Gmail

Ellie Kincaid <kincaid.ellie@gmail.com>

Fwd: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco

Rajvir Dahiya <rdahiya@geneverify.org> Wed, Mar 8, 2023 at 12:06 AM
To: Ellie Kincaid <kincaid.ellie@gmail.com>, rajvir dahiya <rdahiya@gmail.com>

Dear Ms. Ellie Kincaid

Thank you for contacting me regarding the retraction of our Oncogene paper.

Please see below a series of email exchanges between Journal Oncogene and our team of scientists (Authors) regarding this paper.

The major problem was that this paper is about 16 years old and the investigation started in 2016. VA/UCSF committee members asked for original data. The first author who did the experiments left VA/UCSF and could not find the original data because our laboratory was shifted to a different location and our research lab notebooks were stored in a centralized location and after 6-7 years all the old files were discarded. As per NIH guidelines and policies all research data should be stored for 5 years and they kept it for 6-7 years, investigations started 10 years after the publication of data.

All our four papers were retracted due to the fact that all our original lab notebooks with data were discarded by the VA /UCSF after 6-7 years.

As you can see in our email exchange below, we repeated all the experiments and generated new data to satisfy Oncogene Journal. But the VA/UCSF committee forced the journal to retract our papers and penalized us due to the fact we did not have original data notebooks. The VA/UCSF agrees that all our original research notebooks data was stored in a centralized location and discarded because the statute of limitation for keeping the data is 5 years only as per NIH funding guidelines in 2010.

Please look into the reasons for retraction of all 4 papers by the Journals - it clearly states that original data could not be found. The VA/UCSF committee members stated that authors could not find the original data and thus falsified the data. These investigations started in 2016 and continued till 2022. I retired from the UCSF in June 2020.

All the journals that published our papers did not have any problems with the data. But the VA/UCSF committee members forced these journals to retract our papers. It is strange that on one hand VA/UCSF discarded our original research data notebooks and on the other hand they blamed us that we did not have original data and thus we falsified the data.

Please feel free to contact me if you have any further questions.

Thanks and regards

Rajvir Dahiya
Retired Professor Emeritus
UCSF San Francisco

---------- Forwarded message ---------
From: **Dahiya, Rajvir** <RDahiya@ucsf.edu>
Date: Thu, Jul 8, 2021 at 1:17 AM
Subject: Re: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco
To: Lucinda Haines <l.haines@nature.com>
Cc: Shahana <shankhan999@gmail.com>, Tanaka, Yuichiro <yuichiro.tanaka@ucsf.edu>

Dear Lucinda
We have carried out a series of experiments during the last two years to address all the concerns raised by the UCSF / VA investigation committee. All the original data was submitted to your journal and all concerns were addressed. Now under the pressure of UCSF/VA committee, the Editor has decided to retract our paper.
We (all authors) do not agree with the decision to retract our article by the Editors-in-Chief. Please feel free to contact us if you have any questions.
Thank you
With best regards

Rajvir Dahiya, Ph.D.
Professor Emeritus
University of California San Francisco (UCSF)
San Francisco, CA 94121
Phone: 415-861-9970
E-mail: Rdahiya@ucsf.edu

From: Lucinda Haines <l.haines@nature.com>
Sent: Wednesday, June 30, 2021 1:52 AM
To: Dahiya, Rajvir <RDahiya@ucsf.edu>
Subject: RE: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco

Dear Rajvir

Sincere apologies for the time taken to get back to you regarding the below response you sent to the latest round of comments from the editors.
Just prior to receipt of your last email, we received a report from the Investigation Committee on Scientific Misconduct of the Veterans Affair Medical Center, San Francisco, and the University of California San Francisco, which concludes that that several figures are the result of fabrication or falsification. Following receipt of this report the Editors propose that your paper be retracted.

The below retraction note has been drafted and will be circulated to all authors for their approval. Each author will need to confirm individually whether they agree or disagree with retraction.

"The Editors-in-Chief have retracted this article following an investigation by the Investigation Committee on Scientific Misconduct of the Veterans Affair Medical Center, San Francisco, and the University of California San Francisco. The committee concluded that Figures 2b, 4b, 4c, 5a and 5c are the results of fabrication or falsification of data. The Committee could not determine who was responsible for the fabrication or falsification.
[amend as appropriate:] All authors agree to this retraction/ None of the authors agree to this retraction /[author name] agrees to this retraction/[author name] does not agree to this retraction/ [author name] has not responded to any correspondence from the editor/publisher about this retraction."

Kind Regards

Lucinda

Lucinda Haines
Senior Publishing Manager

Springer Nature
The Campus | 4 Crinan Street |London |N1 9XW |UK
T: +44 (0) 207 843 3634

l.haines@nature.com
springernature.com

From: Dahiya, Rajvir <RDahiya@ucsf.edu>
Sent: 20 July 2020 21:29
To: Lucinda Haines <L.Haines@nature.com>
Subject: Fw: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco

[External - Use Caution]

Dear Lucinda
Attached, please find the response to the comments and original data.
We are highly grateful to the editorial board members for giving us a chance to address the concerns. We have really worked very hard and sincerely put all efforts to address each and every comment and generated new data using all appropriate controls. We hope that these responses are satisfactory to the reviewers.

With best regards

Rajvir Dahiya

Rajvir Dahiya, Ph.D.
Professor and Director
Urology Research Center
University of California San Francisco (UCSF) and
Senior Research Career Scientist
Department of Veterans Affairs,
VA Medical Center, San Francisco, CA 94121
Phone: 415-750-6964
E-mail: Rdahiya@ucsf.edu

From: Lucinda Haines <L.Haines@nature.com>
Sent: Monday, June 8, 2020 1:20 PM
To: Dahiya, Rajvir <RDahiya@ucsf.edu>
Subject: RE: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco

Many thanks – I understand the timing of this is somewhat problematic at present!

Kind Regards

Lucinda

Lucinda Haines
Senior Publishing Manager
Springer Nature|The Macmillan Building |4 Crinan Street |London |N1 9XW
Email: l.haines@nature.com
Tel: +44 (0) 207 843 3634

From: Dahiya, Rajvir <RDahiya@ucsf.edu>
Sent: 03 June 2020 08:20

To: Lucinda Haines <L.Haines@nature.com>
Subject: Re: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco

Dear Lucinda

Thank you so much for your prompt response. Due to COVID-19 lockdown and protests in USA, we are restricted to go to the lab for next 2-3 weeks. We have generated more data in response to the reviewers comments and will e-mail you all the data and response after this lockdown is over.
With best regards

Rajvir Dahiya

Rajvir Dahiya, Ph.D.
Professor and Director
Urology Research Center
University of California San Francisco (UCSF) and
Senior Research Career Scientist
Department of Veterans Affairs,
VA Medical Center, San Francisco, CA 94121
Phone: 415-750-6964
E-mail: Rdahiya@ucsf.edu

From: Lucinda Haines <L.Haines@nature.com>
Sent: Wednesday, May 27, 2020 12:13 PM
To: Dahiya, Rajvir <RDahiya@ucsf.edu>
Subject: RE: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco

Dear Rajvir

The editor has now had a chance to look over your point by point response but still has some questions – see in red in the attached.
Unless sufficient responses can be made to the editors questions, it is likely that the next course of action will be to retract this paper.
Please confirm your responses as soon as you can.

Kind Regards

Lucinda

Lucinda Haines
Senior Publishing Manager
Springer Nature|The Macmillan Building |4 Crinan Street |London |N1 9XW
Email: l.haines@nature.com
Tel: +44 (0) 207 843 3634

From: Dahiya, Rajvir <RDahiya@ucsf.edu>
Sent: 20 May 2020 17:49
To: Lucinda Haines <L.Haines@nature.com>
Subject: Re: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco

Oncogene (2007) 26:7647-7655
Knockdown of astrocyte-elevated gene-1 inhibits prostate cancer progression through upregulation of FOXO3a activity.

Dear Lucinda

Here is the point by point response to your comments:

We used siRNA to knockdown the AEG1 gene along with a non-specific control. The results are consistent with the data that is presented in the paper. Original paper used PMO and conventional methods such as PCR and chemiluminescent for Western developing machine. Since this is 13 years old paper and the technology has significantly advanced during this time. Therefore, for repeating these experiments, we used siRNA, advanced quantitative RT-PCR and LI-COR based Western blots and used the LI-COR Odyssey imaging platform (Image Studio) to quantify the band intensities to calculate the changes in protein expression. Again, as you see from the data that even though values are different, the results are consistent with the original paper.

Comment: Please clarify if you used EF1α as a normalization protein in the original paper, which they have now replaced with GAPDH?
Response: This work was done by the first author in 2007, almost 13 years ago. However, we repeated all the experiments in question. Currently we use GAPDH and/or B-actin as endogenous control in our lab for all the experiments and we get consistent expression across all cancers/cell lines. Endogenous control genes are used as loading controls to show that equal amount of proteins have been loaded across all the experimental conditions. In all our repeat experiments GAPDH or B-acting are consistent.

Additional important points to clarify:
Comment (i): Please can you provide quantification values for Figure 1D, as you did in the original paper. I am sure that these will be different and therefore the text will have to be adjusted.
Response: Please see the quantification values in Power Point file, slide 1, Figure 1D. Values are different since now we use LI-COR as mentioned above. However, the text does not need to be adjusted because the results are still the same. Please see the fold increase under the values. Expression is still 3 or more-fold higher (4-20) in cancer cells compared to Normal (RWPE1) cells and also different among cell lines. New values still have the same interpretation as given in result text in original paper.

Comment (ii): New Figure 2B: the control sample (1st lane of the original paper) was missed? In any case, the quantification of bands needs to be redone here too.
Response: The first lane in Figure 2B is the control "untreated samples" showing the endogenous levels of the target gene AEG1 which we already analyzed and is given in Figure 1D. That is why we did not put it in Figure 2B again. The quantification values from the LI-COR Software are provided in Power Point file slide 2 Figure 2B along with fold decrease and percent knockdown. Again, the results are consistent with the original paper, and the text in result section of original paper does NOT need to be adjusted.

Comment (iii): New Figure 4A: It seems that p27 in LNCAP is not increased as it is stated in the original paper (as shown in Figure 4B)?
Response: We have provided more blots in power point file slide 4, Figure 4A p27. We are also providing the modified Jpg file. It is consistent with the original paper and the text does not need to be changed.

v): New Figure 4B: Total FOXO3 levels are not higher in LNCAP cells as stated in the original paper (as a matter of fact, they actually seem to be less)? This again goes against what is written in the original paper.
Response: Active functional form of FOXO3 is phosphor FOXO3 (pFOXO3) and this is much higher in LNCAP cells in our current data consistent with what is explained in the original paper. Figure 4B.

Comment (v): New Figures 5A and especially 5C are not that convincing and as clear as the original ones.
Response: This is EMSA assay and done with siRNA. Original paper had used PMO. The differences between two is surely expected. However, we have provided image J quantification and the values shows significant differences and consistent with the original paper. Please see modified Figures 5A-C with quantification data (JPEG file).

Comment (vi): In the uncropped ppt file what does: A and C labels mean in the blots?
Response: In the ppt file we have raw data. We performed experiments with two siRNAs (A and C). This was to make sure that we get consistent results. However, in the compiled Figures, only one siRNA is shown. We have added the details on each ppt file slides.

We greatly appreciate your editorial board members for allowing us to repeat these experiments. We worked very hard and provided all the raw data for your kind consideration. We believe that your editorial members will find our responses satisfactory and resolve these issues.

Kind Regards

Rajvir Dahiya

Rajvir Dahiya, Ph.D.
Professor and Director
Urology Research Center
University of California San Francisco (UCSF) and
Senior Research Career Scientist
Department of Veterans Affairs,
VA Medical Center, San Francisco, CA 94121
Phone: 415-750-6964
E-mail: Rdahiya@ucsf.edu

From: Lucinda Haines <L.Haines@nature.com>
Sent: Sunday, May 10, 2020 1:45 PM
To: Dahiya, Rajvir <RDahiya@ucsf.edu>
Subject: RE: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco

Dear Rajvir

Firstly sincere apologies for not getting back to you sooner regarding the below email and your response to our enquiry.
I have now had a chance to liaise with our editors. Before we finalise an outcome for this paper, they have a few further questions which they would like answered which I have listed below.
Please provide your response to these:

Please clarify if you used EF1α as a normalization protein in the original paper, which they have now replaced with GAPDH?
Additional important points to clarify:
(i) Please can you provide quantification values for Figure 1D, as you did in the original paper. I am sure that these will be different and therefore the text will have to be adjusted.
(ii) New Figure 2B: the control sample (1st lane of the original paper) was missed? In any case, the quantification of bands needs to be redone here too.
(iii) New Figure 4A: It seems that p27 in LNCAP is not increased as it is stated in the original paper (as shown in Figure 4B)?
(iv) New Figure 4B: Total FOXO3 levels are not higher in LNCAP cells as stated in the original paper (as a matter of fact, they actually seem to be less)? This again goes against what is written in the original paper.
(v) New Figures 5A and especially 5C are not that convincing and as clear as the original ones.
(vi) In the uncropped ppt file what does: A and C labels mean in the blots?

Kind Regards

Lucinda

Lucinda Haines
Senior Publishing Manager
Springer Nature|The Macmillan Building |4 Crinan Street |London |N1 9XW
Email: l.haines@nature.com
Tel: +44 (0) 207 843 3634

From: Dahiya, Rajvir <RDahiya@ucsf.edu>
Sent: 20 November 2019 23:53
To: Lucinda Haines <L.Haines@nature.com>
Subject: Re: Two Oncogene articles under investigation Rajvir Dahiya UCSF / VAMC san Francisco

Dear Lucinda

Oncogene (2007) 26:7647-7655
Knockdown of astrocyte-elevated gene-1 inhibits prostate cancer progression through upregulation of FOXO3a activity.

Here is the response to the comments:

We are grateful to the journal for giving us time to repeat these experiments whose data is in questions. As we mentioned before that the primary author has left my lab 12 years ago and despite our repeated attempts, we could not contact him for the primary data. We used siRNA to knockdown the AEG1 gene and used it along with a non-specific control. The results are consistent with the data that is presented in the paper.

Please find attached the compiled data in a Tiff files as well as the original full membrane scans in PowerPoint. The western blots were performed with red and green labelled secondary antibodies and were developed on a Licor machine. For Figure 5a, c, we performed EMSA and the results are given in PowerPoint slides 5 and 6. The results are consistent with the results given in Paper and thus does not change the results or the conclusion of the paper.
Thank you again for giving us the time to repeat these experiments.
With best regards

Rajvir Dahiya, Ph.D.
Professor and Director
Urology Research Center
University of California San Francisco (UCSF) and
Senior Research Career Scientist
Department of Veterans Affairs,
VA Medical Center, San Francisco, CA 94121
Phone: 415-750-6964
E-mail: Rdahiya@ucsf.edu

From: Dahiya, Rajvir <RDahiya@ucsf.edu>
Sent: Wednesday, September 18, 2019 10:51 AM
To: Lucinda Haines <L.Haines@nature.com>
Subject: Re: Two Oncogene articles under investigation

Dear Lucinda:
Attached, please find the response of one of our papers. We have attached original data and the response.
Oncogene (2005) 24, 6765–6772
Paper Title: Promoter CpG hypomethylation and transcription factor EGR1 hyperactivate heparanase expression in bladder cancer.

Comment: Figure 6 in question: EGR1 and Heparanase bands are similar with different exposures.
Response: The original data published in this paper is based on gel electrophoresis -very old technology in 2005. Now we do not use this gel electrophoresis based technique anymore. To **repeat these experiments we performed quantitative real-time PCR (qRT-PCR) using a latest machine QuantStudio 7 Flex Real Time PCR System. qRT-PCR has been shown to be a robust, highly reproducible and sensitive method to quantitatively track functional gene expression changes under varying experimental conditions.** Utilizing this latest and extremely sensitive technology, we performed three independent experiments with three technical replicates (T1/T2/T3 shown in raw data files) each time. EGR1 expression knockdown was achieved using siRNA in the same manner as mentioned in the paper. T24 cells were transfected with EGR1 siRNA for 48 hours followed by qRT-PCR analysis for gene expression. We used same primer sequences as mentioned in the paper and given below.
Results: We got the same consistent results as were given in the published paper. A significant decrease (p=0.007) in EGR1 levels mRNA levels in T24 human bladder cancer cells transfected with siRNA targeting EGR1 (siEGR) was observed compared to the control siRNA (siControl) (a). Similarly, in the same cells with EGR1 knockdown, a significant decrease (p=0.0055) in the heparnase levels was also observed compared to siControl (b). Compiled results from three independent experiments with three technical replicates in each experiment are given below:

Figure 6: EGR1 siRNA downregulates heparanase gene expression in bladder cancer cell lines. Quantitative RT-PCR showing a significant decrease in EGR1 levels mRNA levels in T24 human bladder cancer cells transfected with siRNA targeting EGR1 (siEGR) and control siRNA (siControl) (a). The knockdown of EGR1 expression also resulted in significant reduction of heparnase levels compared to siControl in the same cells (b). Results represents three independent experiments. P value calculated by student t-test. Bar graph shows mean ± SE.

In summary, based on these experiments, our original data and results are consistent with is data and thus does not alter the summary or conclusion of this paper. .

Second paper entitled "Knockdown of astrocyte-elevated gene-1 inhibits prostate cancer progression through upregulation of FOXO3a activity (Kikuno)" , we are still working on these experiments to address your comments and will send you the data next month.
Thank you so much for your kindness
With best regards

Rajvir Dahiya, Ph.D.
Professor and Director
Urology Research Center
University of California San Francisco (UCSF) and
Senior Research Career Scientist
Department of Veterans Affairs,
VA Medical Center, San Francisco, CA 94121
Phone: 415-750-6964
E-mail: Rdahiya@ucsf.edu

From: Lucinda Haines <L.Haines@nature.com>
Sent: Friday, April 26, 2019 6:50 AM
To: Dahiya, Rajvir <RDahiya@ucsf.edu>
Subject: Automatic reply: Two Oncogene articles under investigation

I am currently out of the office until Tuesday 30th April and will reply to you as soon as i return