Open letter from an anonymous group of experts in response to the anonymous commission report investigating the publications of Catherine Jessus' laboratory

June 12, 2018

Augmented translation of the original document published on May 11, 2018, entitled:

"Lettre ouverte d'un groupe d'experts anonyme concernant le rapport de la commission anonyme ayant enquêté sur les publications dont Mme Jessus est co-auteur"

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1 Background

In September 2017, eleven papers from Catherine Jessus' lab, published between 1998 and 2017, were evaluated and challenged by the post-publication peer-review site *PubPeer*. More precisely, 21 figures with suspicious manipulations have been designated as fraudulent. A commission of inquiry was designated by the UPMC/Sorbonne University and by the CNRS to investigate these allegations of scientific misconduct in the publications of Mrs Jessus and her co-authors. This commission of inquiry, consisting of an unknown number of members who concealed their areas of expertise and their identity, prepared a report that they made public on February 21, 2018 on the following CNRS web page:

- `http://www2.cnrs.fr/sites/communique/fichier/rapport_conclusions.pdf`
- `http://www2.cnrs.fr/sites/communique/fichier/rapport_analyse_detaillee.pdf`
- `http://www2.cnrs.fr/sites/communique/fichier/annexe1.pdf`

The conclusions stated in this report were to absolve Catherine Jessus and her co-authors of all blame and of any scientific fraud.

2 The reasons for this open letter

This open letter was written in response to these conclusions, which are factually diametrically opposed to the findings that emerge from the detailed analysis, article by article, of the same report that is provided below.

The report of the committee of inquiry in fact notes and admits almost all manipulations of images highlighted by *PubPeer* did indeed occur. On the other hand, the report in no way admits that these manipulations of images are fraudulent and justifies them one by one, thanks to false arguments that create an illusion of fairness and objectivity to non-specialists.

However, as evident to any biologists using these techniques, the arguments developed by the commission of inquiry are scientifically baseless. The degree of confusion and factually incorrect pronouncements are such that they reveal the obvious incompetence of this commission of "experts" and discredit its aptitude to give a serious opinion.

The report of the commission has, in the context of this investigation, consequences even more serious than discrediting its own capabilities as an investigative tool and casting serious doubts on the integrity of the host institutions that it represents. The commission actually recommends that this type of image manipulation is perfectly acceptable in the scientific community, whereas, as we explain in detail below, these manipulations are quite simply fraudulent. This kind of data fabrication can in no case be accepted either in a working meeting in a laboratory, nor as part of a presentation to a conference nor in a peer-reviewed journal such as those in which the researchers in biology community publishes.

In this open letter, after a preamble intended for non specialists in Biology, our group of experts, made up of women and men, geneticists, biochemists, cell biologists and molecular biologists, undertook a critical and scientific analysis of each and every one of the 21 figures in question, and resulting in 20 conclusions diametrically opposite to those of the inquiry commission.

3 Preamble for non-experts in biology and/or western-blot

3.1 How to design a biology experiment?

Unlike some experimental sciences which can control all the parameters of their model and can study one variable at a time, living experimental sciences are confronted with a very large number of uncontrolled variables. Designing an experiment therefore consists in keeping constant, as far as possible, the maximum number of parameters and to vary only the element you wish to study.

Let us take an example. Let's try to design an experiment that would measure the effect of a drug "D" on the synthesis of two proteins "Pa" and "Pb". First of all, we must choose the biological model. Among all the possible models (plants, cultured cell lines, bacteria, batrachian eggs or embryos etc.) every biologist has his favourite one. For example, let's choose the batrachian egg the most commonly used in research laboratories, that of xenopus (toad from South Africa). Let's call him "X" and give him the drug D by injection or rather, let's first make the assumption that if D has an effect on Pa and Pb, this should be measurable at a precise concentration. In order to determine this concentration we will inject X with increasing doses of D, i.e. D0 to D5. Then, after injection, X will be ground and homogenized in a liquid called a buffer. The proteins Pa and Pb of X will be then extracted and analyzed by western-blot, a technique that will be explained in the next paragraph.

Let us return to X. X is an individual cellular entity, a unique sample that must receive only one given concentration of drug D by injection. To analyze the effect of six different drug concentrations, we'll have to design an experiment with six samples, X0 to X5. Consequently, X0 will be processed by D0, X1 processed by D1,... X5 by D5, then the samples will be compared to each other.

At this point, you should object and let us know that this experiment is not rigorous. Indeed, if Pa and Pb of the sample number 6 are synthesized in greater quantity than in the other 5 samples, how can we know if this phenomenon is attributable to D5 or an individual characteristic of X5? Indeed you would be right, if X0 to X5 were genetically different, or if they were not the same age, or if they had lived in different environments; there would be too many variable parameters and the results of the experiment would be uninterpretable. That's why biologists choose X0 to X5 as similar as possible: same genetic inheritance, same breeding condition, same age, same feed etc.

But this is not enough because variations can be introduced by the experimental conditions. A rigorous experiment should focus on manipulating X0 to X5 in the same experimental conditions. For this the samples X0 to X5 will be processed by D0 to D5 on same day, even at the same time and with the same instrument, will also be crushed in the same conditions and by the same instrument then will finally be homogenized in the same buffer and placed in identical tubes at the same temperature. At this stage of the experiment, since only the concentration of D varies (from 0 to 5) from one sample to another, it will be possible to determine if D has an effect on Pa and Pb and, if so, from which concentration will D have an effect on Pa and Pb.

Here again, you could raise an objection: indeed X1 to X5 have undergone an injection of drugs with a syringe and thus experienced injection-related stress, which X0 did not because D0 means a drug concentration equal to 0 (and therefore no drug), this stress could have an influence on the synthesis of Pa and Pb. That's the reason why a rigorous experiment will take this possibility into account and X0 will also undergo a injection of the same volume but without drugs, containing only water, the same water that have been used to dilute drugs D1 to D5.

X0 is of crucial importance in this experiment, it is the internal control: it is to X0 that will

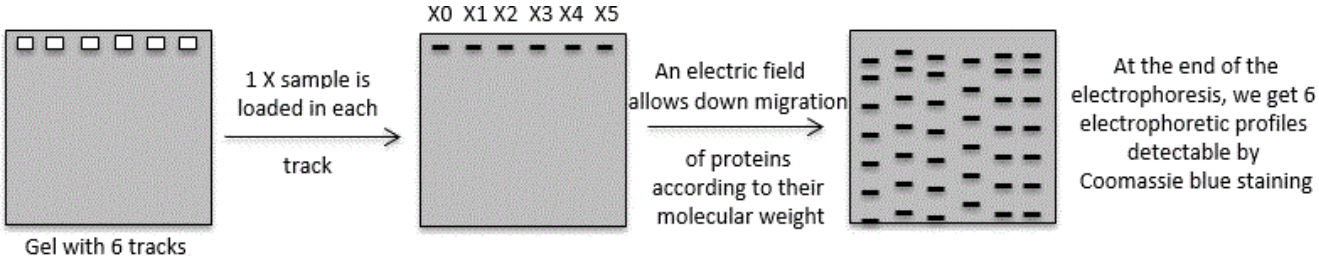


Figure 1: Electrophoresis

be compared the other 5 samples when the results are analyzed. The continuation of the experiment, i.e. the western-blot, will also have to be carried out with the same concern, keep experimental conditions constant for all samples including the internal control.

3.2 What's a western-blot?

It is a three-step technique (electrophoresis, transfer and detection) that allows to visualize one or more proteins given in the form of black bands on a photographic film and to determine, with respect to an internal control, changes in weight and concentration.

Electrophoresis : this step separates a mixture of proteins (*e.g.* proteins contained in X after milling and homogenization) by migrating them through a porous vertical gel (or molecular sieve) under the effect of an electric field. Low molecular weight proteins (small proteins) migrate more easily through the pores of the gel than high molecular weight proteins (large proteins) that are delayed by friction within the gel. Therefore, at the end of electrophoresis, the proteins of the mixture will be separated, the large proteins at the top of the gel, the small ones at the bottom, and the proteins of intermediate weight in the middle. This separation is called an electrophoretic profile.

To carry out this gel, the experimenter mixes very precise volumes of 4 products using graduated pipettes and micro-pipettes. Since there are pipetting uncertainties inherent of the instruments used, the pore size may vary from a gel to another and thus the electrophoretic profile of the same sample will never be strictly identical from one gel to another.

For this reason, we can compare only the electrophoretic profiles of samples that have migrated on the same gel. In our example, it will therefore be necessary that the 6 samples X0 to X5 migrate in the same gel, which is technically possible: the smaller gels have the space for a dozen samples. How to do for experiments that contain more than 10 samples? It is best to use a larger gel, so that all the samples of the experiment migrate in the same gel however if it is not possible we will use 2 different gels, but - be careful! We won't be able to compare them!

How then to interpret the results? Thanks to the internal control sample, the X0 of our example. This X0 will have to be loaded on both gels, so all samples can be compared to this internal control which underwent the same electrophoresis.

Transfer : proteins separated by electrophoresis are moved to another support. For that, a nitrocellulose membrane of strictly the same size as the gel is applied on the gel and then an electric current is applied so as to migrate the proteins from the gel to the membrane. Under these conditions, the place that proteins occupied in the gel at the end of electrophoresis is retained on the membrane.

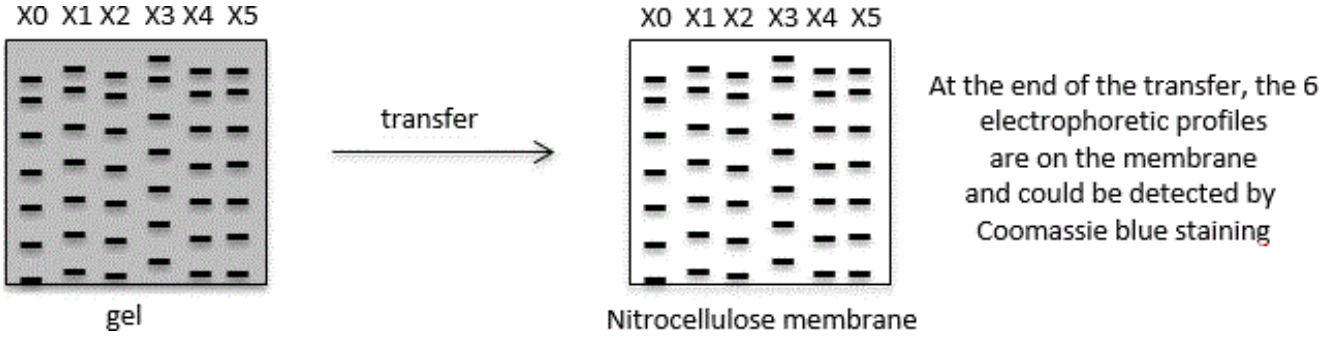


Figure 2: Transfer

Detection : if a single protein P is studied, the protein is detected directly on the membrane with an antibody directed specifically against P.

In the example we have chosen to illustrate (see *figure 3, case n° 1*), we undertake to study 2 proteins Pa and Pb, the first of high molecular weight located in the upper part of the membrane and the second of low molecular weight located in the lower part of the membrane. In order to identify these two proteins, the membrane will be cut out horizontally in 2 parts. The upper part, or top panel, will be incubated with the anti-Pa antibody that will bind specifically to the Pa protein, and the lower panel will be incubated with the anti-Pb antibody that will specifically bind to the Pb protein. Then these antibodies, and therefore the proteins to which they are attached, will be detected as strips on a photographic film by an immunohistochemical reaction that use antibody, enzyme and chemical developer. The intensity of these bands is proportional to the amount of protein, but also to the concentration and the incubation time of the developer; it is therefore essential that the samples were revealed under strictly identical conditions.

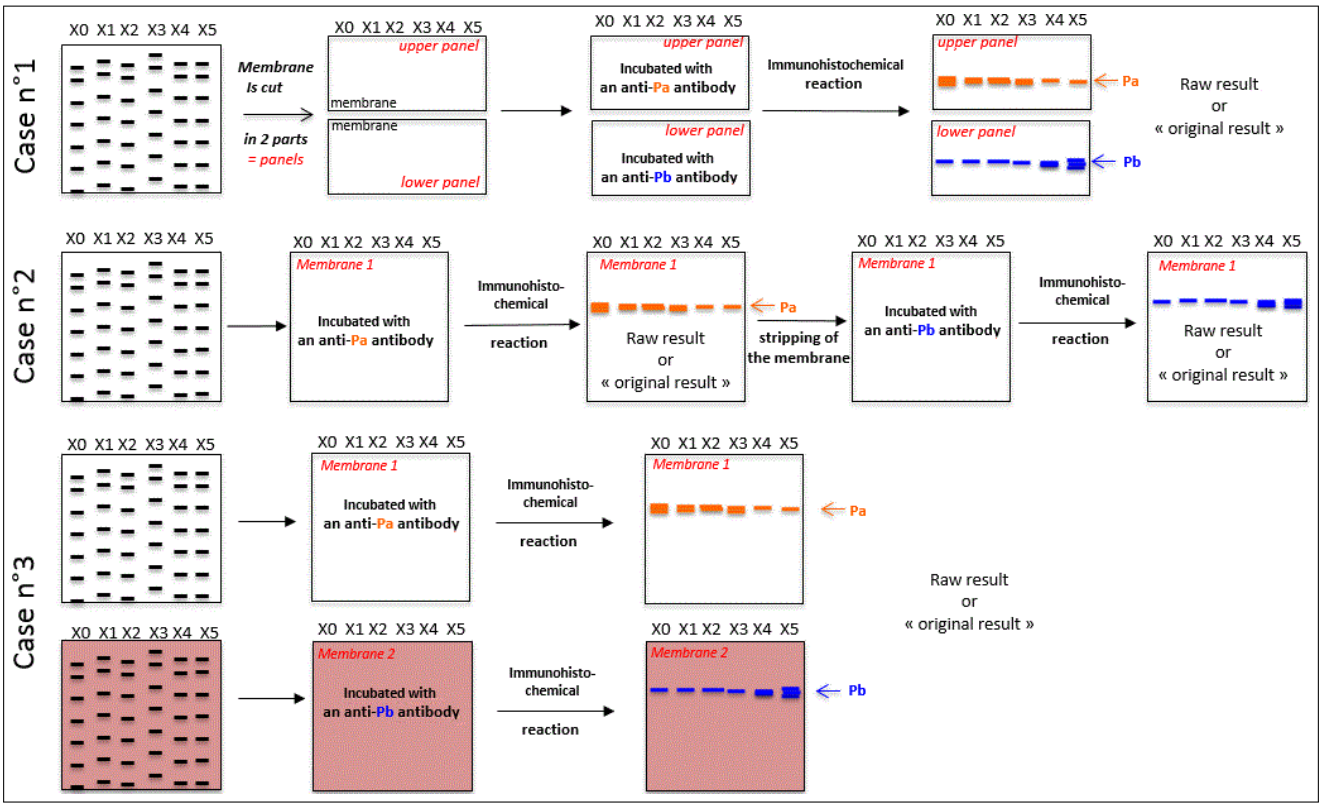


Figure 3: Detection – 3 possible cases

In some cases, the two proteins studied (Pa and Pb) may have the same molecular weight. They will therefore migrate to the same location in the gel and be transferred to the same place on the membrane. Their detection will require a slightly different procedure from the one previously described. Two detections are necessary and are schematized in the figure 3 by cases n°2 and n°3:

- In the case n°2, the first protein is detected, then the membrane once stripped in order to remove the antibodies used for the first detection, is used again for the second detection, the one to identify Pb.
- In the case n°3, two identical gels are made in parallel with the same samples, the proteins contained in the first gel will be transferred to the membrane 1 which will be incubated with the anti-Pa antibody and the proteins of the second gel will be transferred to membrane 2 which will be incubated with anti-Pb Ac.

NB: When the samples are incubated in the presence of radioactive atoms capable of being incorporated into the proteins, the protein detection step does not require the use of an antibodies. The electrophoresis gel containing the radioactively labelled proteins is put directly in contact with an X-ray film in a dark chamber. Radiation emitted by radioactive decay will expose the film by forming strips at the exact location of the proteins in the gel. This detection is called autoradiography.

3.3 How to present the result of a western-blot?

In the case of a western-blot or an autoradiography, the result must be presented so that it can be interpreted by the reader. Thus the presentation must be as close as possible to the original document (or raw result) as schematized in figure 4 (A) of the preamble. In this diagram, the top and bottom panels of the same membrane are separated by a horizontal line (case n°1), the first detection and the second detection of the same membrane are also separated by a horizontal line (case n°2), and two different membranes are separated by a vertical line (case n°3).

Modifications can possibly be made, such as noise attenuation for a better visualization of the bands or the modification of the intensity or the contrast of the bands. These changes, however, have limitations dictated by the interpretation of the experiment itself. The main of these limitations (we have already addressed it in paragraph 1) How to design a biology experiment?) is to keep constant experimental conditions for all samples until the final presentation. Therefore, if background noise attenuation is required, it must be achieved on all samples of the same panel or membrane, as well as for the intensity and contrast. All western-blot image modifications that fit into this framework (see Figure 4) are, by definition, good scientific practices, while outside this framework it is a question of bad scientific practices aiming to manufacture or falsify intentionally a scientific result. We have illustrated these image manipulations in Figure 5.

The withdrawal of some bands corresponding to irrelevant samples does not alter the interpretation of the results and can also be achieved as described in Figure 4, case n°1B to 3B. In this diagram, the electrophoretic profiles X2 and X3 have been removed and both right and left ends of the same gel have been huddled together. However, this type of manipulation called splicing is rarely used in publications for obvious reasons of scientific integrity. Not because they involve scientific misconduct, but because it is impossible, in the absence of the original documents, to tell the difference between the legitimate assembly of distant parts of the same gel, and the fraudulent assembly of two different gels, which cannot be legitimately compared

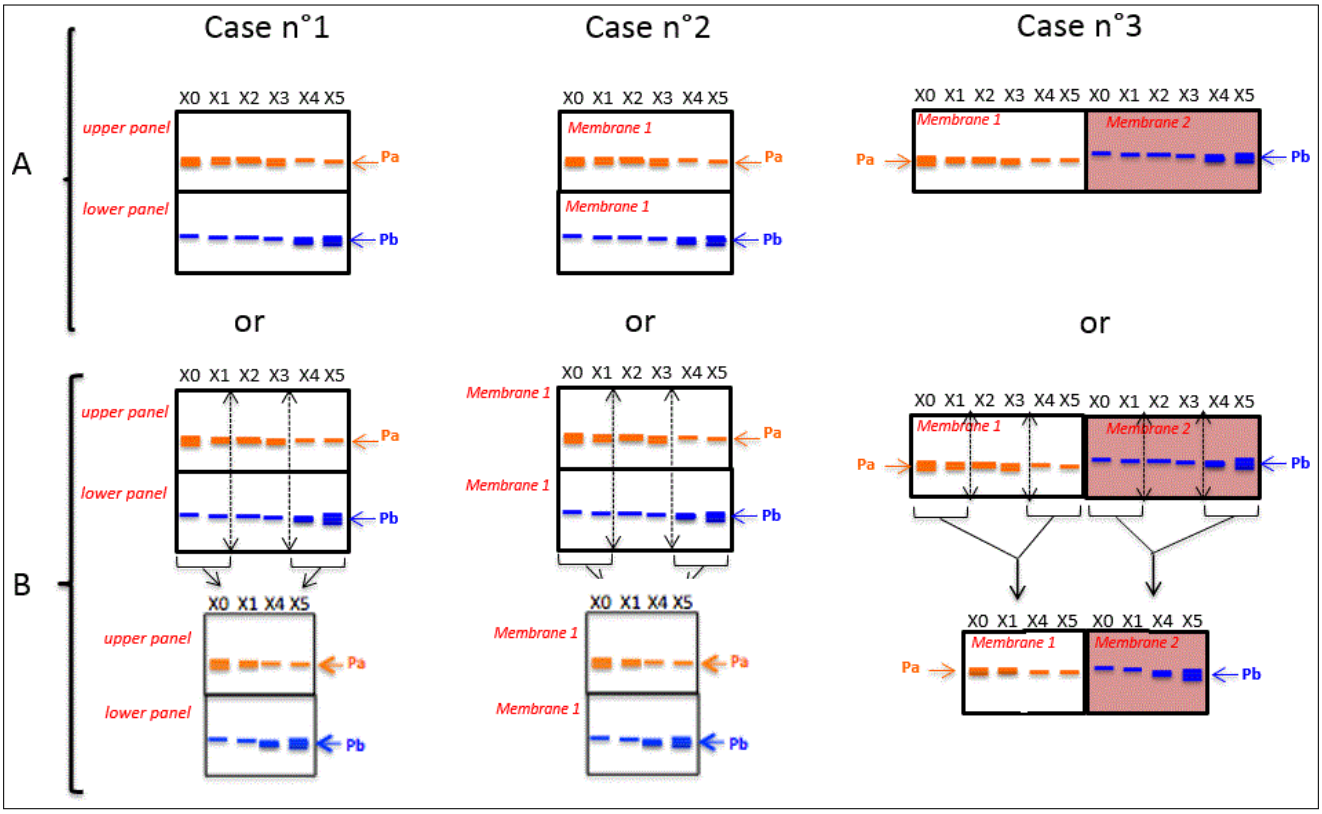


Figure 4: Different constructions of a western-blot figure

(figure 5 cases n°5A, 5B, 6A and 6B). Some journals do tolerate these legitimate assemblies coming from the same gel while other more demanding reviews accept even these legitimate figures only on the condition that access to the raw data results is provided. One such journal is *Cell Cycle* (see Appendix Annex I page 46).

It should be noted that the vast majority of peer-reviewed journals in Biology publish for some years in the section entitled “instructions to authors” a paragraph on image manipulations (see annex) acceptable or not for publication (for review see [Rossner and Yamada, 2004]). This paragraph which was non-existent in the years 1990 has appeared over the past fifteen years and has become increasingly detailed for trying to reduce cases of fraud identified by publishers.

3.4 Archiving of experiments

All experiments (materials, protocols and results) should be carefully recorded daily in the experiment author’s laboratory notebook. This notebook, property of the Research Institution, must be numbered and archived by the laboratory so that it can be found at any time and consulted by the members of the laboratory or by a commission of inquiry[1].

[1] http://www.cnrs.fr/infoslabos/cahier-laboratoire/docs/cahierlabo.pdf

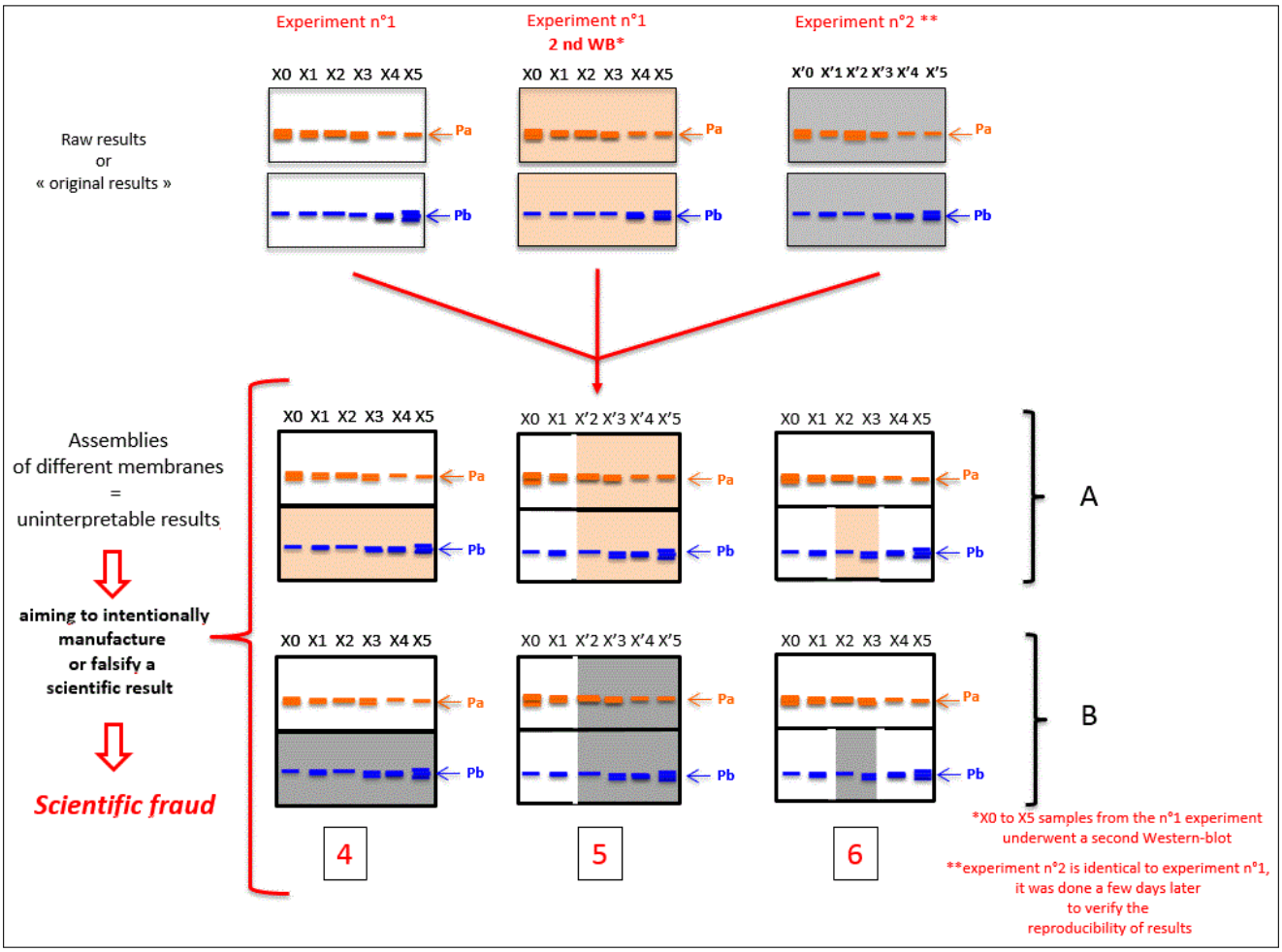


Figure 5: Image manipulations

4 Critical scientific analysis of commission report, article by article

Article 1 Thibier, C., De Smedt, V., Poulhe, R., Huchon, D., Jessus, C., and Ozon, R. (1997). In vivo regulation of cytostatic activity in Xenopus metaphase II-arrested oocytes. Dev Biol 185, 55-66.[2]

We first analyzed the figure 7 of this article challenged by *PubPeer*:

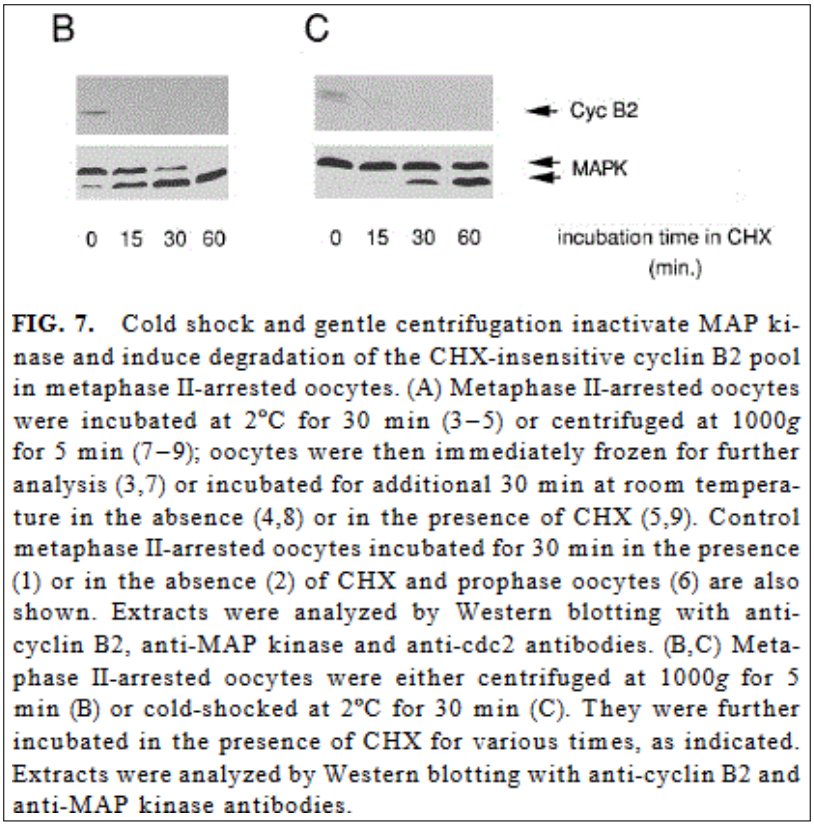


FIG. 7. Cold shock and gentle centrifugation inactivate MAP kinase and induce degradation of the CHX-insensitive cyclin B2 pool in metaphase II-arrested oocytes. (A) Metaphase II-arrested oocytes were incubated at 2°C for 30 min (3–5) or centrifuged at 1000*g* for 5 min (7–9); oocytes were then immediately frozen for further analysis (3,7) or incubated for additional 30 min at room temperature in the absence (4,8) or in the presence of CHX (5,9). Control metaphase II-arrested oocytes incubated for 30 min in the presence (1) or in the absence (2) of CHX and prophase oocytes (6) are also shown. Extracts were analyzed by Western blotting with anti-cyclin B2, anti-MAP kinase and anti-cdc2 antibodies. (B,C) Metaphase II-arrested oocytes were either centrifuged at 1000*g* for 5 min (B) or cold-shocked at 2°C for 30 min (C). They were further incubated in the presence of CHX for various times, as indicated. Extracts were analyzed by Western blotting with anti-cyclin B2 and anti-MAP kinase antibodies.

Figure 6: **Figure 7 of the manuscript**

The organization of the figure 7 and its legend, are very clear and consistent. They tell us that in B as in C, the experiment is designed to make vary only one parameter, the incubation time of xenopus oocytes with the cycloheximide drug (CHX). Thus in experiment B, as in experiment C, all the samples are treated in exactly the same way and undergo either all the same centrifugation (in B), or the same thermal shock (in C).

However, these samples differ from each other in incubation time with CHX for 0, 15, 30 or 60 minutes (min.). In experiment B as in experiment C, 4 samples are from left to right: the internal control (the equivalent of the X0 of the preamble, page 6) treated 0 min with CHX then the samples X15, X30 and X60 treated respectively 15, 30 and 60 min. by CHX.

As explain in the preamble, X15, X30 and X60 can be compared with each other and can be compared with X0, at the condition to undergo the **same** electrophoresis and the **same** transfer on nitrocellulose membrane. As also indicated in the preamble (page 8), the membrane will be divided into two panels, the upper panel incubated with anti-Cyc B2 antibody and the lower panel incubated with the anti-MAPK antibody. After detection with the antibodies, the 2 panels

[2]Corresponding author : R. Ozon, pubmed: 9169050, doi: 10.1006/dbio.1997.8543, issn: 0012-1606

must be reassembled in the respective place they occupied before cutting the membrane, and that is the figure of experiment.

This seems to have been done by the authors, as indicated in the legend and in the presentation of Figures 7B and 7C. It should be noted that the authors fully respected the signal, recommended today, as in 1997, for such assemblies, by separating, on the figure, the upper panels from the lower panels by a white space.

Thus reassembled, each figure allows on the one hand to compare the 4 electrophoretic profiles between them, and on the other hand, within the same panel to compare the intensity of the 4 samples between them. Any additional assembly (*e.g.* inside a panel) from different membranes (as described in Figure 5 of the preamble, case n°5 or 6 page 11), would be completely inappropriate as it would make the experiment uninterpretable.

However, the *PubPeer* site has highlighted two such assemblies in the lower panels of Figures 7B and 7C (Figure 7).

PubPeer allegation indicates that the blue arrows (Figure 7) point to junctions that most probably result from an assembly of two different membranes (and not from an internal splicing (see definition page 9) since they are absent in the two upper panels). If that is true, it is fraudulent image manipulation.

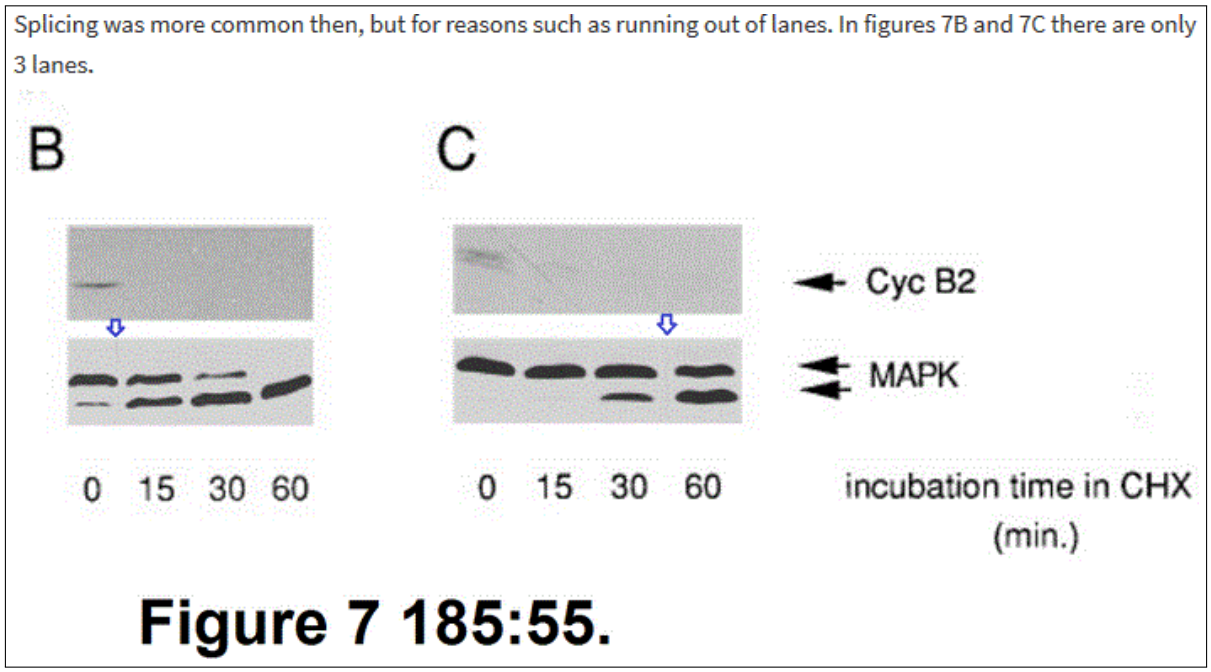


Figure 7: **Figure 7 of the manuscript challenged by *PubPeer***. Blue arrows point to junctions that result from an assembly of two different membranes. This is fraudulent image manipulation.

The inquiry report indicates that the original was not found, which, in all rigour, does not allow it to confirm, nor to invalidate, that assemblies inside the panels were carried out by the authors. However, the committee does not rule out the possibility that these arrangements could have been made and justifies them by three totally irrelevant arguments.

The first argument used is that each incriminated panel was made by the assembly of distinct autoradiographic films but coming from the same experiment. First of all, we notice that the commission confused autoradiography (implementing a protocol using radioactivity to detect molecules) with western-blot (protocol using antibodies coupled to immunochemical reactions of molecules), whereas it is clearly indicated in the legend of the figures, as on the figures, that the detection was performed using antibodies. It is therefore a western-blot and

not an autoradiography. On the other hand, as indicated in the preamble (pages 7 and 8), samples from the same experiment cannot be compared if they have not undergone the three stages of the western-blot together: electrophoresis, transfer and detection. This first argument is therefore not admissible and even discredits the committee in terms of its scientific rigour.

The second argument used consists in legitimising such a montage ("different films but from the same experiment") by claiming that such an assembly is indicated in the legend and that this is a common practice. However, neither in the legend nor in the organization of the figure is such an assembly indicated. Moreover, it is not at all a common practice, because such a practice (see preamble, page9) would not allow the analysis of results and is in fact unacceptable by any scientific journal [Rossner and Yamada, 2004]. This second argument is no more admissible than the first one and reflects the ineptitude of the inquiry commission to understand a legend or interpret a figure.

The third argument used by the commission of inquiry seems to be a criticism to the authors, who did not indicate such a montage by a vertical line inside a panel. However, the commission excuses the authors by then claiming that putting the vertical lines which indicate the assembly of two different membranes, was not yet recommended in 1997. This clarification is absent in the instructions to authors' section of 1997 quite simply because there was no paragraph, at the time concerning the manipulation of images, NOT because this was acceptable. In fact vertical lines were indeed generally used in 1997, including by the authors of this very article, as can be seen at figure 1 of the manuscript (figure 8).)

A vertical line clearly indicates the boundary between two different gels of the same experiment. Thus the reader is advised that he cannot compare the samples of the two different gels. On the other hand, he can fully compare each sample (each post GVBD time) to its internal control (-CHX). The third argument of the commission is therefore totally fallacious, vertical lines have always been good practice to highlight legitimate assemblies (as stated in the preamble page 9).

Our conclusion for this article is that there can be no exoneration of this fraud in the absence of the original experimental result. We remind you that any experiment (material, protocols and results) must be scrupulously recorded daily in the laboratory notebook of the author of the experiment. This notebook, property of the Research Institution, must be archived by the laboratory in order to be found and consulted by the members of the laboratory or by a commission of inquiry. Indeed, only the interpretation of the original result of the experiment can deliver a scientific message.

It is therefore unusual that a commission of inquiry on scientific integrity could not consult the laboratory notebooks containing the details of the experiments and the original results. It is strange that she states that the scientific merits of the article are not challenged while the scientific message of this figure is unavailable. These paradoxes, as well as the inadequate argumentation used by this commission to justify putative assemblies, are a reflection of its total incompetence.

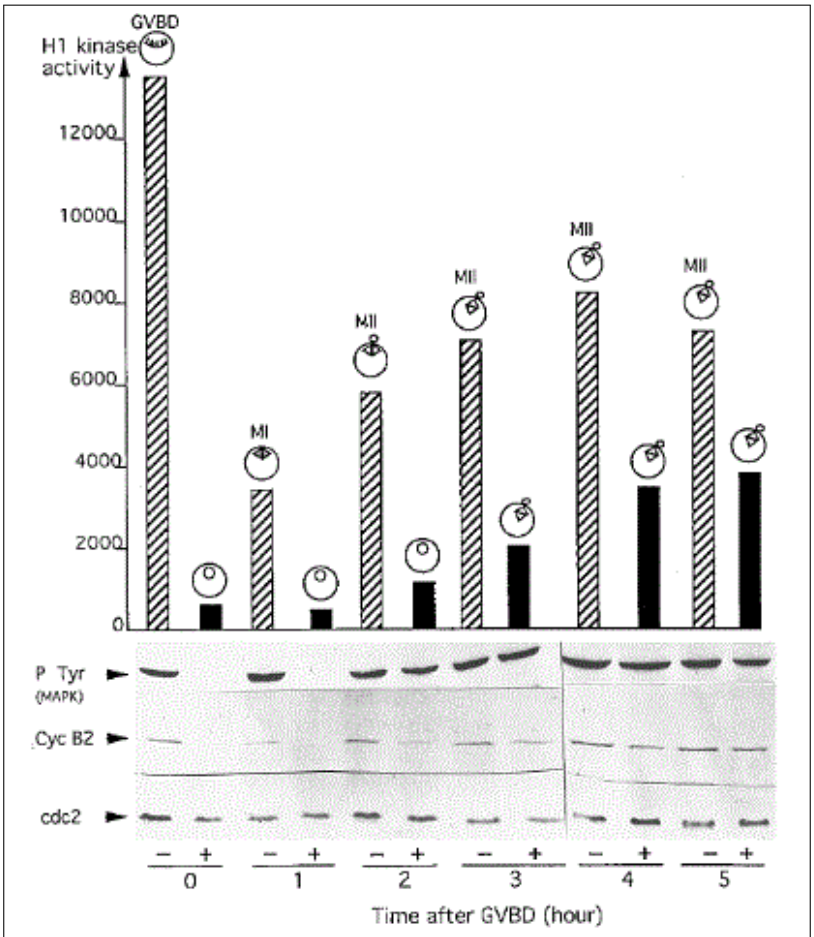


FIG. 1. Effect of CHX on cdc2 kinase and MAP kinase activities and cdc2 and cyclin B2 levels during the post-GVBD period. At GVBD time or at various times after GVBD, maturing oocytes were incubated for 1 hr in the absence (hatched bars and "−") or in the presence (solid bars and "+") of CHX. H1 kinase activity was then assayed, and immunoblotting with anti-phosphotyrosine (top), anti-cyclin B2 (middle), and anti-cdc2 (bottom) antibodies was performed. The presence of a nucleus and the spindle position are schematically represented at time of CHX addition (hatched bars) or after 1-hr CHX treatment (solid bars).

Figure 8: **Figure 1 of the manuscript**

Article 2 Rime, H., Talbi, N., Popoff, M.R., Suziedelis, K., Jessus, C., and Ozon, R. (1998). Inhibition of small G proteins by clostridium sordellii lethal toxin activates cdc2 and MAP kinase in Xenopus oocytes. Dev Biol 204, 592-602.[3]

PubPeer revealed an image manipulation in figure 4 of this article: The sample 2 photographic image boxed in yellow from figure 4A has been copied, pasted and relabelled to make figure 4B. This kind of image manipulation is a deliberate and fraudulent invention of scientific results.

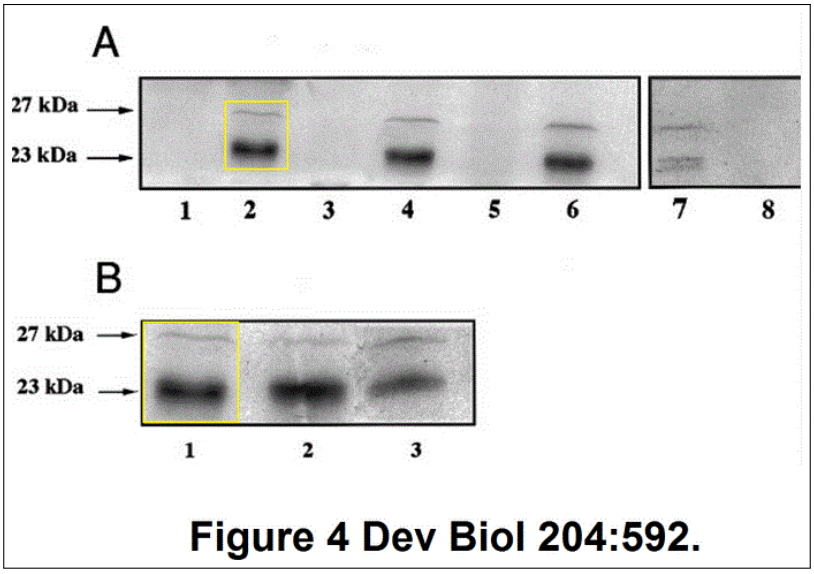


Figure 9: **Figure 4 of the manuscript challenged by *PubPeer***. The sample 2 photographic image boxed in yellow from figure 4A has been copied, pasted and relabelled to make figure 4B. This kind of image manipulation is a deliberate and fraudulent invention of scientific results.

The inquiry report begins by pointing out that the original was not found. As regards this second case of original document not found, and given that the committee still does not take offence, we are entitled to ask ourselves whether this commission of inquiry on integrity is aware of the national charter of ethics for research professions which stipulates:

> *"All raw results (which belong to the Institution) as well as the analysis of the results must be kept in such a way as to allow their verification".*

Despite the absence of an original, the commission admits that there has been duplication of Track 2 (boxed in yellow by *PubPeer*) from figure 4A to figure 4B. The commission affirms that this is not an error but a *"correct"* reuse of this track 2 and *"considers that no correction is necessary"* because *"both panels are from the same experiment"*.

The commission is wrong for three reasons:

First reason. Even if it were the same experimental condition within the same experiment, the autoradiographic image of sample 2, which underwent electrophoresis in track 2 of the gel in figure 4A of the manuscript, should not have been reused to match the autoradiographic image of another electrophoresis gel. As explained in the preamble, the electrophoretic profile of a same sample will never be strictly identical from one gel to another (page 7) and the intensity of the bands will never be identical from one autoradiographic revelation to another (page 8). It is only possible to compare between them, the electrophoresis profiles and the

[3]Corresponding author : R. Ozon, pubmed: 9882492, doi: 10.1006/dbio.1998.9069, issn: 0012-1606.

intensities, of samples having migrated in the same gel and having undergone the same autoradiographic revelation. However, here, the sample '+LT stage IV', having undergone only one electrophoresis and only one autoradiography, can only be compared to samples 1, 3 to 6 of figure 4A of the manuscript. Intentionally reusing the image of this sample to attach it to the image of samples that have migrated into another gel, falls under the cases n° 5B or 6B described in figure 5 of the preamble (page 11). It is an image manipulation aiming to make and/or to falsify a result, making the image uninterpretable.

Second reason. The error is even more serious since the samples are not the same. Track 2 of figure 4A of the manuscript is stated to correspond to proteins extracted from a stage IV oocyte, whereas track 1 of figure 4B is stated to correspond to proteins extracted from a stage VI oocyte (see the legend of figure 4 of the manuscript). Since the images are identical but labelled differently, this means that at least one of these gels represents invention of scientific results and is completely and utterly fraudulent.

Third reason. The commission mentions (as for Article 1) that a vertical line could have marked the boundary between tracks 1 and 2 of figure 4B of the manuscript, but justifies its absence by claiming that the vertical lines, signaling the assembly of two different membranes, were not recommended in 1998. We have already refuted this argument in the previous article. Indeed, no image manipulation was recommended or prohibited by the editors of the time (1998) since there was no paragraph at all concerning the manipulation of western-blot or autoradiographic images. However, vertical lines were used in 1997, as we demonstrated previously for Article 1 (see page 14), and in 1998, as can be clearly seen in figure 4A of the manuscript: the boundary between samples 6 and 7 is clearly marked to indicate that they are different gels. Conversely, in the case of figure 4B, the organization of figure without vertical lines, as well as the legend, suggest that it is the same gel.

Concerning the argument *"no element questioning the scientific message of the article"* already used by the committee in Article 1 and already refuted in our comments, we wish exploit this example to demonstrate that falsification of a result necessarily has consequences on the scientific messages delivered:

> In this article, the experiments of figure 4 carried out *in vitro*, present the results of a glucosylation reaction (glucose binding) of proteins. Xenopus oocyte extracts are incubated in the presence of a glucosyltransferase (LT) which incorporates carbon-14-labelled radioactive glucose into some proteins, including Ras, Rac and Rap proteins (molecular weights around 21 kilodalton (kDa)).
>
> The intensity of the signals, proportional to the incorporation of radioactive glucose into proteins, is analysed by autoradiography during 3 oocyte stages: stage IV (oocyte of 0.8 mm in diameter; prophase stage of meiosis during which vitellogenesis begins), stage VI (oocyte of 1.2-1.3 mm in diameter, in prophase I of meiosis, mature oocyte at the end of vitellogenic growth) and stage VI in metaphase II of meiosis (oocyte of 1.2-1.3 mm in diameter).
>
> In the paragraph "Materials and Methods", sub-paragraph *"in Vitro Glucosylation of Oocytes Extracts"*, of the manuscript (p. 593) it is specified that a hundred oocytes in prophase were used initially in this experiment for the homogenization of each category of oocytes. For each stage studied, the quantity of samples deposited in final in the electrophoresis gel is indicated as being the equivalent of 5 oocytes.
>
> A stage IV xenopus oocyte contains about 14 micro-grams ($14\,\mu g$) of non-vitellogenic proteins; a stage VI oocyte contains about $25\,\mu g$ or about twice as much ([Smith et al., 1984] and [Davidson, 1986]). By depositing an amount equivalent to 5

oocytes in each gel track, a total of $14 \times 5 = 70\,\mu g$ of protein is deposited for the “Stage IV Oocyte” sample and a total of $25 \times 5 = 125\,\mu g$ of protein for the “Stage VI Oocyte” sample. The almost identical signal strength between tracks 2, 4 and 6 of figure 4A thus demonstrates that approximately twice as many proteins incorporated the radioactive glucose in stage IV oocytes (track 2) versus stage VI oocytes (tracks 4 and 6).

In figure 4B, the copy/paste assembly made by comparing a signal obtained from stage IV oocytes (track 1) and signals obtained from stage VI oocytes (track 2 and 3), is incorrect, contrary to what figure out the commission of inquiry. This intentional presentation affects the scientific message of the conclusion of this experiment. It is indeed written in the article (p. 595) that *“This indicates that levels of major substrates of LT do not vary,...”*. However, this experiment shows the opposite because it is quite obvious that the levels of the TL substrate proteins vary between a stage IV oocyte and a stage VI oocyte, which the assembly does not in any case allow to envisage. This montage, which has modified the authentic result, is therefore a falsification that changes the scientific message of the article.

For all these reasons, the committee’s conclusion *“there is no misconduct scientific, no error, nor any element calling into question the messages of the article”* is unacceptable. We seriously doubt that this conclusion has been approved by the *Journal Developmental Biology*. If this had been the case, the committee would have provided proof of this in its report.

Article 3 Karaiskou, A., Jessus, C., Brassac, T., and Ozon, R. (1999). Phosphatase 2A and polo kinase, two antagonistic regulators of cdc25 activation and MPF auto-amplification. J Cell Sci 112, 3747-3756.[4]

PubPeer revealed image manipulations involving identical lanes to represent different experimental results. As seen in figure 10 below, the two lanes boxed in red are identical. The one on the left of figure 3B has been reused to fabricate the lane on the right and also the first lane of figure 5D. The lanes boxed in brown are also identical, the one from figure 3B has been reused to fabricate the second lane of figure 5D. The lanes boxed in blue are also identical, the one from figure 3B having been reused to fabricate the fourth lane of figure 5D. Again, as also seen in figure 11 below, the two lanes boxed in red are identical, one having been reused to fabricate the second. And lastly, as seen in figure 12 below, the lanes boxed in red are also identical, one having been reused to fabricate the other. Thus, 5 recycled images were used to fabricate the needed figures without performing the experiment they were claimed to represent - this kind of image manipulation is deliberate and fraudulent invention of scientific results.

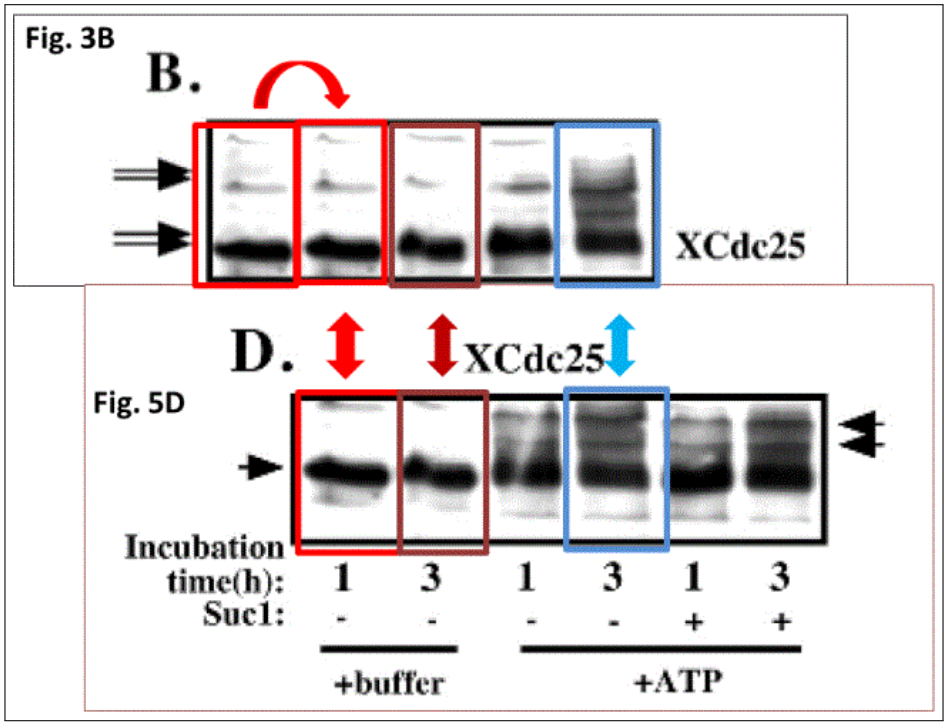


Figure 10: **Figures 3B et 5D of the manuscript challenged by *PubPeer***. The two lanes boxed in red are identical. The one on the left of figure 3B has been reused to fabricate the lane on the right and also the first lane of figure 5D. The lanes boxed in brown are also identical, the one from figure 3B has been reused to fabricate the second lane of figure 5D. The lanes boxed in blue are also identical, the one from figure 3B having been reused to fabricate the fourth lane of figure 5D. This kind of image manipulation is a deliberate and fraudulent invention of scientific results.

In the inquiry report, the commission states that the originals (without specifying which ones) have not all been found. Once again, we are surprised (see our previous comments (pages 14 and 16).

[4]Corresponding author: R. Ozon, pubmed: 10523510, issn: 0021-9533.

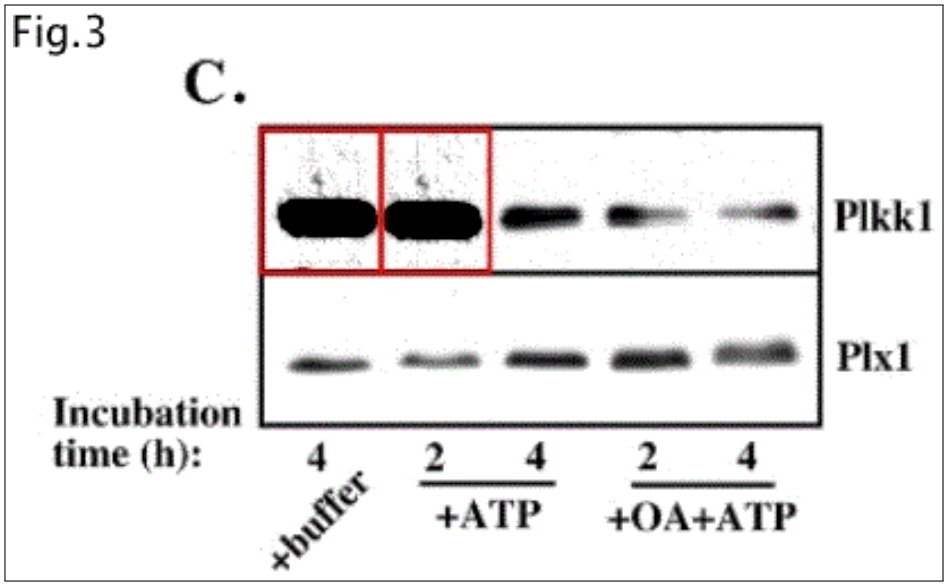


Figure 11: **Figure 3C of the manuscript challenged by *PubPeer***. The two lanes boxed in red are identical, one having been reused to fabricate the second. This kind of image manipulation is a deliberate and fraudulent invention of scientific results.

The commission does not recognize duplications within 3B and 3C gels but recognizes other duplications, and designates them as either *"legitimate duplications"* or *"assembly errors"*.

To justify the so-called legitimate duplications (blue boxes) from the 3B membrane to the 5D membrane, the commission puts forward the same erroneous argument as in the two previous articles, namely that these are the same experimental conditions within the same experiment. We assert that such an argument is inadmissible. The samples from figure 3B may only be reused on the condition that they are part of the same western-blot as the samples from figure 5D. It is absolutely unjustified to reuse the final results from one membrane to connect them to another.

To justify the so-called *"assembly errors"* (red and brown boxes indicated by *PubPeer*) the commission claims that the electrophoretic profiles being similar from one gel to another, the authors did not pick the right gel lanes at the time of the assembly. This argument, whereby the commission attempts to excuse the authors by suggesting 'unintentional' errors is completely misplaced since any assemblies from different membranes can in no case allow a correct interpretation of the experiment and are prohibited by all the scientific journals [Rossner and Yamada, 2004].

The commission claims that these errors have been corrected:

"Ms. Jessus's team found original identical experiments performed at that time. To dispel any ambiguity, it was proposed to replace the incriminated figures by new figures illustrating the same results. These replacements, relating to figures 3 and 5, "were accepted by the journals." We strongly doubt this affirmation since no replacement figure has been published to date. The commission must provide proof of this assertion.

In addition, *"the commission considers that the proposed new figures, stemming from experiments identical to those used to support the article's figures, deliver exactly the same messages as the original figures"*. How could this happen when the original figures has not been found? This argument is baseless.

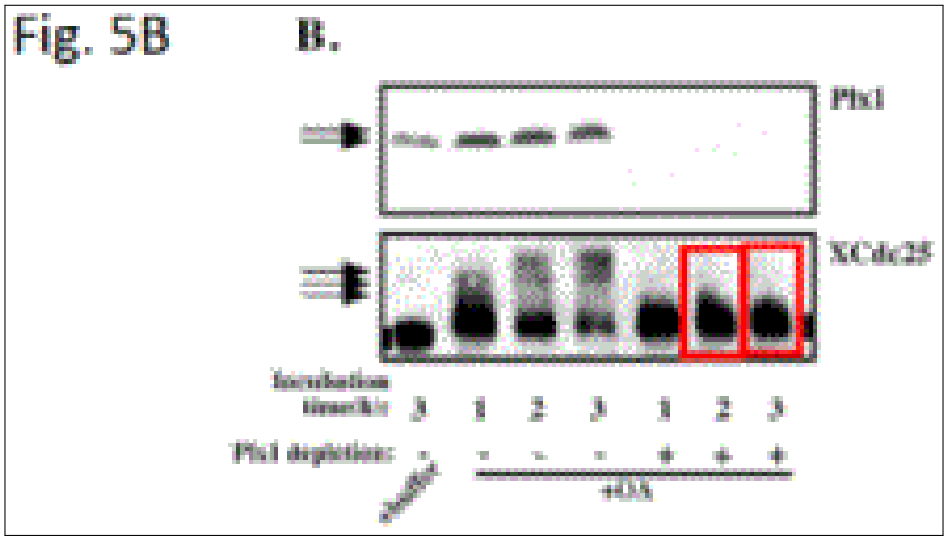


Figure 12: **Figure 5B of the manuscript challenged by *PubPeer***. The two lanes boxed in red are identical, one having been reused to fabricate the second. This kind of image manipulation is a deliberate and fraudulent invention of scientific results.

Article 4 Frank-Vaillant, M., Haccard, O., Thibier, C., Ozon, R., Arlot-Bonnemains, Y., Prigent, C., and Jessus, C. (2000). Progesterone regulates the accumulation and the activation of Eg2 kinase in Xenopus oocytes. J Cell Sci 113, 1127-1138.[5]

PubPeer revealed an image manipulation in figure 8 of this article. The two lanes boxed in yellow (see figure 13), are identical photographic images that have been used in two different figures associated with two different upper Eg2 panels. Furthermore, a slight rotation of the recycled image was performed to try to mask this illicit practice. So, these two identical images claimed to result from different electrophoretic profiles and by consequences from different experimental procedures. This is pure and unadulterated fraud.

In the inquiry report, the committee states that *"the original has not been found. On the other hand, the scans used for the assembly of the figures of this article were found in electronic form and made available to the commission"*.

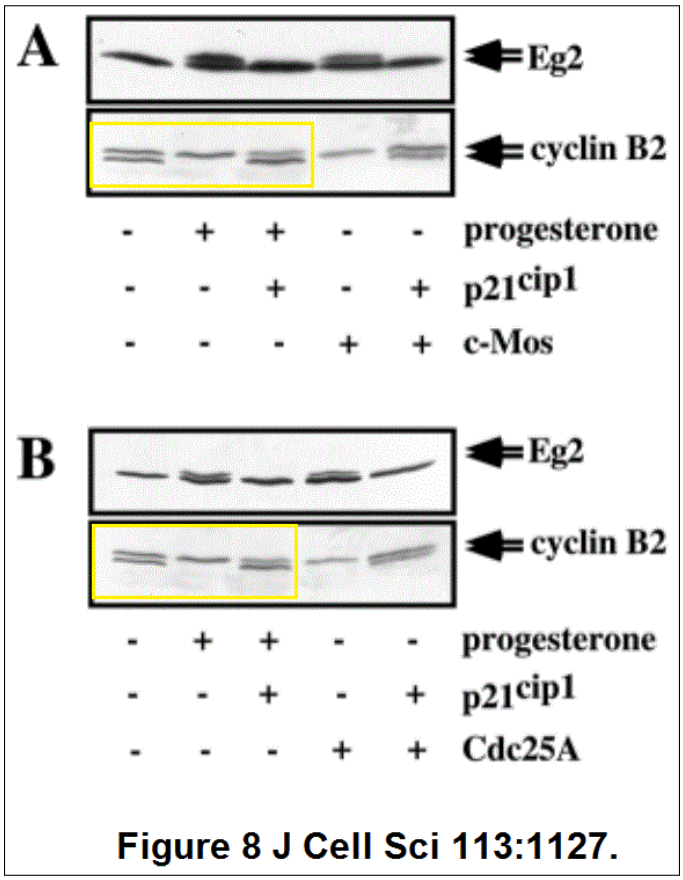


Figure 13: **Figure 8 of the manuscript challenged by *PubPeer***. The two lanes boxed in yellow, are identical photographic images that have been published in two different figures associated with two different upper Eg2 panel and with a slight rotation of the reused image performed to try to mask this illicit practice. This kind of image manipulation is a deliberate and fraudulent invention of scientific results.

The commission in its report found more duplications of western-blot bands than those reported by *PubPeer* in figure 8 of the manuscript (see figure 13). Indeed, it indicates that:

> *"Fig. 6A and Fig. 10B share two Eg2 tracks (same experimental conditions, same legends).*

[5]Corresponding author : C. Jessus, pubmed: 10704364, issn: 0021-9533.

Fig. 7A and Fig. 8B share three tracks Eg2 and Cyclin B2 (same experimental conditions, same legends).

Fig. 8A and Fig. 8B share three Cyclin B2 tracks (same experimental conditions, same legends).”

To justify these duplications, the committee puts forward the same erroneous argument as in the three preceding articles, namely that it is the same experimental conditions within the same experiment and that it is *“justified that the control of the same experiment are reused in several figures when these are all resulting from this same experiment (Eg2 in figures 6A and 10B, Eg2 and Cyclin B2 in figures 7A and 8B, Cyclin B2 in figures 8A and 8B)”*.

We assert that such an argument is inadmissible. The samples from figure 8A can only be reused on the sole condition that they actually come from the same western-blot as the samples from figure 8B; the same applies to 6A and 10B or 7A and 8B. It is absolutely incorrect to retrieve the final results from one membrane to connect them to another (see figure 5 of the preamble)!

This is clearly an image manipulation described in the case n°5A of the figure 5 of the preamble with, in addition here, rotation of the image to try to mask this illicit practice. This type of assembly, if it were transparent as indicated by a vertical boundary, as the commission suggests, would clearly signal that the figure is uninterpretable. But the commission does not seem to realize this, from the beginning of this investigation report, the report has confused the reuse of control samples and the copy and paste of control sample images, a confusion that leads it to conclude unduly and repeatedly *“that there is neither scientific misconduct, nor error, nothing that calls into question the scientific messages of the article”*.

This faulty commission report analysis thereby has serious consequences since it sends the wrong message to what is, and what is not, an acceptable practice.

Article 5 Frank-Vaillant, M., Haccard, O., Ozon, R., and Jessus, C. (2001). Interplay between Cdc2 kinase and the c-Mos/MAPK pathway between metaphase I and metaphase II in Xenopus oocytes. Dev Biol 231, 279-288.[6]

PubPeer revealed multiple image duplications in this paper. These have been indeed confirmed even by the **inquiry report**, which specifies: *"In Fig. 2, Fig. 3, Fig. 4 and Fig. 5: the control tracks ('Pro' and time 0), are identical in the presence or absence of Cip1"*. We surrounded these identical control tracks with rectangles of same color (see figure 14 page 25).

The legends, as well as the organization of these four figures, clearly indicate that for each signal by a given antibody, there are, each time, two subpanels, a -CIP subpanel in which all samples, from PRO to 180, are supposed to have been injected with water, and a +CIP subpanel in which all samples from PRO to 180, are supposed to have been injected with the CIP solution. Therefore the PRO and 0 samples of each pair of -CIP/+CIP subpanels **are not identical** since the first were injected with water and the second with CIP.

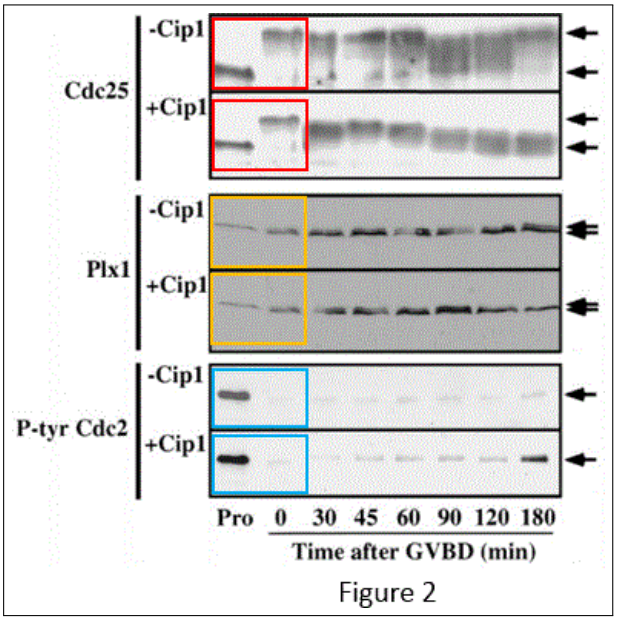
However, systematically, for each pair (-CIP/+CIP) of subpanels, the western-blot images of the PRO and 0 samples were copied from the -CIP subpanels to be pasted (with or without image distortion) to the +CIP subpanels. So two manipulations were performed. First manipulation: images from different membranes were placed together to make it look like the same membrane. Second manipulation: the image of the "PRO and 0 -CIP" samples was duplicated and relabeled as the "PRO and 0 +CIP" samples. This represents fraud involving fabrication of results, pure and simple.

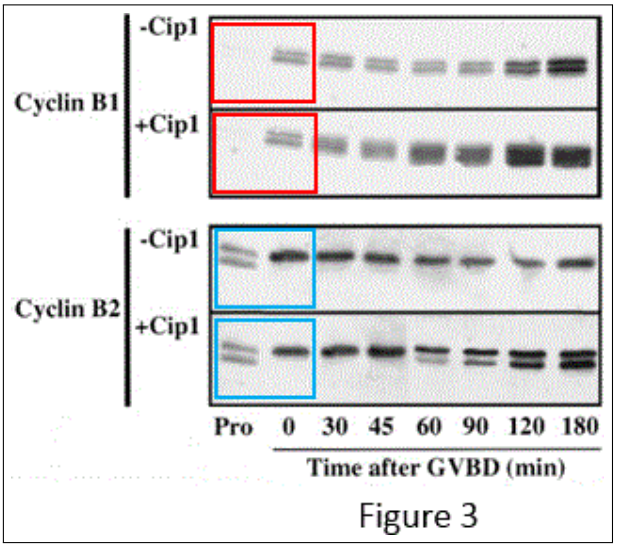
Unbelievably, the commission nevertheless tries to justify this copy/paste by claiming that *"the samples of the Pro and 0 stages were carried out only once before the injection experiment"*, and therefore, would not have been injected at all, neither with water, nor with CIP. If this were indeed the case, the experiment would be methodologically flawed since it would include at least two different parameters compared to the other samples: injection and CIP. As we saw in the preamble, a control should differ from the samples by only one parameter, namely CIP; as CIP is injected, the control without CIP must also be injected, but without CIP, therefore with water (the same water that was used to dilute CIP in the other samples). Therefore, in contradiction to the legend and organization of the figure, the commission indicate that the samples "PRO and 0 +CIP" and "PRO and 0 -CIP" are not at all what they are supposed to be, i.e. the respective controls of the +CIP and -CIP conditions. The commission does not seem to realize that such an affirmation totally negates the conclusion of the experiment.

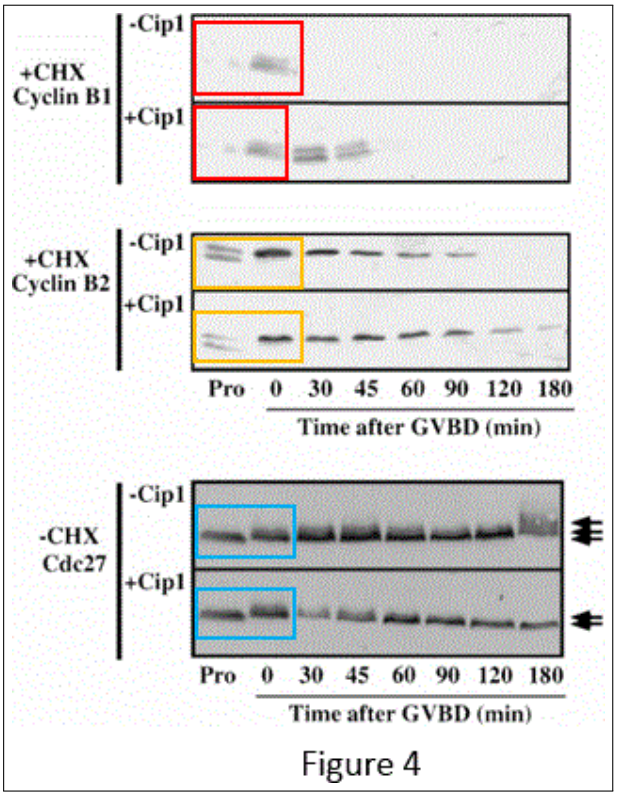
The only thing that seems important to the commission is the pretense that "PRO and 0 +CIP" and "PRO and 0 -CIP" are identical to justify the reuse of the same image from one panel to another. However, since a single image can only result from a single experiment, this means that at least one of the two 'results' was an entire fabrication without resulting from the claimed experimental manipulation!

Furthermore, as we have seen in the preamble (see pages 7 and 8), the electrophoretic profile of a given sample is never strictly the same from one gel to another, and the intensity of a band is never identical from one detection to another. Therefore, even if the reuse of the original "PRO and 0" sample had been relevant, this "PRO and 0" sample would have had to be re-run on the same western-blot as the "+CIP" samples. But it is not a sample reuse that has been made but a copy/paste of images, one of which did not correspond to the experiment it claimed to illustrate. This is simply inventing a result.

[6]Corresponding author : C. Jessus pubmed: 11180968, doi: 10.1006/dbio.2000.0142, issn: 0012-1606.







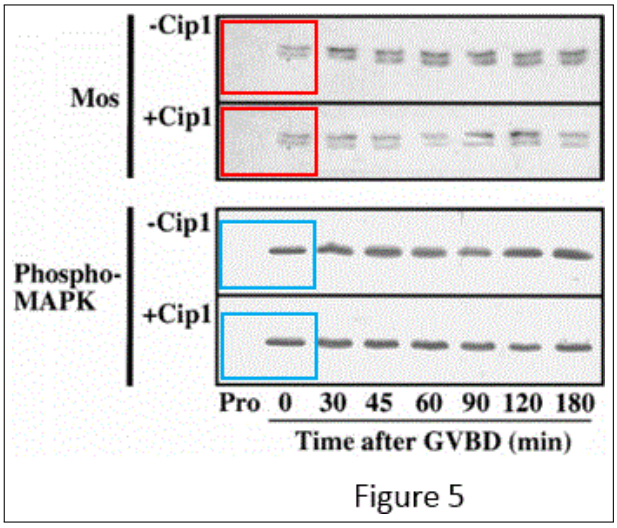


Figure 14: **Figure 2, 3, 4 et 5 of the manuscript**.In each figure, the images surrounded by the rectangles of the same colour are identical, one of which obviously did not correspond to the experiment it claimed to illustrate. This is simply inventing a result.

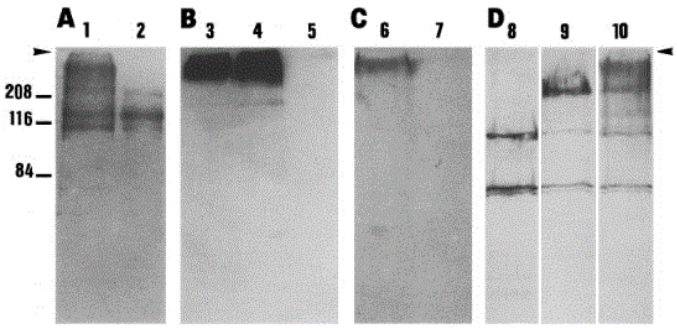


FIG. 1. Immunopurification of mab111 antigen and Western blot analysis of mab10. (A) Coomassie stain analysis of mab111 protein, immunopurified from P7–P9 rat brain urea extracts, and electrophoretically separated on a 10% SDS-PAGE gel. Prior to heat treatment (lane 1), four components with approx MWs of 200–370, 180, 140, and 120 kDa, respectively, are resolved. After boiling in sample buffer for 50 min, only three bands with approx MWs of 180, 140, and 120 kDa become apparent (lane 2). (B) Immunoblot analysis of the protein recognized by mab10. Using rat brain-derived urea extract as sample, incubation with mab10 antibody reveals a 200- to 370-kDa band (lane 3). The protein immunopurified from rat brain extract using a mab111-column is recognized by mab10, staining the 200- to 370-kDa component exclusively (lane 4). Immunoreactivity of mab10 on the mab111 antigen is completely abolished by boiling in sample buffer for 50 min (lane 5). (C) Immunoblot performed with E10 chicken brain urea extracts, using mab10 for immunodetection. Prior to heat treatment (lane 6), the high molecular weight component is stained. It disappears after heat treatment (lane 7). (D) Immunoblot performed with urea extract from P7–P9 rat brain. Unspecific staining with the secondary antibody and the avidine-biotin-system used for immunodetection (lane 8) (see Materials and Methods). Incubation with control antibody anti-DCC reveals that other integral membrane proteins are extracted by the procedure employed and remain intact (lane 9). In these extracts, mab111 recognizes the same high molecular component as mab10 and, in addition, the other minor bands also isolated from the mab111-immunoaffinity column (lane 10). Selected apparent MWs are indicated in kilodaltons on the left. The arrowhead points to the interface between the stacking and running gel.

Figure 15: **Figure 1 of the manuscript**: Monier et al. The Polysialic Acid Moiety of the Neural Cell Adhesion Molecule Is Involved in Intraretina Guidance of Retinal Ganglion Cell Axons. Developmental Biology, 229, 1-14 (2001).

In this article the commission makes multiple errors that clearly highlight its incompetence in:

- designing an experiment with the appropriate controls;
- analyzing a figure and understanding its legend;
- distinguishing between a reuse of control samples and a copy/paste of control sample images.

Under these conditions, the conclusion of the commission of inquiry, claiming they are in agreement with the journal *Developmental Biology*, cannot be taken seriously. As for the recurring argument: *"20 years ago, no journal recommended the addition of lines to indicate assemblies"*, it is an intellectual imposture. Indeed, if a good scientific practice is not specifically formulated in the recommendations of the journal to the authors, this does not authorize the non-respect of this good practice. Non-compliance with a good practice is bad practice no matter what. In addition, the scientific community publishing in *Developmental Biology* followed this good practice in 2001. We consulted the archives of this review of the year 2001 to note it. In the first figure of the first article of the first volume of 2001, we can observe a montage made from 6 different membranes very clearly indicated by vertical white lines between each membrane.

Article 6 Karaiskou, A., Lepretre, A.C., Pahlavan, G., Du Pasquier, D., Ozon, R., and Jessus, C. (2004). Polo-like kinase confers MPF autoamplification competence to growing Xenopus oocytes. Development 131, 1543-1552.[7]

PubPeer revealed image manipulation in figures 2A, 2B, 5C, 6 and 7 of this article. This involved duplication and recycling of identical images of lanes that were copied and pasted on different experiments and labelled as representing different experimental outcomes. This represents a deliberate and fraudulent invention of scientific results.

With regard to figure 2A, the Committee notes that the original has not been found, without any further clarification. With regard to the fifth article, the originals of which are unavailable, one would be entitled to wonder whether the commission actually consulted the laboratory notebooks to try to find the original results supposed to be kept there.

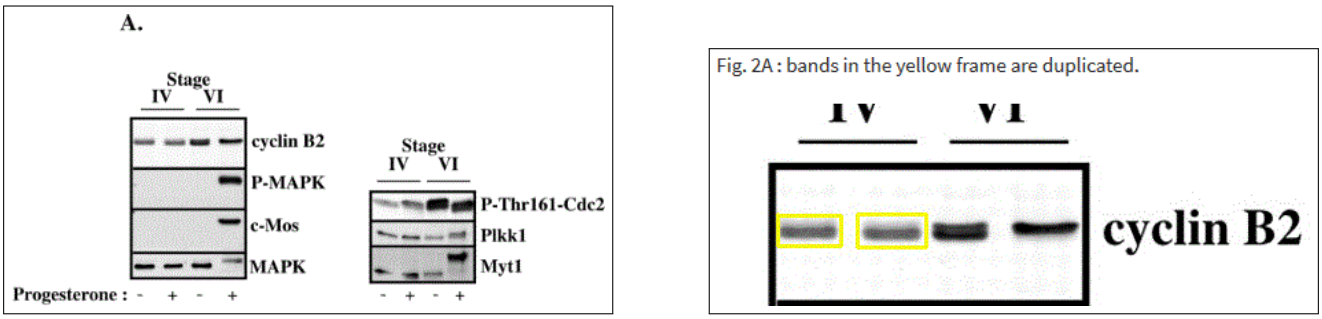


Figure 16: **Figure 2A of the manuscript (original on the left, challenged by *PubPeer* on the right)**. *PubPeer* noted that the lanes boxed in yellow are identical, one having been copied, pasted and relabelled to create the second. This represents a deliberate and fraudulent invention of scientific results.

Indeed, in the absence of an original, if the commission cannot affirm that there exists a duplication, it cannot either, in all rigor, affirm the opposite. Yet this is what it does by writing:

[7]Corresponding author: C. Jessus, pubmed: 14985258, doi: 10.1242/dev.01050, issn: 0950-1991 issn: 1477-9129.

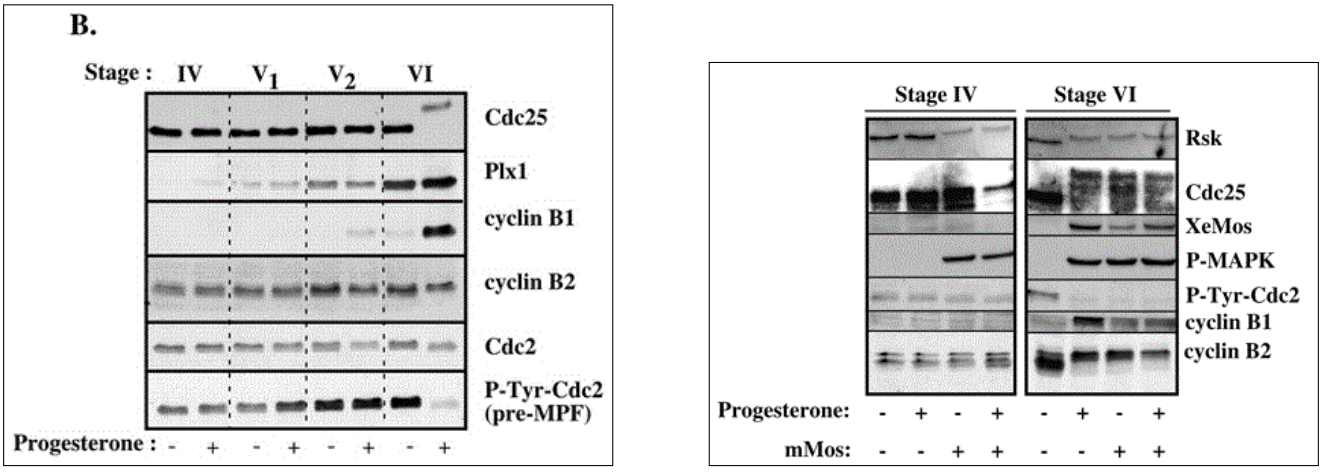


Figure 17: **Figures 1B et 3 of the manuscript**

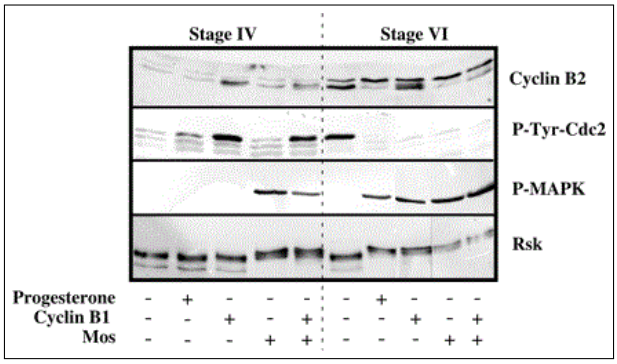


Figure 18: **Figure 6 of the manuscript**

"[...] although there is no duplication in figure 2A [...]". However, the commission adds that "a correction requested by the authors proposes to delete it".

Why would you want to remove this panel fourteen years later if there was really no duplication at the time (2004)? Furthermore, we note that three months after the publication of the survey report, figure 2A was not deleted by the publishers.

The commission furthermore minimizes the importance of a possible manipulation in this panel, in claiming that *"in three other figures of the same article (Figures 1B, 3 and 6: Cyclin level B2)"* the same result is already shown.

However in these three other figures – figures 1B, 3 and 6 of the manuscript, see figures 17 and 18 of this report –, it is not the same result that is highlighted, since they show double bands linked to Cyclin B2 level in stage IV oocytes. While obviously in the figure 2A, only one band is detected in stage IV oocytes.

With regard to figure 2B, the Commission of Inquiry describes it as an analysis of experiments using the northern-blot technique (page 7 of the Inquiry Report). This affirmation is repeated again on page 8 of the report.

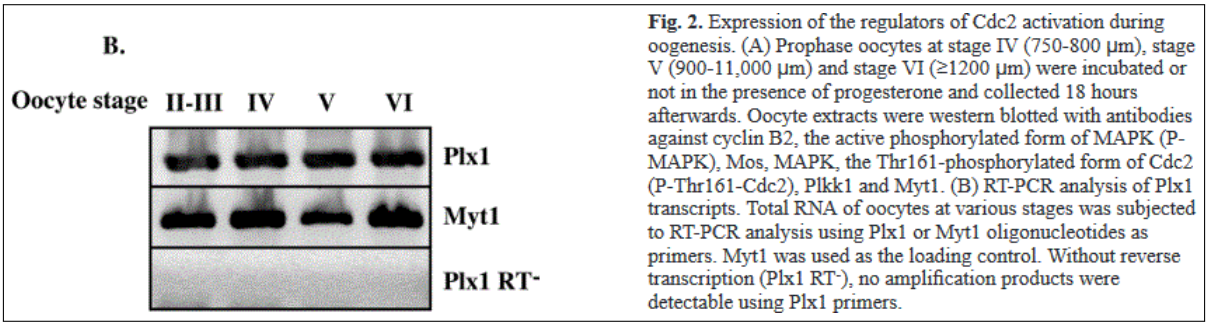


Fig. 2. Expression of the regulators of Cdc2 activation during oogenesis. (A) Prophase oocytes at stage IV (750-800 µm), stage V (900-11,000 µm) and stage VI (≥1200 µm) were incubated or not in the presence of progesterone and collected 18 hours afterwards. Oocyte extracts were western blotted with antibodies against cyclin B2, the active phosphorylated form of MAPK (P-MAPK), Mos, MAPK, the Thr161-phosphorylated form of Cdc2 (P-Thr161-Cdc2), Plkk1 and Myt1. (B) RT-PCR analysis of Plx1 transcripts. Total RNA of oocytes at various stages was subjected to RT-PCR analysis using Plx1 or Myt1 oligonucleotides as primers. Myt1 was used as the loading control. Without reverse transcription (Plx1 RT-), no amplification products were detectable using Plx1 primers.

Figure 19: **Figure 2B of the manuscript**

We are surprised by this confusion in the commission report, completely ignoring the difference between a northern-blot analysis (which allows, the migration of RNA molecules) and an analysis by electrophoretic migration of DNA fragments amplified by the Polymerase Chain Reaction (PCR) method, which the legend of the figure mentions in the manuscript (p. 1546; Fig. 2) (RT-PCR analysis...).

This level of confusion reflects and reveals the incompetence of this commission of inquiry, and casts serious doubt on its credibility as regards its ability to issue a serious opinion on scientific work.

In any case, this figure is the result of an electrophoretic analysis of DNA fragments amplified by PCR. *PubPeer* note that the first signal in track II-III is that coming from two halves

of different signals reassembled in the same track, to give the false appearance of only one signal (see figure 20).

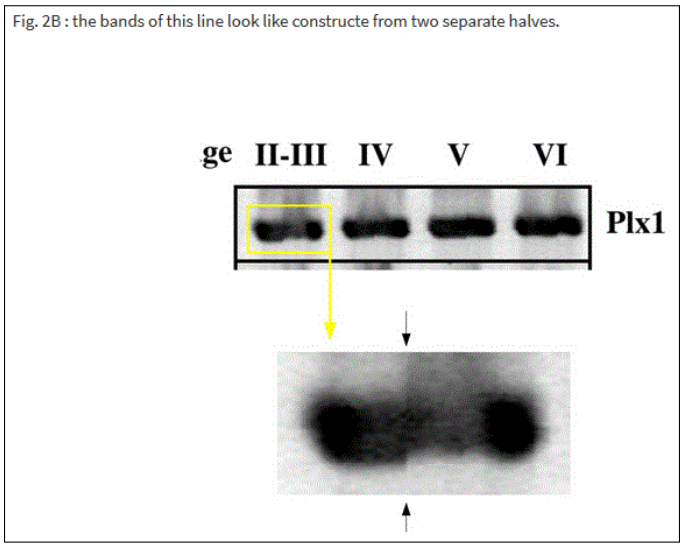


Figure 20: **Figure 2B of the manuscript challenged by *PubPeer***.the first signal in track II-III is a composite made from two halves of entirely different signals reassembled in the same track. This gives the false appearance of only one signal track. This is pure fabrication of a scientific result.

This figure therefore presents a montage suggesting that the II-III signal is similar to that of the other stages studied in this experiment! It is an obvious fabrication, making an image by assembling unrelated signals, which makes the experiment meaningless. It is surprising that the commission of inquiry does not mention it, and chooses to attribute it to an alleged malfunction of a device called GelDoc – such an explanation for this kind of a manipulated image is quite simply technically impossible.

As regards figure 5C, ***PubPeer*** revealed that the lanes boxed in red are identical, one having been copied, pasted and relabelled to create the second. This is intentional and fraudulent fabrication of a scientific result. The **inquiry commission** acknowledges that each subpanel of this figure is formed by the assembly of distinct membranes, but that an error has slipped into the manufacture of the assembly, leading to duplications (framed in red) of observed bands.

If one refers to the good experimental practices recalled in the preamble (see text page 9 and figures 4 and 5), the commission should not conclude that there was an assembly error in the subpanels. On the contrary, it should point out that this type of assembly is inadmissible. Indeed, the figure 5C is created by the assembly of four horizontal panels (black frames) in a rather classical way (see preamble or even legend of the figure) to indicate to the reader that the 6 samples underwent the same electrophoresis and the same transfer onto nitrocellulose membranes. This membrane was then cut into four horizontal bands for each to be developed either following incubation with a particular antibody, or by radioactive emission. Thus from top to bottom, the first panel is incubated with anti-Myc antibody, the second with anti-Cdc25 antibody, the third with anti-P-Tyr-Cdc2 antibody and the fourth by autoradiography. After development, the four panels were reassembled in the respective places they occupied before cutting the membrane (see figure 3 of the preamble, case n°1). Thus reassembled, the figure allows, on one hand, to compare the six electrophoresis profiles between them and, on the other hand, within the same panel, to compare the intensity of the six tracks between them.

Therefore, an assembly inside a single panel is uninterpretable and clearly reveals that tracks 1 and/or 4 of the P-Tyr-Cdc2 panel have been added to hide the original tracks.

In addition, the masked original tapes were those of the internal controls (not treated by 'OA nor B1'), reference elements to which all other tapes with the same experimental conditions must be compared, provided, of course, that they had undergone all the stages of the western-blot together, and therefore that they were on the **same** membrane. This figure is therefore totally fabricated and uninterpretable.

The incompetence of the commission has, in this example, serious consequences because it recommends the continuation of this type of assembly. This could, in no case, be acceptable, neither during a working meeting in a laboratory, nor in presentation at a congress, nor by the rewievers of the newspapers with reading committee as of the review *Development*.

As regards figure 6, ***PubPeer*** note that published version contains several identical duplicated lanes, labeled as emanating from different experimental conditions, and thus quite clearly fraudulent. The **inquiry commission** attempts to excuse this fraud by the affirmation that it was able to observe the original and find that the RsK panel does not contain any duplication. Without this original, it is impossible for us to endorse the committee's conclusions, and it does in no way negate the fact that the published figure was fraudulent.

In contrast, as regards the P-Tyr-Cdc2 panel, the Commission accepts the duplication observed by *PubPeer* (red boxed lanes) but concludes that there was an assembly error and is satisfied with a correction of this assembly (correction which, however, three months after publication of the investigation report, has still not been published in *Development*). But here again, the mistake does not consist in making mistakes in the right parts of the assembly, but in making this type of assembly in the first place. Moreover, if the commission had any wise advice to give to the authors, it would certainly not be to make a new assembly but to repeat the experiment with all the samples on the same electrophoresis gel and the same nitrocellulose membrane.

Indeed, being attentive to the presentation of the figure 6, we notice that it is created by the

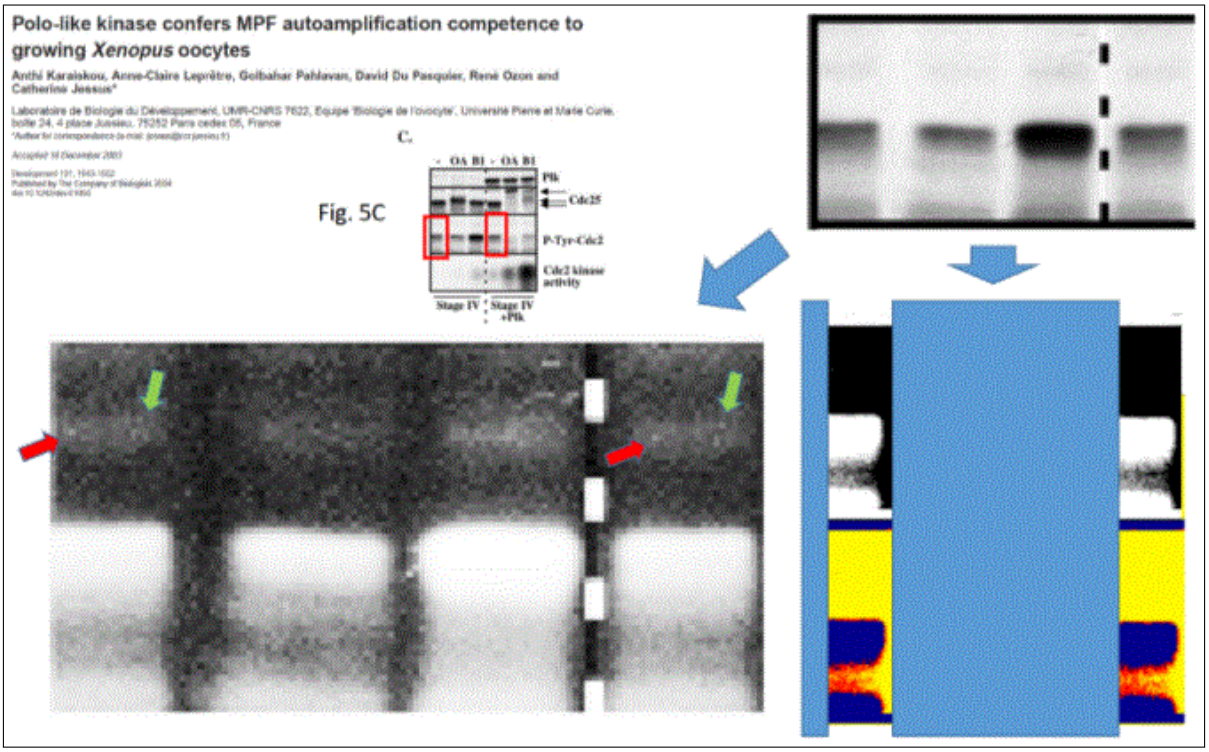


Figure 21: **Figure 5C of the manuscript challenged by *PubPeer***. Lanes boxed in red are identical, having been copied, pasted and relabelled to create the second. This is an intentional and fraudulent fabrication of a scientific result.

assembly of four horizontal panels (framed in black). This type of assembly is quite classic and correct. It indicates (as it is confirmed by the legend of figure) that 1) all samples underwent the same electrophoresis, 2) the same transfer on nitrocellulose membrane, then 3) that the nitrocellulose membrane was cut into four horizontal bands so that each was revealed by a particular antibody : in this case, from top to bottom, the anti-Cyclin antibody B2 for the first panel, the anti-P-Tyr-Cdc2 antibody for the second panel, the anti-P-MAPK antibody for the third panel and last the anti-Rsk antibody for the fourth panel. After immunochemical detection, the four panels were reassembled in their respective places before the membrane was cut. Thus reassembled, the figure allows on the one hand to compare the 10 electrophoresis profiles between them, and on the other hand, within the same panel, to compare the intensity of the 10 tracks between them.

Therefore, an additional assembly inside a single panel is incomprehensible and clearly reveals that track 8 of the P-Tyr-Cdc2 panel has been added to mask the original track.

This additional editing is therefore inadmissible: it is very clearly an intentional manipulation to make believe that tracks 8 and 9 of this panel have the same electrophoretic profile and the same intensity. We would be curious to know which tapes are present on track 8 of the original for having taken the foolish risk of replacing them by a duplication of track 9? The commission of inquiry, which had access to the original, should have included it in its report.

Last, as regards figure 7, The Committee notes for the sixth time that the original has not been found but is still not offended! The Panel also concludes that unintentional errors occurred in the assembly of the figure 7. As for figures 5C and 6, it is still a question of mounting inside a panel. For exactly the same reasons that we have mentioned in the two previous figures, such assemblies are inadmissible: they very clearly denote intentional manipulation to manufacture or falsify a result and make figure uninterpretable.

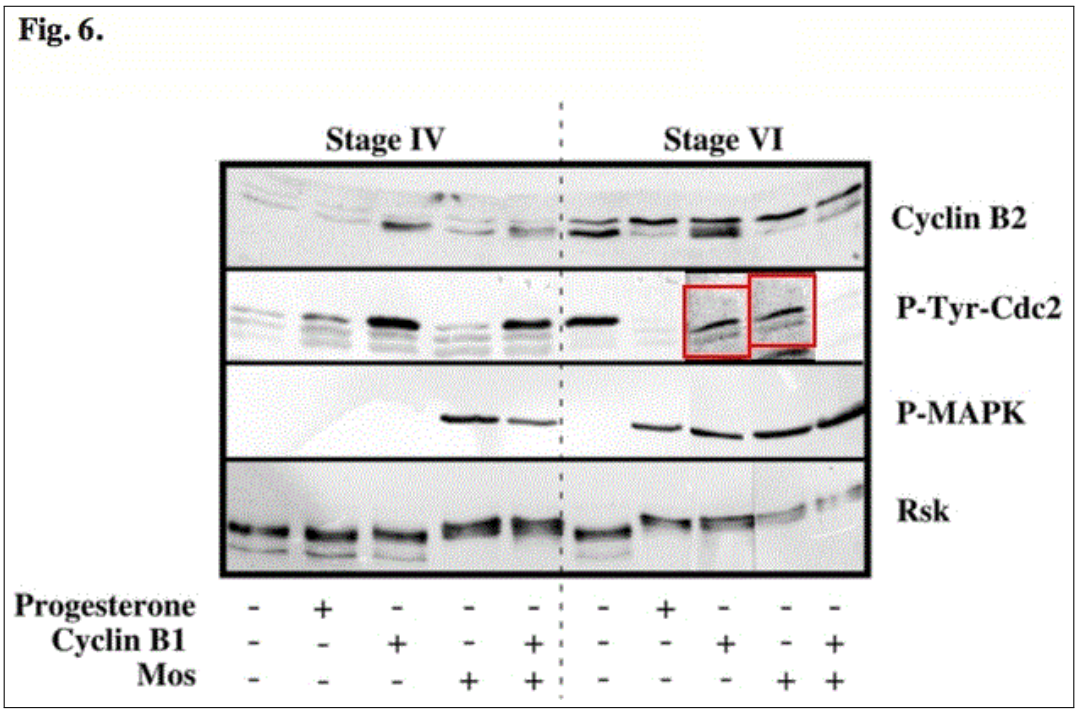


Figure 22: **Figure 6 of the manuscript challenged by *PubPeer***. The two lanes boxed in red in track 8 and 9 of the P-Tyr-Cdc2 panel are identical as also confirmed by the inquiry commission. Track 9 image has been copied and pasted in track 8 probably to mask the original track. This kind of image manipulation is an intentional fabrication and falsification of scientific result.

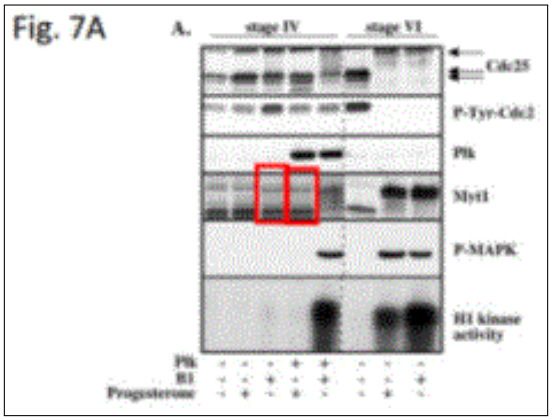


Figure 23: **Figure 7 of the manuscript challenged by *PubPeer***. The two lanes boxed in red are identical as also confirmed by the inquiry commission. One image has been copied, pasted and relabelled to create the second and probably to mask the original track. This kind of image manipulation is an intentional fabrication and falsification of scientific result.

Instead of asking the authors to repeat the experiment with all the samples in the same electrophoresis gel without subpanel assembly (i.e. assembly inside a panel), the commission is satisfied with another assembly. However, if the commission is not competent to understand that an assembly inside a panel is a fraudulent manipulation, it will be just as incompetent to determine whether the corrections made by the authors are correct or not.

In conclusion, all of the commission comments show that it has absolutely no mastery of the techniques used in this section, that it neglects the fundamental importance of the internal controls of each experiment, that it confuses an assembly of legitimate panels with an assembly of illegitimate subpanels, and last, that it confuses unintentional errors with intentional manipulations aimed to deliberately falsify an original result. All the comments of this commission of inquiry are therefore inadmissible and can under no circumstances be taken into consideration either by the institutions or by *Development* journal.

Article 7 Zhao, Y., Haccard, O., Wang, R., Yu, J., Kuang, J., Jessus, C., and Goldberg, M.L. (2008). Roles of greatwall kinase in the regulation of cdc25 phosphatase. Mol Biol Cell 19, 1317-1327.[8]

PubPeer revealed image manipulations in figures 4 and 8B of this article. subpanels shown boxed with the same color in figure 4 and 8B are identical. Those of figure 4 have been copied, pasted (with distortion) and relabelled to create those in figure 8. This kind of image manipulation is deliberate and fraudulent fabrication of a scientific result.

In its report, the **inquiry commission** admits that there has been a duplication of the green boxed subpanel of figure 4 in figure 8B. she affirms that it is not an error but an intentional reuse, and *"considers that no correction is necessary"* because *"it is justified that the control of the same experiment are reused in several figures when these are well resulting from this same experiment"*.

[8]Corresponding author : M. Goldberg, pubmed: 18199678, doi: 10.1091/mbc.E07-11-1099, issn: 1939-4586 issn: 1059-1524.

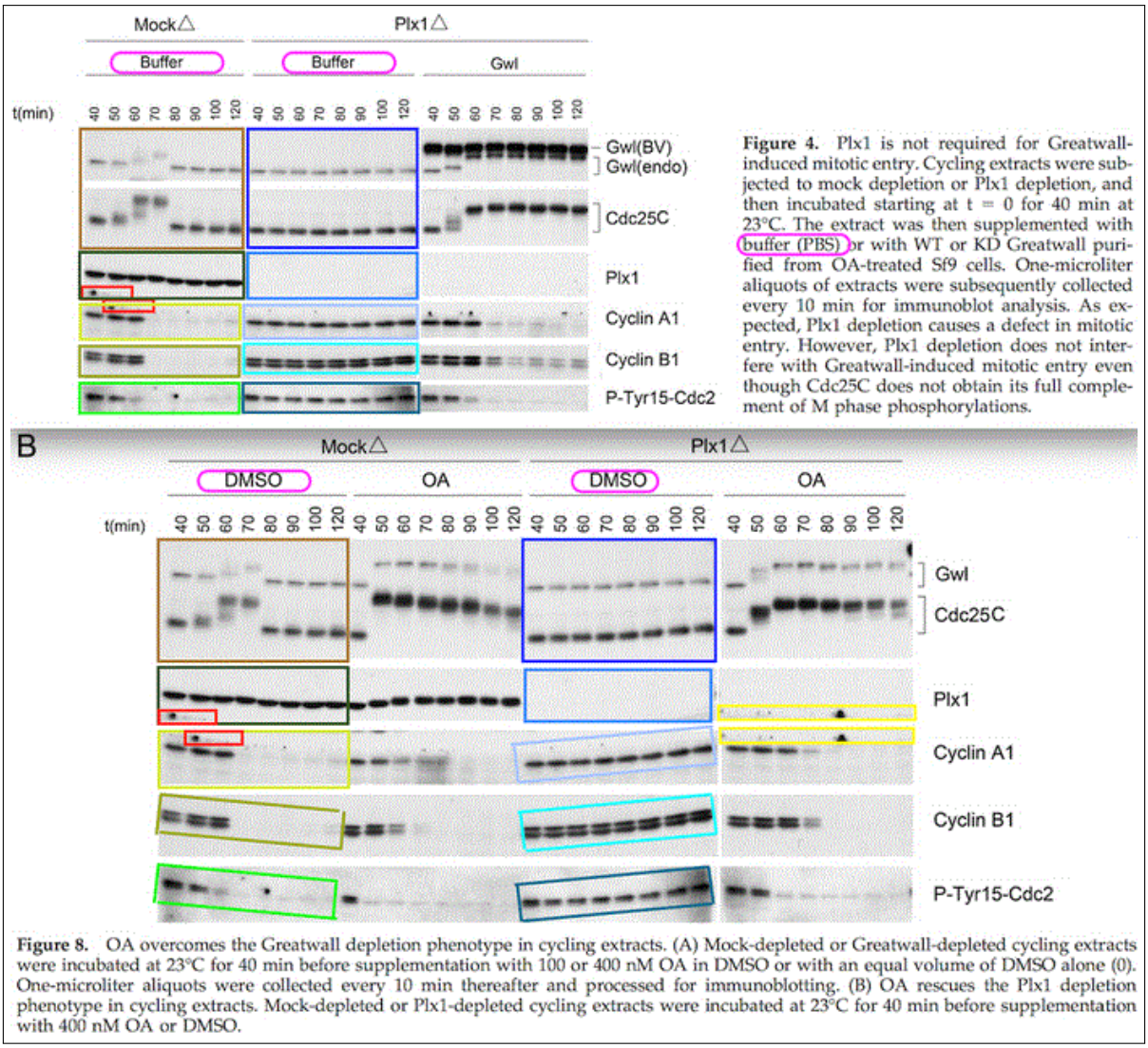


Figure 24: **Figures 4 et 8B of the manuscript challenged by *PubPeer***. subpanels boxed with the same color are identical. Those of figure 4 have been copied, pasted (with distortion) and relabelled to create the figure 8. This kind of image manipulation is a deliberate and fraudulent fabrication of a scientific result.

The commission is wrong for several reasons: First reason, even if it were the same experiment, the image of the internal controls used in the western-blot of the figure 4 “Buffer” panel should not have been reused in the assembly of another western-blot. As we explained in the preamble (see page 7), if too many samples do not allow the use of the same electrophoresis gel to carry out their migration, it is possible to carry out two different gels. The internal control of the experiment will then have to be run on two western-blots; the first with samples from figure 4 and the second with samples from figure 8. A copy/paste of the image of the control samples in a second montage is not at all equivalent to a reuse of the control samples in a second western-blot. To confuse the two demonstrates the scientific incompetence of this commission.

Second reason, the error is even more gross since the duplicated lanes are not the same samples, those of figure 4 are re-suspended in “Buffer”, while those of figure 8B are announced as being re-suspended in DMSO (DiMethylSulfOxide). Moreover, a recent analysis in *PubPeer*, even more scrupulous than the previous one, shows that there was not only one copy/paste, but ten copy/paste from figure 4 to figure 8B with image distortion to try to mask this illegal practice.

Despite this, the commission concludes *“that there is neither scientific misconduct, nor error, no element calling into question the messages of the article. It is justified that the controls of the same experiment are reused in several figures when these are all resulting from this same experiment. The Commission considers that no correction is necessary”*.

The formulation of such a conclusion by a commission of inquiry on scientific integrity is totally obscene as it expressly encourages cheating through manipulations of images such as those described in figure 5 of the preamble case n°4A and 5A. Such montages are uninterpretable and therefore do not deliver any scientif message only a totally falsified one.

Article 8 Dupre, A., Buffin, E., Roustan, C., Nairn, A.C., Jessus, C. and Haccard, O. (2013). The phosphorylation of Arpp19 by Greatwall renders the auto-amplification of MPF independently of PKA in Xenopus oocytes. J. Cell Sci. 126, 3916-3926.[9]

PubPeer revealed image manipulations in figures 4D and S4 of this article. In figure 4D the background pattern has been modified only in some areas and not uniformly on all of the samples on the membrane. This is intentionally falsifying a scientific result. In figure S4, an additional track has been inserted in the middle of the pMAPK subpanel. Insertion of a track from a different membrane or insertion of a track of an unrelated sample from the same membrane in order to mask an original result are both fabrication/falsification of a scientific result.

About figure 4D :

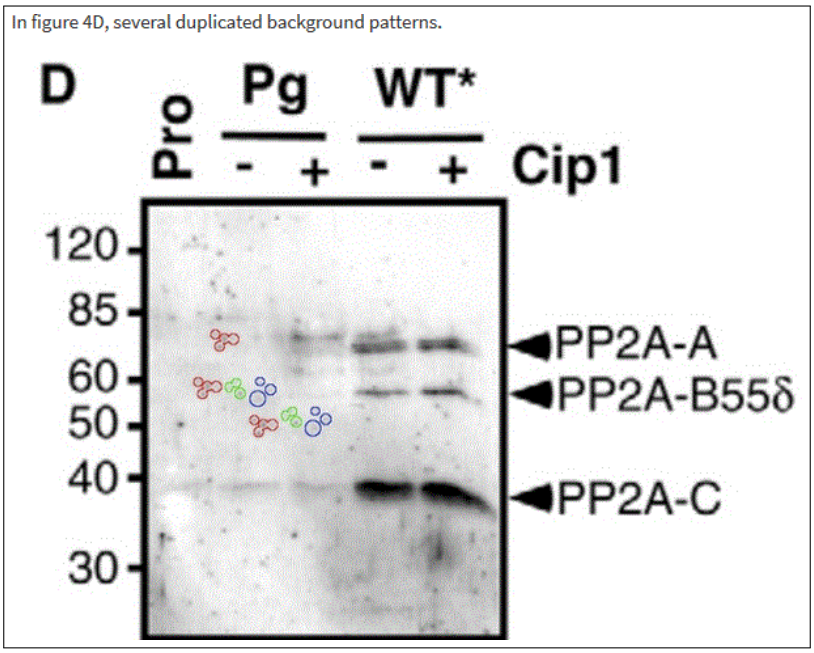


Figure 25: **Figure 4D of the manuscript challenged by *PubPeer***. The background pattern has been modified in some areas of the membrane and not others, in this way falsely giving the impression of uniformity on the membrane . This falsifies the deduced scientific result.

The committee concedes that reducing the background on some parts of the membrane, but not homogeneously on the whole membrane, is indeed a bad scientific practice. The committee claims that the original figure was sent by the authors to *J. Cell. Science* for replacement. However, no correction has been published by the journal to date, which makes us doubt the honesty of the commission.

About figure S4, the Commission acknowledges that Track 5 of the pMAPK panel has been cut from another part of the same gel, and inserted between Tracks 4 and 6.

If this track had been made from the same gel, it would also have undergone the same nitrocellulose membrane transfer and detection as samples of the same gel. However, the background noise of this track is clearly less intense than that of bands 1 to 4 and 6 to 8.

[9]Corresponding author : O. Haccard doi: 10.1242/jcs.126599, pubmed: 23781026, issn: 0021-9533 issn: 1477-9137.

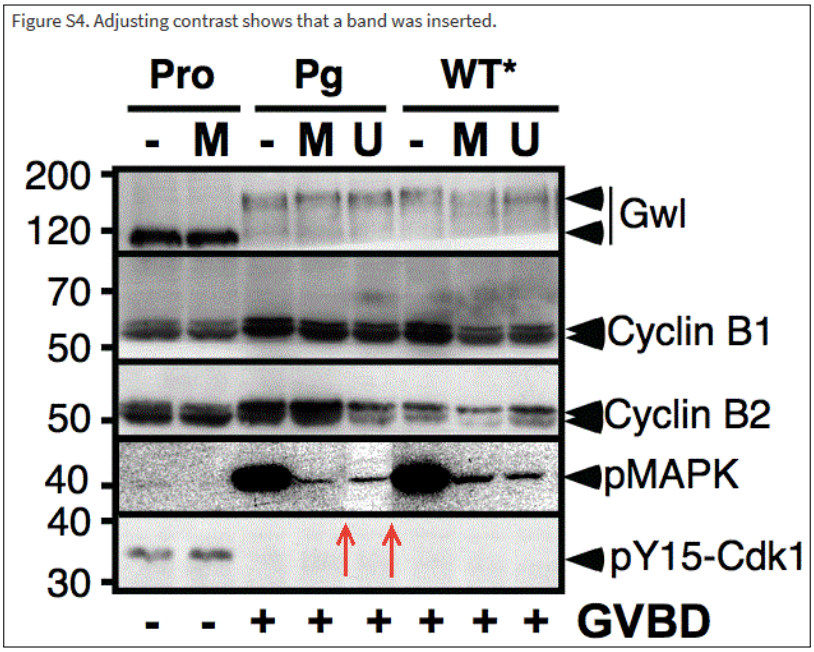


Figure 26: **Figure S4 of the manuscript challenged by *PubPeer***. A track has been inserted in the middle of the pMAPK subpanel. Insertion of a track from a different membrane or insertion of a track of an unrelated sample from the same membrane in order to mask an original result are both fabrication/falsification of a scientific result.

This track have been therefore most probably cut from a membrane that had undergone immunochemical detection different from the other tracks. As we explained in the preamble (see page 8), its intensity cannot be compared with the other bands of the same subpanel. Moreover, whatever the origin of the inserted track (whether from the same or from a different membrane) as no insertion have been made in any other subpanels of figure S4, this track insertion has been done to mask an original result.

We are very surprised that the commission does not qualify this deliberate insertion as bad scientific practice and does not require a replacement figure that has not been manipulated.

As for the recurring argument: “The time of publication of this article corresponds to a time of transition in the presentation of figures where the desirable indication of insertions was not yet the norm”. We have refuted it several times by proving that a good practice or that a bad scientific practice is independent of the year of publication, and by giving several examples, showing that since 1997, the use of black or white vertical lines indicating assemblies between different membranes was indeed the norm, practiced by the scientific community, and even by C. Jessus co-author of this article.

Whatever the case, with or without vertical lines, this type of insertion transgresses the limits of interpretation of a western-blot. Not acknowledging this is an admission of incompetence by the Commission of Inquiry.

Article 9 Dupre, A., Daldello, E.M., Nairn, A.C., Jessus, C., and Haccard, O. (2014). Phosphorylation of ARPP19 by protein kinase A prevents meiosis resumption in Xenopus oocytes. Nature communications 5, 3318.[10]

PubPeer revealed image manipulations in figures 2A and 3B of this article:

- Concerning figure 2A: we fully agree, for once, with the technical arguments put forward by the committee to explain the similarity of the yellow framed bands. This is the case figure described in figure 4 of the preamble.
- Concerning figure 3B: we were also able to observe the original figure presented in the supplementary data of the article. It is indeed an assembly of strips coming from the same gel as the one schematized in figure 5 (case B) of the preamble.

[10]Corresponding author: O. Haccard. Two first authors: equal contribution, pubmed: 24525567, doi: 10.1038/ncomms4318, issn: 2041-1723.

Article 10 Daldello, E.M., Le, T., Poulhe, R., Jessus, C., Haccard, O., and Dupre, A. (2015). Fine-tuning of Cdc6 accumulation by Cdk1 and MAP kinase is essential for completion of oocyte meiotic divisions. J Cell Sci. 128, 2482-2496.[11]

PubPeer revealed manipulations of images in figure 4B of this article (see figure 27 below): the two subpanels boxed in red are identical. One has been copied, pasted and relabelled to create the other. This kind of image manipulation is deliberate and fraudulent fabrication of a scientific results

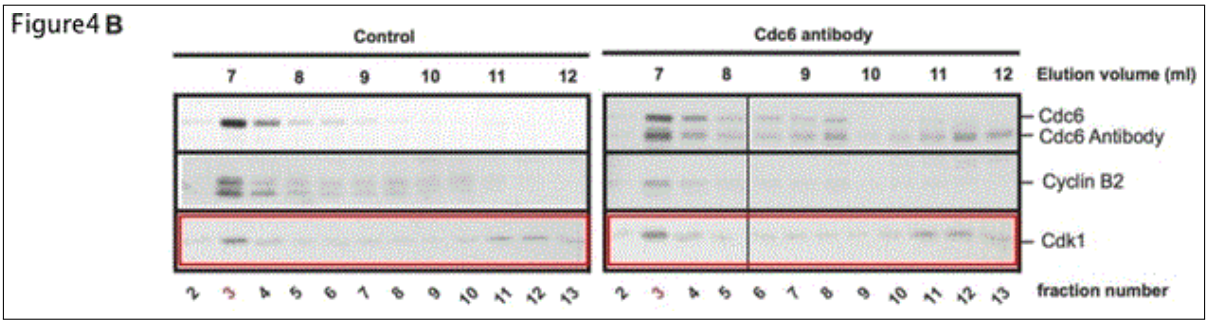


Figure 27: **Figure 4B of the manuscript challenged by *PubPeer***. The two subpanels boxed in red are identical. One has been copied, pasted and relabelled to create the other. This kind of image manipulation is deliberate and fraudulent fabrication of a scientific results.

In its report, the **committee of inquiry** states that it had access to the original results and acknowledges that there was *"a gross error when mounting the figure"* in other words a coarse copy/paste (red boxes) of the lower left panel instead of the lower right panel. The commission of inquiry requested and obtained a correction from the authors. This patch was sent to the *Journal of Cell Science* which accepted it and published it on February 1, 2018.

One can be pleased that the **commission of inquiry** has recognized a fraudulent image manipulation by qualifying it of "gross error". It is indeed typically a 5B type falsified assembly (see figure 5 of preamble), recognized as deliberate and fraudulent fabrication of scientific result, found several times in previous articles but then presented as "correct reuses". Note the total incoherence of the committee's work between the beginning and end of its report.

[11] Corresponding author : A. Dupré, pubmed: 26092930, doi: 10.1242/jcs.166553, issn: 0021-9533 issn: 1477-9137.

Article 11 Dupre, A., Haccard, O. and Jessus, C. (2017). The greatwall kinase is dominant over PKA in controlling the antagonistic function of Arpp19 in Xenopus oocytes. Cell Cycle 16, 1440-1452.[12]

PubPeer revealed image manipulations in figures S1B and S2B of this article. Red arrows (see Figure 28) point to junctions that result from an assembly of two different membranes or two different parts of a same membrane. In the first case it is recognized as fraudulent image manipulation, only in the latter case is it acceptable.

In its report, the inquiry commission states that she had access to the originals and there-

[12]Corresponding author : A. Dupré. Three authors : equal contribution, signature by alphabetical order, pubmed: 28722544, doi: 10.1080/15384101.2017.1338985, issn: 1538-4101 issn: 1551-4005.

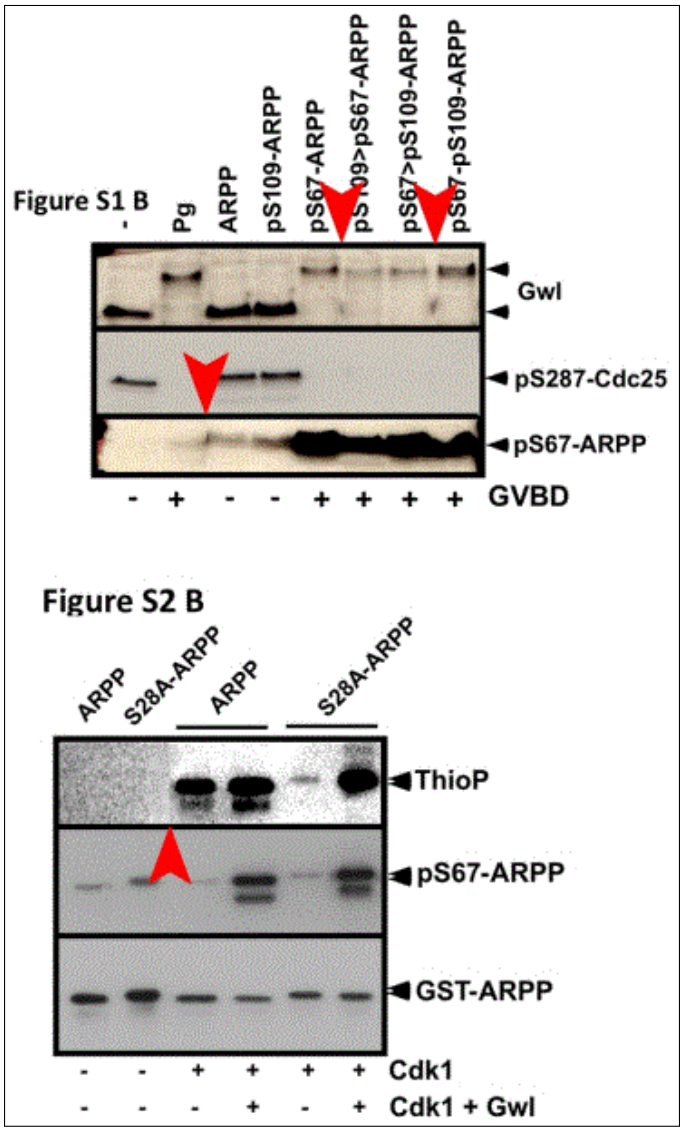


Figure 28: **Figures S1B et S2B of the manuscript challenged by *PubPeer***. Red arrows point to junctions that result from an assembly of two different membranes or two different parts of a same membrane. In the first case it is recognized as fraudulent image manipulation, only in the latter case is it acceptable. The inquiry commission confirm these both kind of image manipulation have been made.

fore could confirm assemblies inside the three panels (indicated by the red arrows in *PubPeer*). It also indicates that some of these assemblies (without specifying which ones) consisted in bringing together distant parts of the same gel and others in bringing together different gels. Whereas the assembly of distant parts of the same gel (or membrane) is scientifically acceptable (see case n°1B to 3B in figure 4 of the preamble), we have explained on several occasions (see figure 5 of the preamble and our comments for the previous articles) that assembly, bringing together different gels or membranes, is scientifically non rigorous and makes figure uninterpretable; the commission should have recognised such manipulation as intentionally fraudulent, instead of justify it.

Again, and despite observing the originals, the commission was unable to distinguish between legitimate assemblies and uninterpretable assemblies involving intentional fraudulent manipulation.

The commission points out that the authors sent Cell Cycle corrections not concerning the two figures incriminated by *PubPeer* (S1B, S2B) but concerning three others figures S1A, 1A and 2A.

The need to address such a patch explicitly indicates that this article contained not two figures, but five figures from incorrect assemblies.

With these new corrected figures, and their originals provided, readers can now interpret the results in a correct way but still cannot do so for figures S1B and S2B, which have still not been corrected.

The commission ends its analysis on a very strange note about these three new figures corrected by the authors and accepted by Cell Cycle: “Note that on this occasion, the journal did not ask to add a vertical line to mark the re-assembly junctions.”

The vertical lines, as explained in the preamble and illustrated in figure 8 of Article 1, serve to indicate the assembly of two distinct membranes. In the case of the three new figures that the authors have submitted to the journal Cell Cycle, the originals available online allow us to see very clearly that there are no assemblies made from separate membranes but only one assembly made from bands remote from the same membrane. It would therefore have been irrelevant if Cell Cycle had asked for a vertical line!

What is the committee looking for in writing this? To cause confusion? to justify the absence of vertical lines of the figures S1B, S2B that were not corrected? Or is it simply a reflection of its own confusion when faced with a scientific domain of which it has absolutely no comprehension.

5 Conclusion

With the exception of the comments and conclusions concerning the two figures of Article 9, all of the arguments and conclusions of this commission are factually incorrect. This leaves us all very perplexed as to the rigour and professionalism with which it conducted its investigation.

Since all of *PubPeer*'s allegations involve possible manipulation of western-blot images or autoradiography, the work of such a commission of inquiry must consist in comparing the original western-blot and autoradiographs with the incriminated published figures. Furthermore, the commission must acknowledge that recycling of identical images that are then relabeled and re-used in different experimental figures represents invention of scientific results and therefore out-and-out fraud.

When confronted by such blatant fabrication, a commission of inquiry should furthermore obtain the original documents in the laboratory archives in order to verify if any experimental data ever did, indeed, exist. It would seem that the commission was satisfied, as it indicates in the conclusions of its report "The commission asked Mrs Jessus to provide the original documents used to assemble the incriminating figures". However, Mrs Jessus could have provided only two thirds of the results since the commission affirmed at least 7 original documents (out of 21) were not found. While the national code of ethics for research professions clearly stipulates that "All raw results (which belong to the Institution) as well as the analysis of the results must be kept in such a way as to allow their verification". It is strange that a commission of inquiry on scientific integrity makes no comment on the absence of such a large number of original documents and does not itself look for them in the various laboratory notebooks of the authors of the challenged articles.

The position taken by the commission of inquiry is to note and admit almost all of the image manipulations highlighted by *PubPeer*. These comprise non homogeneous attenuation of background noise (article 8 figure 4D) and 18 reuses (copy/paste type) of images (articles 1 to 8 and 10 to 11).

However, the commission does not accept that such blatant manipulations are evidence of intentional fraud! In spite of these 18 falsifications of characterized images, the commission uses confusing and scientifically baseless arguments to try to justify the majority of them after having classified them into three distinct categories :

- Category 1: reuse (or duplication) of control sample images in several figures (Article 2, Article 3, Article 4, Article 5 and Article 7). The commission claims that this represents "legitimate" reuse, affirms that "there is no error intended in the reuse", or that "the conditions of each experiment have been reproduced". It explains that "it is justified for controls of the same experiment to be reused in several figures when these are resulting from the same experiment" and even goes so far as to mention three more such manipulated figures, containing reuses of images of control samples, beyond than those detected and exposed by *PubPeer* (in Article 5).

  However, as we have shown, this argument is completely senseless. The commission confuses the reuse of control samples (meaning that the experimental samples themselves were reused as controls in a different experiment) with a simple copy/paste of control sample images, which is not at all the same thing! In the first case, the reuse is scientifically correct, it consists in subjecting the control samples to an additional western-blot with other samples from the same experiment. In the second case (which is the case of the incriminated articles), it is scientifically incorrect. The control samples did not undergo a second western-blot analysis on the same membrane as the new set of experimental samples. Instead, the images from one Western blot were

attached to images from another Western blot run independently, making the resulting figures uninterpretable! This confusion of the commission of inquiry, which states unduly and repeatedly "that there is neither scientific misconduct, nor error, nor element calling into question the scientific messages of the article." highlights their total incompetence.

- Category 2: manipulations of images other than control samples, which consists of bringing together (or inserting) various distant parts of the same membrane (Article 8 – figures S4 – and Article 11) or of different membranes (Article 1, Article 6 – figure5C – and Article 11) into a single figure panel.

  We have explained on several occasions (see figure 5 of the preamble and our comments for Article 1, Article 6 and Article 11) that the latter type of assembly (bringing together different gels or membranes) is not scientifically correct since the samples whose images are brought together have not come from the same western-blot or from the same autoradiography. They are therefore not comparable, which makes the figures meaningless. The commission should have recognized such manipulations as intentionally fraudulent, instead of justifying it.

  The assembly of distant parts of the same gel (or membrane) is indeed scientifically acceptable (see preamble page 9). However, this is probably not the case in these manuscripts. When we carefully analyze the organization and background noise of figures S4 in Article 8 and S1B and S2B in Article 11, it is not a question of assembling distant parts of the same membrane (see case n°3 of the preamble), but of assembling different pieces of different membranes (case n°6 of the preamble), very clearly done to give the illusion that they all came from the same membrane. This represents intentional scientific fraud.

  Again, and despite observation of some originals, the commission was not able to distinguish between "legitimate" assemblies and uninterpretable assemblies involving intentional fraudulent manipulation to make believe that samples from the same figure all came from the same western-blot or the same autoradiography.

- Category 3: reuse (or duplications) of images of non-control samples that are found twice in the same panel (under part of a western-blot – figures 3 and 5B from Article 3, figures 6 and 7 of the Article 6) or reuse of images of control samples that are found in two different panels (Article 10). In other words, demonstrable fabrication and invention of data, as only one of the images could possibly correspond to an experimental result.

  Whereas this is exactly the same type of copy/paste and relabelling of fraudulent images as the previous cases, this time the commission recognizes that these are errors. However, by a completely fallacious reasoning consisting in making believe that a panel would be an assembly of various parts (as is in a way a puzzle) the commission minimizes these errors by making them pass for unintentional errors, of misguided mistakes which would have led the authors to be mistaken of parts at the time of the assembly! But here the mistake does not consist in inserting the wrong panel during assembly of a complex figure, but in duplicating images and relabeling them in different ways to supposedly represent different experimental results. This furthermore does not address the additional fallacy of making complex figures containing assemblies of non-comparable results originating from different gels in the first place! As a further attempt at excuse, the commission states that these errors have been corrected. However, to date, only figure 4B of Article 10 has been the subject of a *corrigendum* published by *J. Cell Science*.

One wonders what the commission sought by carrying out such a classification of the 18 manipulations of images into three categories? Obviously trying to exonerate 13 of them and minimize the fraudulent intent of the other 5.

This attempt is useless, as we have demonstrated article by article, figure after figure, the 18 reuses of images are all falsifications aimed at making people believe that samples from the same panel have originated from the same western-blot, for some, or aimed at masking an original result, for others.

Since the Commission refers to it many times in its analysis, it should be noted that the vast majority of peer-reviewed journals in Biology have for some years now published in the section entitled "Instructions to Authors" a paragraph on acceptable image manipulation for publication (see [Rossner and Yamada, 2004] and Annex I). This paragraph, which did not exist in the 1990s, has appeared over the last fifteen years and has become increasingly detailed in an attempt to reduce cases of fraud identified by publishers.

However, the advice recommended in this paragraph does not make the law, with non-retroactive effect, on how to determine what is a good or bad scientific practice since the good or bad scientific practices are independent of the year of publication of this paragraph in journals. Good or bad practices are determined by the technical limitations for interpreting the results of each technique and each experiment as we have explained in the preamble. Performing, analyzing and rigorously presenting each experiment within these limitations (in this case, for the western-blot technique, all samples to be compared must have undergone the same western blot run from the beginning to end) is a good practice. Violating these limits, demonstrates an absence of rigor and constitutes a bad scientific practice because the conclusions drawn from such analysis are not upheld by the experiment.

Contrary to what the commission tries to insinuate throughout its analysis, if a good scientific practice is not formulated in the recommendations of the journals to the authors, this does not authorize the non-respect of this good practice. Non-compliance with a good (interpretable results) practice is bad (uninterpretable results) practice, whether the experiments were conducted in 1997 as in 2017!

As for the argument put forward by the committee in Article 1, Article 2, Article 3, Article 4, Article 5, Article 6 and Article 7, it is particularly disconcerting. For all these articles, the committee ends its analysis by declaring that nothing calls into question the scientific messages of the article. On this occasion, we wish to indicate to the commission that does not seem to be familiar with experimental sciences, that a scientific experiment is designed to answer a question and the answer to this question is provided by the raw (or original) result of the experiment and it alone. However, for Articles 1 to 7, the original documents have precisely not or not all been found. What is the commission's basis for declaring that the article's scientific message is not modified when it was not able to consult it? Furthermore, even if these findings ultimately prove to have scientific validity, it in no way exonerates the authors from using fabricated and invented data in the actual published manuscript.

On the contrary, the accumulation of fraudulent practices by this laboratory over a period of 20 years, combined with a significant loss of original documents, should have seriously alerted the commission of inquiry concerning the scientific message delivered by the articles.

In conclusion, all of the Board's comments show that it has absolutely no mastery of the techniques used in the articles, that it neglects the fundamental importance of the internal controls in each experiment, that it confuses an assembly of legitimate panels with an assembly of illegitimate subpanels, and that it confuses unintentional errors with intentional manipulations such as relabeling and recycling identical images which are aimed at deliberately fabricating a desired experimental result.

The arguments of this commission of inquiry are rhetorical exercises and dishonest pleas which have no scientific basis. They are also irresponsible because they encourage image manipulation. They could under no circumstances be taken into consideration by reputable Institutions or journals such as *Developmental Biology*, *Journal of Cell Science*, *Development*, *Molecular Biology of The Cell* and *Cell Cycle*.

References

[Davidson, 1986] Davidson, E. H., editor (1986). *Gene Activity in Early Development (Third Edition)*. Academic Press, New York, third edition edition.

[Rossner and Yamada, 2004] Rossner, M. and Yamada, K. M. (2004). What's in a picture? the temptation of image manipulation. *The Journal of Cell Biology*, 166(1):11–15.

[Smith et al., 1984] Smith, L. D., Richter, J. D., and A., T. M. (1984). Regulation of translation during oogenesis. *Molecular Biology of Development*, pages 129 – 143.

Annex I Extracts from instruction to authors

The articles incriminated by *PubPeer* were published in the following scientific journals : *"Cell cycle"*, *"Development"*, *"Journal of cell science"* and *"Developmental Biology"*. Each of these journals publishes instructions for authors. Here is for each of them, the extract of these instructions concerning image manipulations.

In *"Cell cycle"*

"Since blots are used as primary evidence in many scientific articles, editors may require deposition of the original photographs of blots on the journal's website."

In *"Development"*

- "Do not add to, alter, enhance, obscure, move or remove a specific feature of an image – the focus should be on the data rather than its presentation (*e.g.* do not 'clean up' backgrounds or remove/obscure imperfections and non-specific bands).
- Adjustments should be applied to the whole image so no specific feature of the original data, including background, is obscured, eliminated or misrepresented as a consequence. Any non-linear adjustments must be disclosed in the appropriate figure legends and in the Materials and Methods section.
- The splicing of multiple images to suggest they represent a single micrograph or gel is not allowed.
- Any grouping or consolidation of data (*e.g.* removal of lanes from gels and blots or cropping of images) must be made apparent (i.e. with dividing lines or white spaces) and should be explicitly indicated in the figure legends.
- A positive and a negative control and a set of molecular weight markers must be indicated on all images of gels and blots.
- High-contrast gels and blots are unacceptable (i.e. no white backgrounds) – grey backgrounds are expected.
- The same data in whole or part should not be presented in multiple figures (*e.g.* loading controls; different exposures of the same gel), unless explicitly stated and justified.
- Previously published data in whole or in part (*e.g.* loading controls) should not be presented.
- All figures containing micrographs must contain a scale bar.
- Image acquisition methods must be described in the Materials and Methods or figure legends.
- Individual data should not be used across multiple figures, unless this is because of experimental design (for example, when multiple experiments are performed simultaneously using a single control experiment), in which case this must be clearly stated in each figure legend.

In *"Journal of cell science"*

- Adjustments should be applied to the whole image so no specific feature of the original data, including background, is obscured, eliminated or misrepresented as a consequence. Any alterations, such as non-linear adjustments (*e.g.* changes to gamma settings), must be disclosed in the appropriate figure legends and in the Materials and Methods section.
- The splicing of multiple images to suggest they come from a single micrograph or gel is not allowed.
- Any grouping or consolidation of data (*e.g.* removal of lanes from gels and blots or cropping of images) must be made apparent (i.e. with dividing lines or white spaces) and should be explicitly indicated in the figure legends.
- At least several band widths should be retained above and below cropped bands.
- A positive and a negative control and a set of molecular weight markers must be indicated on all images of gels and blots.
- High-contrast gels and blots are unacceptable (i.e. no white backgrounds) – grey backgrounds are expected unless otherwise justified.
- The same data in whole or part should not be presented in multiple figures (*e.g.* loading controls; different exposures of the same gel), unless explicitly stated and justified.
- Previously published data in whole or in part (*e.g.* loading controls) should not be presented.

In *"Developmental Biology"*

Whilst it is accepted that authors sometimes need to manipulate images for clarity, manipulation for purposes of deception or fraud will be seen as scientific ethical abuse and will be dealt with accordingly. For graphical images, this journal is applying the following policy: no specific feature within an image may be enhanced, obscured, moved, removed, or introduced. Adjustments of brightness, contrast, or color balance are acceptable if and as long as they do not obscure or eliminate any information present in the original. Nonlinear adjustments (*e.g.* changes to gamma settings) must be disclosed in the figure legend.