Scandalous withdrawn of a published research paper

Cognition and behavior in sheep repetitively inoculated with aluminum adjuvant-containing vaccines or aluminum adjuvant only
By: Asín J, Pascual-Alonso M, Pinczowski P, Gimeno M, Pérez M, Muniesa A, de Pablo L, de Blas I, Lacasta D, Fernández A, de Andrés D, María GA, Reina R, Luján L
Published in: Pharmacological Research, Elsevier (doi: 10.1016/j.phrs.2018.10.019).

This is the story of a scientific misconduct and editor & editorial corruption. An accepted paper in Pharmacological Research (Elsevier) was withdrawn last March 8th 2019 by the editor without a single reason other than non-declared conflicts of interest, fear of science and for sure pressure from external, not-revealed forces. You can read the story in the following emails and make your own conclusions. Our paper links the use of aluminum as vaccine adjuvant with behavioral changes in sheep and it must be extremely relevant to the field of vaccine safety that has forced them to behave in such a non-scientific, corrupted way. People involved in this scandalous issue are:

Main responsible individuals:

1) Emilio Clementi
Editor, Pharmacological Research. Professor at the University of Milan.
emilio.clementi@unimi.it
2) Anne Marie Pordon
Publisher of Pharmacology and Pharmaceutical Sciences titles for Elsevier.
a.pordon@elsevier.com

Scientific misconduct: *They both decided to withdraw the paper without any scientific reason, before contacting me for the first time (January 11th, 2019). Reasons for this are only known by them. They must give the explanations that they have denied to me.*

Accomplices:

1) Elia Biganzoli
Department of Clinical Sciences and Community Health. University of Milano.
elia.biganzoli@unimi.it

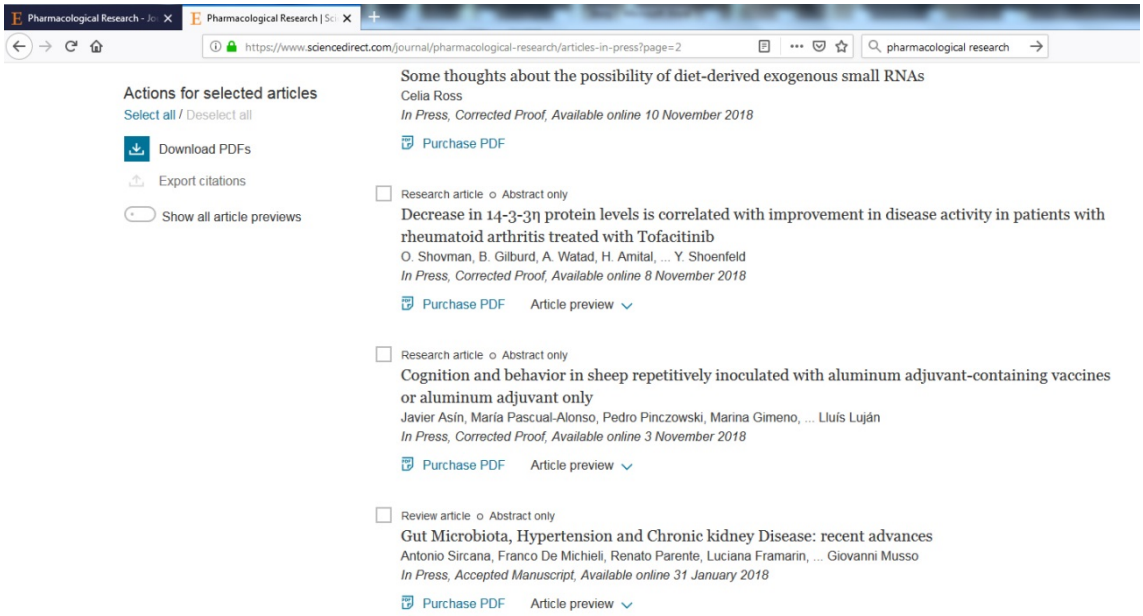
Scientific misconduct: *Necessary accomplice of a fake, biased statistical review, highlighting 'limitations' only he can see. He must explain the reason for his acts.*

2) Pasquale Maffia
Senior Lecturer in Immunology. University of Glasgow.
pasquale.maffia@glasgow.ac.uk
3) Sonia Radice
Faculty of Medicine and Surgery. University of Milano.
sonia.radice@unimi.it

Scientific misconduct: *Spectators from the very beginning of a scientific misbehave that do nothing about and therefore agree.*

Brief summary of key facts:

A paper entitled 'Cognition and behavior in sheep repetitively inoculated with aluminum adjuvant-containing vaccines or aluminum adjuvant only', from which I am the corresponding author is presented, reviewed, accepted and published on line in Pharmacological Research (Elsevier) on the 3rd November, 2018. See screen capture:



On January 11th, 2019, I receive an email from the same editor that had accepted the paper (E. Clementi): He is very worried for some anonymous concerns he has received about the published paper and urges for a response or he will withdraw it. Suspiciously enough, from the very beginning, he invites me to withdraw the paper myself, something that I cannot agree upon (of course) and something that should be absolutely unacceptable for a scientific editor to suggest at this stage (see page 5 in this pdf).

'Concerns' (pages 6-7) are written in a manner to deceive and to give the appearance of 'scientific credibility', but they totally lack scientific foundation. Significantly, they are full of malicious comments and many conceptual mistakes. All of them are answered in due time (see pages 14-21): not a single problem stands after my review. Upon receiving this answer, E. Clementi involves a statistical expert (Elia Biganzoli), to 'analyze the material' (page 22). However, Biganzoli's response is to make another, further review without any mention neither to the previous 'concerns' nor my answers, thus indicating all 'concerns' had been answered unquestionably. Biganzoli starts his review by saying 'the work is focusing a very delicate issue in science', which gives an idea of the bias he has (page 24). Biganzoli makes some observations ('limitations' he says) and -significantly- he mentions a well-known pseudoscientific internet activist (David Hawkes) as if the main problem of our paper is that one of his references is missing (page 25). Even in these strongly biased circumstances, he clearly recommends to publish the paper as it is (page 24). The response by E. Clementi is to withdraw the paper, without any scientific reason, on the basis of some of these 'observations' made by E. Biganzoli (page 26), avoiding Biganzoli's main conclusion. In the limit of the insult, Clementi offers me to resubmit the paper while he withdraws it: indescribable. I immediately

react and show that not a single observation from E. Biganzoli is scientifically sound (pages 27-30) and I indicate I will only accept the publication of the paper as it is in an issue of the journal, as there is no a single scientific problem. The paper is finally withdrawn on the 8th of March by E. Clementi (page 34), committing scientific misconduct as there are no scientific reasons to do it. The reasons why they do this must be investigated.

Role played by Elsevier delegate (A.M. Pordon) in this issue is just as scandalous. She fully supports this scientific misconduct, trying to justify the unjustifiable (page 31). Note her sentence: 'We are withdrawing the paper (…)', i.e., she is part of all this and fully responsible. The withdrawn decision was already taken before contacting me for the first time. The other actors, Pasquale Maffia and Sonia Radice are blamed for acting as spectators of a scientific crime, not making any effort in defending science in the face of a terrible injustice: a true scientific prevarication.

The truth needs to be known. Please, read the emails below and realize about the problem: science that indicates that vaccine safety is not as strong as we are told is withdrawn from publication without scientific reasons: they want to avoid people knowing the truth, they need to keep on saying there are no published papers indicating lack of safety in aluminum vaccine adjuvants. This needs to be changed as soon as possible. You can act and I'm calling you to act:

1) Write the people implicated in this scandal (emilio.clementi@unimi.it, a.pordon@elsevier.com, elia.biganzoli@unimi.it, pasquale.maffia@glasgow.ac.uk, sonia.radice@unimi.it). Ask them the reasons for their acts: why science questioning vaccine safety is being removed without any scientific reason, which are their conflict of interests, who has told them to commit this scientific misconduct, where their scientific integrity is, etc. If they are not able to give an answer, all of them must resign (or fired) from their jobs: an editor that it is not independent must immediately resign, personal for an editorial supporting this scandal must immediately resign, professors at university with no scientific integrity have nothing to teach and they must immediately resign.

2) Write Elsevier (see Elsevier.com for contacts). Ask them if it is editorial policy to withdrawn papers without scientific basis, ask who has pressured them to act like this, ask why they tolerate scientific misconduct and misbehavior among their employees and their editors, and ask them to restitute the withdrawn paper immediately and to apologize.

3) Distribute this pdf as much as you can: your contacts, institutions, associations… Place this pdf in any web page you might think appropriate. Use social media to disseminate. We need a massive response.

4) Contact journalists. There must be journalists in this planet ready to report the links between those pharmaceutical companies, editorials and editors that actively (and in a very corrupted way) work to stop the truth about aluminum and vaccine safety to be known by the general public.

Of course, you can mention my name as the responsible for disclosing these email conversations: I never act anonymously.

Lluís Luján
Department of Veterinary Pathology
University of Zaragoza, Spain
Lluis.Lujan@unizar.es

March 10th, 2019

Assumpte	**concerns on your article Cognition and behavior in sheep repetitively inoculated with aluminum adjuvant containing vaccines or aluminum adjuvant onlyY PHRS_2018_1341**
Remitent	Emilio Clementi <emilio.clementi@unimi.it>
Destinatari	<Lluis.Lujan@unizar.es>
Cc	Anne Marie Pordon <a.pordon@elsevier.com>, Pasquale Maffia <pasquale.maffia@glasgow.ac.uk>, Sonia Radice <sonia.radice@unimi.it>
Data	2019-01-11 18:15

- Asin et al.,concerns.pdf (~51 KB)

Dear Prof Luján,

I am writing to you about your manuscript entitled "Cognition and behavior in sheep repetitively inoculated with aluminum adjuvantcontaining vaccines or aluminum adjuvant only", which we recently accepted for publication (still in ahead of print status).

We received serious concerns from the readership about a series of aspects of it.

I summarise them for you here below:

- Very small cohort sizes
- Possible Influence of extreme outliers on statistical relationships not addressed
- Data presented in some figures possibly exceeding the number of animals involved
- Graphical representations of data including items that appear not explained in the legend, or elsewhere
- High numbers of relationships (>200) statistically assessed with a low rate of significance (<9%), raising concerns about p hacking
- Findings of statistical significance difficult to reconcile with data presented (mean, median, IQ range, SE)
- The overwhelming majority of statistically significant findings were from two behavioural tests which have not apparently been validated for the model chosen

Details of the concerns are enclosed in the attached file, please do have a look at them. In these circumstances it is our policy to contact the authors and give a possibility to answer to the concerns received.

Given the circumstances we also require that you send us, or make us available otherwise, all the raw data of the experiments in a format suitable for statistical analyses which we may need to run independently.

I encourage you to take this letter of mine seriously. We will keep the manuscript on hold till we reach a final decision

We offer you also the possibility to withdraw the manuscript if you desire so. In this case all proceedings regarding this case will come to a halt

with best regards

Emilio

Prof. Emilio Clementi, Mus. M., M.D., Ph.D.
Head, Unit of Clinical Pharmacology,
Fatebenefratelli-Sacco Hospital, University of Milano
Editor in Chief, Pharmacological Research
Member in the Executive Committee,
The International Union of Basic and Clinical Pharmacology, IUPHAR
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Concerns from the readership

Very low cohort sizes, n = 7. There does not appear to be any power calculation to validate this choice of cohort size. This is a very low cohort size with other papers by these authors having group sizes more than double this.

The low cohort sizes appear to have an effect on statistical relationships. An example of which can be seen in Table S5. The measurement in this table is time spent in leaving the first area (latency). As a result it would be expected that all numbers would be integers and between 0 and 300 seconds, the time spent in the behavioural test. There is a statistical difference between the Group C on Day 1 and on Day 2, however if the mean and interquartile range was mapped out for Day 1 a set of values that matches the data set very well (same data except for a minor difference in SD (18.01 vs 18.17)) is 0, 2.5, 3, 7, 7, 7, 51.5. Apart from the question of how the IQ is 2.5, the major issue with this data is the extreme outlier, 51.5 - which nearly double the other six values combined. If this single outlier is removed a simple Student's t test demonstrates that the difference is no longer significant.

Data presentation is not straightforward. Figure 3 Group B is presented as two yellow boxes where the interquartile range on the Winter test falls completely within the interquartile range of the Summer test. The data sets in S26 show the respectively IQ ranges are 5 – 16 and 5 – 11. It is never adequately described but it appears that the circles (also stars on other graphs) are indicators of outliers. For the Summer cohort the upper IQ limit is 16 but there appears to be an outlier at ~42 compared with a single outlier for the Winter cohort of ~23. Whilst impossible to understand without the raw data and the way the analysis was exactly performed it appears to be another example of a single outlier causing a difference to become statistically significant as the original p value was 0.045 which is very close to the limit for acceptance.

The concerns on the apparent outliers are increased when Figure 5 (associated with Supplementary Table S27) is examined, as the Group A Summer cohort has eight of these markers (one circle, seven asterix), considering that the n value is only seven this is highly confusing. The upper IQ limit is 5 and all of these markers are beyond this, as is the mean of 6.61. If eight markers are beyond the IQ3 then it is safe to assume that at least 32 data points are involved in this analysis. The median is also only 1 which means that 16 of these data points are either 1 or zero, and another seven are above 21. This indicates that there is a large variation in this single set of data which is a red flag for the behavioural protocol. Are these outliers from a single animal?

Where do all the data points come from? If further calculations are made, based on the fact the total of the mean x n will equal a whole number (because interactions are measured as integers not fractions), then the two closest n values which give a whole number when multiplied by the mean , and are over 32, are 41 and 59. As the error is given as Standard error (SE = square root of SD) it means the mean ± SD with these two n values would be 6.61 ± 10.50, and 6.61 ± 12.6 respectively. If the n values were the same for the Group A Winter figures the respective mean ± SD would be 2.67 ± 4.61 and 2.67 ± 3.84. These data demonstrate that with an n value of either 41 or 59 (which are the two lowest that can be represented by this data on the assumption that the asterisks and dots are outliers) the mean of the summer and winter data falls within a single standard deviation from the mean of the other value.

In the data presented in the Supplementary section (which reflects the data presented in the Figures in the Main manuscript) there are no less than 213 interactions examined statistically, of which only 8.9% are statistically significant. This raises the issue that the statistically significant results in this study have occurred purely by chance and are only detected because of the large number of relationships tested. However over 63% of the statistically significant results came from the behavioural tests (home pen individual and social behaviour observations). As a result it is likely that with a statistically significant rate of only less than 3.3% the findings in the non-behavioural tests are likely to be the result of chance alone, especially considering that the seven different statistically significant results all occur individually rather than in a pattern.

These behavioural tests which produced the majority of the significant findings are problematic. In both the Methods and Results (both Individual Behaviour and Social behaviour sections) no references are given for the protocol used. In the Discussion the authors claim that their behavioural protocols are 'extensively validated' using references 24 – 35.

However if these references are looked at, there is very little evidence of these protocols being validated. It is well established that different strains of animal respond differently to behavioural stressors (van Gaalen and Stecler, Behav Brain Res, 2000 and Romeyer and Bouissou, Applied Animal Behav Science, 1992 – which is Ref 35 in Asin et al.) ; references 24, 26, 27, 29, 31, 32, 34, and 35 are excluded as they use different strains of sheep, and often a different gender (females compared to the males in the current study). Reference 28 was a study which was undertaken in sheep at 30 days of age which is a very different developmental stage to the sheep in the current study which were not even recruited until they were three months old. Finally the few remaining references looked at different behavioural paradigms than the ones identified as 'Behavioural tests: home pen individual and social behaviour observations'. Reference 25 was a conference abstract only and looked at individually housed animals not group housed animals as examined in this study (and this is obviously key when examining social behaviours). Reference 30 examined sheep in a choice maze by showing them 25 pairs of sheep faces. Finally Reference 33 is a generalized review of fear in a variety of species and no specific protocols are included or assessed relating to the 'behavioural tests' used in the current study. So in short the majority of statistically significant findings in this study were from unvalidated behavioural tests.

Assumpte	**Re: concerns on your article Cognition and behavior in sheep repetitively inoculated with aluminum adjuvant containing vaccines or aluminum adjuvant onlyY PHRS_2018_1341**
Remitent	Lluís Luján <Lluis.Lujan@unizar.es>
Destinatari	Emilio Clementi <emilio.clementi@unimi.it>
Cc	Anne Marie Pordon <a.pordon@elsevier.com>, Pasquale Maffia <pasquale.maffia@glasgow.ac.uk>, Sonia Radice <sonia.radice@unimi.it>
Data	2019-01-11 19:10

Dear Prof. Clementi,

I have just received this email and let me say I'm quite surprised about it. It is just too late to start a discussion now but of course we will answer all your points once we have studied them. I will contact you next week.

Yours sincerely,

Lluís Luján

A 2019-01-11 18:15, Emilio Clementi escrigué:

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> Given the circumstances we also require that you send us, or make us available otherwise, all the raw data of the experiments in a format suitable for statistical analyses which we may need to run independently.

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Data	2019-01-14 14:40

Dear Prof. Clementi,

Your email took me by surprise. Until this point I have only received praise and encouragement about our paper. It is, of course, anyone's prerogative to review and question published science by sending a Letter to the Editor but these letters are not given anonymity. I do not understand why this case is different.

We can and indeed we will address the comments made by this individual. Actually, it will be easy for us to refute/discuss all of them, one by one. We will also make our raw data available to you for independent statistical analysis should this be necessary once we have answered the queries raised by this individual.

Professor Clementi, I am sure that you are aware that there are individuals that write letters very similar to this one to editors of literally every paper that is published that questions the safety of vaccines, whether human or animal vaccines. This may be a legitimate complaint questioning the science published in our paper but at least, it should be transparent.

In any case, we are already preparing a reply to these comments. You will receive this document shortly.

Yours sincerely,

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Data	2019-01-14 15:13

Dear Prof Lujan,
thank you for your feedback

Please make sure to sustain your points with analyses of the data showing that numbers are correct and significance do exists
Be as detailed as possible including if needed tables, and disaggregation of data to make this case the easiest possible to solve, I do hope with a favourable outcome. Take all the time needed to do it in the most accurate way

best regards

Emilio

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Data	2019-01-14 15:50

Dear Prof. Clementi,

I will follow your advices, no doubt about it.

Yours sincerely,

Lluís Luján

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Data	2019-01-28 16:10

Dear Prof Luján,
I am writing to you to know about my letter to you of the 11th January requesting your reply to the comments to you article.
Two weeks have elapsed since then and I desire to know at which stage you are in preparing the reply and the raw data. We ought to receive them by the end of this week, in the absence of which we would have to withdraw the article.
Please do let me know

best regards

Emilio

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Data	2019-01-28 19:27

Dear Prof. Clementi,

The response is ready to be sent but I'm at the moment in France until tomorrow. You will have my comments on your computer on Wednesday early morning, do not worry. By the way, you will see there is nothing in those comments that stand a minimal scientific review.

Sorry for this delay, yours sincerely

Lluís Luján

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Assumpte	**Answers to concerns on article CY PHRS_2018_1341**
Remitent	Lluís Luján <Lluis.Lujan@unizar.es>
Destinatari	Emilio Clementi <emilio.clementi@unimi.it>
Cc	Anne Marie Pordon <a.pordon@elsevier.com>, Pasquale Maffia <pasquale.maffia@glasgow.ac.uk>, Sonia Radice <sonia.radice@unimi.it>
Data	2019-01-30 00:52

- Response to concerns PHRS_2018_1341.docx (~37 KB)

Dear Prof. Clementi,

Thank you for the opportunity to respond to the comments on our paper. As requested, we have reviewed these comments and our paper in full and, importantly, in good faith. The time taken for all this is the only reason for this delay, for which I apologize.

Prof. Clementi, when I submitted this paper to your journal, the data had been checked a thousand times and I was absolutely sure of the contents. After this revision I'm even surer about it. In reading our reply to the comments you will quickly appreciate that they have almost no scientific foundation. Indeed, they are written in a manner to deceive and to give the appearance of 'scientific credibility'. I know authors that have received very similar 'complaints' where the objective of the complainer is always to get a published paper retracted and to discredit the authors' reputation forever. Most of these 'complaints' come from a few sources that rarely -if ever- reveal their conflicts of interests when they make their so-called complaint. Specifically, comments made by this individual in this occasion constitute the perfect example of cherry picking (or the fallacy of incomplete evidence): "the act of pointing to individual data that seem to confirm a particular position while ignoring a significant portion of data that may contradict that position". In the more than thirty years of my life as a researcher and university lecturer, this is the first time that something similar happens to one of my studies and I have worked and published extensively in the field of animal health, including vaccines. Some people in the field of vaccine safety seem to judge papers by the topic and not by the science.

We have complied with your request in full and we now consider this issue closed. However, something does need to be done about these individuals whose only purpose seems to be to prevent the publication of high quality science where the conclusions go against their significant interests.

Of course, if you would have any further doubt or question about our paper or would like to check our data base, please, just contact me again.

With best wishes

Lluís Luján

Answers to "Concerns from the readership"

PARAGRAPH 1

Very low cohort sizes, n = 7. There does not appear to be any power calculation to validate this choice of cohort size. This is a very low cohort size with other papers by these authors having group sizes more than double this.

Let's state a basic notion: Power calculation for determining cohort sizes is an ideal scenario for epidemiologic studies and not a necessary pre-requisite, as the sentence above seems to indicate. It is, therefore, just a recommended procedure that always depends on available funds. In our paper power calculation was performed but it was limited by a very tight budget, as the 21 animals had to be maintained at least 16 months, something that is very expensive. Sheep need appropriate facilities, specialist care and suitable research spaces, a combination of factors not easy to find for studies implying large animals. In any case, this comment is spurious: results soundly demonstrate that even with the size of our cohorts, very relevant significant differences appeared in many of the evaluated parameters, invalidating the questioning on the size of cohorts. Only in the case of no significant results at all, one could assume than the size cohort was perhaps too small to demonstrate the hypothesis.

Contrarily to what this individual says, we normally work with groups of this size. Our last experimental study using lambs (*Pinczowski et al., Veterinary Pathology 2017, Vol. 54(3) 413-424*) included 15 lambs divided in three groups (6, 6 and 3 lambs per each group). Results were outstanding enough to merit a highly positive editorial in the issue where it was published (*Highland, Veterinary Pathology 2017, Vol. 54(3) 353-354*).

PARAGRAPH 2

The low cohort sizes appear to have an effect on statistical relationships. An example of which can be seen in Table S5. The measurement in this table is time spent in leaving the first area (latency). As a result it would be expected that all numbers would be integers and between 0 and 300 seconds, the time spent in the behavioural test. There is a statistical difference between the Group C on Day 1 and on Day 2, however if the mean and interquartile range was mapped out for Day 1 a set of values that matches the data set very well (same data except for a minor difference in SD (18.01 vs 18.17)) is 0, 2.5, 3, 7, 7, 7, 51.5. Apart from the question of how the IQ is 2.5, the major issue with this data is the extreme outlier, 51.5 - which nearly double the other six values combined. If this single outlier is removed a simple Student's t test demonstrates that the difference is no longer significant.

All this paragraph is based on a misleading reasoning: remove outliers to use parametric tests (Student's t test, in this case). As stated in the paper, our data are not normally-distributed and in consequence we needed to use non-parametric tests: our data cannot be evaluated using parametric tests in most of the cases. Actually, we have reviewed the data without that outlier (that this individual mentions) and data from day 1 become normal but not data from day 2. Therefore, even in this analysis we

are obliged to use a non-parametric
approach. https://en.wikipedia.org/wiki/Nonparametric_statistics
Non-parametric tests evaluate data depending on rank of specific data in a series of data and they are not so depending on the specific value of each data. Moreover, the tests we have applied are paired statistics, a very powerful tool as there are auto control values within the same analysis.
We recommend the reading of this comment in the blog of Minitab that indicates the use of non-parametric tests when analyzing data with outliers (http://blog.minitab.com/blog/applying-statistics-in-quality-projects/why-you-should-use-non-parametric-tests-when-analyzing-data-with-outliers).
As a conclusion, removing outliers is only justifiable if a known factor could have affected the validity of that value, which was never the case. Removing an outlier just because it is an outlier is essentially wrong. This is textbook knowledge and our students would not make such mistake. In any case, removing outliers for the data to fit the hypothesis is not scientific and it is indeed not our way of analyzing data.

The IQ range is 2.5 because it was calculated using the most appropriate statistic tool, the Tukey's hinges (https://stats.idre.ucla.edu/spss/output/descriptive-statistics/). By the way, checking the numbers this individual has created to demonstrate his/her hypothesis, they are several mistakes: there should not be a zero value and the median should be the value in the middle of the ordered list of values, implying that 50% of data are below this value and 50% are above the median.

PARAGRAPH 3

Data presentation is not straightforward. Figure 3 Group B is presented as two yellow boxes where the interquartile range on the Winter test falls completely within the interquartile range of the Summer test. The data sets in S26 show the respectively IQ ranges are 5 – 16 and 5 – 11. It is never adequately described but it appears that the circles (also stars on other graphs) are indicators of outliers. For the Summer cohort the upper IQ limit is 16 but there appears to be an outlier at ~42 compared with a single outlier for the Winter cohort of ~23. Whilst impossible to understand without the raw data and the way the analysis was exactly performed it appears to be another example of a single outlier causing a difference to become statistically significant as the original p value was 0.045 which is very close to the limit for acceptance.

In this paragraph there are several mistakes, some crucial:
1) This comment is about Fig 4 which is 'Social behavior' (and not Fig 3 which is 'Individual behavior').
2) Circles and asterisks: They need no explanation as in SPSS (the universal pack for statistics) 'normal outlier' or 'atypical values' are represented by circles whereas extreme outliers are represented by asterisks (by the way, not *'starts'* as this individual says). I'm afraid this is again basic knowledge (https://en.wikipedia.org/wiki/Box_plot).
3) Fig 4 is included in the 'Social behavior' part of the study. As it is perfectly explained in point 2.4.3., observations were performed on 7 individually-identified animals, during 7 days: this means 49 observations per group and round. In other words, there are 49 data in each group (box) and 294 (49x6) data behind the whole Fig. 4.

Therefore, the fact that there are a total of 4 atypical values and only one true outlier in Fig. 4 is simply an anecdote and the reasoning this individual makes, irrelevant. Remarkably, this individual pays a great deal of attention to the fact that one significant value in Fig. 4 is p=0.045 (*'very close to the limit for acceptance'*) but at the same time this individual misses that there are four significant differences p<0.001 just in the same figure: these results deserve no comment…

Not to leave any comment without answer: the explanation of outliers and non-parametric test has been done in the previous paragraph.

PARAGRAPH 4

The concerns on the apparent outliers are increased when Figure 5 (associated with Supplementary Table S27) is examined, as the Group A Summer cohort has eight of these markers (one circle, seven asterix), considering that the n value is only seven this is highly confusing. The upper IQ limit is 5 and all of these markers are beyond this, as is the mean of 6.61. If eight markers are beyond the IQ3 then it is safe to assume that at least 32 data points are involved in this analysis. The median is also only 1 which means that 16 of these data points are either 1 or zero, and another seven are above 21. This indicates that there is a large variation in this single set of data which is a red flag for the behavioural protocol. Are these outliers from a single animal?

Again, a misleading comment based on a wrong assumption: The n value of each box is 49 (294 data in total in the Figure) and all the effort this individual makes to squeeze numbers to prove his/her hypothesis is useless. By the way, we have reviewed all data again in the search of a single or small cohort of animals that might be diverting data (and results): there is no a single animal that is constantly outlier. On the contrary, data are very homogeneously distributed among animals in all groups.

PARAGRAPH 5

Where do all the data points come from? If further calculations are made, based on the fact the total of the mean x n will equal a whole number (because interactions are measured as integers not fractions), then the two closest n values which give a whole number when multiplied by the mean , and are over 32, are 41 and 59. As the error is given as Standard error (SE = square root of SD) it means the mean ± SD with these two n values would be 6.61 ± 10.50, and 6.61 ± 12.6 respectively. If the n values were the same for the Group A Winter figures the respective mean ± SD would be 2.67 ± 4.61 and 2.67 ± 3.84. These data demonstrate that with an n value of either 41 or 59 (which are the two lowest that can be represented by this data on the assumption that the asterisks and dots are outliers) the mean of the summer and winter data falls within a single standard deviation from the mean of the other value.

The same mistakes once again: Sample size in behavioral analysis is 49 (7 daily observations for each of 7 animals by group), and it is a non-sense the assumptions and deductions about 41 and 59 as n value (it is so easy to read the M&M section 2.4.3!). Moreover, this individual insists on using parametric tests for non-normally-

distributed data. Using these equivocal assumptions, this individual creates wrong data that -simply- do not deserve attention.

Remarkably, there are again basic mistakes in this paragraph. First of all, SE is not the square root of SD; it is the ratio between SD and square root of sample size (https://en.wikipedia.org/wiki/Standard_error). Secondly, there is a wrong interpretation between SD and SE, and their corresponding intervals. When we calculate the probability interval (or confidence interval of a distribution) as sample mean ± Z·SD we obtain a descriptive result of variability of data (when confidence level is 95%, Z is equal to 1.96, rounded to 2 for further calculations in this explanation). For instance, for a sample of weight of 100 animals with mean = 10 kg and SD =2 kg, we get an interval of 6 to 14 kg, that means that 95% of animals are between 6 and 14 kg, and 5% are below 6 kg or above 14 kg. When we use the SE to calculate a similar interval (mean ± Z·SE) we are calculating a confidence interval for an estimation (the mean in this case), and in our example, SE will be equal to 0.2 (2 divided by square root of 100) so the confidence interval is 3.6 to 4.4 kg, and it means that we have a confidence of 95% that population mean (μ) is between these values. So, the first probability interval (based on SD) is a description of the population (distribution) and the confidence interval (based on SE) is an inference of the population mean (precision of the estimation from a sample). And here the most important point: the parametric tests are based on the overlapping of the second confidence intervals, and not on the overlapping of probability intervals as is incorrectly stated by this individual. Moreover, as it has been already said, these interpretations this individual makes about SE would only be valid if our data would be normally distributed, which is not our case.

PARAGRAPH 6

In the data presented in the Supplementary section (which reflects the data presented in the Figures in the Main manuscript) there are no less than 213 interactions examined statistically, of which only 8.9% are statistically significant. This raises the issue that the statistically significant results in this study have occurred purely by chance and are only detected because of the large number of relationships tested. However over 63% of the statistically significant results came from the behavioural tests (home pen individual and social behaviour observations). As a result it is likely that with a statistically significant rate of only less than 3.3% the findings in the non-behavioural tests are likely to be the result of chance alone, especially considering that the seven different statistically significant results all occur individually rather than in a pattern.

As it has been said at the first sentence of this reply, the cohort size -perhaps- did not allowed us to demonstrate other significant results in the cognition section of our paper. However, this does not mean that these differences do not exist. Not to be able to reject the null hypothesis does not automatically mean the null hypothesis is true. It may simply mean that there might not be enough evidences to reject it. For us, it would have been much easier not to show the results on cognition (where there are only a few significant results) in the paper and only to publish the results on behavior, where differences are outstanding. However, we are honest scientists and as such, we

do not hide data. We just wanted to clearly show all gathered information for the readers to be able to make an objective judgement.

Remarkably, this individual focusses and maliciously criticizes a part of the study (non-behavioral assessments), completely ignoring the rest. However, the sentence *'are likely to be the result of chance alone'* is clearly released to attack the whole paper. If all significant results in this paper are the *'result of chance alone'* then our results are closer to a miracle than to anything else: control group (age and sex matched animals) never showed any difference in any of the cognitive or behavioral assessments performed, whereas all changes appeared in the aluminum and vaccine group, only… of course, following this misleading interpretation, just by chance… This individual misses that in Fig. 7, the only significant result is actually in the control group, demonstrating a lower cortisol level in winter in the control animals, whereas both aluminum and vaccine groups show the same values than in summer. Following this malicious interpretation this is again, pure chance.

FINAL PARAGRAPH

These behavioural tests which produced the majority of the significant findings are problematic. In both the Methods and Results (both Individual Behaviour and Social behaviour sections) no references are given for the protocol used. In the Discussion the authors claim that their behavioural protocols are 'extensively validated' using references 24 – 35.

However if these references are looked at, there is very little evidence of these protocols being validated. It is well established that different strains of animal respond differently to behavioural stressors (van Gaalen and Stecler, Behav Brain Res, 2000 and Romeyer and Bouissou, Applied Animal Behav Science, 1992 – which is Ref 35 in Asin et al.) ; references 24, 26, 27, 29, 31, 32, 34, and 35 are excluded as they use different strains of sheep, and often a different gender (females compared to the males in the current study). Reference 28 was a study which was undertaken in sheep at 30 days of age which is a very different developmental stage to the sheep in the current study which were not even recruited until they were three months old.

Finally the few remaining references looked at different behavioural paradigms than the ones identified as 'Behavioural tests: home pen individual and social behaviour observations'. Reference 25 was a conference abstract only and looked at individually housed animals not group housed animals as examined in this study (and this is obviously key when examining social behaviours). Reference 30 examined sheep in a choice maze by showing them 25 pairs of sheep faces. Finally Reference 33 is a generalized review of fear in a variety of species and no specific protocols are included or assessed relating to the 'behavioural tests' used in the current study. So in short the majority of statistically significant findings in this study were from unvalidated behavioural tests.

These comments are so misleading that they need a proper answer starting from the basis of what it is a study on animal behavior.

Animals are exposed to many endogenous and exogenous stress factors along their productive life and early behavioral responses are indicative of a stressor/s to which the animal cannot adapt. Scientific behavioral studies imply two complementary approaches: behavioral tests & behavioral assessments. Behavioral tests are developed to challenge animals and measure how they cope with those challenges (measured as frequencies of behavior and duration of responses). Behavioral assessments consist in observing animals under certain circumstances both individually and socially, to record the frequencies and time each animal dedicates to a certain behavior. Our study was planned to evaluate behavioral responses of sheep under a certain challenge (inoculation of PBS, aluminum alone or aluminum-containing vaccines) and it was performed using both, behavioral tests & behavioral assessments, as any proper study in behavior should do. The use of these two simultaneous approaches gives the reader a holistic vision of the phenomenon that happens after these inoculations and of the post-vaccine phenomenon in sheep.

Regarding behavioral assessments, the scan sampling (instantaneous) and continuous sampling techniques are universally stablished and they have been widely used for decades to assess behavioral changes of all kind, irrespectively of species, breed, age, sex, etc. This can be checked in the most important textbook in this topic "Martin & Bateson. Measuring Behaviour: An Introductory Guide. Cambridge University Press; 1986, 1993 and 2007", a book with more than six thousand cites in Google Scholar (we decided to cite several studies to demonstrate the flexibility of these techniques and because they easier to find, instead of citing a highly-specialized book alone). The scan sampling is used to measure behavioral states that require some time (eating, drinking, walking…) and the continuous sampling is used to measure relatively short behavioral events (affiliations, aggressions, etc.). Both techniques are complementary and allow deciphering how animals distribute their behavior under a certain stressor. These studies are sampling techniques for measuring behavioral frequencies and they can be adapted to all sorts of conditions (species, age, sex, state, type of production, type of farm…) without further validation, as counting defined behaviors needs no validation, only expert recognition. They are not tests on themselves; they are assessments to detect biologically significant behavioral changes (in its frequency or magnitude). In our work, all behaviors studied have been previously defined (Supplementary Table S2 and Supplementary Table S3) and we only measured their frequency to detect increases, decreases or no changes, when comparing the different groups. Contrarily to what this individual says, the same techniques have been previously used in very similar circumstances in ruminants (*Galindo 2000. The relationships between social behaviour of dairy cows and the occurrence of lameness in three herds. Res Vet. Sci. 69:75-9*; *Galindo 2002. Effects of lameness of dairy cows. J Appl Anim Welf Sci. 5:193-201*) and in sheep of the same breed (*Teixeira 2012. Effect of straw on lamb welfare, production performance and meat quality during the finishing phase of fattening. Meat Sci, 92:829-36*). Therefore, the insinuation made by this individual of "no validation of behavioral tests" is more than just a wrong statement.

Our study demonstrates that aluminum is a robust stressor that causes a non-specific response (chronic stress) to sheep in its different presentations, i.e.; it is the base of a syndrome, the ovine ASIA syndrome. In our study, the effect of this stressor could be detected in changes of the frequency of certain behaviors, thus indicating the capacity

of the stressor to change behavior. However, our results do not point to a remarkable impairment of sheep cognition. Presence or absence of a behavior does not necessarily mean tissue damage either temporal or irreversible. Therefore, a responsible reading of our paper indicates that the non-specific response to the stressor exists but our study is not able to discern if the damage exists or if it is temporal or not: more studies are needed. We would like to underline that our study was part of a much bigger project that included, among others, pathology and genetics studies. We have demonstrated subcutaneous, long-lasting inoculation site lesions in the form of aluminum-containing granulomas in the same sheep included in this paper in Pharmacological Research (*Asín 2018, Granulomas following subcutaneous injection with aluminum adjuvant-containing products in sheep, Veterinary Pathology; doi: 10.1177/0300985818809142*), thus providing a morphological basis for both, the biological response to the stressor and the syndrome. We have also demonstrated a very important genetic expression rearrangement in the same sheep (*Varela-Martínez 2018, Molecular signature of aluminum hydroxide adjuvant in ovine PBMCs by integrated mRNA and microRNA transcriptome sequencing, Frontiers in Immunology (Vaccines and Molecular Therapeutics); doi: 10.3389/fimmu.2018.02406*), thus indicating a profound genetic effect of subcutaneously-inoculated aluminum, further supporting the response to the stressor and the systemic effects of the syndrome.

Not to leave any comment by this individual without answer: the publications quoted above from van Gaalen and Stecler 2000 (*Behavioural analysis of four mouse strains in an anxiety test battery*) and from Romeyer and Bouissou 1992 (*Assessment of fear reactions in domestic sheep, and influence of breed and rearing conditions*) compare the reactions of different mouse strains or different sheep breeds under different stressors. This is misused to argue about the breed of our sheep. Remarkably, in our study, extremely homogenous animals were challenged by the same stressor (aluminum in different forms), which is the completely opposite approach to the above-quoted papers. The reasoning of this individual insinuating that our results are not valid because this approach has not been used in this breed and in this age is not just untrue (as demonstrated above): our system validated itself every single day of the experiment, as there was a totally-matched control group for comparison with the treatment groups, a fact that this individual misses again.

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Data	2019-01-30 17:57

Dear Prof Luján,
thank you for your e mail and the clarification.

we will now proceed with the analysis of the material you sent us and let you know in due course. As already anticipated, please do be prepared to send in the raw data should our statistical editor, Prof Elia Biganzoli, require them

best regards

Emilio

Prof. Emilio Clementi, Mus. M., M.D., Ph.D.
Head, Unit of Clinical Pharmacology,
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Data	2019-01-30 18:41

Dear Prof. Clementi,

No problem. If required, our epidemiologist and statistical expert (Dr. Ignacio de Blas) will be ready to assist him in any question on how to interpret the excel sheet containing the data and on how the analysis was performed.

Yours sincerely,

Lluís Luján

A 2019-01-30 17:57, Emilio Clementi escrigué:

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Data	2019-02-13 10:34

Dear Emilio,

I was reading the paper and related material of Asín et Al. with Prof. Luján as corresponding Author. I was considering in addition cited and not cited literature on ASIA.

The work is focusing a very delicate issue in science, calling for suitable research to clarify many controversial aspects.

Although the relevant topic, the paper is showing many relevant limitations on the ground of research methodology which I list below.

1. Also considering the chosen endpoints, blindness was necessary to implement the experiment.
2. Another relevant point is random sampling. The experimental animals within each treatment group were kept in the same herd, this is clearly against the assumption of independent sampling of the observations, underlying the chosen statistical analysis methods.
3. As additional questionable point, the use of PBS as control should be definitely reconsidered, since the local effects caused by the vaccine and the aluminum adjuvant.

On the basic statistical ground, the limitations are also clearly evident. It is mentioned the b risk value for type II error, but no formal calculation for sample size was presented to justify the sample size (assuming a correct random independent sampling)

A mixed model ANOVA approach was expected to account for repeated measures on the same experimental units. The naive use of test for the departure from normality assumption is not correct since the lack of significance is not proving normality.

Multiple comparisons are requiring a suitable procedure for controlling overall type I error risk.

However, following the above points, I don't think that withdrawal of the paper should be advised. In my experience, the cited limitations are unfortunately frequent in animal experiments. Withdrawing the paper for these reasons would imply a similar action on many other works. At present this option would not be sustainable.

The exploratory nature of the paper is implicit, results and conclusions should not be scored more than expected. The finding should be suggestive of additional higher level research for better clarifying the role of vaccines and aluminum adjuvant.

The author themselves suggest to keep the results as preliminary. At the end of the Discussion section the statement: *"Pathology performed at the end of the experimental period showed that Vaccine and Adjuvant-only inoculated animals presented persistent subcutaneous granulomas at the inoculation site with active migration of Al-laden macrophages to the regional lymph nodes. These granulomas likely act as a continuous and non-specific inflammatory stimulus and they could have somehow contributed to the behavioral changes observed in the present work"*

Beside any statistical interpretation according to incorrect p-values, the alternative interpretation of the findings shed a completely different light on the starting hypothesis of ASIA. The Authors honestly acknowledged this issue.

In conclusion, this work should be considered as exploratory and hypothesis generating, without being conclusive on any aspect.

The Journal in response to the criticism, possibly biased by advocacy, which is a disgraceful attitude in science as any other methodological limitation, could promote an editorial action on the ASIA topic. The relevant citation of the work by David Hawks et Al. on Journal of Autoimmunity 59, 2015, 7784: "Revisiting adverse reactions to vaccines: A critical appraisal of Autoimmune Syndrome Induced by Adjuvants (ASIA)" was actually missed in the present paper, showing that the controversy on the vaccines matter should be definitely framed in a more aseptic science context.

With best regards,

Elia

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Dear Prof Luján,
thank you for your e mail and the clarification.

we will now proceed with the analysis of the material you sent us and let you know in due course. As already anticipated, please do be prepared to send in the raw data should our statistical editor, Prof Elia Biganzoli, require them

best regards

Emilio

Prof. Emilio Clementi, Mus. M., M.D., Ph.D.
Head, Unit of Clinical Pharmacology,
Fatebenefratelli-Sacco Hospital, University of Milano
Editor in Chief, Pharmacological Research
Member in the Executive Committee,

Assumpte	**on the article by Asin et al**
Remitent	Emilio Clementi <emilio.clementi@unimi.it>
Destinatari	Lluís Luján <Lluis.Lujan@unizar.es>
Cc	Anne Marie Pordon <a.pordon@elsevier.com>
Data	2019-02-19 15:33

dear Prof Lujan
as you have seen we have completed our analysis of the issues related to your article. We have decided that the best course of action is that we withdraw the paper in its present form while allowing you to resubmit a revised version that takes into account the criticisms raised by our Statistical Editor in the comments he sent also to you. Please when ready just submit the article to us with a point by point reply in which you describe how you have modified the article and we will assess whether this is sufficient to allow its final publication.

best regards

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Via GB Grassi 74,
20157 Milan, Italy
Tel: +3902 50319640
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Fax: +3902 50319682
e mail: emilio.clementi@unimi.it

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Cc	<pasquale.maffia@glasgow.ac.uk>, Sonia Radice <sonia.radice@unimi.it>, Elia Biganzoli <elia.biganzoli@unimi.it>
Data	2019-02-19 16:00

Prof Clementi,

This is clearly non-justified. We have answered all “Concerns” and we haven’t had a chance to respond to the statistic review recently done. This is terribly unfair and responds to other reasons, not-scientific. This is causing us a terrible damage to our work, our prestige and future scientific contributions. Please, do not do it. We can respond to the last comments immediately, to ensure our work has no problem.

I will report this to the Committee on Publication Ethics (COPE) and I will treat this as a scientific misconduct.

Lluís Luján

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Data	2019-02-19 16:09

- Responses to Prof Biganzoli.docx (~18 KB)

Please, find attached the document we had already prepared to the comments made by Proif. Biganzoli.

There is nothing to change, sorry

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Although the relevant topic, the paper is showing many relevant limitations on the ground of research methodology which I list below.

1. Also considering the chosen endpoints, blindness was necessary to implement the experiment.

*2.4.1. Cognitive test: T-maze: "Video recordings of each test were **blindly** evaluated by a trained researcher".*

*2.4.2. Cognitive test: Open Field Test (OFT) and Novel Object Test (NOT): From the recordings, the observer (MPA) **blindly** calculated time the animal spent walking, exploring, standing, and trying to escape, among others parameters.*

*2.4.3. Behavioral tests: home pen individual and social behavior observations: After the experiment had concluded, a trained researcher (MPA) analyzed the videos consecutively in a **blind** manner.*

All the behavioral analyses were performed fully bind. Statistical analyses were also performed in a blind manner using unrelated coding for the groups.

2. Another relevant point is random sampling. The experimental animals within each treatment group were kept in the same herd, this is clearly against the assumption of independent sampling of the observations, underlying the chosen statistical analysis methods.

This is an experimental study, so the selected animals were randomly assigned to each group of treatment. Random sampling is indicated for observational studies, which was not the case.

To isolate 21 animals from each other in independent boxes for 15 months and fulfill animal welfare rules is just impossible. Moreover, how could we measure interactions between sheep if they are isolated from each other?

3. As additional questionable point, the use of PBS as control should be definitely reconsidered, since the local effects caused by the vaccine and the aluminum adjuvant.

If Prof. Biganzoli knows of any better reagent than PBS to be used as control in similar experiments, please, let us know.

On the basic statistical ground, the limitations are also clearly evident. It is mentioned the β risk value for type II error, but no formal calculation for sample size was presented to justify the sample size (assuming a correct random independent sampling)

As explained in our preview rebuttal letter, power calculation of sample size was limited by budget, facilities and ethical recommendation by the Ethics Commission.

A mixed model ANOVA approach was expected to account for repeated measures on the same experimental units. The naive use of test for the departure from normality assumption is not correct since the lack of significance is not proving normality.

A mixed model ANOVA approach was carried out, described in Mat & Met as “General lineal model”.

Regarding “repeated measures” we did not measured more than one time the same value. We carried out the same measurement along time in the same individual, meaning “paired measures”. They were analyzed with Wilcoxon and Student T test for paired samples, depending on normality (see point 2.6. in the paper).

We demonstrated the lack of normality of many of our data and therefore we used non-parametric tests.

Multiple comparisons are requiring a suitable procedure for controlling overall type I error risk.

2.6. Statistical analysis. Unpaired comparisons were performed using an ANOVA (A) Test (or Welch’s t-test (We) if variances were not homogeneous based on a Levene’s test) and a post hoc Duncan’s test (parametric tests), or a Kruskal-Wallis (KW) test and a post hoc Dunn’s test (non-parametric test).

In this paragraph we established the use of Duncan or Dunn’s test for multiple comparisons. This was again explained in every table of the paper.

The relevant citation of the work by David Hawks et Al. on Journal of Autoimmunity 59, 2015, 7784: "Revisiting adverse reactions to vaccines: A critical appraisal of Autoimmune Syndrome Induced by Adjuvants (ASIA)" was actually missed in the present paper, showing that the controversy on the vaccines matter should be definitely framed in a more aseptic science context.

“The relevant citation of the work by David Hawks” (Hawkes) is a review of previous scientific works. Authors express many personal opinions and conclusions are based on their own conceptions, all of them fully arguable. Their conclusions have been extensively discussed in other publications (*Segal, Dahan, Sharif, Bragazzi, Watad, Howard, Amital. 2018. The value of Autoimmune Syndrome Induced by Adjuvant (ASIA) - Shedding light on orphan diseases in autoimmunity. Autoimmunity Reviews 17:440–448*). Similar opinions by this individual and colleagues have already been totally refuted by us (*Ameratunga R, Langguth D, Hawkes D. 2018. Perspective: Scientific and ethical concerns pertaining to animal models of autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA). Autoimmun Rev 17(5):435-439*. **See answer in:** *Gherardi RK, Crépeaux G, Authier FJ, Luján L Animal studies are mandatory to investigate the poorly understood fate and effects of aluminum adjuvants administered to billions of humans and animals worldwide. Autoimmunity Rev 17(7):735-737*).

In any case, it is pernicious for science to consider that a review (such in this case) totally ends a scientific topic. The paper by Hawkes is simply another opinion along a scientific discussion. Clearly, as Prof. Biganzoli says, this topic needs unbiased science, freedom from any conflicts of interests.

Assumpte	**RE: on the article by Asin et al**
Remitent	Pordon, Anne Marie (ELS-AMS) <A.Pordon@elsevier.com>
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Data	2019-02-19 16:24

Dear Dr. Luján,

I wanted to step in here to say that your manuscript is not being retracted – which implies wrongdoing and could damage your professional reputation. We are withdrawing the paper, which does not imply misconduct in any way. There will be simply a statement that says "This paper has been withdrawn at the request of the _____" (Authors or Editors in the blank.)

Best,
Anne Marie

-----Original Message-----
From: Lluís Luján [mailto:Lluis.Lujan@unizar.es]
Sent: 19 February 2019 16:10
To: Emilio Clementi <emilio.clementi@unimi.it>
Cc: Pordon, Anne Marie (ELS-AMS) <A.Pordon@elsevier.com>; Pasquale Maffia <pasquale.maffia@glasgow.ac.uk>; Sonia Radice <sonia.radice@unimi.it>; Elia Biganzoli <elia.biganzoli@unimi.it>
Subject: Re: on the article by Asin et al

*** External email: use caution ***

Please, find attached the document we had already prepared to the comments made by Proif. Biganzoli.

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Data	2019-02-19 16:29

Sorry, the damage is the same and there is no reason (scientific) to do it, as we have demonstrated. Not even one. This is devastating for us.

There must be another solution, which I ask for

Lluís Luján

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Data	2019-02-19 17:21

Dear Prof. Clementi and others,

From the very beginning this has been a highly unusual action by the editor. An accepted paper, published “on line first” can be criticized but it is unacceptable that these criticisms are done anonymously. We all know this should have involved a Letter to the Editor, as one can see in the published issues of the journal. However, I preferred to be patient as I knew there were no scientific problems with my article and responded to all issues, not leaving even one standing. My rebuttal was then checked by a statistician which advice was to maintain the paper. To my surprise, on no scientific grounds, the decision is to withdraw the on line published paper. The reasons stated by the editor are some allegations made by this statistician that, again, can be refuted totally, as I have done just a while ago. Under no circumstances I agree with any action being taken by the editor/editorial with respect to my published paper. I can only accept the publication in its present form. I will report any other action to COPE and beyond if necessary to defend my work, my dignity as a researcher and the future of our research.

Professor Clementi, I am sure that you are aware that most of these ‘complaints’ come from the same source, an individual called David Hawkes or some of his accomplices (you can read about this person in this blog http://www.ghostshipmedia.com/2017/10/15/profile-passionate-vaccine-advocate/). These individuals are paid by the vaccine industry to contest any published paper where there might be any suggestion that a vaccine is not 100% safe. Individuals such as Hawkes masquerade as ‘scientists’ when they are simply individuals with significant vested interests and, rarely if ever do they reveal such interests when they make their so-called complaints.

Therefore, I’ll ask once more for the reason of the action you want to carry out with my paper and where this action is sanctioned within your publishing agreement with Elsevier. Where does it say that an anonymous and unfounded complaint can be made against published science? Where does it say that you are not given the opportunity to respond to 'so-called' independent review by a statistician? Where does it say that your published paper can be 'withdrawn' while all of this anonymous criticism is acted upon?

This is being terribly unfair for all of us. There are brilliant PhD students behind this work, reputed colleagues internationally known and many other reasons. I’m asking you to reconsider your decision and simply publish the paper. There is no a single scientific reason to do a different action. I will immediately act if I see this happening to my published paper.

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e/article/pii/S1043661818313732

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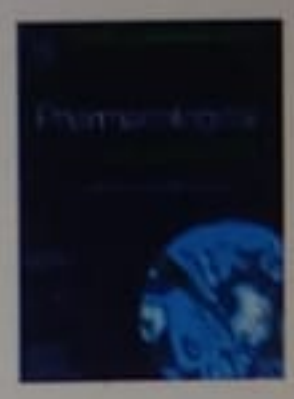
Pharmacological Research

Available online 3 November 2018

Withdrawn Article in Press



WITHDRAWN: Cognition and behavior in sheep repetitively inoculated with aluminum adjuvant-containing vaccines or aluminum adjuvant only

Javier Asín [a, 1], María Pascual-Alonso [b, 1], Pedro Pinczowski [a], Marina Gimeno [a], Marta Pérez [c, d], Ana Muniesa [a, d], Lorena de Pablo-Maiso [e], Ignacio de Blas [a, d], Delia Lacasta [a, d], Antonio Fernández [a, d], Damián de Andrés [e], Gustavo María [b, d], Ramsés Reina [e, 2], Lluís Luján [a, d, 2]

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https://doi.org/10.1016/j.phrs.2018.10.019

This article has been withdrawn at the request of the editor.

The Publisher apologizes for any inconvenience this may cause.