

CITY UNIVERSITY OF NEW YORK
FINAL INVESTIGATION REPORT OF
Associate Professor Hoau-Yan Wang, Ph.D.

Report Summary

This report summarizes the investigation conducted by a committee of research-active faculty at the City University of New York that was tasked with an examination of 31 allegations, described to us by the Office of Research Integrity, of research misconduct made against Dr. Hoau-Yan Wang, an associate medical professor in the CUNY School of Medicine. Here we describe our investigation, which took place over approximately ten months and consisted of an examination of the data cited in the allegations, interviews of Dr. Wang, a member of his lab, several administrators at the CUNY School of Medicine and CCNY, and a senior editor representing the ethics team for the *Public Library of Science (PLOS)* series of journals. The committee also reviewed Dr. Wang's responses to allegations, any image files referenced in and provided along with these responses, and additional material provided by Wang, including an analysis of blot images by Dr. Charles Spruck.

The committee has found evidence highly suggestive of deliberate scientific misconduct by Dr. Wang for 14 of the 31 allegations. However, we were unable to objectively assess the merit of the allegations due to the failure of Dr. Wang to provide underlying, original data or research records and the low quality of the published images that had to be examined in their place. For the majority of the publications identified in the allegations, we recommend that editorial action be taken to demand verifiable original data and determine, based on these, if the misconduct described in allegations has indeed taken place.

Finally, our investigation has revealed long-standing and egregious misconduct in data management and record keeping by Dr. Wang. It appears likely that no primary data and no research notebooks pertaining to the 31 allegations exist. It is for this reason that it was not possible for this committee to objectively determine how figures were created from the experiments described in the publications cited in the allegations. Dr. Wang has therefore failed to provide the data and research records necessary for the committee to directly address the concerns surrounding the published work under identified in the allegations. Thus, the integrity of Dr. Wang's work remains highly questionable.

Nature of Allegations

On September 13, 2021, Dr. Tony Liss, Provost and Senior Vice President for Academic Affairs at the City College of New York (CCNY), received a letter from Dr. Alexander Runko, the Director of the Division of Investigative Oversight at the Office of Research Integrity (ORI), informing Dr. Liss that ORI had received allegations of research misconduct from the National Institutes of Health (NIH) against Dr. Hoau-Yan Wang, Associate Medical Professor, City College of New York (CCNY). The letter from

ORI outlined nine specific allegations pertaining to work reported in eight publications, a poster presented at a conference, and an NIH grant proposal. Following the reception of this letter, ORI notified CCNY of additional allegations made against Dr. Wang, bringing the total number of allegations to 31. These allegations are listed in the word document “NIH Allegation Summary 1 thru 31 10.8.31.docx” that was provided by ORI and is included in the files accompanying this report. In all 31 allegations, Dr. Wang has been accused of falsification and/or fabrication of data, the vast majority of which consists of western blot data described in approximately 30 publications over the course of nearly 20 years. More specifically, for most allegations, Dr. Wang is accused of duplicating, cutting and pasting, or altering western blot images, thereby presenting falsified or fabricated biochemical data.

Research Sponsor and Grant Support

The committee was tasked with summarizing the funding and spending by Dr. Wang’s lab at CCNY over the nearly 20 years over which the alleged misconduct took place. These are the funding sources and expenditures for Dr. Wang’s lab, according to the CUNY Research Foundation.

Description	5R01MH116463-03	5R01MH116463-04	1RF1AG059621-01	1RF1AG059621-01	5R01AG057658-03	5R01AG057658-04	5R01AG057658-05	1R44AG065152-01
Budget Period	12/01/2020-11/30/2021	12/01/2021-11/30/2022	07/01/2020-06/30/2021	7/01/2021-06/30/2022	03/01/2020-02/28/2021	03/01/2021-02/28/2022	03/01/2022-02/28/2023	06/01/2020-12/31/2021
Expenditures								
Release time	10,237	14,716	11,758	11,758	9,881	14,822	13,693	8,646
Salary								
Research Assistant	48,438.46	25,836.75	29,030.34	94,145.71	34,260	33,000	64,800	16,320
Graduate Assistant	0	0	11,600	11,600	12,000	59,844.12	0	0
Fringe Benefits	24,043.13	16,911.62	17,223.86	42,938.72	18,147	42,871.07	30,951	10,176
Research Supplies	18,630	4,500	119,246.51	56,779	39,597	65,638.87	35,899	33,628
Other Independent contractor	0	0	0	0	0	0	0	1,350
Equipment maintenance	875	1,750	5,250	7,000	1750	3,500	1750	0
Travel	608	-0.35	4,437.97	6,837.97	1565	3,203	1687	0
Budget Adjustments/T transfers	-43,288.36		-174,098.63	0	-121,058.04	-328,072.70	0	0
Facilities & Admin Cost	58,614.05	36,316.99	119,165.09	137,697.23	66,804	144,140.98	84805	39,968
Total	118,157.28	100,031.01	143,613.14	368,756.63	62,945.96	68,947.34	233,585	110,088

Research Misconduct Committee and University Policies and Procedures for CUNY Misconduct Investigations

The research misconduct committee was charged by the Vice Provost for Research in accordance with the guidelines described in CUNY’s Policy Regarding the Disposition of Allegations of Research Misconduct, which can be found here:

<https://www.cuny.edu/wp-content/uploads/sites/4/page-assets/about/administration/offices/legal-affairs/policies-resources/Research-Misconduct-1.pdf>

The committee was tasked with assessing the merits of each of the 31 specific allegations of research misconduct against Dr. Wang and provide a conclusion as to whether research misconduct did or did not occur. Upon the determination that such misconduct did occur, the committee was charged with: 1.) Indicating if the research misconduct represented falsification, fabrication, or plagiarism, and if it was intentional, knowing, or in reckless disregard; 2.) Summarizing the facts and the analysis that support the conclusion and considering the merits of any reasonable explanation provided by Dr. Wang. 3.) Identifying the research sponsor that supported the work in question. 4.) Determining if any publications need correction or retraction. 5.) Identifying the person(s) responsible for the Research Misconduct.

Scope of Investigation

Having reviewed the 31 specific allegations raised against Dr. Wang and the material provided by CCNY to the research misconduct committee, reading the report produced by the initial inquiry at CCNY, and examining Dr. Wang's response to this inquiry, the committee agreed that each allegation could be objectively assessed through an examination of the primary research materials pertaining to the figures cited (primary scans of the films used to visualize western blots along with research notebooks and other records describing the preparation and execution of these blots). The committee therefore requested original blot scans and research records pertaining to each allegation from Dr. Wang. In our initial letter to Dr. Wang, we informed him of the existence of 31 allegations and asked that he initially respond to a subset of these using primary research materials to address the specific concerns raised in each allegation. It was the committee's desire to examine how data from the original uncropped images of western blots were used to create the figures cited in each of these allegations, compare our findings to Dr. Wang's response to each allegation, and make an assessment regarding whether misconduct had taken place for each of the specific concerns. The committee reasoned that establishing a correspondence between the shapes and molecular weights of the bands shown in the published figures with the shapes and molecular weights of the bands present on the original blot or blots used to create the figures in question would provide a definitive falsification of allegations against Dr. Wang.

The committee requested that CUNY hire an independent image consultant to examine all the publications and materials provided by Dr. Wang. However, after working on these allegations for nearly three months, this consultant precipitously withdrew their services, citing legal risks to themselves and their business. The committee therefore examined all the images cited in the allegations, along with Dr. Wang's responses and associated images for the allegations. The committee also attempted to create a timeline of actions taken by CCNY and CUNY to secure research materials from the Wang lab and conduct the initial inquiry. Finally, the committee conducted interviews with Dr. Wang, a member of his lab (Dr. Pei), various administrators at CCNY, and an Editor at *PLoS* who oversaw the examination of data

from five publications that were retracted from *PLoS ONE*. The committee chose to interview the Editor at PLoS based on the fact that *PLoS ONE* had not only taken the extraordinary step of retracting five of Dr. Wang's publications but also discovered evidence of research misconduct in his response to the concerns raised by *PLoS* editors.

Details of Investigation and Research Records and Evidence Reviewed

Though it was our intention to examine all primary data upon which the western blots identified in the specific allegations were based, we were unable to acquire any such material. In response to our requests, Dr. Wang sent many digital images, either organized within PowerPoint presentations, embedded in his response to the committee, or as single image files, containing what he claimed were the underlying data pertaining to the subset of the 31 allegations to which Wang was initially asked to respond. Some of these images were described by Dr. Wang as higher resolution versions of the published figures. In no instance did Dr. Wang provide any material that could be reasonably recognized as original, uncropped blots (images that included clear film/blot edges and molecular weight markers). In his response to our investigation, Dr. Wang has protested that our definition of original blot data is unreasonably strict. However, our definition is shared by ORI, for whom this report is written. The third-party analysis of Dr. Wang's work by Dr. Spruck was also based on images that are clearly not original data. It also became clear from our interviews with Dr. Wang and, Dr. Zhe Pei, a post-doctoral Research Associate in the Wang lab, that the lab did not employ notebooks to record the details of the preparation or execution of the western blot Experiments performed in the lab.

According to Dr. Wang and Dr. Pei, details of blot preparation and sample loading were written on loose sheets of paper and were typically discarded after the blots were run and data had been quantified from the blots. No other primary records were maintained. Rather, quantitative measures from blot scans were placed in Excel spreadsheets. This revelation is difficult to reconcile with the detailed synopsis of blot preparation provided by Dr. Wang in response to the draft of this report for some of the allegations. During our interview with Dr. Wang, he revealed that his laboratory did not record the file names of densitometer scans in these spreadsheets, nor did these spreadsheets appear to contain information that would allow for a clear understanding of how samples were prepared or loaded. Thus, even if unedited images of films or film scans exist, it does not appear to be possible to determine how data were acquired or which original western blots were used to create the figures cited in each of the 31 allegations.

According to Dr. Wang, material pertaining to western blot experiments were organized in folders, and folders were stored in boxes within the lab. During our interview, Dr. Wang confirmed that some of these folders contained at least a portion of the original films used to visualize western blots. However, he stated that a significant number of boxes containing research records were thrown away in response to a

request from CCNY to clean the lab during the COVID-19 pandemic. Officials at CCNY were not able to confirm this. Furthermore, as CUNY faculty, none of the committee members were directed to throw away research material during the pandemic and are not aware of other colleagues who were asked to do so. In our experience, labs were asked to decontaminate but not discard belongings. Therefore, this claim by Dr. Wang remains contentious. Dr. Wang stated the Dr. Pei, a post-doctoral research scientist in his lab, was present when boxes of research material were thrown away. Dr. Pei acknowledged that she was asked to clean the lab and that some films were likely thrown away. We were not able to determine, during our interviews with Dr. Wang and Dr. Pei, how much of the material removed from Dr. Wang's lab may have represented research records pertinent to the 31 allegations. However, it is clear from our interviews with Dr. Wang and Dr. Pei that maintaining such physical records was not a priority and that long-term record keeping was largely limited to the storage of cropped image files and excel spreadsheets containing densitometer measurements on lab computers and, in some cases, printouts of spreadsheets. Dr. Wang reported that the densitometer used for most of his western blot work is no longer functional and that at least one hard drive containing original densitometer files had been destroyed by CCNY IT when they sequestered data from the Wang lab. The committee notes a repeated pattern of blaming CCNY for the lack of data management by Dr. Wang.

Throughout our interview with Dr. Wang, he insisted that the images he provided to the committee and to editors who had made inquiries, and that the digital files he provided represented uncropped, underlying blot data. However, in no instance did such data include the blot/film edges expected of uncropped blot images. Furthermore, during our interview with Dr. Wang, he confirmed that all gels run in the experiments in question were loaded with molecular weight markers. However, there is not a single case in which the data presented to us by Dr. Wang as uncropped blots contained such markers. We conclude therefore, the Dr. Wang has failed to provide data that can be verified as unmanipulated, uncropped, underlying primary western blot data, as defined by ORI. It is not clear to this committee why some editors have accepted such material as original underlying blots from Wang in response to inquiries regarding misconduct allegations.

Despite his failure to maintain and share original research records with this committee, Dr. Wang's response to this draft report claims that this committee's analysis "materially inhibits Dr. Wang's ability to meaningfully and adequately respond to allegations" and references a "vagueness" in our allegations. We contend, however, that such vagueness is an unavoidable product of the need to examine low quality published images rather than verifiable original data. Throughout Dr. Wang's response to our draft report, he resorts to the same adjustment of image contrast and levels that were used as the basis of the original allegations, sometimes providing an analysis of images from other studies published in the same journal issue. We contend that the degrees of freedom involved is such image adjustments and the low quality and resolution of the published images make this approach untenable for the direct assessment of the allegations. Furthermore, we maintain that original blot images, as we have defined them, along with research records would offer a straightforward means

of determining if the shapes and relative positions of the bands shown in published figures reflect the true and unmanipulated outcomes of the original experiments.

During our interview it also became clear that the preparations of western blot experiments are starkly siloed in Dr. Wang's laboratory, with lab members preparing the samples and Dr. Wang running the gels, visualizing the blots, and preparing the figures. Thus, Dr. Wang would appear to be the only member of his lab who ran and visualized western blots for most experiments involving this technique. Given the extent of the allegations of misconduct against Dr. Wang, this practice should be noted.

Having determined that we would not be given access to uncropped underlying data and verifiable research records, we therefore examined the published images and determined the extent to which the aberrations described in the allegations and/or editorial statements were visible. We also confirmed that no verifiable underlying data (uncropped, original images of blots containing clear edges and molecular weight markers) were among the materials provided by Dr. Wang. We also examined image analyses provided by ORI, any PubPeer threads pertaining to the publications in question, and the analysis conducted by Dr. Spruck. The committee also conducted an interview with Dr. Maria Zalm to discuss the Editorial retraction of five of Dr. Wang's publications in *PLoS ONE* and the nature of the material Dr. Wang provide *PLoS* editors in response to their inquiry into allegations of research misconduct in these studies. Finally, early in our investigation, we requested that CUNY/CCNY provide access to all image files sequestered from Dr. Wang's office and lab computers. CUNY and CCNY were initially wholly unresponsive to these requests. It was not until approximately six months later, when the committee conducted an interview with Dr. Vincent Boudreau, CCNY President, that we made some headway in gaining access to the image files sequestered from Wang's computer.

At the direction of President Boudreau, CCNY IT provided access to 647 image files (518 jpeg, 127 tiff, and 3 bmp files), all of which the committee examined. During the interview with Dr. Wang, he referred to "thousands" of images stored on his devices, though it was conceded by his lawyers that it was not possible to track these images to research records, further demonstrating the lack of data management in the Wang lab. Based on this, we do not think that the files provided by CCNY represent the majority of image files that were likely present in Dr. Wang's lab when files were copied by CCNY IT. Among these files, only a few represented uncropped blots with molecular weight markers. That is, the bulk of the images made available to us by CCNY did not represent uncropped and unmanipulated western blot data, nor was it possible to match these images to any of the publications cited in the 31 allegations.

Finally, it should be noted that we first requested Dr. Wang to address a subset of the allegations (1-8 and 22) in writing before our interview. We were surprised to discover during our interview with Dr. Wang that he was apparently unaware of allegations 9-21 and 23-31, despite having informed Dr. Wang of the existence of 31 allegations in our initial correspondence and stating that we would first examine a subset of the allegations. We therefore requested during the interview that he provide us with any original data or records pertaining to any of 31 allegations and immediately sent Dr. Wang the full list of allegations from ORI. However, in his follow-up response

to the committee, Dr. Wang did not address these additional allegations, nor did he provide any data or research records pertaining to them. Our draft report therefore indicated Wang's failure to respond to or provide material pertaining to allegations 9-21 and 23-31. In his response to the draft report, Dr. Wang stated that he was never asked to respond to all 31 of the allegations. The committee contests this, but granted Dr. Wang additional time to provide responses, which have been incorporated into the final draft of this report. We were surprised to learn that CCNY had never shared the full allegations list with Dr. Wang, but do not understand why Dr. Wang did not immediately inquire about the full list when informed of the full number of allegations against him.

Dr. Wang's Response to the Draft Report

In his response to the draft of this report, Dr. Wang has accused the committee of being prejudiced against him, failing to follow the CUNY guidelines for this investigation, and of lacking a basic understanding of western blot analysis. We as a committee contest these assertions unequivocally. Our only stake in this investigation has been the objective assessment of the allegations for ORI as charged by the CUNY office of research. We have worked closely, throughout this entire investigation, with a CUNY administrator with extensive experience with research misconduct investigations. Furthermore, three out of four of the committee members routinely conduct experiments involving protein biochemistry and two out of four routinely conduct and publish western blot experiments. These assertions by Dr. Wang regarding the committee and its investigation should not distract from our central finding that Dr. Wang has failed to maintain the data and research records that would have allowed for a direct and transparent assessment of the allegations against him. Though we acknowledge that a significant number of the publications concern data published over a decade ago, Dr. Wang has been unable to provide original data or records even for his most recent publications. He is therefore responsible for the inability of this committee to make an objective assessment for even a single allegation. Notwithstanding the specific data retention policies of CUNY and the NIH, Dr. Wang's failure to store original data and maintain research records is reckless and clearly not in keeping with the standard practices in the field. It is our conclusion that this amounts to significant research misconduct.

Specific Allegations

Note: Dr. Wang failed to provide the committee any original, uncropped western blot data with which to directly address the allegations below, nor did he share research records (such as lab notebooks) pertaining to these data. The committee was therefore forced to examine the data as presented in published figures and to use adjustments of brightness and contrast to these images to determine if the aberrations described in the allegations were present. Because we have been forced to rely on the published figures for our investigation, we have chosen, for the sake of brevity, not to reproduce those images in this report.

Allegation 1 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 4A, S2A and S7 by duplicating, cutting and pasting, or altering the plots in Figure 4, and Supplementary Figures 2, S3 and S7 in the following publication:

Banerjee A, Wang HY, Borgmann-Winter KE, MacDonald ML, Kaprielian H, Stucky A, Kvasic J, Egbujo C, Ray R, Talbot K, Hemby SE, Siegel SJ, Arnold SE, Sleiman P, Chang X, Hakonarson H, Gur RE, Hahn CG. Src kinase as a mediator of convergent molecular abnormalities leading to NMDAR hypoactivity in schizophrenia. *Mol. Psychiatry* 2015; 20(9):1091-100.

The concerns of this allegation stem from distinct aberrations in band shapes and backgrounds associated with western blot data in the cited figures. The committee agrees that there are substantive concerns surrounding the data reported in this publication. However, given the low quality of the published images and the nature of the concerns, Dr Wang's failure to provide us with uncropped, unmanipulated images of the blots in question make it impossible to address the allegations objectively. We cannot therefore render a conclusion regarding misconduct in this allegation. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field. The integrity of Dr. Wang's work in this case remains highly questionable.

In figure 4A, the authors present the results of an experiment in which the binding of Src to SH-2 binding domain is tested in the presence of SCZ. The committee found image aberrations that may be consistent with the fabrication/manipulation of the data in this figure, which includes the following: The last band for Src (SCZ at 10nM peptide) slightly protrudes beyond the right side of the blot, falling into the background of the figure, beyond the blot background's edge. The blot background immediately surrounding each band of the figure is unexpectedly lighter compared the background levels across the majority of the blot. The lighter background follows a nearly perfectly rectangular pattern around the bands, which suggest cutting and pasting of these bands into the figure. The Src band for CTL at 10 nM of peptide looks almost perfectly rectangular, suggesting potential cutting and pasting of this band onto the blot. We find additional possible evidence of the cutting and pasting of bands onto blots displayed in figures S2A, S3 and S7. In Dr Wang's response to our investigation, he states that these data were not generated in his laboratory but were prepared and submitted by a co-author of the paper, Dr. Hahn from the Department of Psychiatry at the University of Pennsylvania. We are therefore not discussing the allegations for these three supplemental figures in this report.

In response to this allegation, Dr. Wang referred the committee to his response to CCNY's initial inquiry, dated December 23rd, 2021 and provide a series of images in his response to the preliminary draft of this report. In these documents, Dr. Wang acknowledged that his laboratory had prepared and submitted Figure 4A. Dr. Wang insists that he has provide the committee with an "uncropped blot image" containing the

bands shown in Figure 4a. However, this image does not contain film edges or molecular weight markers and no research records have been shared with the committee recording the preparation of the blot in question. Instead, Dr. Wang provided the committee digital images that cannot be confidently identified as coming from original scan of a full blot. The digital images provided by Dr. Wang do not explain why the Src band is protruding from the right side of the blot in the figure, since cutting the blot presented in the report would have presumably cut the corresponding portion of the band or additional background pixels along the entire blot. Our analysis of the image provided by Dr. Wang also revealed that, although the shape and length of the Src bands in the digital image are quite similar to that of the figure presented in the paper, they do not seem to match.

Dr. Wang did not provide original uncropped blots for this allegation, nor did he provide a compelling explanation for the unexplained patterns found in the original figure of the paper. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, original blots, nor has he maintained notebooks describing the preparation of western blots in his laboratory. This revelation is clearly at odds with his repeated assertions that he has provided the committee with original blot scans. No funding source was reported in this publication for Dr. Wang. Due to Dr. Wang's failure to provide original data (original, uncropped, unmanipulated blots) and the absence of a compelling explanation for the aberrations found in the figure in question (Figure 4A), the committee recommends that the editors of *Mol. Psychiatry* attempt to obtain full uncropped and unmanipulated blots of the underlying figure, which Dr. Wang has clearly failed to provide in his response to the inquiry. The committee would like to emphasize that digital images, which Dr. Wang has consistently submitted as original blots, are not original data and thus are insufficient for objectively addressing the allegations of misconduct.

The western blot presented in figure 4A was performed in the laboratory of Dr. Wang. Thus, Dr. Wang would therefore be responsible for the alleged research misconduct for the data displayed in this figure. A. Stucky, an author affiliated with the laboratory of Dr. Wang, who is also reported to have participated in generating this data, and C-G Han, the corresponding author of the manuscript, may also bear some measure of responsibility.

Allegation 2 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 4D and 4E by duplicating, cutting and pasting, or altering the plots in the following publication:

Talbot K, Wang HY, Kazi H, Han LY, Bakshi KP, Stucky A, Fuino RL, Kawaguchi KR, Samoyedny AJ, Wilson RS, Arvanitakis Z, Schneider JA, Wolf BA, Bennett DA, Trojanowski JQ, Arnold SE. Demonstrated brain insulin resistance in Alzheimer's disease patients is associated with IGF-1 resistance, IRS-1 dysregulation, and cognitive decline. *J Clin Invest.* 2012 Apr;122(4):1316-38.

The concerns in this allegation arise from incongruities in the backgrounds of blot panels displayed in Figures 4D and 4E. The committee agrees that there are substantive concerns surrounding the data reported in this publication. Dr. Wang's failure to provide original uncropped images of the blots in question make it impossible to address the allegations objectively. We cannot therefore render a conclusion regarding misconduct in this case. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field. Dr. Wang's work in this case therefore remains highly questionable.

In figure 4D, the bands for IGF-1R β pY^{1135/1136} show a different background around lanes 2 and 3 (from left to right). This darker background intensity forms a nearly perfect rectangle in both cases, resulting in a linear cut in the background, which may be indicative of cutting/pasting of bands from another blot onto the figure. In figure 4D, the bands for IGF-1R β pY¹¹³¹ and IRS-2 show shading/significantly lighter background around the bands, which may be indicative of cutting/pasting of these bands into the figure. In figure 4E, all the bands for IRS-1 pY, IRS-1 pS and P13K p85 α show a lighter than expected background in the region immediately surrounding the bands, which may be indicative of cutting/pasting of these bands into the figure. In addition, the committee found inconsistencies in Figure 4B. For the IRS-1 pY bands, the first band (left to right) shows lighter, nearly rectangular background around the band and a vertical cut in the background (to the right of the band), which may be indicative of cutting/pasting.

In response to this allegation, Dr. Wang referred to his response to CCNY's initial inquiry and provided two images in his response to the preliminary draft of this report. In his response, Dr. Wang failed to provide images of original blots. Instead, he included digital images, which Dr. Wang referred to as "original western blots", corresponding to figure 4D (IGF-1R β pY¹¹³¹) and 4E (IRS-1 pY, IRS-1 pS and P13K p85 α). Our analysis of the digital images submitted indicate that the images provided by Dr. Wang in response to this allegation are clearly not images of original uncropped blots, as they do not contain film/blot edges or molecular weight markers. In the IGF-1R β pY¹¹³¹ blot provided, the background pattern does not match with that of the figure presented in the paper. Bands 2, 3 and 4 show a darker background area on top of each band in the figure presented in the paper, which is absent in the digital blot provided by Dr Wang. The digital images provided for the blots presented in 4E show a diminished contrast in the background compared to the blots in the published figure, however, the lighter background areas around the bands are still visible. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, original blots, nor has he maintained notebooks describing the preparation of western blots in his laboratory.

No funding source was reported in this publication for Dr Wang. Due to the lack of provision of original data (uncropped, unmanipulated blots) and the absence of a compelling explanation for the aberrations found in the figures in question (Figure 4D and 4E), the committee recommends that the editors of *J. Clin. Invest.* attempt to examine the uncropped, unmanipulated blot scans for of the underlying figures. The committee would like to emphasize that digital images, which Dr Wang has consistently submitted as original blots, are not original data and thus are insufficient for an objective assessment of these allegations.

The western blot presented in figures Figure 4B, 4D and 4E were performed in the laboratory of Dr. Wang. Thus, Dr. Wang would be responsible for the alleged research misconduct in this allegation. Kalindi P. Bakshi and Andres Stucky, two authors affiliated with the laboratory of Dr. Wang, who are also reported to have participated in generating this data, and Steven Arnold, as the corresponding author of the manuscript, may bear a measure of responsibility for the integrity of the data in this publication.

Allegation 3 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 5A and 6 by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Capuano AW, Khan A, Pei Z, Lee KC, Bennett DA, Ahima RS, Arnold SE, Arvanitakis Z. Insulin and adipokine signaling and their cross-regulation in postmortem human brain. *Neurobiol Aging* 2019; 84: 119-130

The concerns described in this allegation stem largely from unexpected vertical discontinuities in several western blot panels, suggesting the undisclosed splicing of blots from different gels. Wang did not provide any of the original data that were used to generate the figures in question (Figure 5A and 6). Dr. Wang acknowledged the splicing of the bands for the blots shown in figure 5A, which was not disclosed in the figure legend. Dr Wang's failure to provide us with uncropped, unmanipulated images of the blots combined to create the figures in question makes it impossible to address the allegations objectively. We cannot therefore render a conclusion regarding misconduct in this case. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field. Dr. Wang's work in this case therefore remains highly questionable.

In figure 5A, there is a vertical discontinuity in the background between lanes 8 and 9 (top panel) and lanes 4 and 5 (bottom panel) which may indicate splicing of blots, which was not disclosed in the figure legend. In figure 6A, there is a significant difference in blot backgrounds for the three blots presented. In addition, the bands in the blots for IRS-1 and Py^{1150/1151}IR β look extremely similar, despite representing independent blots using antibodies against different proteins with significant differences in MW.

In response to this allegation, Dr. Wang referred to his response to CCNY's initial inquiry and provided additional information in his response to the draft of this report, including images taken directly from the publication or adjusted for contrast. However, Dr. Wang failed to provide images of the original, uncropped blots. Instead, his response includes a series digital images, which Dr. Wang referred to as "original western blots", accounting for the bands showing at the top and bottom panels of figure 5A, and for those in figure 6A (IRS-1, pY^{1150/1151}IR β , pY⁹⁶⁰IR β and IR β). The analysis of the digital images submitted by Dr. Wang reveal that, for figure 5A, the digital files provided are consistent with the splicing of the blots, as acknowledged by Dr. Wang.

This splicing was not disclosed in the figure legend of the publication. For figure 6A, Dr. Wang explained that each panel was generated separately, which could explain the difference in the background found in the images. However, the remarkable similarity in the bands of blots for IRS-1 and pY^{1150/1151}IR β , and the presence of areas with lighter background around some of those bands may be indicative of cutting/pasting of the bands into the figure.

The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, original blots, nor has he maintained notebooks describing the preparation of western blots in his laboratory. The work described in this publication was supported by the National Institutes of Health, United States grants P30 AG10161, R01 AG15819, R01 NS084965, and RF1 AG059621. However, the recipients of each of these grants are not identified in the publication. The failure to provide original, uncropped blots, or notebooks or other records describing the preparations of the blots presented in figure 6A leave significant doubts regarding the nature of the data presented. As corresponding author on the study and the member of the lab who runs the bulk of all western blots in his lab, Dr. Wang is responsible for the maintenance of original data and research records and has clearly failed in this case to properly manage the data described in this publication.

Allegation 4 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 3 (right panel), 8B, 10A and 12 by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Lee KC, Pei Z, Khan A, Bakshi K, Burns LH. PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer's disease pathogenesis. *Neurobiol Aging* 2017; 55: 99-114. [The list of allegations provided by ORI also states that Figure 8B in this publication also appears as Figure 3B of the NIH grant proposal for R01 AGO73350-01.]

The concerns described in this allegation stem from discontinuities in the background intensities of blot panels in the figures cited. Dr. Wang failed to provide the original western blot data that were used to generate the figures in question. Dr. Wang's failure to provide us with a compelling explanation or uncropped, unmanipulated images of the blots in question make it impossible to address the allegations directly. We cannot therefore render an objective conclusion regarding misconduct in this case. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field. The integrity of Dr. Wang's work in this case therefore remains highly questionable.

In figure 3 (right panel), the second band (from right to left, 10-month AD Tg, PTI (-)) is surrounded by a rectangle of distinctly darker background, which may indicate cutting and pasting of the band into the figure. In figure 8B, for the IR β blot panel, there is strong evidence of splicing between lanes 4 and 5, and lanes 12 and 13. The bands situated between the apparent cuts (in lanes 1-4, 5, 6-12 and 13-16) reside at distinct

heights on the blot. Furthermore, the bands for IRS-1 do not show the same alignment pattern as that of the blot shown on top, despite representing the same blot using antibodies against different proteins. In figure 8B, for the Py^{1150/1151}IR β blot, bands corresponding to the same protein product do not form the expected straight line. This unexpected variation in band could reflect cutting/pasting of bands into the figure. In figure 8B, for the Py⁹⁶⁰IR β blot, stark vertical discontinuities in blot background and unexpected variation in band heights are strong evidence of undisclosed splicing between bands 2 and 3. In figure 8C, the bands of the blot for Arc are also not aligned as one would expect from the same protein products. For the β -Actin control panel below the Arc blots, the bands also do not appear to be as aligned as expected for the same protein products. However, in this case the variations do not track with the pattern of variations observed for the Arc bands above, despite representing the same blot using antibodies against different proteins. These aberrations might also be indicative of the cutting/pasting of bands into the figure. In figure 10A, for the TLR4 blot, there is an abrupt shift in band height between lanes 6 and 7, which together with the alignment pattern of the lanes are consistent with cutting/pasting of bands into the figure. In figure 10A, for the α 7nAChR blot, stark vertical discontinuities in the blot background are strong evidence of undisclosed splicing between lanes 9 and 10. In figure 12 (top panel), the NR1 blot has 12 bands, whereas the PLC γ 1 blot has 13 bands, despite representing the same samples. In figure 12, vertical incongruities in the background of the NR1 blot and a shift in band height between lanes 8 and 9 are consistent with undisclosed splicing. Likewise, a vertical incongruity in background and shift in band height is also visible in the PLC γ 1 blot panel a between lanes 10 and 11, are further evidence of undisclosed splicing. In addition, the PSD-95 blots in figure 12 shows abrupt shifts in band heights and alignment patterns strongly indicative of splicing between blots. This is further suggested by clear differences in background intensity and pattern between lanes 1-10 and lanes 11-13.

In his reply to this allegation, Dr. Wang referred to his response to CCNY's initial inquiry and provided a series of images in his response to the draft of this report. In these documents, Dr. Wang fails to provide the full original blots. Instead, the initial response to our investigation included one digital image for Figure 3, which Dr. Wang referred to as an "original western blot." Additional images were presented in Dr. Wang's response to the draft of this report for figures 8B, 10A and 12, none of which are full images of uncropped original blots. Absent the provision full, uncropped blots, we simply cannot objectively assess the verity of Dr. Wang's figure or the merit of the allegations. Serious concerns therefore remain regarding the integrity of these data.

An expression of concern was published by the *Neurobiology of Aging* in May 2022, based on multiple concerns with the western blot data described in the publication. According to the editors, the authors provided a detailed response, including images of relevant uncropped western blots and photomicrographs. Upon analysis of the submitted images the Editor in Chief concluded that there was not compelling evidence of data manipulation intended to misrepresent the results. However, Dr. Wang did not provide original uncropped blots for this allegation to this committee and the committee's interview with Dr. Wang revealed that he has not

retained images of uncropped, original blots, nor has he maintained notebooks describing the preparation of western blots in his laboratory.

Pain Therapeutics, Inc. funded this work except for the C14-labeling of PTI-125, which was produced for biodistribution studies under NIH grant number 4R44AG050301. Due to the lack of provision of original data (uncropped, unmanipulated blots) the committee recommends that the editors of *Neurobiology of Aging* confirm that Dr. Wang has indeed provided uncropped, unmanipulated blots for the figures in question, as claimed by Dr Wang in his response to the inquiry. The committee would like to emphasize that digital images, which Dr. Wang has consistently submitted as original blots, are not original data and thus are unacceptable when responding to the allegations. If such original data have been provided, the editors should provide the images for the figures in question and a full description of the analysis done to settle the allegations. Should the editors determine that uncropped and unmanipulated data have not been provided by Dr. Wang, the publication should be retracted. The western blot presented in the figures in questions were performed in the laboratory of Dr. Wang. As corresponding author on the study and the member of the lab who runs the bulk of all western blots in his lab, Dr. Wang would be responsible for the alleged research misconduct in this allegation.

Allegation 5 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 8A, 8E and 9A by duplicating, cutting and pasting, or altering the plots in the following publication:

Meade GM, Charron LS, Kilburn LW, Pei Z, Wang HY, Robinson S. A model of negative emotional contagion between male-female rat dyads: Effects of voluntary exercise on stress-induced behavior and BDNF-TrkB signaling. *Physiol Behav.* 2021 May 15; 234:113286

The concerns described for this allegation stem from vertical discontinuities in western blot images in multiple figure panels. Dr. Wang failed to provide the original data that were used to generate the figures in question. Dr. Wang's failure to provide uncropped, unmanipulated images of the blots in question, make it impossible to address the allegations objectively. We cannot therefore render a conclusion regarding misconduct in this case. Due to this fact, the integrity of Dr. Wang's work in this case remains highly questionable. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field.

In figure 8A, the blot for irisin shows a sharp vertical artifact between lanes 1 and 2, and between lines 2 and 3, and could reflect of the splicing of lanes from separate blots. In figure 8E, the blot panel for Arc shows clear sharp vertical edge which appears to cut the band in the second lane from right. The blot for β -Actin also shows a sharp vertical edge on the left side of the second band from the left. These features may reflect the splicing of lanes from different blots. In figure 9A, the blot for β -Actin shows a sharp vertical edge on the left side of the second band from the left. The NT3 panel also

shows a pronounced linear transition in background intensity in the area above the second band from the left. These features may be consistent with the splicing of lanes from different blots. Finally, there are several aberrations in figure 7B, which may likewise indicate gel splicing in this figure. For example, there is an abrupt shift in band heights in the Py-TrkB145 blot, between lanes 2-3 and 6-7 and a vertical discontinuity is also observed in the N-Shc blot panel.

In response to this allegation, Dr. Wang referred to his response to CCNY's initial inquiry, in which he acknowledged the splicing of blots based on a "scientifically defensible decision to reorder some of the samples for production in the Figures." He also claimed that the journal and its reviewers had evaluated the original blots used to construct the published images. However, we note that Dr. Wang's response to our investigation and to CCNY's initial inquiry did not include original, uncropped blots or any other images representing the blots as they appeared before the disclosed splicing. Dr. Wang provided a more detailed response to this allegation in response to the draft of this report. We note that this response included a highly specific summary of the preparation of the blots in question, one that presumably relied on detailed research records. We note that, despite our request to share such records with the committee, none have been shared by Dr. Wang.

In May of 2022, the journal published a corrigendum to the publication, in which the authors acknowledged that they had "relocated entire columns of images from the original western blots", which according to them had "created visual imperfections on the images of a few individual bands", included in figures 7, 8 and 9. The committee does not consider this explanation sufficient to settle the issues raised in this allegation. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, original blots, nor has he maintained notebooks describing the preparation of western blots in his laboratory..

This research presented in this publication was supported by NIHRO1AG057658 and NIHFR1AG059621. Dr Wang is the principal investigator in both grants. Due to the absence of original data (original, uncropped blots) in Dr. Wang's response, the committee recommends that the editors of *Physiology & Behavior* confirm that Dr. Wang has indeed provided uncropped images of the underlying blots (and not cropped digital images, which Dr. Wang consistently has submitted as original blots). If such original data has been provided, the editors should provide the images for the figures in question and a full description of the analysis done to settle the allegations. Should the editors determine that uncropped and unmanipulated data were not provided by Dr Wang, the publication should be retracted. The western blot presented in the figures in questions were performed in the laboratory of Dr. Wang. As corresponding author on the study and the member of the lab who runs the bulk of all western blots in his lab, Dr. Wang is responsible for the integrity of the data in this allegation.

Allegation 6 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 9A by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang S, Li B, Solomon V, Fonteh A, Rapoport SI, Bennett DA, Arvanitakis Z, Chui HC, Miller C, Sullivan PM, Wang HY, Yassine HN. Calcium-dependent cytosolic phospholipase A2 activation is implicated in neuroinflammation and oxidative stress associated with ApoE4. *Mol Neurodegener.*2021;16(1): 26

The concerns described in this allegation stem from discontinuities in western blot background signals consistent with the cutting and pasting of specific bands onto the blot image. Based on the retraction by the authors of the initially published paper, the data published in the subsequently published manuscript, the removal of Dr. Wang as an author along with the data generated in his laboratory from the subsequently published manuscript, we conclude that there are likely major issues with the data provided by Dr. Wang in the original publication. Dr. Wang failed to provide uncropped images of data that were used to generate the figures in question. Dr. Wang's failure to provide uncropped, unmanipulated images of the blots in question, make it impossible to address this allegation objectively. We cannot therefore render a conclusion regarding misconduct in this case. Due to this fact, the integrity of Dr. Wang's work in this case remains highly questionable. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field.

Upon the adjustment of image levels, brightness, and contrast of the blot images in figure 9A, several unexpected aberrations appear. In figure 9A, the panel marked as "+ 0.1 μ M A β 42" shows a white ring surrounding the band in lane 7 of the top blot panel (p-cPLA2). In addition, several bands in the top and bottom panels are surrounded by patterns of background signal that are distinct from the rest of the blot. In figure 9A, panel marked as "+ 0.1 μ M rApoE4 A β 42", in the top original (p-cPLA2) bands 5 and 6 are surrounded by a rectangular cloud of lighter background intensity than the rest of the figure, suggesting cutting/pasting of these bands into the figure.

This publication was retracted online on 4 February 2022 by the authors, though Dr. Wang appears to contest this in his response to the draft of this report. According to the retraction note, the authors retracted the publication due to the concerns raised about the western blot data Dr. Wang provided in figure 9. The authors indicated that they were collecting new data and that they intended to submit a new manuscript for peer review. This study was re-published by *Mol. Neurodegener.* later in 2022. Dr Wang was removed as an author and the data he had provided in the original publication was also removed from the new Fig 9. In the legend of the new figure the authors stated that phosphorylated cPLA2 (p-cPLA2) levels were very low and therefore were not being shown in the blots of the new figure. Most of the bands named in the allegations from the retracted article were those corresponding to the blots for phosphorylated cPLA2, prepared in Dr. Wang's laboratory. Some of these bands showed very intense signals for phosphorylated cPLA2 (p-cPLA2) in the original figure. The data presented for p-cPLA2 expression in the new manuscript following the retraction therefore differ significantly from the results Dr. Wang originally presented in Figure 9A.

In his reply to this allegation, Dr. Wang referred this committee to his response to CCNY's initial inquiry, in which he first listed a series of technical explanations for the aberrations found in figure 9. He also presented a cropped digital image for the "+ 0.1 μ M rApoE4 A β 42" sample and claimed that the area with lighter background around the bands in question was in fact irregular and not rectangular. Dr. Wang did not provide original uncropped blots for this allegation to the committee. The committee concludes that the images and explanation provided by Dr. Wang do not sufficiently address the concerns of the allegation. The committee's interview with Dr. Wang revealed that he has not maintained notebooks describing the preparation of western blots in his laboratory.

No funding source was reported in this publication for Dr. Wang. The publication in question has been retracted and no further editorial action is needed. The western blots presented in the figures in questions were performed in the laboratory of Dr. Wang. As member of the lab who runs the bulk of all western blots in his lab and the source of the data that precipitated the retraction of the first publication, Dr. Wang is responsible for the research misconduct in this allegation.

Allegation 7 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 3A by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Pei Z, Lee KC, Lopez-Brignoni E, Nikolov B, Crowley CA, Marsman MR, Barbier R, Friedmann N, Burns LH. PTI-125 Reduces Biomarkers of Alzheimer's Disease in Patients. *J Prev Alzheimers Dis.*2020; 7(4): 256-264.

The concerns in this allegation stem from background incongruities apparent in figure 3A. Dr. Wang did not provide the committee the original data used to generate the figure in question. Dr. Wang's failure to provide us with a compelling explanation and uncropped, unmanipulated images of the blots in question make it impossible to address the allegations directly. We cannot therefore render an objective conclusion regarding misconduct in this case. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field. Dr. Wang's work in this case therefore remains highly questionable.

In figure 3A, for the pT²³¹Tau blot panel, a rectangular box with a distinctly lighter different background surrounds the band in lane 9. There is also a suspicious vertical streak in lane 8 of the same blot panel. In his reply to this allegation, Dr. Wang referred the committee to his response to CCNY's initial inquiry, in which he described a series of technical reasons to account for the aberration found in figure 3A. He also presented digital images said to contain the data shown in figure 3, to which he refers to as "original blots" in his initial response to the investigation and as a "high definition raw blot" in his response to the draft of this report. However, these images do not include film edges or molecular weight markers and therefore cannot be considered original data by this committee. The unexpectedly light rectangular pattern can also be seen in

the submitted digital images. Dr. Wang stated that he believes the rectangular pattern of lighter background is due to “a piece of scotch tape remaining on the underlying, previously exposed film, to which the smaller unexposed film, cut to fit the size of the gel, was taped.” In this response to these allegations, Dr. Wang cites the analysis of Dr. Charles Spruck, supporting this explanation. However, the provision of a full uncropped blot that displayed the lighter background behind the band in question would have allowed for this issue to be settled objectively. It is not clear why original data and research records from such a recent publication were not presented to the committee. Finally, Dr. Wang mentioned that this study was confirmed by an independent laboratory, and cited the results presented in a poster-presentation (AAIC July 2021). However, the data showed in two figures of the referenced poster (figures 4 and 5), described as different representations of the same data, don’t match (data points not consistent between the two figures).

Though it is possible that semi-transparent tape might produce the aberration described for figure 3A, it is remarkable that the region in question appears to be so regular in its rectangularity and that it so neatly frames the band in question. Dr. Wang did not provide the committee with original uncropped blots for this allegation and the committee does not think that Dr. Wang’s response sufficiently addresses the concerns of the allegation. The committee’s interview with Dr. Wang revealed that he has not retained images of uncropped, original blots, nor has he maintained notebooks describing the preparation of western blots in his laboratory.

This study was funded by an NIH grant award AG060878 from the National Institute on Aging. Due to lack of provision of original data (original, uncropped blots), the committee recommends that the editors of *The Journal of Prevention of Alzheimer’s Disease* request that Dr. Wang provide uncropped images of the underlying blots (not cropped images, which Dr. Wang consistently has submitted as original blots). If such original data are provided, the editors should provide the images for the figures in question and a full description of the analysis done to settle the allegations. Should the editors determine that uncropped and unmanipulated data are not provided by Dr. Wang in response to these allegations, the publication should be retracted. The western blots presented in the figures in questions were performed in the laboratory of Dr. Wang. As corresponding author on the study and the member of the lab who runs the bulk of all western blots in his lab, Dr. Wang would be responsible for the alleged research misconduct in this allegation.

Allegation 8 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 5B and 10A by duplicating, cutting and pasting, or altering the plots in the following publication:

Stucky A, Bakshi KP, Friedman E, Wang HY. Prenatal Cocaine Exposure Upregulates BDNF-TrkB Signaling. *PLoS One* 2016 Aug 5;11(8):e0160585.

The concerns described in this allegation stem from a vertical discontinuity between lanes near bands in the top hippocampus blot panel shown in figure 5B. Furthermore, rectangular discontinuities are present in the backgrounds framing subsets of bands in the blot panels displayed in figure 10A. This publication was editorially retracted by the editors at *PLoS* on March 30, 2022, based on concerns regarding apparent duplications in figures 2, 5, 9, and 10, partial overlap of blots in figure 1, vertical discontinuities in figures 5 and 6, vertical and horizontal discontinuities in figures 8, 9, 10, and 11, and on Dr. Wang's response to editorial concerns over the data presented in these figures. The committee finds no compelling reason to dispute the assessment of the *PLoS* editorial board that research misconduct occurred in this case. However, we acknowledge that the absence of original data or research records makes a full and objective assessment impossible.

Examination of figure 5B reveals several aberrations. First, we observed a stark vertical incongruity between lanes 3 and 4 of the pS⁴⁷³-Akt1 blot for hippocampus, in addition to light background halos surrounding the bands of this blot and an unexpected horizontal discontinuity in the background, with the bottom half of the blot having a significantly darker background level. The incongruity may be the result of the splicing of lanes from different blots. Though not the best practice, this may not reflect misconduct. The halos around the bands in this case may be a product of image compression and effects of the adjustment of low-resolution figures. The horizontal discontinuity is difficult to explain and may indeed reflect a modification of the underlying data. Examination of figure 10A revealed aberrations in background patterns for the Beta-Actin blot shown for hippocampus and the pro-BDNF blot shown for prefrontal cortex. Specifically, lane three of the Beta-Actin blot for the hippocampus has a noticeably lighter background intensity than the other 5 lanes, suggesting that the image contains a single lane from another blot. However, this variation in background is not observed for the pro-BDNF blot.

In response to CCNY's initial inquiry, Dr. Wang explains the vertical incongruity in figure 5A by stating that the blot panel had indeed been combined from two separate blots, and he cited this in his response to our investigation. Dr. Wang also stated that the background aberrations described for figure 10A were due to be "artifacts of the extreme contrast adjustment and reduction of brightness conducted by the petitioners on the low-resolution images." We do not think that such adjustments can explain the rectangular discontinuities in blot background described above. In response to both editorial concerns from *PLoS* and to our investigation, Dr. Wang provided what he stated were uncropped original blots and, in his response to the draft of this report, presents a series of images upon which contrast and levels have been adjusted. However, the materials provided by Wang to this committee were clearly not original uncropped blots. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab. Dr. Wang's failure to store original data and maintain research records relevant to this publication clearly not in keeping with accepted standards in the field.

According to our interviews with Dr. Maria Zalm, the data provided to the *PLoS* editors by Dr. Wang also did not contain film edges or molecular weight markers and were not recognized by the *PLoS* editors as unmanipulated, uncropped images of the original western blots. Dr. Wang provided an explanation for the similarities in band shapes across panels in figures 2, 5, 9, and 10, stating that this was due to the re-probing of the same blots. However, the data provided by Dr. Wang did not, in the committee's final assessment, provide compelling explanations for the other irregularities described above, which, once again, could have been addressed objectively through an examination of original data and research records. As described in the retraction notice for this publication, among the images provided by Dr. Wang in response to editorial concerns, there are multiple instances of highly similar patterns of background noise that are shared by multiple blot images, and these patterns appear in images provided to address concerns with other *PLoS One* studies published between 2008 and 2016. Dr. Wang states that this overlap in background is due to scanner noise. However, we find it impossible to believe that such noise would remain stable over the span of eight years.

The work in the study was supported by the National Institutes of Health, grant number 41545-00-02-05, awarded to Eitan Friedman, a co-author on the study. This publication was retracted by the editors of *PLoS*. No further editorial action is required. As senior and corresponding author and the author who ran the bulk of all western blots in publication, Dr. Wang is responsible for the research misconduct in this case and for the failure to maintain and make available original data and research records.

Allegation 9 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 4 and 5 by duplicating, cutting and pasting, or altering the plots in the following poster presentation:

Wang HY, Pei Z, Xu Q, Brunelle L, Burns L, Thornton GB. SavaDx, a novel plasma biomarker to detect Alzheimer's disease, confirms mechanism of action of simufilam. Poster presented at: Alzheimer's Association International Conference (AAIC) July 31-August 4, 2021. San Diego, USA.

The concerns described in this allegation stem from the discordance between two figures (4 and 5) purported to display the same results in different ways. Figures 4 and 5 do not represent western blots but are presented as different representations of the levels of plasma P-tau181, with figure 4 taking the form of a scatterplot and figure 5 taking the form of what the authors refer to as a spaghetti plot (paired line plots). We agree with the allegation that the data said to represent levels P-tau181 on day 28 of treatment do not correspond. It is not possible to match some large proportional changes in figure 5 with the scatterplots of percent changes in figure 4. We conclude that the data plotting presentation was misleading and lacking in rigor. We therefore agree that this allegation has merit but cannot eliminate the possibility that this was due to carelessness.

Our assessment of figures 4 and 5 confirmed the lack of correspondence between the percent change data shown in figure 4 and the apparent changes in concentration depicted in figure 5. For example, a single placebo patient appeared to display a 1.5x change in P-tau181 (top red dot in placebo treatment in figure 4), but such a change is not observed in any of the placebo patients in figure 5 green lines). Furthermore, a single patient in the 100mg treatment appears to display an approximately two-fold change in P-tau181 in figure 5, however the expected corresponding data point is not seen in figure 4. Though we are unable to determine the cause of these aberrations, it is possible that the apparent mismatches may have been caused by errors in the preparation of the poster. If the data were fabricated, more care would have likely been taken to avoid such obvious mismatches between graphs.

Dr. Wang did not respond to this allegation in his initial response to this investigation, and states in his response to the draft of this report that he was never asked to do so. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. In his response to the draft of this report, Dr. Wang states that the data in this allegation were not created by his lab, but rather by Quanterix and the laboratory of Dr. Xu Xian. This allegation does not correspond to a publication. Therefore, no additional editorial action is recommended. This work was funded by NIH/NIA grants AG057329 & AG060878. As presenting author on this poster, Dr. Lindsay Burns is responsible for the errors in this poster.

Allegation 10 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 2, 4A and Supplementary Figure 2 by duplicating, cutting and pasting, or altering the plots in the following publication:

Chang-Gyu Hahn, Hoau-Yan Wang, Dan-Sung Cho, Konrad Talbot, Raquel E Gur, Wade H Berrettini, Kalindi Bakshi, Joshua Kamins, Karin E Borgmann-Winter, Steven J Siegel, Robert J Gallop & Steven E Arnold. Altered neuregulin 1–erbB4 signaling contributes to NMDA> receptor hypofunction in schizophrenia. *Nature Medicine* 2006; 12, 824–828.

The concerns described in this allegation arise from differences in background between lanes that contain sample and those that appear to be blank. Furthermore, some of the figures suggest unusual “halos” around bands. We conclude that while these anomalies are concerning, it is difficult to determine with certainty if they are artifacts of image compression, digital contrasting of published, low-resolution images, or represent manipulation of the data. We cannot therefore render an objective conclusion regarding misconduct in this case. However, Dr. Wang's failure to store original data and maintain research records relevant to this publication is clearly not in keeping with accepted standards in the field. Though we observe the halos described in the allegations, these do not appear to frame individual bands as might be expected if a section of gel were cut and pasted or an area enhanced with differing contrast. Furthermore, while figures

appear to be over-exposed, it is possible that these aberrations were caused by image compression.

Dr. Wang did not respond to this allegation in his initial response to this investigation, and states in his response to the draft of this report that he was never asked to do so. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. In his response to the draft of this report, Dr. Wang did not provide original uncropped blots for this allegation but included images from other studies published in *Nature Medicine* that have been adjusted to show halos like those described in the allegations and concludes that the halos described are artifacts "caused by image processing software used by the journal." While we acknowledge that this may indeed explain the halos, we believe that this allegation could have been most transparently addressed and settled with original, uncropped blot images, rather than the same adjustments of published images that his accusers have employed against Dr. Wang, an approach that this committee has been forced to take due to the absence of original data and research records.

The work in allegation 10 was supported by grants from the National Institutes of Health (MH64045 and MH63946). Given Dr. Wang's failure to provide original data or research records pertaining to these allegations, we recommend that the *Nature Medicine* request uncropped images of the underlying blots (images containing film edges and weight markers) and make a determination regarding this allegation. As senior and corresponding author on this study, Steven E Arnold is responsible for the integrity of the data it contains.

Allegation 11 repeats the one of the specific concerns regarding allegation 10. Specifically, it states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Supplementary Figure 2 by duplicating, cutting and pasting, or altering the plots in the same publication listed in allegation 10. Please see our conclusions regarding Supplementary figure 2, in our response to allegation 10 above. In his response to the preliminary draft of this report, Dr. Wang accuses the committee of listing this allegation again in order to "inflate it's allegations against" him. In fact, as stated in our draft report, we are using the list of allegations that ORI provided to CCNY and that CCNY provided to this committee.

Allegation 12 states Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 3 and 5 by duplicating, cutting and pasting, or altering the plots in the following publication:

Hoau-Yan Wang, Mathew L. MacDonald, Karin E. Borgmann-Winter, Anamika Banerjee, Patrick Sleiman, Andrew Tom, Amber Khan, Kuo-Chieh Lee, Panos Roussos, Steven J. Siegel, Scott E. Hemby, Warren B. Bilker, Raquel E. Gur & Chang-Gyu Hahn.

mGluR5 hypofunction is integral to glutamatergic dysregulation in schizophrenia.
Molecular Psychiatry 2020;25:750–760

The concerns described in this allegation stem from a background “halo” effect surrounding several bands in the RGS4 blot shown in Fig. 3, unexpected similarities between bands in this blot, background regions that are unexpectedly lighter than surrounding background areas, and regions that appear to partially obscure bands in the mGluR5 blot shown in figure 5C. We agree that the halo effects in figure 3 are suspicious, but without access to the uncropped, original blots, it is not possible to determine if this was due to data manipulation. The committee also concludes that the lighter background regions described for Figure 5 may indeed represent intentional fabrication of data. However, we acknowledge that the absence of original data or research records makes a full and objective assessment impossible.

Both aberrations described in the allegations are visible in the published figures. Though the halos described for figure 3 are problematic, we cannot eliminate the possibility that this was due to compression effects. The lighter background areas described for Fig. 5C, however, appear to be highly rectangular and appear only for select bands. These aberrations may indicate the pasting of regions of interest from another blot, or the manipulation of levels of contrast within rectangular regions of interest over the original blot. Dr. Wang did not respond to this allegation in his initial response to this investigation and states in his response to the draft of this report that he was never asked to do so. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY’s Office of Research. In his response to the draft of this report, Dr. Wang once again failed to provide original uncropped blots for this allegation or to provide a compelling explanation for aberrations described in the allegation. Dr. Wang, in responding to similar allegations has suggested that tape stuck to the film or background noise was responsible for such aberrations. However, neither of these explains the rectangular nature of the background aberrations or the consistent positioning of these aberrations relative to the bands in question. Dr. Wang’s failure to store original data and maintain research records relevant to this publication is clearly not in keeping with accepted standards in the field.

The work in allegation #12 was supported by RO1-MH075916 and P50-MH096891 to Chang-Gyu Hahn. Given Dr. Wang’s failure to provide original data or research records pertaining to these allegations, we recommend that the editors of *Molecular Psychiatry* request uncropped images of the underlying blots (containing film edges and weight markers). Failure to provide them should be cause for retraction. As first author on the study and the author who ran the western blots in question, Dr. Wang bears responsibility for the misconduct described and for the failure to maintain and make available original data and research records. As senior author, Chang-Gyu Hahn may also bear some responsibility for this misconduct.

Allegation 13 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures a and c by duplicating, cutting and pasting, or altering the plots in the following publication:

Hoau-Yan Wang, Andres Stucky, Chang-Gyu Hahn, Robert Wilson, David Bennett and Steven Arnold. BDNF-trkB signaling in late life cognitive decline and Alzheimer's disease. *Translational Neuroscience* 2011(2), 91-100.

It is not clear from this allegation which figure is being referred to. However, the image analysis provided by ORI raises concerns for figure 1C. We do not see clear issues with figure 1A but have examined only the low-resolution published image (see below). We have therefore focused our attention on figure 1C. This allegation would appear to stem from a clear difference in background for the right two lanes of the pY-ERK2 blot. Without access to the original, uncropped and unmanipulated blot images, it is not clear if this represents fabrication or the splicing of lanes from separate blots. We agree that the unexpected and stark differences in background between the left pair and right pair of lanes is of significant concern, but our reliance on the markedly low-quality image from the publication does not allow us to make a definitive conclusion regarding misconduct in this case.

The discontinuity in blot background between lanes 2 and 3 is striking upon the adjustment of image levels and contrast. This discontinuity could be explained by the splicing of two gels. It is not clear that this was done with the intention to mislead or misrepresent data. Dr. Wang did not respond to this allegation in his initial response to this investigation, and states in his response to the draft of this report that he was never asked to do so. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. In his response to the draft of this report, Dr. Wang acknowledges that the blots were rearranged to organize samples and that this *post-hoc* reorganization of lanes was necessary because he was blind to sample identification during the preparation of the blots. Dr. Wang did not provide original uncropped blots for this allegation and his failure to store original data and maintain research records relevant to this publication clearly not in keeping with accepted standards in the field. The integrity of the data shown in the publication therefore remains highly questionable.

The work in this publication was supported by grants from the National Institute on Aging (P30AG10161, R01AG15819, R01AG024871, P30AG10124, and R01AG03947). The publication does not identify the awardees of these grants. Given Dr. Wang's failure to provide original data or research records pertaining to this allegations, we recommend that the editors of *Translational Neuroscience* request uncropped images of the underlying blots (containing film edges and weight markers) for an examination of the merits of these allegations. As first author and the member of his lab who ran the western blots in question, Dr. Wang bears responsibility for the failure to maintain and make available original data and research records. As senior and

corresponding author, Steven E. Arnold also bears responsibility for the integrity of this publication and the management of its underlying data.

Allegation 14 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 1 and c by duplicating, cutting and pasting, or altering the plots in the following publication:

Konrad Talbot, Hoau-Yan Wang, Hala Kazi, Li-Ying Han,¹ Kalindi P. Bakshi, Andres Stucky, Robert L. Fuino, Krista R. Kawaguchi, Andrew J. Samoyedny, Robert S. Wilson, Zoe Arvanitakis, Julie A. Schneider, Bryan A. Wolf, David A. Bennett, John Q. Trojanowski, and Steven E. Arnold. Demonstrated brain insulin resistance in Alzheimer's disease patients is associated with IGF-1 resistance, IRS-1 dysregulation, and cognitive decline. J Clin Invest 2012; 122(4):1316-1338.

Based on our reading of the image analysis summary provided by ORI, we suspect that the allegation was written in error, as the major issue appears to be related to western blot data in figures 4D and 4E. This allegation would appear to stem from the same images described in allegation two above, which focuses on a conspicuously lighter background pattern surrounding bands in lanes 2-4 of the IGF-1R β pY1131 blot in figure 4D and around most of the bands in figure 4E. In our draft of allegation 14, we concluded that the blots in question in figures 4D and 4E were fabricated intentionally. As Dr. Wang states in his response to the draft report, we reached a more cautious conclusion in allegation 2, pointing to aberrations consistent with the manipulation of blot data, but refrained from reaching a definitive conclusion due the failure of Dr. Wang to provide research records or original, uncropped blot data. We acknowledge our lack of consistency here. This, in part, was because the committee members were forced to make "qualitative" assessment of manipulated images in lieu of any raw and original data.. This discrepancy, yet again, highlights the central contention of this investigation that it is impossible to provide an objective assessment of the allegations against Dr. Wang without the provision of research records and original data. Once again, Dr. Wang's failure to store original data and maintain research records relevant to this publication are not in keeping with accepted standards in the field. The integrity of the data shown in this publication therefore remains highly questionable.

This work was supported by grants from the National Institute on Aging (NIA) to the ROS (R01 AG15819) and the Alzheimer Disease Centers at the University of Pennsylvania (P30 AG10124) and Rush University (P30 AG10161). Absent the provision of original uncropped plots, the study in question should be retracted. While finalizing this report we became aware of additional concerns concerning the western blot data presented in this publication. This further illustrates the need for the editors to request original underlying data and examine the merits of both the old and new allegations pertaining to this study. Dr. Wang is a co-first author on this study and likely bears some responsibility the blots in question. Furthermore, as senior and

corresponding author, Steven E. Arnold bears some share of responsibility for the integrity of the data in this study.

Allegation 15 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 6 by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Capuano AW, Khan A, Pei Z, Lee KC, Bennett DA, Ahima RS, Arnold SE, Arvanitakis Z. Insulin and adipokine signaling and their cross-regulation in postmortem human brain. *Neurobiol Aging* 2019;84:119-130.

Based on our reading of the image analysis summary provided by ORI, we suspect that the allegation was written in error, as the major issue appears to be related to western blot data in figure 5A. The concerns raised in this allegation stem from a vertical discontinuity between lanes 8 and 9 in the top two blot panel and between lanes 4 and 5 in the bottom two blot panels. We conclude that the vertical discontinuities are most consistent with lanes from different blots being spliced together. While not best practice when undisclosed in the publication, we cannot conclude that that this was done to intentionally misrepresent the data. This may simply represent the need to run multiple gels to accommodate all the samples of a large experimental run.

The stark light vertical background lines between the lanes indicated above are clearly apparent in the images. In response to other allegations involving similar background aberrations, Dr. Wang had stated that his lab did not have the capacity to make gels large enough to run all lanes on the same gels and therefore spliced lanes from more than one gel/blot. In his response to the draft of this report, Dr. Wang acknowledges that the vertical discontinuities reflect the rearrangement of lanes from separate blots in the figures. Dr. Wang did not provide the uncropped blots that were combined to create the figure in question, nor did he share research records that specify the lanes from each original blot that contributed to the published figure. While it may be justified to splice lanes from different gels to report a result in a publication, the committee notes that under such circumstances, it becomes even more pertinent to retain original blots with molecular weight markers to establish the integrity of the reported data. Dr. Wang's failure to store original data and make available the research records relevant to this publication clearly not in keeping with accepted standards in the field and fails to address the allegation directly and transparently.

The work in allegation 15 was supported by NIH P30 AG10161, R01 AG 15819, R01 NS084965, and RF1 AG059621. Due to the absence of any compelling explanation for the aberrations found in the figure in question and the failure to provide original underlying data (uncropped blots including edges and molecular weight markers), the committee recommends that the editors of the *Neurobiology of Aging* request that Dr. Wang provide uncropped images of the underlying blots (not cropped images, which Dr. Wang consistently has submitted as original blots). If such original data are produced, the editors should provide the images for the figures in question and a full description of

the analysis done to settle the allegations. As senior and corresponding author on this study, Dr. Wang is responsible for the integrity and management of the data in question.

Allegation 16 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in numerous figures by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Li W, Benedetti NJ, Lee DH. Alpha 7 nicotinic acetylcholine receptors mediate beta-amyloid peptide-induced tau protein phosphorylation. J Biol Chem. 2003 Aug 22;278(34):31547-53

This allegation appears to stem from unexpected variations in the background patterns of western blots displayed in figures 1a, 1c, 1d and 2b. We conclude that while these anomalies are highly suspicious, it is difficult to determine with certainty if they are artifacts of image compression, digital contrasting of published, low-resolution images, or represent manipulation of the data.

Examination of the blot panels in questions confirm unexpected variations in background patterns, with a darker, rectangular area around the bands with regions of background further from the band characterized by no background signal at all. Upon the adjustment of levels and contrast of the blot images cited in the allegation, individual bands appear to be closely surrounded by small nearly rectangular regions of higher background signal and each band appears to have a uniquely sized halo of background signal. In contrast, most of the background regions across the blot panel appear to have no signal at all. However, similar nearly rectangular regions of background signal also appear behind panel labels, as if they had been cut and pasted from another figure rather than formatted directly onto the blot. These aberrations may reflect the cutting and pasting bands from another gel onto the larger blot. However, it is possible that these aberrations are compression artifacts from the low-resolution images contained in the pdf of the publication.

In this response to the draft of this report, Dr. Wang confirms the background patterns described in the allegation and compares these to adjusted images from another study, one not conducted by Dr. Wang, in the same issue of the journal. He finds similar background aberrations in these adjusted images, consistent with the compression of digital images being their cause. Dr. Wang did not share uncropped original blots for the experiments in question, which would have provided the most direct and transparent means of addressing the allegation. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field.

No sources of support are identified in the publication. As first author on this study Dr. Wang likely bears some responsibility for the blots in question. Furthermore, as senior and corresponding author, Daniel H. S. Lee bears some share of responsibility for the integrity and management of the data in this study.

Allegation 17 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in figures by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Burns LH. Gbetagamma that interacts with adenylyl cyclase in opioid tolerance originates from a Gs protein. *J Neurobiol.* 2006 Oct;66(12):1302-10.

The concerns described in this allegation stem from the appearance of background aberrations and/or sharp linear edges in the bands of the western blot data. Aberrations can be observed in the backgrounds of blot panels in figures 2, 3, and 4 when the contrast is increased, revealing nearly rectangular clouds of higher background intensities in regions immediately surrounding individual bands. In addition, several individual bands have unexpectedly stark linear edges in the blot panels of figures 3 and 4. We conclude that, while these anomalies are highly suspicious, it is difficult to determine with certainty whether they are artifacts of image compression, digital contrasting of published, very low-resolution images, or represent manipulation of the data.

The suspicious background pattern observed in the blot panels of figures 2, 3, and 4 are clearly present upon adjustment of the image contrast levels. In contrast, most of the background regions across the blot panel appear to have no background signal at all. However, similar nearly rectangular regions of background signal also appear behind panel labels, as if they had been cut a pasted from another figure rather than formatted directly onto the blot. These aberrations are consistent with cutting and pasting bands from another gel onto the larger blot. However, it is possible that these aberrations are compression artifacts from the low-resolution images contained in the pdf of the publication. Examination of the blot panels in figures 3 and 4 also revealed instances of unexpected stark linear edges in some bands.

Dr. Wang did not respond to this allegation in his initial response to this investigation, and states in his response to the draft of this report that he was never asked to do so. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. In his response to the draft of this report, Dr. Wang included figure panels from the publication in question that he subjected adjustments of sharpness and contrast, confirming the patterns we described in our report and, he states, consistent with the aberrations being the product of the journals image processing software. He also acknowledges that the published blot images contain bands from two different gels. Dr. Wang claims to have included "raw" images in this response, however these are clearly not original blot images, as they do not contain film edges or weight markers and clearly do not include the entirety of the films from the gels combined to create the final image panels. Dr. Wang also failed to provide research records that would allow the committee to identify the lanes from separate blots that were combined to create the published blot images. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor

has he maintained notebooks describing the preparation of western blots in his lab. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field.

No funding source was reported in this publication. As first and corresponding author in this study, Dr. Wang bears responsibility for the failure to maintain and make available original data and research records.

Allegation 18 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in figures by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Frankfurt M, Burns LH. High-affinity naloxone binding to filamin A prevents mu opioid receptor-Gs coupling underlying opioid tolerance and dependence. *PLOS ONE*. 2008 Feb 6;3(2):e1554.

The concerns described in this allegation primarily arise from the data presented in Figures 1 and 7, which contain suspicious patterns suggestive of fabrication. Specifically, horizontal and vertical artifacts in Figure 1A may indicate the splicing of lanes from different blots. Furthermore, panels in Figure 7A appear to be more similar than expected from independent data, suggestive of data duplication to fabricate results. Dr. Wang did not provide any of the underlying data that used to generate the figures in question. However, based on the retraction of this publication by the editors of *PLoS ONE*, the committee's interview with Dr. Zalm from the *PLoS* editorial team and, and careful visual analysis of the reported data, we conclude that this allegation holds merit. We find no compelling reason to dispute the findings of the *PLoS* editors. However, we must note that the failure of Dr. Wang to provide original data or research records pertaining to this case prevents us from making an objective assessment of this allegation.

Our analysis of the published figures confirmed the presence of horizontal and vertical irregularities in the blot panels of figure 1A between lanes 4-5 and around multiple bands in figure 7A. No positive control samples were included in the experiment summarized in figure 1C. Based on the publisher's retraction, Dr. Wang appears not to have provided any original data demonstrating appropriate positive control for figure 1C. We also agree that the data in Figure 7A representing NLX and FLNA²⁵⁵⁰⁻²⁵⁶⁰ appear to be more similar than expected from independent blot data. Dr. Wang did not respond to this allegation in his initial response to this investigation, and states in his response to the draft of this report that he was never asked to do so. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. Dr. Wang did not provide uncropped blots or research records pertaining to the blots in his response to the draft of this report. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab. Dr. Wang's failure to

store original data and maintain research records is clearly not in keeping with accepted standards in the field. In his response to the draft of this report, Dr. Wang explains the apparent duplication of bands figure 7 by stating a blot image "...was inadvertently copied..."

The publisher's editorial team conducted a thorough analysis of the data in question and gave Dr. Wang the opportunity to address the concerns described. It is clear from our interview with Dr. Maria Zalm, that the images provided by Dr. Wang not only failed to resolve most of the issues described in the retraction notice, but also themselves display hallmarks of fabrication. The *PLoS* editors provided the committee with the images provided by Dr. Wang in his response to their concerns. Once again, these images do not appear to represent original, uncropped images of the original blots (they do not represent full blots with edges included in the image and contain no weight markers). As described in the retraction notice for this publication, among the images provided by Dr. Wang in response to editorial concerns, there are multiple instances of highly similar patterns of background noise that are shared by multiple blot images, and these patterns appear in images provided to address concerns with other *PLoS One* studies published between 2008 and 2016. The committee agrees that the misconduct described in this allegation warranted a retraction of the publication. No further editorial action is recommended. The work described in this publication was supported by Pain Therapeutics, Inc. As corresponding author in this study, Dr. Wang bears responsibility for the misconduct in this allegation.

Allegation 19 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in figures by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Burns LH. Naloxone's pentapeptide binding site on filamin A blocks Mu opioid receptor-Gs coupling and CREB activation of acute morphine. *PLoS One*. 2009;4(1):e4282.

The concerns described in this allegation primarily arise from the data presented in Figures 1, 2 and 5, which contain suspicious patterns suggestive of fabrication. These include unexpectedly distinct regions of background intensities in the blot panels displayed in figure 1A and vertical irregularities suggestive of splice lines can be seen in the plot panels of figures 2A and 5A. Based on the retraction by the editors of this publication, our interview with a representative of the *PLoS* editorial team who handled the analysis leading to retraction, and our own analysis of the published data and the data provided by Wang to *PLoS*, we conclude that this allegation holds merit. We find no compelling reason to dispute the findings of the *PLoS* editors. However, we must note that the failure of Dr. Wang to provide original data or research records pertaining to this case prevents us from making our own objective assessment of this allegation.

Our examination of the published figures confirmed the aberrations described above. In figure 1A, the background noise behind the top portions of lanes 1 and 2 does not match with the background in other regions of the blot. The aberration appears as a

highly rectangular region of distinct background intensity. There also appear to be smaller background aberrations surrounding the bands in lanes 4 and 5. In figure 2A lane 9 appears to be missing from the bottom-most MOR blot on the left, in that there is no background signal at all in this lane, and there is a thick vertical discontinuity in the background of the bottom-most MOR blot on the right between lanes 6 and 7. In figure 5A the background behind lanes 7-9 are much darker than the background behind lanes 1-6.

Dr. Wang did not respond to this allegation in his initial response to this investigation, and states in his response to the draft of this report that he was never asked to do so. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. Dr. Wang did not provide original uncropped blots or research records pertaining to this allegation. In his response to the publisher, Dr. Wang claimed that the observed irregularities in Figures 1 and 5 were a consequence of scanner artifacts. Dr. Wang acknowledged that a sample lane (VAAGL + Morphine 60 Min) in Figure 2 was inadvertently cropped out upon publisher's inquiry and provided a replacement figure. In his response to *PLoS*, Dr. Wang acknowledged that a sample lane (VAAGL + Morphine 60 Min) in Figure 2 was inadvertently cropped out and provided a replacement figure. In addition, no positive control samples were included in the blots displayed in figure 2A and, according to *PLoS*'s retraction notice, Dr. Wang failed to provide original data demonstrating appropriate positive control for this experiment. In his response to the draft of this report, Dr. Wang states that "it is impossible...to remember in specific, particular detail what occurred more than fourteen years ago..." but acknowledges the likelihood that the blots were spliced to create the final figures.

The publisher's editorial team conducted a rigorous analysis of the underlying data and communicated with Dr. Wang, giving him the opportunity to address the concerns raised. However, the response provided by Dr. Wang was not deemed sufficient to provide confidence in the integrity of the data, thereby leading the editors to retract this publication. Based on the publisher's analysis of the underlying data provided by Dr. Wang, the pixel patterns in blot backgrounds appeared much more similar than would be expected to other images provided in response to concerns pertaining to other *PLoS ONE* studies published by Dr. Wang. Dr. Wang did not respond to this allegation, nor did he provide underlying data or research records. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field.

The committee agrees with *PLoS*'s decision to retract the publication. No further editorial action is recommended. The work described in this publication was supported by Pain Therapeutics, Inc. As first author on the study and the person who performs the western blots in his lab, Dr. Wang is responsible for the research misconduct in this allegation. As senior and corresponding author on this publication, Dr. Lindsay H. Burns also bears some measure of responsibility.

Allegation 20 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 1 and 5 by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Stucky A, Liu J, Shen C, Trocme-Thibierge C, Morain P. Dissociating beta-amyloid from alpha 7 nicotinic acetylcholine receptor by a novel therapeutic agent, S 24795, normalizes alpha 7 nicotinic acetylcholine and NMDA receptor function in Alzheimer's disease brain. J Neurosci. 2009 Sep 2;29(35):10961-73.

This allegation arises from the data presented in Figures 1 and 5, which contain suspicious patterns suggestive of fabrication. Specifically, there appear to be three regions of distinct background intensities in the top blot panel displayed in Figure 1C that do not match the rest of the blot or the Beta-Actin blots shown below, the latter of which has uniform background levels across the blot. Furthermore, unexpected rectangular discontinuities are apparent in the three out of the five blot panels presented in figure 5A. Based on our analysis of the published images, we confirm the presence of the aberrations described in for the data shown in Figures 1 and 5 and that these may be consistent with knowing fabrication by Dr. Wang. However, we must note that the failure of Dr. Wang to provide original data or research records pertaining to this case prevents us from making an objective assessment of this allegation.

Adjusting levels of contrast for the alpha7nAChR blots shown in figure 1C reveals three distinct levels of background intensity: the lightest intensity background is seen behind lanes 1-4, dark intensities are observed in lanes 5 and 9 as distinct narrow vertical bands centering the lanes, and intermediate levels are seen behind lanes 6-8. Though this may reflect the assembly of the final figure from 3 different blots, these background differences are not observed in the Beta-Actin blots, that presumably come from the same blots as the alpha7nAChR bands. Several of the rectangular irregularities in the blot panels are visible even without contrast adjustment in Figure 5A. Adjustment of image levels reveals three aberrations: In the first blot panel there is a rectangular halo of lighter background behind the bands in lanes 7 and 8. In the second panel there is a stark rectangular band of lighter than expected background immediately below the bands in every lane. Finally, there is again, in the fourth blot panel, a rectangular halo of lighter background behind the bands in lanes 3 and 4. These aberrations are most consistent with the cutting and pasting of bands and lanes from other blots onto the images in question or the adjustment of specific rectangular regions of interest within the image.

Dr. Wang did not respond to this allegation in his initial response to this investigation, and states in his response to the draft of this report that he was never asked to do so. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. In his response to the draft of this report, Dr. Wang includes an analysis of the published figures and makes a case that the aberrations

described in the allegation are caused by the imaging processing software used the Journal. Furthermore, Dr. Wang cites the fact that the Editor of the Journal of Neuroscience reviewed the “raw blot images provided...and reached the conclusion that that there was no evidence of data manipulation.” However, we note that no original images of the blots in question were provided to the committee, and it is not clear what is meant by “raw blot images.” The committee’s interview with Dr. Wang revealed that he has not retained images of uncropped blots, nor has he maintained notebooks describing the preparation of western blot experiments in his lab. Dr. Wang’s failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field.

An expression of concern published was by the journal on January 19, 2022, based on “concerns about western blots in this study.” In this expression of concern, the editors state that they await the results of CUNY’s investigation before taking further action. We recommend that the editors of *The Journal of Neuroscience* confirm that Dr. Wang has indeed provided uncropped images of the underlying blots (containing film edges and molecular weight markers). If these have indeed been provided, the editors should provide a full description of the analysis that was done to settle each of the allegations above and provide images of the underlying data to the readers. Should the editors determine that uncropped and unmanipulated data have not been provided by Dr. Wang, the publication should be retracted. This work was supported by grants from Institut de Recherches Internationales Servier in France. As first and the corresponding author on the study and the person who performed the western blots in his lab, Dr. Wang is responsible for the research misconduct in this allegation.

Allegation 21 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 1 by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Bakshi K, Shen C, Frankfurt M, Trocmé-Thibierge C, Morain P. S 24795 limits beta-amyloid-alpha7 nicotinic receptor interaction and reduces Alzheimer's disease-like pathologies. *Biol Psychiatry*. 2010 Mar 15;67(6):522-30.

The concerns described in this allegation arise from unexpected variations in the background surrounding specific bands in the blot panels displayed in Figure 1A. The NIH imaging analysis provided by ORI also mentions similar aberrations throughout the remaining figures. We conclude that the aberrations associated with the blots in figure 1a could be consistent with the fabrication of western blot data via the cutting and pasting of specific bands onto the blot image or to adjustment of image levels for subsets of bands within a rectangular region of interest. However, we must note that the failure of Dr. Wang to provide original data or research records pertaining to this case prevents us from making an objective assessment of this allegation.

Our analysis revealed that the background signal surrounding the alpha7nChR bands in lanes 2-6 of the topmost blot appears to be significantly different from the

background noise of the overall blot, including the regions surrounding lane 1. This is clear without adjusting the levels of image but becomes starkly clear when adjustments are made. The adjustment of the published image in figure 1 for brightness and contrast reveals an unexpectedly linear edge to the relatively light background intensity just to the left of band 2 in the top panel. Furthermore, there is a stark horizontal discontinuity in the bottommost alpha7nChR blot panel in figure 1A. The background behind the control Beta-Actin bands for both blot panels has extremely low signal compared to the blots displaying the alpha7nChR bands. In addition, supplementary figure 2 displayed at least three regions of unexpectedly rectangular discontinuities in background signal, which also center specific bands or lanes in the blot. In this case the resolution of the published images appears sufficiently high to the committee to argue against the possibility that the aberrations have been caused by image compression and digital contrasting of the published images. Dr. Wang contests this conclusion in his response to the draft report. The aberrations in figure 1A appear to be consistent with the manipulation of the blot image, either through the cutting and pasting of bands onto the blot image, or to the selective manipulation of bands 2-6 through the adjustment of image levels within a rectangular region of interest over these bands.

In response to this draft report, Dr. Wang presents what he refers to as "...raw high-resolution blot images submitted to the journal more than a decade ago." However, once again, these are clearly not uncropped blots, as they lack both film edges and molecular weight markers. Dr. Wang has repeatedly insisted that the cropped manipulated data he has provided the committee is "raw data". At the same time, Dr. Wang has argued that it is not possible to provide raw data for publications dating back 10 years. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field and prevent an objective assessment of this allegation.

This work was supported by grants from Institut de Recherches Internationales Servier in France. Based on the presence of aberrations consistent with misconduct throughout figures of this publication, we recommend that that the editors of *Biol. Psychiatry* request uncropped images of the underlying blots (containing film edges and molecular weight markers). If these are provided, the editors should provide a full description of the analysis that was done to settle each of the allegations above and provide images of the underlying data to readers. Should the editors determine that uncropped and unmanipulated data have not been provided by Dr. Wang, the publication should be retracted. As first and the corresponding author on the study and the person who performed the western blot experiments, Dr. Wang is responsible is responsible for this misconduct and for the failure to maintain and make available original data and research records.

Allegation 22 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 2, 5 and 9 by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Bakshi K, Frankfurt M, Stucky A, Goberdhan M, Shah SM, Burns LH. Reducing amyloid-related Alzheimer's disease pathogenesis by a small molecule targeting filamin A. *J Neurosci*. 2012 Jul 18;32(29):9773-84.

The concerns described in this allegation stem from western blot data presented in Figures 2, 5 and 9 in which unexpected rings of lighter background narrowly surround bands and unexpected discontinuities in background levels appear across the blots. In addition, there appear to be several instances in which individual bands representing different samples have complex and unexpectedly similar shapes. Some of the aberrations described in the allegation pertaining to Figure 5 may be artifacts of image compression, or digital contrasting of published, low-resolution images. Due to the lack of any original data from Dr. Wang, we find this western blot data highly questionable. Our analysis agrees with the contention that multiple bands in figure 2A, 2C, and 2D appear to be identical. We also observed the ring artifacts surrounding each band when we increased the contrast in these panels. Based on these observations, we confirm the presence of aberrations consistent with fabrication of the western blot in figure 2. We also detected unexpected differences in background levels across the NR1 blot displayed in figure 5. Lanes 1-4 have a darker background than lanes 5-8 and there is a clear rectangular halo of very light background surrounding the band in lane 1. Though the differences behind lanes 1-4 and 5-8 may represent the splicing of lanes from different blots, the halo specifically surrounding the band in lane one may reflect the cutting and pasting of the band from another blot or from the adjustment of levels specifically within a region of interest centering the band in lane 1. Our analysis confirms that the bands displayed in figure 9A are oddly shaped and appear be much more similar than expected. Though we agree that these features of the blot are highly problematic, we do not think that, without access to primary underlying data, we can make an objective assessment of this allegation. However, given the absence of original data or research records, the data described in this figure should therefore be considered with suspicion.

In his initial response to this investigation, Dr. Wang did not provide any clarification for the artifacts in Figure 5. Rather, Dr Wang provided .jpg images embedded in power PowerPoint files, which he presented as representing underlying data. However, these images clearly did not represent uncropped blots containing film edges and molecular weight markers. In his response to the draft of this report, Dr. Wang presented adjusted images taken from the publication and states that his analysis reveals no evidence of these aberrations. Once again, Dr. Wang has failed to provide original data and records that would allow for the objective assessment of these allegations. Original, uncropped plots displaying the bands reported in the figures with the shapes and relative positions shown in the figures, would address the allegations transparently and directly. Therefore, the committee concludes that Dr. Wang's response to this allegation is not sufficient and that he has failed to provide the committee access to the original data that were used to generate the figures in question.

In a corrigendum to this publication, the authors provided what they referred to as “original uncropped blots” to the editors, but these are clearly not full, uncropped blots, as there are no film edges visible in these images and they do not include the molecular weight markers expected of an uncropped blot. It is not clear why the editors accepted these images as uncropped blots. Dr. Wang’s response to this allegation cites the corrigendum for the publication and the conclusion from the editors of *J. Neurosci.* that there was “no evidence of manipulation.” However, the files provided by Dr. Wang in response to this allegation cannot be considered original, unmanipulated data. Due to the absence of any research records or original data, the integrity of this entire study remains highly questionable. The committee’s interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab. Dr. Wang’s failure to store original data and maintain research records relevant to this publication clearly not in keeping with accepted standards in the field.

This work was supported by Pain Therapeutics, Inc. An expression of concern published by the journal on January 19, 2022, based on “concerns about western blots in this study.” In this expression of concern, the editors state that they await this investigation before taking further action. Based on our consideration of this allegation we recommend that the editors of *J. Neurosci.* confirm that uncropped images of the underlying blots (containing film edges and molecular weight markers) were provided by Dr. Wang. If these were indeed provided, the editors should provide a full description of the analysis that was done to settle each of the allegations above and provide images of the original, uncropped blot images to their readers. Should the editors determine that uncropped and unmanipulated data have not been provided by Dr. Wang, the publication should be retracted. We also note that the data provided by Wang to the editors of *J. Neurosci.*, did not appear to be original, unmanipulated data. In addition, credible concerns have been raised about apparent misconduct in the images provided to the editors by Dr. Wang. As first and corresponding author on the study and the person who performed the western blot experiments, Dr. Wang would be responsible for any research misconduct that occurred in this case and is responsible for the failure to maintain and make available original data and research records.

Allegation 23 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 9 and 11 by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Lee KC, Pei Z, Khan A, Bakshi K, Burns LH. PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer's disease pathogenesis. *Neurobiol Aging* 2017;55:99-114.

The ORI allegations summary appears to have made an error in this case. Figure 9 does not contain western blot data and the NIH image analysis identifies several figures other than figures 9 and 11. The summary of NIH’s image analysis provided by ORI

identifies issues regarding the data shown in figures 3, 5, 8, 10, and 12 (see also our conclusions for allegation 24, below, which pertains specifically to figure 5 in this publication). The majority of the concerns raised for this publication involve aberrations in the background surrounding western blot bands. In addition, a vertical discontinuity is observed in background of the blot shown figure 8 and the bands appear to be distorted. The authors mention that the blots shown in figure 10a were “stripped and reprobed” but a vertical discontinuity can be seen in the background for the α 7nAChR blot but not for the other two blots in the same figure. Furthermore, in figure 12, the number of bands in the top blot panel (12) does not match number of bands in the bottom panel (13).

We agree that there are multiple substantive concerns surrounding the data reported in this publication. However, once again, Dr Wang’s failure to provide the committee with an explanation or the uncropped images of the blots in question make it impossible to address the allegations objectively. Dr. Wang’s failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field. The integrity of Dr. Wang’s work in this case therefore remains highly questionable. However, due to the lack of original data, the committee cannot make a clear assessment for allegations arising from figures 3, 8, 10 and 11. Though the aberrations could be consistent with misconduct, we cannot eliminate the possibility that some of the aberrations described could be caused by compression artifacts and effects of adjustment of levels, brightness, and contrast of low-resolution published images. Dr. Wang did not provide uncropped blots for these allegations, nor did he provide a compelling explanation for the unexpected and problematic background patterns observed.

Our analysis of Figure 12 confirms the simple observation that the number of bands in the top (12; NR1) does not match with number of bands in the bottom panel (13; PLC γ 1). In the expression of concern published by the journal, the authors acknowledge that “NR1 loading controls in Figure 12 were not measured from stripped re-probed gels as indicated in the published report; they were run on separate gels and one lane was omitted in Figure 12”. Dr. Wang did not provide uncropped images or research records that would allow us to objectively determine if misconduct occurred in this case. The committee’s interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab.

Based on reader concerns, the journal issued an expression of concern for this publication in 2022. This expression of concern states that the authors provided a detailed response to the concerns described, including images of relevant uncropped blots. However, such data was not provided to the committee by Dr. Wang and similar statements by other journal have been made even in instances in which Dr. Wang clearly did not provide images of uncropped original blots. The expression of concern concludes that “the editors did not find compelling evidence of data manipulation intended to misrepresent the results.” However, the editors go on to list additional serious errors with the publication that, in the opinion of this committee, place the verity of the publish data into serious doubt. Though Dr. Wang requested a corrigendum to

correct these errors, the editors appear to have halted further action on until CUNY's investigation is completed..

According to the acknowledgements section, "PTI funded this work except for the C¹⁴-labeling of PTI-125, which was produced for biodistribution studies under NIH grant number 4R44AG050301." Though the committee could not make an objective determination with regard to data manipulation in this case, Dr. Wang's failure to provide uncropped blots, notebooks, or other records describing the preparations of these blots, leave significant doubts regarding the integrity of the data presented. Given Dr. Wang's failure to provide a response to these allegations to this committee, we recommend that the editors of *Neurobiology of Aging* confirm that Dr. Wang has indeed provided uncropped images of the underlying blots (containing film edges and molecular weight markers). If these have indeed been provided, the editors should provide a full description of the analysis that was done to settle each of the allegations above and provide images of the underlying data to readers. Should the editors determine that uncropped and unmanipulated data have not been provided by Dr. Wang, the publication should be retracted. As first and the corresponding author on the study and the person who performed the western blot experiments, Dr. Wang is responsible for the failure to maintain and make available original data and research records. As senior author on this publication, Dr. Lindsay H. Burns also likely bears a measure of responsibility for the integrity of the publication and the management of its underlying data.

Allegation 24 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 5 by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Lee KC, Pei Z, Khan A, Bakshi K, Burns LH. PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer's disease pathogenesis. *Neurobiol Aging* 2017;55:99-114.

This allegation stems from irregularities in the background of the blot panels displayed in figure 5: halos of lighter background appear to surround individual bands and there are additional discontinuities in the blot backgrounds. As stated for allegation 23, we agree that there are substantive concerns surrounding the data reported in figure 5. However, once again, Dr Wang's failure to provide the committee with an explanation or the uncropped images of the blots in question make it impossible to address the allegations objectively. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field. The integrity of Dr. Wang's work in this case therefore remains highly questionable. Due to the lack of original data, the committee cannot make a clear assessment for allegations arising from figures 5. Though the aberrations are consistent with misconduct, we cannot eliminate the possibility that some of the aberrations described could be caused by compression artifacts and effects of adjustment levels, brightness, and contrast of low-resolution published images.

Our analysis of figure 5 confirms that the observations made by the allegation; there are clear and abnormal geometric cuts in figure 5A, which could be indicative of the cutting and pasting of bands onto the blot image. However, without access to verifiable uncropped images of the original blot, it is impossible to objectively determine the explanation for this unexpected background pattern, as it may be due to image compression and the alteration of levels, brightness, and contrast of a low-resolution image. In his response to the draft of this report Dr. Wang includes adjusted images taken from the published figures and acknowledged removing two lanes from the original blots for the final published images. Once again, this allegation could have been directly addressed by presenting uncropped blots displaying the bands shown in the published figure with the same shapes and molecular weights but with the additional lanes expected from research records, which, based on his response to this allegation, Dr. Wang has apparently retained. However, neither original data nor research records were shared with the committee. Instead, Dr. Wang's response to this allegation is based solely on the adjustment of published images to support his explanation that the aberrations cited were caused image processing used by the publisher. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab.

Based on reader concerns, the Journal issued an expression of concern for this publication in 2022. The expression of concern published by the editors states that the authors provided a detailed response to the concerns described, including images of relevant uncropped blots. However, such data was not provided to the committee by Dr. Wang. and similar statements by other journal have been made even in instances in which Dr. Wang clearly did not provide images of uncropped original blots. The expression of concern concludes that "the editors did not find compelling evidence of data manipulation intended to misrepresent the results." However, the editors go on to list additional serious errors with the publication that, in the opinion of this committee, place the verity of the publish data into serious doubt. Though Dr. Wang requested a corrigendum to correct these errors, the editors appear to have halted further action until CUNY's investigation is completed.

According to the acknowledgements section, "PTI funded this work except for the C¹⁴-labeling of PTI-125, which was produced for biodistribution studies under NIH grant number 4R44AG050301." Though the committee could not make an objective determination regarding data manipulation in this case, Dr. Wang's failure to provide original, uncropped blots, or notebooks or other records describing the preparations of these blots leave significant doubts regarding the nature of the data presented. We recommend that the editors of *Neurobiology of Aging* request uncropped images of the original blots that include blot edges and molecular weight markers. If these have indeed been provided, the editors should provide a full description of the analysis that was done to settle each of the allegations above and provide images of the underlying data to readers. Should the editors determine that uncropped and unmanipulated data have not been provided by Dr. Wang, the publication should be retracted. As first and the corresponding author on the study and the person who performed the western blot

experiments, Dr. Wang is responsible for the failure to maintain and make available original data and research records. As senior author on this publication, Dr. Lindsay H. Burns also likely bears a measure of responsibility for the integrity of the publication and the management of its underlying data.

Allegation 25 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data figures by duplicating, cutting and pasting, or altering the plots allegation in the following publication:

H.-Y. Wang, Z. Pei, K.-C. Lee, E. Lopez-Brignoni, B. Nikolov, C. A. Crowley, M. R. Marsman, R. Barbier, N. Friedmann & Lindsay H. Burns. PTI-125 Reduces Biomarkers of Alzheimer's Disease in Patients. *The Journal of Prevention of Alzheimer's Disease* 2020;7:256–264.

This allegation stems from a conspicuously lighter background region surrounding a single band in Figure 3A. This allegation appears to be a duplication of allegation seven. Please our summary of allegation seven above.

Allegation 26 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data figures by duplicating, cutting and pasting, or altering the plots in the following publication:

Robinson S, Mogul AS, Taylor-Yeremeeva EM, Khan A, Tirabassi AD, Wang HY. Stress Diminishes BDNF-stimulated TrkB Signaling, TrkB-NMDA Receptor Linkage and Neuronal Activity in the Rat Brain. *Neuroscience*. 2021 Jul 21:S0306-4522(21)00358-4.

The concerns described in this allegation stem from the apparent duplications of blot data shown in Figures 4 and 7. Specifically, the bottom blot of 4A appears to have been duplicated and rotated 180 degrees and presented again in Figure 7A. Furthermore, the blot shown in Figure 4B (top row) is highly similar to the blot presented in Figure 7B despite representing independent blots using antibodies against different proteins. Based on a close examination of the top blots in Figures 4B and 7B, we conclude that the blots shown in 4B and 7B, though similar in some ways, are distinct. We therefore do not find a preponderance of evidence supporting the conclusion that bands have been duplicated in this case.

These allegations were the subject of a corrigendum in which the authors explain the issue with 4A and 7A as a mistake in the preparation of the figure. However, the authors provide no explanation for why the blots shown in 4B and 7B look so unexpectedly similar. However, close examination of the blots in 4B and 7B revealed apparent differences in the shapes of the bands and in the background regions below the bands. In their corrigendum, the authors provide what they refer to as “original uncropped blots”, but these are clearly not full, uncropped blots, as there are no film

edges visible in these images and they do not include the weight markers expected of an uncropped blot. It is not clear why the editors accepted these images as uncropped blots. Dr. Wang's response to this allegation cites the corrigendum for the publication and the conclusion from the editors of *Neuroscience* that there was "no evidence of impropriety." Dr. Wang did not provide uncropped blots to the committee, nor did he provide any research records pertaining to the blots in question. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field.

This work was supported by the following NIH grants to Dr. Wang: NIH RO1 AG057658, R01 MH116463 and NIH FR1 AG059621. We find no clear evidence that the blots shown in 4B and 7B are duplications of the same data and do not recommend editorial action in this case. However, the failure to provide original, uncropped blots, or notebooks or other records describing the preparations of these blots leave significant doubts regarding the nature of the data presented. As senior author on the study and the member of the lab who runs the bulk of all western blots in his lab, Dr. Wang was responsible for the maintenance of original data and research records and has clearly failed in this case to properly manage the data described in this publication. As corresponding author of this study, Dr. Siobhan Robinson may also bear some responsibility for the lack of data management.

Allegation 27 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 4, 5, 5a and 6 by duplicating, cutting and pasting, or altering the plots in the following publication:

Stucky A, Bakshi KP, Friedman E, Wang HY. Prenatal Cocaine Exposure Upregulates BDNF-TrkB Signaling. *PLoS One* 2016 Aug 5;11(8):e0160585.

This paper was editorially retracted by *PLoS* on March 30, 2022, based on an expanded set of concerns regarding data shown in figures 1, 2, 5, 6, 8, 9, 10, and 11. These concerns included apparent duplications of blot data and many irregularities in blot backgrounds, including both vertical and horizontal irregularities most simply explained by the cutting and pasting of images onto blots and/or the splicing of blots. The committee has found no compelling reason to dispute the assessment of the *PLoS* Editorial board that research misconduct occurred in this case and that Dr. Wang fabricated western blot data through the manipulation of images. However, once again, Dr Wang's failure to provide the committee with an explanation or the uncropped images of the blots in question make it impossible for the committee to address the allegations objectively. For this publication, Dr. Wang was accused of: 1.) duplicating blot data across panels with molecular weight sizes that do not appear to be consistent across duplications (Fig 1B,D,E,F); 2.) the duplication of Beta-Actin blot data across multiple figures (Figs. 2, 5, 6, 9, 10, and 11); 3.) the splicing images onto blots (Figs. 5B

and 6A), and 4.) an irregularly light region of background intensity forming a rectangle surrounding a single band on a blot shown in Fig. 10A.

It is clear from our interview with Dr. Maria Zalm, that the underlying data provided by Dr. Wang not only failed to resolve most of the issues described in the retraction notice, but also display hallmarks of fabrication. The *PLoS* editors provided the committee with the images provided by Dr. Wang in his response to their concerns. Once again, these images do not appear to represent original, uncropped images of the original blots (they do not represent full blots with edges included in the image and contain no weight markers). In his response to these concerns, Dr. Wang stated that the apparent duplications across Figures 2A, 5A, 9A, and 10A were due to the use of the same re-probed blots across these figures. In his response to the remaining concerns, Dr. Wang stated that the artifacts and overlaps were not due to fabrication but were the product of either the splicing of blots or were due to artifacts caused by material attached to the original films. As described in the retraction notice for this publication, among the images provided by Dr. Wang in response to editorial concerns, there are multiple instances of highly similar patterns of background noise that are shared by multiple blot images. Furthermore, these patterns appear in images provided to address concerns with other *PloS One* studies published between 2008 and 2016. Dr. Wang states that this overlap in background is due to scanner noise. However, we find it impossible to believe that such noise would remain stable across the span of eight years.

In his response to the draft of this report, Dr. Wang claimed the "...Committee copy and pasted its prior analysis from Allegation 8 without supplying any analysis" and requested that this allegation be removed for this reason. However, the draft report had described distinct analyses for these two allegations, though it did contain prose referring to the *PLoS* Editorial actions that was repeated in the other allegations pertaining to publications retracted by *PLoS*. It is not clear why Wang does not recognize the analysis unique to this allegation. Wang stated that he reserves the right to "supplement his response to the Draft Report" if this allegation was not removed. However, we see no compelling reason for this, as this section of the report clearly contains analysis unique to allegation 27.

According to the acknowledgements, this study was funded by an NIH grant (41545-00-02-05), that was listed as awarded to Eitan Friedman. This publication was retracted by the editors of *PLoS*. No further editorial action is recommended. As senior and corresponding author on the study and the member of the lab who runs the bulk of all western blots in his lab, Dr. Wang is responsible for the research misconduct in this allegation.

Allegation 28 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figure 6 by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Li W, Benedetti NJ, Lee DH. Alpha 7 nicotinic acetylcholine receptors mediate beta-amyloid peptide-induced tau protein phosphorylation. J Biol Chem. 2003 Aug 22;278(34):31547-53

This allegation stems from unexpected background patterns in the blots displayed in Fig. 6. We conclude that, while these anomalies are highly suspicious, it is impossible to determine with certainty whether they are artifacts of image compression, digital contrasting of published, low-resolution images, or represent manipulation of the data.

Upon the adjustment of levels and contrast of the blot shown in Figure 6, individual bands appear to be closely surrounded by small rectangular regions of background signal. Specifically, each band appears to be closely surrounded by small, nearly rectangular regions of higher background signal and each band appears to have a uniquely sized halo of background signal. Similar rectangular regions of background signal also appear behind the KD size numbers and panel labels, as if they had been cut-and-pasted from another figure rather than formatted directly onto the blot. Thus, the individual bands of the blots in Figure 6, along with figure labeling, have the appearance of having been cut and pasted onto a blank background.

Dr. Wang did not provide an explanation for these aberrations in response to our investigation and claims that he was not asked to do so in his response to the draft of this report. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. In his response to the draft of this report, Dr. Wang includes an analysis of the published figures and other figures from the same issue of the journal and makes a case that the aberrations described in the allegation are caused by the imaging processing software used. Once again, Dr. Wang failed to provide original images of uncropped blots or records the experiments described in the figure in question. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field.

No research sponsor or grant number was reported in this publication. Given the unexplained background patterns and the absence of an explanation from Dr. Wang, we think that this publication should be held in suspicion until uncropped, original blots are provided to address the allegations directly. As the first author on the study who oversaw and ran the western blots in his lab, Dr. Wang is responsible for the failure to maintain and make available original data and research records. As senior and corresponding author, Dr. Daniel H. S. Lee also bears a measure of responsibility for the integrity of this study.

Allegation 29 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data Figures 5a and 12a by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Friedman E, Olmstead MC, and Burns LH. Ultra-low-dose naloxone suppresses opioid tolerance, dependence and associated changes in mu opioid receptor-G protein coupling and Gbetagamma signaling *Neuroscience* 2005;135:247–261

The concerns described in this allegation stem from unexpectedly similar bands appearing across multiple blots and the appearance of stark linear discontinuities between lanes in Figure 5. In addition, Figure 12 appears to contain a western blot that have been duplicated and presented as completely independent data in a subsequent publication. For this specific concern, see Allegation 21, above.

Based on concerns raised for the aberrations described above, the editors asked the authors for original, uncropped western blots. However, the images provided by the authors are clearly cropped images of blots and therefore do not represent original underlying data. We conclude that while the anomalies described in this allegation are suspicious, it is impossible to objectively assess their merit without access to original uncropped blot images. The unexpectedly high similarities in bands represent may represent the cutting, pasting, and modest distortion of the same data onto multiple regions of the figure, but, as presented in the publication, one can distinguish between the proposed duplicate bands. Furthermore, the stark vertical discontinuities present may be indicative of the cutting and pasting of bands onto the figure but may also reflect undisclosed reordering of lanes for clarity, a dubious practice when unacknowledged, but not one that necessarily rises to the level of egregious misconduct.

In response to our investigation and claims that he was not asked to do so in his response to the draft of this report. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. Dr. Wang did not provide original uncropped images of the blots used for this figure, and a failure to store original data and maintain research records relevant to this publication is clearly not in keeping with accepted standards in the field. The committee's interview with Dr. Wang revealed that he has not retained images of uncropped, unmanipulated blots, nor has he maintained notebooks describing the preparation of western blots in his lab, which represents an egregious failure to manage data and research records. In Dr. Wang's response to editorial concerns over Figure 5, he presents what are referred to as uncropped blots. However, these images do not contain film edges or weight markers. Nor do these blots cover all the bands reported in figure 5. It is not clear to the committee why these were accepted as uncropped, original blot data or why the respondent was not expected to provide blots covering all bands.

We recommend that the editors of *Neuroscience* request that Dr. Wang provide uncropped images of the underlying blots (containing film edges and molecular weight markers). If these have indeed been provided, the editors should provide a full description of the analysis that was done to settle the allegations described above and provide images of the underlying data to readers. The work described in this publication was funded by Pain Therapeutics, Inc. As first and corresponding author on the study and the author who ran the bulk of all western blots in the publication, Dr. Wang is

responsible for the failure to maintain and make available original data and research records. As senior author, Dr. Lindsay H. Burns may also bear some responsibility for the misconduct described above.

Allegation 30 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data Figure 7a by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang H-Y, Burns LH. Naloxone's Pentapeptide Binding Site on Filamin A Blocks Mu Opioid Receptor–Gs Coupling and CREB Activation of Acute Morphine. *PLoS ONE* 2009 4(1): e4282.

The NIH allegations list appears to have made an error in this case, as there is no Figure 7A. There is a Figure 7, which is not divided into multiple labeled panels and does not contain western blot data. However, this publication was editorially retracted by the editors at *PLoS* on March 30, 2022, based on concerns regarding Figures 1, 2, and 5 and on Dr. Wang's response to editorial concerns over the data presented in these figures. The committee finds no compelling reason to contest the assessment of the *PLoS* editorial board that research misconduct occurred in this case and that Dr. Wang fabricated western blot data through the manipulation of images. Dr. Wang claimed that he was not asked to respond to this allegation in his response to the draft of this report. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. In his response to the draft of this report, Dr. Wang failed to present original uncropped blots or research records pertaining to this allegation. Without access to such material, the committee has no evidence upon which to make its own assessment.

As described in the published retraction, we confirmed that a rectangular region of lower background intensity is apparent behind two of the five bands on the top right blot shown in Figure 1A. This region begins just above the two bands and extends below them, nearly to the bottom of the blot image. Furthermore, as described in the retraction notice, we confirmed that the rightmost band in this same blot has a rectangular region of higher background intensity. This region is smaller than the region behind the two leftmost bands. We also confirmed the presence of vertical discontinuities in background intensity in the blot shown in the bottom row of blots in Figure 2A. This aberration is consistent with the cropping out of a single lane in the left column, and the undisclosed splicing of blots. We also confirmed the presence of additional vertical discontinuities in background levels that suggested further undisclosed splicing in one of the blots shown in Figure 5A (lowermost blots).

According to our interviews with Dr. Maria Zalm, the data provided to the *PLoS* editors by Wang do not contain film edges or weight markers and were not recognized by the *PLoS* editors as unmanipulated uncropped images of the original western blots. Furthermore, the data provided by Wang did not in any way explain the irregularities

described above. As described in the retraction notice for this publication, among the images provided by Dr. Wang in response to editorial concerns, there are multiple instances of highly similar patterns of background noise that shared by multiple blot images, and these patterns appear in images provided to address concerns with other *PLoS One* studies published between 2008 and 2016. Dr. Wang states that this overlap in background is due to scanner noise. However, we find it impossible to believe that such noise would remain stable across the span of eight years.

This study was funded by Pain Therapeutics, Inc. This publication was retracted by the editors of *PLoS*. No further editorial action is recommended. As first and corresponding author on the study and the author who ran the bulk of all western blots in the publication, Dr. Wang is responsible for the failure to maintain and make available original data and research records. As senior author, Dr. Lindsay H. Burns may also bear some responsibility for the misconduct described above.

Allegation 31 states that Dr. Wang falsified and/or fabricated western blot data and plots of clinical trial data in Figures 6 and 10b by duplicating, cutting and pasting, or altering the plots in the following publication:

Wang HY, Lee KC, Pei Z, Khan A, Bakshi K, Burns LH. PTI-125 binds and reverses an altered conformation of filamin A to reduce Alzheimer's disease pathogenesis. *Neurobiol Aging* 2017;55:99-114

The summary of NIH's image analysis provided by ORI identifies issues regarding the data shown in figures 5, 8, 10, and 12. Based on reader concerns, the Journal issued an expression of concern for this publication in May of 2022. The allegation claims that the patterns and intensities of background signal immediately surrounding the bands on the TLR4 blot of figure 5A, are clearly distinct from the background across the blot. Furthermore, the allegation points to a vertical discontinuity in the in bottom blot shown in figure 8B and unexpected background patterns consisting of patches of only two different background intensities in the blots shown in 8C. Additionally, a vertical discontinuity is observed in central blot shown in figure 10A. Finally, a vertical discontinuity is present in the top two blots shown in 12A. In this case the rightmost 4 bands in the top blot are surrounded by a pattern of background noise that is clearly distinct from that surrounding the other bands. For the bottom blot, this discontinuity only applies to the rightmost 3 bands, however one band appears to be missing from this blot. We agree that there are multiple substantive concerns surrounding the data reported in this publication. However, once again, Dr Wang's failure to provide original us with an explanation or uncropped images of the blots in question make it impossible to address the allegations objectively. Dr. Wang's failure to store original data and maintain research records is clearly not in keeping with accepted standards in the field. Due to these negligent practices, the integrity of Dr. Wang's work in this case remains highly questionable.

Our analysis of Figure 5A confirms the observations made by the allegation; there are clear clouds of lighter background noise immediately surrounding each blot, which could be indicative of the cutting and pasting of bands onto the blot image, or the adjustment of levels of the bands within a free-drawn region of interest immediately surrounding each band. However, without access to verifiable uncropped images of the original blot, it is impossible to objectively determine the explanation for this unexpected background pattern. Our analysis of figure 8B revealed patterns in the background that, though presenting a line-like pattern between bands 2 and 3, did not reveal the straight vertical line suggested by the allegation. Our analysis of figure 8C confirmed the presence of the background patches described. Our analysis of Figure 10A confirmed the presence of a vertical discontinuity (thin line) the middle blot, but not the top or bottom blot. Finally, our analysis of figure 12A, confirmed the distinct background patterns behind the rightmost 4 bands in the top blot and the rightmost 3 bands of the bottom blot, along with the obvious absence of one (the rightmost) band in the bottom blot.

In his response to the draft of this report, Dr. Wang claims that he was not asked to respond to this allegation. Though the committee disputes this, we acknowledge the confusion caused on this point by the hand-off of the misconduct investigation from CCNY to CUNY's Office of Research. In his response, Dr. Wang failed to provide uncropped images of the original blots or research records pertaining to the experiments described in these figures. However, he does acknowledge that some blot images were created by combining lanes from different blots, which was necessitated by the sample sizes, and the inadvertent cropping a single image. According to the expression of concern by the editors, Dr. Wang "provided a detailed response, including images of relevant uncropped western blots and, photomicrographs, as the editor requested." Based on our experience during this investigation, we have serious doubts that uncropped images were provided to the editors, and this would not be the first time that editors have accepted something other than true underlying data. Nevertheless, the expression of concern concludes that, based on their analysis of the materials provided by Dr. Wang, "the editors did not find compelling evidence of data manipulation intended to misrepresent the results." However, the editors go on to list additional serious errors with the publication that, in the opinion of this committee, place the verity of the publish data into even more serious doubt. Though Dr. Wang requested a corrigendum to correct these errors, the editors appear to have halted further action on this publication until CUNY's investigation is completed. Except for the issue raised for figure 8B, we agree that the issues described in these allegations raise serious doubts. However, Dr. Wang's failure provide uncropped images or research records prevents the committee from objectively determining if misconduct occurred.

According to the acknowledgements section, "PTI funded this work except for the C¹⁴-labeling of PTI-125, which was produced for biodistribution studies under NIH grant number 4R44AG050301." Given Dr. Wang's failure to provide a response to these allegations to this committee, we recommend that the editors of *Neurobiology of Aging* confirm that Wang has really provided the journal uncropped images of the original blots that include blot edges and molecular weight markers. If these have indeed been

provided, the editors should provide a full description of the analysis that was done to settle each of the allegations above and provide images of the underlying data to readers. Should the editors determine that uncropped and unmanipulated data have not been provided by Dr. Wang, the publication should be retracted. As first and corresponding author on the study and the member of the lab who runs the bulk of all western blots in his lab, Dr. Wang is responsible for the research misconduct in this allegation. As senior author, Dr. Lindsay H. Burns may also bear some responsibility for the misconduct described above.

To summarize the major conclusion of our findings, Dr. Wang's failure to provide underlying raw data or research records has prevented the committee from making a definitive conclusions regarding misconduct and the integrity of the data in majority of the allegations remains highly suspect. Dr. Wang's failure to store original data and research records represents a major break from the standards of the scientific community. Based on our examination of the published figures cited in each allegation, we recommend that editorial action be taken in for the publications referenced in allegations 1-5, 7, 10-17, 20, 22-25, 28, 29, and 31.

Ongoing and Pending Research Support

We were informed that there are currently no pending proposals for research support. Dr. Wang is currently being supported as a co-Investigator on an NIH grant. (1R01AG057658-01) awarded to Konrad Talbot at Loma Linda University.

Addendum

An additional allegation of research misconduct was received by the committee on April 18th, 2023, while this report was being finalized.

This allegation pertains to the reporting and analysis of Elisa assay in the following publication:

Zoe Arvanitakis, Hoau-Yan Wang, Ana W. Capuano, Amber Khan, Bouchra Taï, Frederick Anokye-Danso, Julie A. Schneider, David A. Bennett, Rexford S. Ahima, Steven E. Arnold: Brain Insulin Signaling, Alzheimer Disease Pathology, and Cognitive Function. *Ann Neurol.* 2020 September; 88(3): 513–525.

The concerns in this allegation stem from the analysis of Elisa experiments and the analysis of raw optical density (OD) values for two sample types without normalizing the OD values to a standard curve. Additionally, Table 2 reports identical means and interquartile ranges for Elisa values for the two groups of the samples analyzed.

The committee agrees that the identical values reported in Table 2 are of concern. It is indeed true that 10-15% variation is routinely observed in Elisa values and given the large sample size ($n=75$) of the reported data, variation in the mean value is to be expected. Given that Dr. Wang has not shared research records or raw data for even one of the 31 original allegations in this investigation, the committee does not think it worth delaying this report further to request the data and research records necessary to make an objective assessment. Based on our experience during this investigation, we find it highly unlikely that such material would be provided by Dr. Wang. The committee recommends that the editors of the journal request more information about the Elisa experiments described in this publication from the corresponding author of the article, Dr Arvanitakis.

From the onset of our investigation, the committee has asserted that the only objective way to make an objective assessment of each allegation of research misconduct was to examine the scans of the original blots used to create the figures in question. We defined original blots as primary densitometer scans with clear film edges and molecular weight markers. As we have discussed in previous meetings with ORI and in the introduction to our report, a central challenge and frustration of this investigation was the failure of the respondent to provide any verifiable original data or research records. This situation forced the committee to rely on the published figures as presented in the PDF files downloaded from the publishers' websites. The images taken from these publications were often of markedly low quality and suffered from low resolution and compression artifacts that became apparent when brightness and contrast were adjusted to attempt to address each specific allegation.

In our draft report we concluded that a preponderance of evidence supported the conclusion of knowing scientific misconduct by Dr. Wang for 14 of the 31 allegations. In these 14 cases, the committee felt that the quality of the published images was sufficiently high to eliminate compression artifacts as explanations for the aberrations described in the specific allegations. However, the respondent, in his sprawling response to the draft report, describes instances in which images of similar quality to those examined in these 14 cases, and published in the same journal issues, can be shown to display effects of low resolution and image compression. The respondent also identified apparent inconsistencies in our assessments of various allegations, reaching the conclusion of misconduct for some allegations, but failing to make that assessment for others based on the same evidence.

Already frustrated by the respondent's inability to provide even a single datum or notebook in response to any allegation, the committee decided that it would be most conservative to conclude that the respondent's failure to provide data or records prevented us from making an objective assessment in any case. ***But to be clear, the committee concludes that Dr. Wang's inability or unwillingness to provide primary research materials to this investigation represents egregious misconduct.*** This failure, the troubling research practices described in our report, and the clear indications of misconduct in his response to PLoS editorial concerns, is highly suggestive of longstanding and deliberate scientific misconduct by Dr. Wang. However, absent access to primary research materials, it is not possible to make definitive assessments for the 31 specific allegations. This is a source of deep frustration to the committee, which spent the better part of a year actively attempting to provide an objective investigation into these serious charges against Dr. Wang.