict. The scientific community should open a debate about how it wants to deal with suspicions of misconduct, and how it wants to protect itself from perversion of all sorts. Directions of reflections and possible improvements include: (i) the development of sophisticated documentation and archiving systems (including electronic lab books) to ensure a better tracking of the data back to their origin; (ii) the re-appropriation of discussion forums by the different scientific societies; (iii) the development of procedures to better coordinate clarification efforts by the concerned parties (editors, funding bodies, research institutions).

5. Recommendations

The commission considers that the following actions should be taken both as measures to address the damage created and in order to prevent similar problems in the future.

5.1. Immediate actions to address the damage to the data

We recommend that the implicated authors draw very clear lines between the papers that contain problems that are due to mistakes, and those that are problematic due to a wilful distortion of the facts. Although it is obviously the journal's prerogative, the former (category 2) papers, particularly those containing well documented intentional manipulations (PLoS Pathogens 2013 9:e1003435; Plant Cell 2004 16: 1235; Science 2006 313: 68; PNAS 2006 103: 19593 and EMBO J 2010 29: 1699), should be retracted through OV's requests as being non-factual, irrespectively of whether the reported observations have been reproduced by others. Given that primary data exist and experiments were correctly conducted and documented, the commission does not propose retraction of the trio of papers with shared loading controls (EMBO J 2012 31:2553; Science 2010 328: 912; Nat. Genetics 2007 39: 84). Corrected figures should be submitted to the journals. Papers in categories 3 and 4 can be 'repaired' through publication of corrections in order to re-establish a faithful documentation of primary data. Our investigations have established that the vast majority of the data originally produced have been conserved faithfully and are of sufficient quality. Therefore, issuing these corrections rapidly should be possible. Doing this will send a strong sign that accuracy of documentation precedes interpretation and is an essential step in the long road towards re-establishing trust in the OV group.

5.2. Further action to correct the working culture in the OV laboratory

It appears essential to the commission that, in order to avoid future misconduct driven by an excessive rush to publish, the OV laboratory is reduced to a manageable size on a single site, at ETHZ. Procedures inside the laboratory need to be improved along the lines proposed by OV himself. Internal restructuring at ETH is also

recommended. The OV laboratory needs to be better integrated with those of the neighbouring laboratories in related fields, for example by integrating these teams in an Institute of Plant Biology with all the organs needed to foster administrative, technical, and scientific exchanges between its research teams. This should promote a healthy debate about scientific procedures and greatly reduce the probability of misconduct.

5.3. Strengthening scientific culture and education at ETH

The emergence of platforms such as *PubPeer* is a sign that the misconduct established in this investigation is not an isolated case. While PubPeer is a valuable forum, many comments that the commission inspected viewed the problem from the side of the advantages that the “cheaters” may obtain as a result of their misconduct. This is not the whole picture. The primary victim of misconduct is the scientific enterprise; the misrepresentation of data works against science. Students need to be taught this even more extensively than they are already. The commission feels that courses in epistemology and, specifically, in what constitutes misconduct should be mandatory for science students and scientists alike. Such courses should induce reflection and discussion on what approaches sustain the open-minded and open-ended progress of science and what constitutes misconduct. The best teachers may be those who have a deep experience of being at the leading edge of research.

5.4. Reprimand

The commission regards this as a serious case where an appropriate reprimand is required. It was not in the commission's mandate to propose disciplinary procedures.

[redacted]

Report completed on June 17, 2015