

IN THE COURT OF COMMON PLEAS OF ALLEGHENY COUNTY, PENNSYLVANIA

ARAVIND R. TARUGU,

CIVIL DIVISION

and

G.D. - 19- 11584

DR. RAJU C. REDDY

COMPLAINT IN CIVIL ACTION

Plaintiffs,

Filed on behalf of Plaintiffs,

v.

Aravind R. Tarugu and Dr. Raju C. Reddy

JOURNAL OF BIOLOGICAL CHEMISTRY

and

Counsel of Record for this Party:

AMERICAN SOCIETY OF BIOCHEMISTRY
AND MOLECULAR BIOLOGY,

James McNally, Esquire
PA ID No. 78341

Defendants.

Jonathan A. Cass, Esquire
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JURY TRIAL DEMANDED

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15 August 2019
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GD-19-011584

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NOTICE TO DEFEND

You have been sued in Court. If you wish to defend against the claims set forth in the following pages, you must take action within twenty (20) days after this complaint and notice are served, by entering a written appearance personally or by an attorney and filing in writing with the Court your defenses or objections to the claims set forth against you. You are warned that if you fail to do so, the case may proceed without you and a judgment may be entered against you by the Court without further notice for any money claimed in the Complaint or for any claims or relief requested by the Plaintiff. You may lose money or property or other rights important to you.

YOU SHOULD TAKE THIS PAPER TO YOUR LAWYER AT ONCE. IF YOU DO NOT HAVE A LAWYER, GO TO OR TELEPHONE THE OFFICE SET FORTH BELOW. THIS OFFICE CAN PROVIDE YOU WITH INFORMATION ABOUT HIRING A LAWYER.

IF YOU CANNOT AFFORD TO HIRE A LAWYER, THIS OFFICE MAY BE ABLE TO PROVIDE YOU WITH INFORMATION ABOUT AGENCIES THAT MAY OFFER LEGAL SERVICES TO ELIGIBLE PERSONS AT A REDUCED FEE OR NO FEE.

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COMPLAINT AND JURY DEMAND

AND NOW, comes Plaintiffs, Mr. Aravind R. Tarugu (“Mr. Tarugu”), and Dr. Raju C. Reddy, MD (“Dr. Reddy”), by and through their undersigned counsel, and hereby file the within Complaint against Defendants, Journal of Biological Chemistry, Inc. (the “JBC”) and American Society for Biochemistry and Molecular Biology, Inc. (the “ASBMB”) (the JBC and the ASBMB collectively, “Defendants”). As set forth below, Mr. Tarugu and Dr. Reddy bring claims against Defendants sounding in defamation, which causes of action arise from Defendants publication of false and defamatory statements which accuse Mr. Tarugu and Dr. Reddy of falsifying data in an academic research article published in the Journal of Biological Chemistry, thereby severely injuring Mr. Tarugu’s and Dr. Reddy’s professional reputations, as well as causing each to suffer significant mental anguish and personal humiliation. For their Complaint, Mr. Tarugu and Dr. Reddy (the “Authors”) aver as follows:

THE PARTIES

1. Plaintiff, Mr. Tarugu is an individual residing in the Commonwealth of Pennsylvania.

2. At all relevant times, Mr. Tarugu was, and still is, an employee of the University of Pittsburgh (the “University”).

3. Plaintiff, Dr. Reddy is an individual residing in the Commonwealth of Pennsylvania.

4. At all relevant times, Dr. Reddy was, and still is, a Visiting Associate Professor of Medicine at the University’s Department of Medicine, as well as the Chief of Pulmonary Division, Department of Veteran Affairs, Pittsburgh Healthcare System (the “VAPHS”).

5. Upon information and belief, defendant JBC, is a corporation, incorporated in the State of Maryland, and is a wholly owned subsidiary of the ASBMB.

6. The JBC publishes scientific articles which fall under the scientific fields of chemistry, biochemistry, biophysics, systems biology, RNA biology, immunology, microbiology, neurobiology, epigenetics, and computational biology, among others.

7. Upon information and belief, the JBC has its principle place of business in the State of Maryland.

8. Defendant ASBMB is a corporation incorporated in the State of Maryland.¹

9. The ASBMB is a society comprising of roughly 12,000 members, and owns and operates a number of different scientific publications, including the JBC.

10. Upon information and belief, the ASBMB regularly publishes scientific articles

¹ MARYLAND BUSINESS EXPRESS,
<https://egov.maryland.gov/BusinessExpress/EntitySearch/BusinessInformation/F15818081> (last visited August 5, 2019) (showing the ASBMB’s current registration status as a business in good standing in the State of Maryland).

by itself, and through its subsidiaries, such as the JBC.

11. Upon information and belief, the ASBMB has its principle place of business in Rockville, Maryland.²

JURISDICTION AND VENUE

12. The Court has jurisdiction over the subject matter of this action pursuant to 42 Pa.C.S.A. § 931.

13. Upon information and belief, the JBC is a wholly owned subsidiary of the ASBMB, and is incorporated under the laws of the State of Maryland, with its principal place of business in the State of Maryland.

14. Upon information and belief, the ASBMB is incorporated under the laws of the State of Maryland, with its principal place of business in the State of Maryland.

15. Dr. Reddy is a citizen of the Commonwealth of Pennsylvania.

16. Mr. Tarugu is a citizen of the Commonwealth of Pennsylvania.

17. At all relevant times, Dr. Reddy and Mr. Tarugu were, and remain, employees of the University, a public university of the Commonwealth of Pennsylvania.

18. Mr. Tarugu and Dr. Reddy are two of the co-authors of Lakshmi SP, Reddy AT, Zhang Y, Scirba FC, Mallampalli RK, Duncan SR, and Reddy RC, The Journal of Biological Chemistry 289(10):6383-6393 (2014), “Down-regulated peroxisome proliferator-activated receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)” (the “Article”), a scientific article published on behalf of the University. **Exhibit A**

² AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, www.asbmb.org (last visited August 5, 2019) (stating ASBMB’s address is 11200 Rockville Pike, Suite 302, Rockville, MD 20852-3110).

19. Upon information and belief, the Defendants knew that the Authors were citizens of the Commonwealth of Pennsylvania, are employees of the University, and published the Article on behalf of the University.

20. The defamatory statements, as discussed in detail below, published by the Defendants were specifically directed at the Authors, who are residents and employees of the Commonwealth of Pennsylvania, and therefore were directed at the Commonwealth of Pennsylvania.

21. The brunt of the harm and injury to the Authors' reputations within the scientific community at the University, and their local community, occurred in the Commonwealth of Pennsylvania, the focal point of the Defendants' tortious conduct.

22. As such, this Court may exercise personal jurisdiction over the Defendants pursuant to 42 Pa.C.S.A. § 5322 insofar as the Defendants directly caused harm and tortious injury in the Commonwealth of Pennsylvania, from outside the Commonwealth of Pennsylvania.

23. Venue is properly laid in this Court under Pa.R.C.P. 1006, because (i) the Authors' causes of action arose in Allegheny County, and (ii) transactions and/or occurrences, out of which the Authors' causes of action arose, took place in Allegheny County.

STATEMENT OF FACTS

The Joint Inquiry and Investigation

24. On December 24, 2013, Dr. Reddy and Mr. Tarugu, along with five other co-authors, published the Article in the Journal of Biological Chemistry.

25. The Article assessed the actions of peroxisome proliferator-activated receptor γ (gamma) ("PPAR γ ") in pulmonary epithelial cells of chronic obstructive pulmonary disease

(“COPD”)³ patients.

26. The Article includes nine (9) figures with multiple subpanels, which consist of: measurement of cytokine and chemokine levels, determination of cellular ROS levels, HDAC activity, transcription factor DNA binding activity assays, CHIP assays, quantitative real-time PCR, and siRNA experiments, among other things.

27. The Article also consists of 147 immunoblots lanes,⁴ with a total of 644 individual bands,⁵ presented in support of the conclusions made within the main body of the Article.

28. On October 8, 2015, the Authors were notified that they would be subject to an inquiry (the “Inquiry”) to determine, among other things, the provenance of certain immunoblots used in Figure 5E.

29. Specifically, the Inquiry was focused on whether the left lane in the left panel in the β -actin blot of Figure 5E was the same as the left lane in the right panel of the pMSK1 blot, but just oriented differently.

30. Figure 5, of which 5E is a part, is comprised of data from multiple experiments conducted by the Authors, and is presented in the Article to support the finding that PPAR γ activation decreases CSE-induced cytokine production and oxidative stress by modulating NF- κ B.

31. Figure 5E specifically displays an immunoblot showing levels of COX-2, NOX4,

³ COPD is a progressive lung disease that is presently a leading cause of death in the United States.

⁴ An immunoblot—also known as a Western Blot—is a method employed by researchers to detect specific proteins present in tissue samples.

⁵ Proteins separated in a porous gel form thin, sharply defined shapes referred to as “bands” and a horizontal row of bands is referred to as a “lane.”

pIKK α , p-I κ B α , p-MSK1, and NF- κ B p65.

32. Graphically, Figure 5E includes 18 lanes of immunoblots scanned by the Authors using a LICOR Imaging System.⁶ *See* Exhibit A at 6388.

33. A part of the data provided in Figure 5E includes pMSK1 with vehicle/OA-NO₂ treatment, which was not central to the Article or the conclusions made therein.

34. The Inquiry panel met on February 1, 2016, and was conducted jointly by the University and the VAPHS.

35. At the request of the VAPHS, the University led the Inquiry, and was responsible for collecting and examining evidence, as well as hearing and observing oral testimony provided by witnesses.

36. Upon completion of the Inquiry, on February 18, 2016, the Panel issued an inquiry report (the "Inquiry Report") which did not recommend that a formal investigation be conducted.

37. On February 18, 2016 the Authors were given a copy of the Inquiry Report, and were told that "the Panel recommended that the procedure be terminated without an investigation and without a finding of misconduct."

38. On or about April 26, 2016, and coming as a great surprise to the Authors, Assistant Dean of Academic Affairs for the University, Dr. Saleem A. Khan ("Dean Khan"), notified the Authors that they would be subject to an investigation concerning the provenance of Figure 5E in the Article because The Office of Research Oversight of the Department of Veteran Affairs (the "VA ORO") had lingering reservations about the Inquiry Report.

39. The University and the VAPHS formed an "Investigative Board," and agreed that

⁶ A LICOR Imaging System is designed to scan and analyze immunoblots.

the University would lead the investigation.

40. On July 15, 2017, the Investigative Board issued its report which opined that Mr. Tarugu had reused the p-MSK1 immunoblot within Figure 5E (the “Investigative Board Report”).

41. After receipt of the Investigative Board Report, both the University and the VA ORO issued separate determinations (the “University Determination” and the “VA ORO Determination”), both of which the Authors appealed.

42. The Authors appealed the University Determination to the University’s appeal panel (the “University Appeal Panel”) on November 27, 2017.

43. The Authors similarly sought to appeal the VA ORO Determination, and filed a formal appeal on December 14, 2017 with the VA ORO.

44. On or about March 29, 2018, the University Appeal Panel issued its report unanimously overturning the Investigative Board’s decision (the “University Appeal Panel Report”), thereby absolving Mr. Tarugu of any research misconduct.

45. In doing so, the University Appeal Panel determined that “intention was not proven by a preponderance of evidence, including a lack of proof for purposeful image manipulation.”

46. The panel also noted the lack of a motive, as the figure panel at the center of the investigation was not essential for the paper’s conclusions.

47. The University Appeal Panel relied upon independent experts in reaching its conclusion that the first lane from the lower β -actin immunoblot in Figure 5E was not reused in the right pMSK1 immunoblot also present in Figure 5E.

48. On April 4, 2018, then University Provost Patricia Beeson, adopted the University

Appeal Panel Report in her final decision after appeal (the “University’s Final Decision”).

49. Subsequently, a panel of scientist-investigators and legal counsel for the National Institutes of Health (NIH) Office of Research Integrity (ORI) conducted a thorough and complex review and accepted the University’s decision concluding that no misconduct or reuse of the immunoblot occurred.

50. However, notwithstanding the University’s Final Decision in favor of Mr. Tarugu, and the weight of the supporting evidence, on May 25, 2018, the VA ORO erroneously denied the Author’s appeal of the VA ORO Determination, reasserting that in Figure 5E, the first band from the lower β -actin immunoblot was reused as the first band in the right pMSK1 immunoblot (the “VA ORO Findings”).

51. The VA ORO Findings were not based on a preponderance of evidence as required by the VHA Handbook 1058.02, Department of Veterans Affairs, Veterans Health Administration (2014).

52. The VA ORO Findings included a corrective action plan for Mr. Tarugu which, among other things, directed him to notify the JBC by August 10, 2018 of the VA ORO Findings.

Defendants’ Independent Examination Outside the Scope of the Joint Investigation

53. In compliance with the VA ORO’s corrective action plan, on August 10, 2018, Mr. Tarugu notified the JBC, by letter addressed to Dr. Kaoru Sakabe, the ASBMB’s Data Integrity Manager, of the VA ORO Findings (the “Notice”). *See Exhibit B.*

54. With his Notice, Mr. Tarugu provided a copy of the University’s Final Decision, which had been redacted at the recommendation of the University.

55. In the Notice, Mr. Tarugu vigorously disputed the VA ORO Findings and

maintained that no action should be taken by the JBC with regard to the Article.

56. Mr. Tarugu asserted that the VA ORO's conclusion that the first band in the right panel of the pMSKI blot was reused was erroneous and contrary to the preponderance of evidence, and provided the JBC independent expert reports in support of his contention.

57. On August 16, 2018, the JBC initiated its examination of Figure 5E, and then unilaterally expanded its examination beyond the scope of the VA ORO Findings, and the Notice that Mr. Tarugu had provided to the JBC (the "JBC Examination").

58. Specifically, on August 16, 2018, without explaining why, the JBC requested that the Authors provide the original data for Figures 3C, 4C, and 5E.

59. Figure 3, of which 3C is a part, is presented in the Article to support the finding that CSE down-regulates anti-inflammatory transcription factors PPAR γ and GR- α .

60. Figure 3C specifically displays an immunoblot of nuclear GR- α and acetylation of immunoprecipitated GR- α .

61. Whereas Figure 4, of which 4C is a part, is presented in the Article to support the finding that CSE down-regulates HDAC2 and increases chromatin acetylation.

62. Figure 4C specifically displays immunoblots showing acetyl- and phospho-histone H3 (Lys-9/Ser-10) and total histone H3; acetylated (Lys-12) and total histone H4.

63. In the spirit of cooperating with the JBC Examination, on August 20, 2018, the Authors provided all data relevant to the JBC's request.

64. On August 21, 2018, the JBC requested that the Authors provide further documents, this time seeking acquisition of zip files from the LICOR Imaging System used by the Authors during their research.

65. While the Authors desired to be cooperative, on August 22, 2018, the Authors

informed the JBC that they no longer had access to the requested files because the LICOR Imaging System used to generate the images was no longer operational and had been replaced by an upgraded system.

66. The Authors, through their counsel, also stated “[p]lease let me know if there is anything else I can do to assist you.” See **Exhibit C**.

67. Despite their offer, the Authors did not receive any further communications from the JBC regarding the availability of data from the LICOR system.

68. On August 23, 2018, Dr. Sakabe requested that the Authors produce an unredacted copy of the University’s Final Decision.

69. On or about August 29, 2018, Dr. Sakabe also requested that the Authors provide the original data for Figures 1A and 6A (the “Additional Figures Request”).

70. Figure 1, of which Figure 1A is a part, is presented in the Article to support the finding that PPAR γ expression and activity are decreased in COPD.

71. Figure 1A specifically displays an immunoblot for PPAR γ in tissue extracts of pathologically normal (non-COPD; n=6) and COPD (n=6) lung (top panel) and in whole-cell extracts of HBE cells obtained from normal and COPD subjects (bottom left panel) followed by densitometric analysis (bottom center panel).

72. The bottom right panel shows DNA binding activity of PPAR γ in non-COPD and COPD tissue extracts measured using an ELISA-based assay.

73. Whereas Figure 6, of which 6A is a part, is presented in the Article to support the finding that PPAR γ activation reverses CSE-induced changes in PPAR γ , GR- α , and HDAC2, as well as in chromatin acetylation.

74. Figure 6A specifically displays immunoblots showing nuclear levels of PPAR γ ,

GR- α , and HDAC2.

75. It also displays immunoblots showing acetyl- and phospho-histone H3 (Lys-9/Ser-10) and total histone H3, as well as acetylated (Lys-12) and total histone H4.

76. On August 30, 2018, the Authors responded to Dr. Sakabe and politely declined to provide an unredacted copy of the University's Final Decision, and the data responsive to Additional Figures Request.

77. They did so because the University's Final Decision had been redacted at the suggestion of Dean Khan to protect Mr. Tarugu's confidential information. *See Exhibit D.*⁷

78. The Authors also declined to provide the data responsive to the Additional Figures Request because the request substantially deviated from the scope of the subject matter of the VA ORO Findings and the Notice, as well as Mr. Tarugu's obligation to notify the JBC of the VA ORO Findings with respect to Figure 5E.

79. However, in an effort to better understand the basis for the Additional Figures Request, the Authors requested that the JBC clarify why it had made the request, and for what purpose.

80. Although the JBC never responded to the Authors' request, on September 12, 2018, in a further attempt to demonstrate their good faith intentions, the Authors provided the requested images for Figures 1A and 6A.

81. They also reaffirmed their willingness to continue to cooperate in any way they could with respect to additional questions the JBC may have had regarding the β -actin and pMSK1 blots in Figure 5E. *See Exhibit E.*

JBC/ASBMB's Failure to Exercise reasonable Diligence in Ascertaining the Truth

⁷ Exhibits include attachments redacted when originally transmitted between the parties.

82. On August 31, 2018, Dr. Sakabe told the Authors that in addition to the alleged duplication in Figure 5E, the JBC had determined that “[t]he PPAR γ blot from Fig 1A was reused in Fig 6A as pAcK-H3 and H3” and that “[t]he Lamin B1 blot from Fig 3C was reused in Fig 4C as H3” (the “JBC Findings”). *See Exhibit F.*

83. Dr. Sakabe did not offer any explanation or justification for the JBC Findings, but, rather, simply stated that “the Editors are requesting that the [A]uthors withdraw the [A]rticle.” *Id.*

84. Perplexed by the JBC’s unexplained and unsupported determinations, on September 6, 2018, the Authors contacted Dr. Sakabe to express their confusion, and to request that Dr. Sakabe provide “the journal’s basis/analysis for determining that the images were reused.”

85. They made the request so that they could address the JBC’s obvious concerns regarding the images, and, by doing so, assist the JBC in its analysis of the applicable images to ensure that the JBC correctly, and in an unbiased fashion, arrived at the truth—that the images had not been reused as alleged.

86. In an apparent refusal to be transparent or to engage with the Authors in good faith to ascertain the truth, on September 7, 2018, Dr. Sakabe responded that the information requested by the Authors on September 6, 2018 had already been provided with the JBC Findings contained within Dr. Sakabe’s August 31, 2018 email.

87. The immunoblot images provided by the Authors readily demonstrate that the images are unique and distinct and were not re-used.

88. The JBC Findings were devoid of any information that addressed the source of the images used in the JBC’s analysis, the software tools and methodologies it used to conduct the

analysis, or any interpretations the JBC was able to derive from its analysis.

89. The JBC Findings did not otherwise include any additional explanatory language.

90. The so-called analysis and basis for the JBC Findings, as delivered to the Authors, merely consisted of pictorial information with a small amount of highlighting.

91. This complete lack of information prevented the Authors from understanding how the JBC reached its conclusions regarding image duplication and reuse.

92. Moreover, the JBC's lack of transparency, and refusal to provide critical information, prevented the Authors from meaningfully responding to the JBC's prior inquiries that were well beyond the scope of the Notice, and hampered the Authors efforts to aid the JBC in ascertaining the truth.

93. Upon information and belief, the JBC only utilized snapshots of images taken from a .pdf copy of the Article to perform its image analysis, and simply applied a color gradient analysis to Figures 1A, 6A, and 5E to determine if the images were duplicated.

94. Upon information and belief, the JBC utilized a naked eye comparison of figures 3C and 4C.

95. An analysis based on snapshots of images and/or naked eye comparisons of images that have been produced as part of a highly technical and sophisticated experimentation, is wholly inadequate.

96. Upon information and belief, the JBC failed to perform histogram equalization, image segmentation, sobel gradient, thresholding, or any other relevant technique on any of the images provided to the JBC.

97. Had the JBC employed the above referenced techniques as part of its analysis, it would have been able to conclusively determine that each and every image contained in the

Article was unique and distinct.

98. On or about September 12, 2018, the Authors responded to the JBC's September 7, 2018 email in detail, and explained why the analysis included in the JBC Findings was deficient and did not support the JBC's conclusion of duplication and reuse (the "Authors' Response").

99. With the Authors' Response, the Authors provided a total of 37 images related to the five figures and a detailed and rigorous image analysis addressing each figure (the "Image Analysis").

100. The Authors performed and provided the Image Analysis because the information provided by the JBC to support its analysis was woefully inadequate, and the JBC had ignored the Authors' multiple requests to provide additional information that explained the JBC Findings and erroneous conclusions.

101. The Image Analysis utilized the following techniques:

NIH Office of Research Integrity (ORI) Advanced Forensic Actions tools in Adobe Photoshop: In this process, histogram equalized images are applied with advanced dark or light areas and advanced gradient map to determine the similarities or differences between images. The preset actions allow the user to limit personal biases.

Image segmentation, thresholding, and sobel gradient in MATLAB Image Processing Toolbox: In this process, histogram equalized images are portioned into regions based on the pixel characteristics of the image. This process discloses the discontinuities in pixel values and indicated edges, and eliminates biases as the process is performed as a coded program.

Reference to notebook entries: Along with image analysis and original images, the Authors provided lab notebook entries related to Figure 5E β -actin and pMsk1 performed approximately 6 months apart by two different researchers.

102. The Image Analysis highlighted several key differences between the images,

including (a) several differences in excised borders of membrane and its size, (b) the presence of protein marker lanes in the blots, (c) several differences in heatmaps and gradient maps of images and bands; and (d) several differences in the backgrounds of the images.

103. The Image Analysis conclusively demonstrated that each immunoblot used in the Article is, in fact, unique and distinct.

104. As part of the Authors' Response, they also included the results of an independent forensic image analysis performed by Dr. John Russ, an expert in the field, which similarly found that the images utilized in the Article were unique and distinct. *See* Ex. G at 13.

105. On the same day that she received the Authors' Response, Dr. Sakabe inexplicably responded, in conclusory fashion, that

Because [the Authors] refused to provide the original data and images for figures 1A and 6A, any criticism of the JBC processes are the result of [the Authors'] failure to provide requested and required information. The images in the PDF provided are of too poor quality for JBC to analyze. The data shown in the attachment for figures 3C and 4C do not appear to correspond with what is presented in the [Article]. The quality of the data provided on August 20 was of such poor quality that we requested the native files, but none were provided. Finally, we requested full copies of the investigation reports to determine the rigor and completeness of the committee's investigation.

See Exhibit G.

106. At no time prior to September 12, 2018 did the JBC ever raise any issues concerning the quality of images provided by the Authors.

107. The JBC grossly mischaracterized the nature of its correspondence with the Authors, which was pointed out in detail via letter correspondence on September 14, 2018.

108. The JBC's refusal to reconsider the JBC Findings, even after the Authors had exposed inaccuracies in its findings, both forensically and procedurally, demonstrates that the JBC failed to exercise reasonable diligence in pursuit of the truth with regard to the accuracy of

the relevant images. *See Exhibit H.*

109. The JBC thereafter referred the matter to the ASBMB Publications Committee (the “Publications Committee”) for review. *See Exhibit I.*

110. In yet another attempt to ensure that Defendants were engaged in a reasonable and diligent search for the truth, on or about September 19, 2018, the Authors asked the JBC to: (a) “provide a copy of the Editors’ analyses and reports describing the techniques they used to review the data/images we provided from August 10, 2018 through September 14, 2018,” (b) “confirm that our September 14 emails (and all attachments) were shared with the Editors,” (c) “forward the guidelines/policies which will apply to and govern the Publications Committee’s consideration of this matter,” and (d) “confirm that all of our communications with [Dr. Sakabe], beginning with our August 10, 2018 letter, will be made available to the ASBMB Publications Committee.” *See Exhibit J.*

111. Again, Dr. Sakabe, the JBC, and now the ASBMB failed to engage meaningfully with the Authors.

112. Other than providing a hyperlink to the JBC’s website, Defendants refused to share any of the reports, processes, policies, or methods employed by the JBC in its image analysis.

113. On September 21, 2018, the Authors, by way of letter correspondence to Dr. Enrique M. De La Cruz, Chair of the Publications Committee, again tried to ensure that the Defendants were adhering to appropriate procedures, were diligently examining all the relevant data, and were diligently considering evidence that conclusively showed that the images were not reused. *See Exhibit K.*

114. Although Dr. Sakabe acknowledged receipt of the letter addressed to Dr. De La

Cruz on October 1, 2018, Defendants failed to forward to the Authors the requested guidelines or policies which applied to the Publications Committee's consideration of the Article.

115. In fact, the Authors did not receive any communications from the Defendants until November 21, 2018.

116. Upon information and belief, the ASBMB failed to adequately consider, in good faith, the evidence provided by the Authors.

117. It was only then that the Defendants advised, after an alleged careful consideration of the matter, that the Publications Committee had determined that the "images had been reused to represent different experimental conditions," and that the Article was to be retracted.

118. On November 30, 2018, in a final effort to engage with Defendants, the Authors contacted Dr. Gerald Hart, President of the ASBMB, Barbara Gordon, Executive Director at the ASBMB, and Nancy Rodnan, Senior Director of Publications at the ASBMB. *See Exhibit L.*

119. However, the Authors did not receive a response.

120. Thereafter, on or about December 6, 2018, the Defendants retracted the Article and published the retraction notice (the "Retraction") on their publically accessible webpage.

121. The Retraction states in full:

Retraction: Down-regulated peroxisome proliferator-activated receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible proinflammatory phenotype in chronic obstructive pulmonary disease (COPD).

Sowmya P. Lakshmi, Aravind T. Reddy, Yingze Zhang, Frank C. Scieurba, Rama K. Mallampalli, Steven R. Duncan and Raju C. Reddy

VOLUME 289 (2014) PAGES 6383–6393

This article has been retracted by the publisher. The right pAcK-H3 and H3 immunoblots from Fig. 6A were reused in Fig. 1A as PPAR γ . The right Lamin B1 immunoblot from Fig. 3C was reused in Fig. 4C as the right H3 immunoblot. In Fig. 5E, the first lane from the lower β -actin immunoblot was reused in the right pMSK1 immunoblot.

JOURNAL OF BIOLOGICAL CHEMISTRY, <http://www.jbc.org/content/294/1/69> (last visited August 5, 2019).

122. The Retraction contains three separate and distinct, false and defamatory statements.

123. The first false and defamatory statement is that “[t]he right pAcK-H3 and H3 immunoblots from Fig. 6A were reused in Fig. 1A as PPAR γ .”

124. The second false and defamatory statement is that “[t]he right Lamin B1 immunoblot from Fig. 3C was reused in Fig. 4C as the right H3 immunoblot.”

125. The third and final false and defamatory statement is that “[i]n Fig. 5E, the first lane from the lower β -actin immunoblot was reused in the right pMSK1 immunoblot.”

126. On or about January 4, 2018 the Retraction was publically posted by the twitter handle @Sciblotter.

127. @Sciblotter is a twitter handle dedicated to tweeting alerts to its subscribers which detail instances where scientific articles have been retracted.

128. @Sciblotter’s sole function is to report on article retractions.

129. @Sciblotter has thousands of followers, who, upon information and belief, are largely comprised of members of the academic and scientific communities of which the Authors are members of.

COUNT I

(Defamation Seeking Permanent Injunctive Relief – The JBC and The ASBMB)

130. The Authors incorporate by reference the foregoing paragraphs of this Complaint

as if set forth at length herein.

131. By agreeing to publish the Retraction, the Defendants caused the publication of false statements and misrepresentations of fact to the scientific community.

132. Moreover, upon information and belief, the Defendants are directly responsible for, and proximately caused, @Sciblotter's mass dissemination of the defamatory and false statements contained in the Retraction to thousands of members of the academic and scientific community.

133. As media defendants, the Defendants were obligated to exercise reasonable care and diligence to ascertain the truth of the statements they would publish about the Authors.

134. The Defendants published the three offending statements in the Retraction with want of reasonable care and diligence to ascertain the truth of each statement contained therein.

135. The Defendants did so because they blatantly disregarded and failed to adequately evaluate the data and images provided by the Authors.

136. The Retraction contains three distinct false and defamatory statements: (a) "The right pAcK-H3 and H3 immunoblots from Fig. 6A were reused in Fig. 1A as PPAR γ ," (b) "The right Lamin B1 immunoblot from Fig. 3C was reused in Fig. 4C as the right H3 immunoblot," and (c) "In Fig. 5E, the first lane from the lower β -actin immunoblot was reused in the right pMSK1 immunoblot."

137. The three statements in the Retraction can fairly and reasonably be construed to imply defamatory meaning in that each of the three offending statements is patently false.

138. The Authors did not, in fact reuse images, rather they utilized individual, distinct, and unique images in and throughout the Article.

139. The statements indicate that the basis for the Article's retraction was the alleged

reuse of images within the Article.

140. An accusation that an image has been surreptitiously reused in a scientific article is tantamount to an accusation of data falsification and research misconduct, the ultimate breach of trust one can commit within the scientific community.

141. Moreover, the defamatory meaning could not be more evident to the Authors, for the impression it would naturally engender in the minds of the average persons among whom it was intended to circulate—the Authors' academic peers—is obvious to the Authors as both harmful and untrue.

142. Adding insult to injury is the fact the Retraction was non-consensual.

143. The Authors understand that the Retraction directly implicates and directly applies to them, in that the Retraction lists the Authors by name.

144. That the Authors were not distinctly identified as the individuals implicated by the false and defamatory statements in the Retraction is immaterial.

145. Within the sphere of academia (the audience for the publication of the journal at issue) the meaning of each statement is clear—the authors of the Article were found to have improperly reused images in the Article.

146. As career academics, the Authors also understand the gravity of such a statement being published to the public at large, and the reputational harm and impact it has caused and will continue to cause.

147. Due to the publication of the Retraction by the Defendants, the Authors have already suffered significant impairments to their reputation and standing within the University community, as well as within the greater academic community as a whole.

148. Dr. Reddy and Mr. Tarugu have had professional opportunities delayed and or

revoked.

149. In addition, the retraction of the Article has caused the Authors to suffer severe mental anguish and personal humiliation.

150. The Defendants abused their status as conditionally privileged entities when they negligently published the Retraction.

151. Given the overwhelming data and contrary detailed and rigorous Image Analysis provided by the Authors, a reasonably prudent person under the circumstances would have engaged with the Authors in good faith and sought to engage in an open evaluation of the data and available analysis presented, prior to publishing the Retraction.

152. However, both of the Defendants failed to engage in a transparent and good faith process.

153. Upon information and belief, had the Defendants actually provided the requested information and worked with the Authors, as opposed to against them, in pursuit of the truth, the Authors would have been able to conclusively and convincingly show the Defendants the images at issue were not duplicated or reused.

154. Upon information and belief, the Defendants ignored the Image Analysis provided by the Authors which conclusively shows that the images were not reused or duplicated.

155. Similarly, upon information and belief, the Defendants failed to perform histogram equalization, image segmentation, sobel gradient, thresholding, or any other relevant technique on any of the images provided to the Defendants.

156. The Defendants' failure to do so was a gross departure from their duty to exercise reasonable care and diligence to ascertain the truth.

157. The Defendants were negligent in their publication of the false and defamatory statements contained in the Retraction.

158. Because the images were not, in fact, reused or duplicated, the three statements published in the Retraction are false, and erroneously brand the Authors as liars.

159. The Defendants actions have actually and proximately caused, and continue to actually and proximately cause, damage to the Authors, their reputations and livelihoods.

160. The public dissemination of the Retraction, and the defamatory statements it contains, effects an ongoing and continuous injury on the Authors reputations and personal wellbeing.

161. As such the Authors have a clear right to relief.

162. The Authors' reputations cannot be repaired or restored as long as the Defendants publically maintain, and hold out, the statements within the Retraction to be true when they are not.

163. No remedy at law will provide adequate relief in lieu of a withdrawal of the Retraction.

164. Moreover, the on going and continuous nature of the injury inflicted by the Retraction has prevented and will continue to stymie the Authors' career advancement, the repair of their reputations, and the clearing of their names as honest and reputable scientists.

165. Should the Retraction be allowed to stand, even greater injury will result to the Authors' reputations, and their careers will continue to be unjustly derailed further.

WHEREFORE, Mr. Tarugu and Dr. Reddy request that the Court (i) enter judgment in their favor and against the Defendants, (ii) award a Permanent Injunction to Mr. Tarugu and Dr. Reddy enjoining the Defendants from publically displaying or further disseminating the

Retraction, and requiring Defendants to otherwise withdraw the Retraction from all publically available sources, and (iii) award Mr. Tarugu and Dr. Reddy such other relief as this Court deems just and proper.

COUNT II
(Defamation Seeking Monetary Damages – The JBC)

166. The Authors incorporate by reference paragraphs 1 through 129 of this Complaint as if set forth at length herein.

167. By agreeing to publish the Retraction, the JBC caused the publication of false statements and misrepresentations of fact to the scientific community.

168. Moreover, upon information and belief, the JBC is directly responsible for, and proximately caused, @Sciblotter's mass dissemination of the defamatory and false statements contained in the Retraction to thousands of members of the academic and scientific community.

169. As a media defendant, the JBC was obligated to exercise reasonable care and diligence to ascertain the truth of the statements it would publish about the Authors.

170. The JBC published, on behalf of the ASBMB, the three offending statements in the Retraction with want of reasonable care and diligence to ascertain the truth of each statement contained therein.

171. It did so because it blatantly disregarded and failed to adequately evaluate the data and images provided by the Authors.

172. The Retraction contains three distinct false and defamatory statements: (a) "The right pAcK-H3 and H3 immunoblots from Fig. 6A were reused in Fig. 1A as PPAR γ ," (b) "The right Lamin B1 immunoblot from Fig. 3C was reused in Fig. 4C as the right H3 immunoblot," and (c) "In Fig. 5E, the first lane from the lower β -actin immunoblot was reused in the right pMSK1 immunoblot."

173. The three statements in the Retraction can fairly and reasonably be construed to imply defamatory meaning in that each of the three offending statements is patently false.

174. The Authors did not, in fact reuse images, rather they utilized individual, distinct, and unique images in and throughout the Article.

175. The statements indicate that the basis for the Article's retraction was the alleged reuse of images within the Article.

176. An accusation that an image has been surreptitiously reused in a scientific article is tantamount to an accusation of data falsification and research misconduct, the ultimate breach of trust one can commit within the scientific community.

177. Moreover, the defamatory meaning could not be more evident to the Authors, for the impression it would naturally engender in the minds of the average persons among whom it was intended to circulate—the Authors' academic peers—is obvious to the Authors as both harmful and untrue.

178. Adding insult to injury is the fact the Retraction was non-consensual.

179. The Authors understand that the Retraction directly implicates and directly applies to them, in that the Retraction lists the Authors by name.

180. That the Authors were not distinctly identified as the individuals implicated by the false and defamatory statements in the Retraction is immaterial.

181. Within the sphere of academia (the audience for the publication of the journal at issue) the meaning of each statement is clear—the authors of the Article were found to have improperly reused images in the Article.

182. As career academics, the Authors also understand the gravity of such a statement being published to the public at large, and the reputational harm and impact it has caused and

will continue to cause.

183. Due to the publication of the Retraction by the JBC, on behalf of the ASBMB, the Authors have already suffered significant impairments to their reputation and standing within the University community, as well as within the greater academic community as a whole.

184. Dr. Reddy and Mr. Tarugu have had professional opportunities delayed and or revoked.

185. In addition, the retraction of the Article has caused the Authors to suffer severe mental anguish and personal humiliation.

186. The JBC abused its status as a conditionally privileged entity when it negligently published the Retraction.

187. Given the overwhelming data and contrary detailed and rigorous Image Analysis provided by the Authors, a reasonably prudent person under the circumstances would have engaged with the Authors in good faith and sought to engage in an open evaluation of the data and available analysis presented, prior to publishing the Retraction.

188. However, the JBC failed to engage in a transparent and good faith process.

189. Upon information and belief, had the JBC actually provided the requested information and worked with the Authors, as opposed to against them, in pursuit of the truth, the Authors would have been able to conclusively and convincingly show the JBC the images at issue were not duplicated or reused.

190. Upon information and belief, the JBC ignored the Image Analysis provided by the Authors which conclusively shows that the images were not reused or duplicated.

191. Similarly, upon information and belief, the JBC failed to perform histogram equalization, image segmentation, sobel gradient, thresholding, or any other relevant technique

on any of the images provided to the JBC.

192. The JBC's failure to do so was a gross departure from its duty to exercise reasonable care and diligence to ascertain the truth.

193. The JBC was negligent in its publication of the false and defamatory statements contained in the Retraction.

194. As a result of the images not having been reused or duplicated, the three statements published in the Retraction are false, and erroneously brand the Authors as liars.

195. The JBC's actions have actually and proximately caused, and continue to actually and proximately cause, damage to the Authors, their reputations and livelihoods.

WHEREFORE, Mr. Tarugu and Dr. Reddy request that the Court (i) enter judgment in their favor and against the JBC, (ii) award damages to Mr. Tarugu and Dr. Reddy in an amount to be determined at trial, but otherwise in excess of Thirty-Five Thousand Dollars (\$35,000.00), and (iii) award Mr. Tarugu and Dr. Reddy such other relief as this Court deems just and proper.

COUNT III
(Defamation Seeking Monetary Damages – The ASBMB)

196. The Authors incorporate by reference paragraphs 1 through 129 of this Complaint as if set forth at length herein.

197. Like the JBC, by agreeing to publish the Retraction the ASBMB caused the publication of false statements and misrepresentations of fact to the scientific community.

198. Similarly, upon information and belief, the ASBMB is also directly responsible for, and proximately caused, @Sciblotter's mass dissemination of the defamatory and false statements contained in the Retraction to thousands of members of the academic and scientific community.

199. As a media defendant, the ASBMB was obligated to exercise reasonable care and

diligence to ascertain the truth of the statements it would publish about the Authors.

200. The ASBMB published the three offending statements in the Retraction with want of reasonable care and diligence to ascertain the truth of each statement contained therein.

201. It did so because it blatantly disregarded and failed to adequately evaluate the data and images provided by the Authors.

202. The Retraction contains three distinct false and defamatory statements: (a) “The right pAcK-H3 and H3 immunoblots from Fig. 6A were reused in Fig. 1A as PPAR γ ,” (b) “The right Lamin B1 immunoblot from Fig. 3C was reused in Fig. 4C as the right H3 immunoblot,” and (c) “In Fig. 5E, the first lane from the lower β -actin immunoblot was reused in the right pMSK1 immunoblot.”

203. The three statements in the Retraction can fairly and reasonably be construed to imply defamatory meaning in that each of the three offending statements is patently false.

204. The Authors did not, in fact reuse images, rather they utilized individual, distinct, and unique images in and throughout the Article.

205. In the sphere of academia, a notice of retraction issued by a peer reviewed journal, based upon allegations of image reuse, is tantamount to a finding of research misconduct and data falsification, the ultimate breach of trust one can commit within the scientific community.

206. The defamatory meaning could not be more evident to the Authors, for the impression it would naturally engender in the minds of the average persons among whom it was intended to circulate—the Authors’ academic peers—is obvious to the Authors as both harmful and untrue.

207. The Authors understand that the Retraction directly implicates and directly applies to them, as the Retraction lists the Authors by name.

208. That the Authors were not distinctly identified as the individuals implicated by the false and defamatory statements in the Retraction is immaterial.

209. Within the sphere of academia (the audience for the publication of the journal at issue) the meaning of each statement is clear—the authors of the Article were found to have improperly reused images in the Article.

210. As career academics, the Authors also understand the gravity of such a statement being published to the public at large, and the reputational harm and impact it has caused and will continue to cause.

211. Due to the publication of the Retraction by the ASBMB, the Authors have already suffered significant impairments to their reputation and standing within the University community, as well as within the greater academic community as a whole.

212. Dr. Reddy and Mr. Tarugu have had professional opportunities delayed and or revoked.

213. In addition, the retraction of the Article has caused the Authors to suffer severe mental anguish and personal humiliation.

214. The ASBMB abused its status as a conditionally privileged entity when it negligently published the Retraction. Given the overwhelming data and contrary detailed and rigorous Image Analysis provided by the Authors, a reasonably prudent person under the circumstances would have engaged with the Authors in good faith and sought to engage in an open evaluation of the data and analysis presented, prior to publishing the Retraction.

215. The ASBMB failed to do so, and failed to engage in a transparent and good faith process.

216. Upon information and belief, had the ASBMB actually provided the requested

information and worked with the Authors, as opposed to against them, in pursuit of the truth, the Authors would have been able to conclusively and convincingly show the ASBMB the images at issue were not duplicated or reused.

217. Upon information and belief, the ASBMB ignored the Image Analysis provided by the Authors which conclusively shows that the images were not reused or duplicated.

218. Similarly, upon information and belief, the ASBMB failed to perform histogram equalization, image segmentation, sobel gradient, thresholding, or any other relevant technique on any of the images made available to the ASBMB. The ASBMB's failure to do so was a gross departure from its duty to exercise reasonable care and diligence to ascertain the truth.

219. The ASBMB was negligent in its publication of the false and defamatory statements contained in the Retraction.

220. As a result of the images not having been reused or duplicated, the three statements published in the Retraction are false, and erroneously brand the Authors as liars.

221. The ASBMB's actions have actually and proximately caused, and continue to actually and proximately cause, damage to the Authors, their reputations and livelihoods.

222. As a media defendant, the ASBMB had a duty to exercise reasonable care and diligence in ascertaining whether the images purported to be reused by the Authors in the Article were not in fact distinct and unique prior to publishing statements that they were not.

223. They failed to do so.

WHEREFORE, Mr. Tarugu and Dr. Reddy request that the Court (i) enter judgment in their favor and against the ASBMB, (ii) award damages to Mr. Tarugu and Dr. Reddy in an amount to be determined at trial, but otherwise in excess of Thirty-Five Thousand Dollars

(\$35,000.00), and (iii) award Mr. Tarugu and Dr. Reddy such other relief as this Court deems just and proper.

Respectfully submitted,

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Attorneys for Plaintiffs,

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Dated: 8/15/2019

CERTIFICATION OF COMPLIANCE

I certify that this filing complies with the provisions of the *Public Access Policy of the Unified Judicial System of Pennsylvania: Case Records of the Appellate and Trial Courts* that require filing confidential information and documents differently than non-confidential information and documents.


James McNally, Esq. 8/15/19
Date

Down-regulated Peroxisome Proliferator-activated Receptor γ (PPAR γ) in Lung Epithelial Cells Promotes a PPAR γ Agonist-reversible Proinflammatory Phenotype in Chronic Obstructive Pulmonary Disease (COPD)*[§]

Received for publication, November 20, 2013, and in revised form, December 20, 2013. Published, JBC Papers in Press, December 24, 2013, DOI 10.1074/jbc.M113.536805

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Background: The mechanistic role of peroxisome proliferator-activated receptor γ (PPAR γ) in chronic obstructive pulmonary disease (COPD) is poorly understood.

Results: COPD and cigarette smoke exposure down-regulated PPAR γ and produced inflammation that PPAR γ agonists reversed through multiple pathways.

Conclusion: PPAR γ plays a pivotal role in COPD.

Significance: PPAR γ agonists may be the first effective treatment for COPD.

Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory condition and a leading cause of death, with no available cure. We assessed the actions in pulmonary epithelial cells of peroxisome proliferator-activated receptor γ (PPAR γ), a nuclear hormone receptor with anti-inflammatory effects, whose role in COPD is largely unknown. We found that PPAR γ was down-regulated in lung tissue and epithelial cells of COPD patients, via both reduced expression and phosphorylation-mediated inhibition, whereas pro-inflammatory nuclear factor- κ B (NF- κ B) activity was increased. Cigarette smoking is the main risk factor for COPD, and exposing airway epithelial cells to cigarette smoke extract (CSE) likewise down-regulated PPAR γ and activated NF- κ B. CSE also down-regulated and post-translationally inhibited the glucocorticoid receptor (GR- α) and histone deacetylase 2 (HDAC2), a corepressor important for glucocorticoid action and whose down-regulation is thought to cause glucocorticoid insensitivity in COPD. Treating epithelial cells with synthetic (rosiglitazone) or endogenous (10-nitro-oleic acid) PPAR γ agonists strongly up-regulated PPAR γ expression and activity, suppressed CSE-induced production and secretion of inflammatory cytokines, and reversed its activation of NF- κ B by inhibiting the I κ B kinase pathway and by promoting direct inhibitory binding of PPAR γ to NF- κ B. In contrast, PPAR γ knockdown via siRNA augmented CSE-induced chemokine release and decreases in HDAC activity, suggesting a potential anti-inflammatory role of endogenous PPAR γ . The results imply that down-regulation of pulmonary epithelial PPAR γ by cigarette smoke promotes inflammatory pathways and dimin-

ishes glucocorticoid responsiveness, thereby contributing to COPD pathogenesis, and further suggest that PPAR γ agonists may be useful for COPD treatment.

Chronic obstructive pulmonary disease (COPD)² is a progressive disease that, due to lack of effective treatment (1), is a leading cause of death in the United States and worldwide. It is characterized by chronic pulmonary inflammation and long term tissue destruction that impairs respiratory gas exchange. The major risk factor for COPD is exposure to cigarette smoke, which contains noxious inflammatory and oxidant agents. Once established, COPD continues to progress even with smoking cessation or available treatments.

The mainstay of treatment for most inflammatory diseases is glucocorticoid therapy, but in COPD patients it provides only short term benefit (2). Recent studies have attributed such glucocorticoid ineffectiveness to decreased activity of the corepressor histone deacetylase 2 (HDAC2) (3), an essential component of a major mechanism of glucocorticoid action. Oxidative stress (4, 5) and cigarette smoke (6) reduce HDAC2 levels in airway epithelial cells, thereby impairing the anti-inflammatory effectiveness of glucocorticoid receptor (GR- α) activation.

The ligand-activated transcription factor peroxisome proliferator-activated receptor γ (PPAR γ), a member of the nuclear hormone receptor superfamily, exerts strong anti-inflammatory and antioxidant effects (7, 8) by down-regulating activity of nuclear factor- κ B (NF- κ B) and other pro-inflammatory transcription factors via multiple mechanisms. These actions might be pathophysiologically or therapeutically relevant to COPD, but the potential roles of PPAR γ and its agonists in responses to

* This work was supported by a Merit Review award from the United States Department of Veterans Affairs and National Institutes of Health Grant HL093196 (to R. C. R.).

[§] This article contains supplemental Tables 1 and 2.

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² The abbreviations used are: COPD, chronic obstructive pulmonary disease; HDAC2, histone deacetylase 2; PPAR γ , peroxisome proliferator-activated receptor γ ; GR- α , glucocorticoid receptor; HBE, human bronchial epithelial; CSE, cigarette smoke extract; Rosi, rosiglitazone; OA-NO₂, 10-nitro-oleic acid; IKK, I κ B kinase; ROS, reactive oxygen species; p, phosphorylated.

Role of PPAR γ Down-regulation and Activation in COPD

cigarette smoke exposure and COPD have previously been poorly characterized. Known PPAR γ agonists include the synthetic thiazolidinediones, used to treat type 2 diabetes, and various endogenous compounds. Physiologically relevant endogenous PPAR γ agonists remain to be identified, but plausible candidates include nitrated fatty acids, which constitute one of the largest blood-borne pools of biologically active nitrogen compounds (9) and circulate in concentrations sufficient to activate PPAR γ (10).

Here we assessed the anti-inflammatory potential of PPAR γ in pulmonary epithelial cells of people with and without COPD and on smoke-induced epithelial responses. We also explored its mechanistic relationships with key transcription/signaling factors including the NF- κ B pathway, GR- α , and HDAC2. We found that PPAR γ expression and activity are down-regulated in human bronchial epithelial (HBE) cells from COPD patients and those exposed to cigarette smoke extract (CSE) *in vitro*, whereas proinflammatory pathways are up-regulated. Treating lung epithelial cells with either the thiazolidinedione rosiglitazone (Rosi) or the endogenous PPAR γ agonist 10-nitro-oleic acid (OA-NO₂) reversed these CSE effects and the accompanying decreases in GR- α and HDAC2. PPAR γ agonists also blocked CSE-induced inflammatory cytokine and chemokine production and ROS production by reversing the CSE-induced increase in NF- κ B activity through multiple PPAR γ -mediated mechanisms. Conversely, PPAR γ knockdown augmented CSE responses. These findings raise the possibility that PPAR γ agonists may be therapeutically useful for treating COPD, and furthermore, may reverse COPD patients' resistance to anti-inflammatory steroid therapy by restoring impaired HDAC2 activity.

EXPERIMENTAL PROCEDURES

Cells—H292 cells were obtained from the ATCC (Rockville, MD) and maintained in RPMI medium supplemented with 10% FBS, 10,000 units/ml penicillin, and 10,000 μ g/ml streptomycin (HyClone, Logan, UT). Normal human bronchial epithelial cells and diseased human bronchial epithelial (COPD) cells were obtained from Lonza (Walkersville, MD) at passage 1 and used at passages 2–8. Cells were grown and maintained in bronchial epithelial cell growth medium (BEGM), supplemented with 10% FBS, 0.4% bovine pituitary extract, 0.1% insulin, 0.1% human EGF, 0.1% hydrocortisone, 0.1% GA-1000, 0.1% retinoic acid, 0.1% transferrin, 0.1% triiodothyronine, epinephrine, penicillin, and streptomycin (HyClone). Cells were cultured at 37 °C in a humidified atmosphere of 5% CO₂, 95% air in tissue culture flasks, plates, or dishes. Monolayer cultures at 90% confluence were deprived of serum for 24 h prior to treatment.

Patient Lung Tissue Samples—Human lung tissues were obtained from excess pathologic tissue after lung transplantation and organ donation, under a protocol approved by the University of Pittsburgh Institutional Review Board. COPD lung tissues were obtained from explanted lungs of subjects with advanced COPD, and control lungs were donated lungs not suitable for transplantation from the Center for Organ Recovery and Education (CORE). Lung tissues were stored at –80 °C until future usage.

Preparation of Cigarette Smoke Extract—CSE was prepared by slowly bubbling smoke from one research-grade cigarette

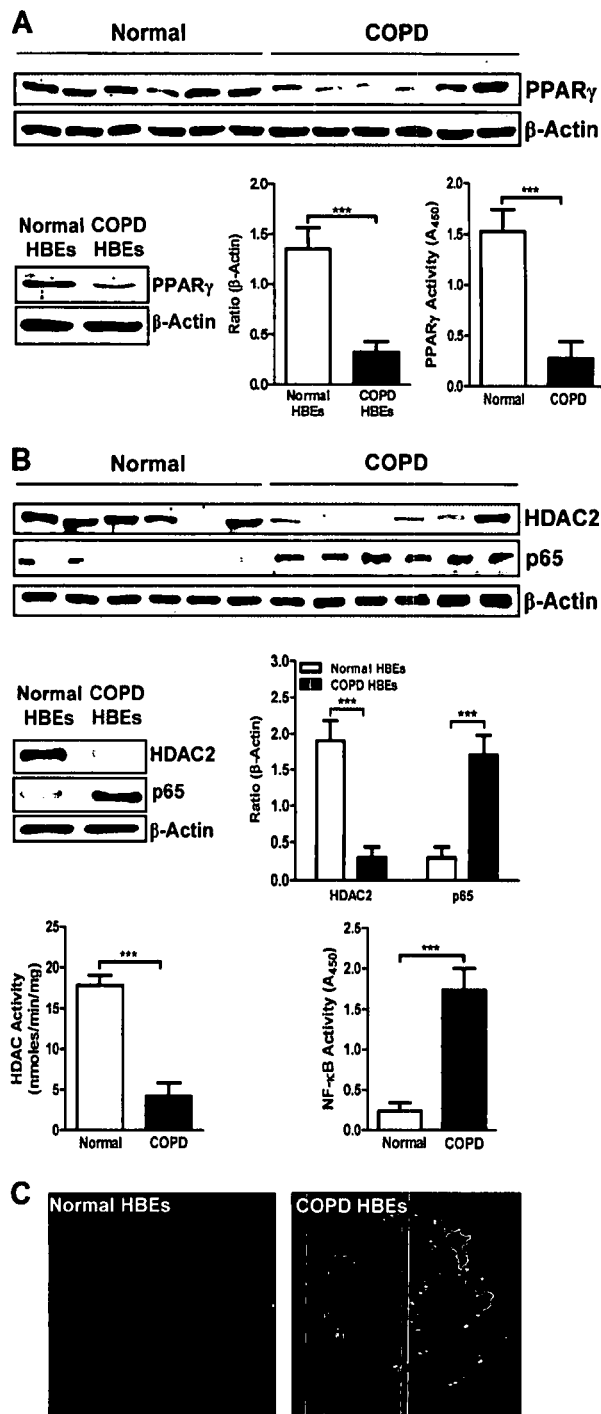


FIGURE 1. PPAR γ expression and activity are decreased in COPD. A, Western blots for PPAR γ in tissue extracts of pathologically normal (non-COPD; $n = 6$) and COPD ($n = 6$) lung (top panel) and in whole-cell extracts of HBE cells obtained from normal ($n = 6$) and COPD ($n = 6$) subjects (bottom left panel) followed by densitometric analysis (bottom center panel). Bottom right panel, DNA binding activity of PPAR γ in non-COPD and COPD tissue extracts measured using an ELISA-based assay. B, Western blots and densitometric analysis for HDAC2 and p65 from lung (top panel) and HBE cells (middle left panel) as described in A. Bottom left panel and bottom right panel, HDAC deacetylase (bottom left panel) and p65 DNA binding activities (bottom right panel) measured by ELISA-based assays, as described in A. C, intracellular ROS levels in normal and COPD HBE cells, assessed by confocal microscopy. Data are representative of three independent experiments; ***, $p < 0.001$.

(3R4F; Kentucky Tobacco Research and Development Centre, University of Kentucky, Lexington, KY) into 10 ml of medium according to the Federal Trade Commission (FTC) protocol,

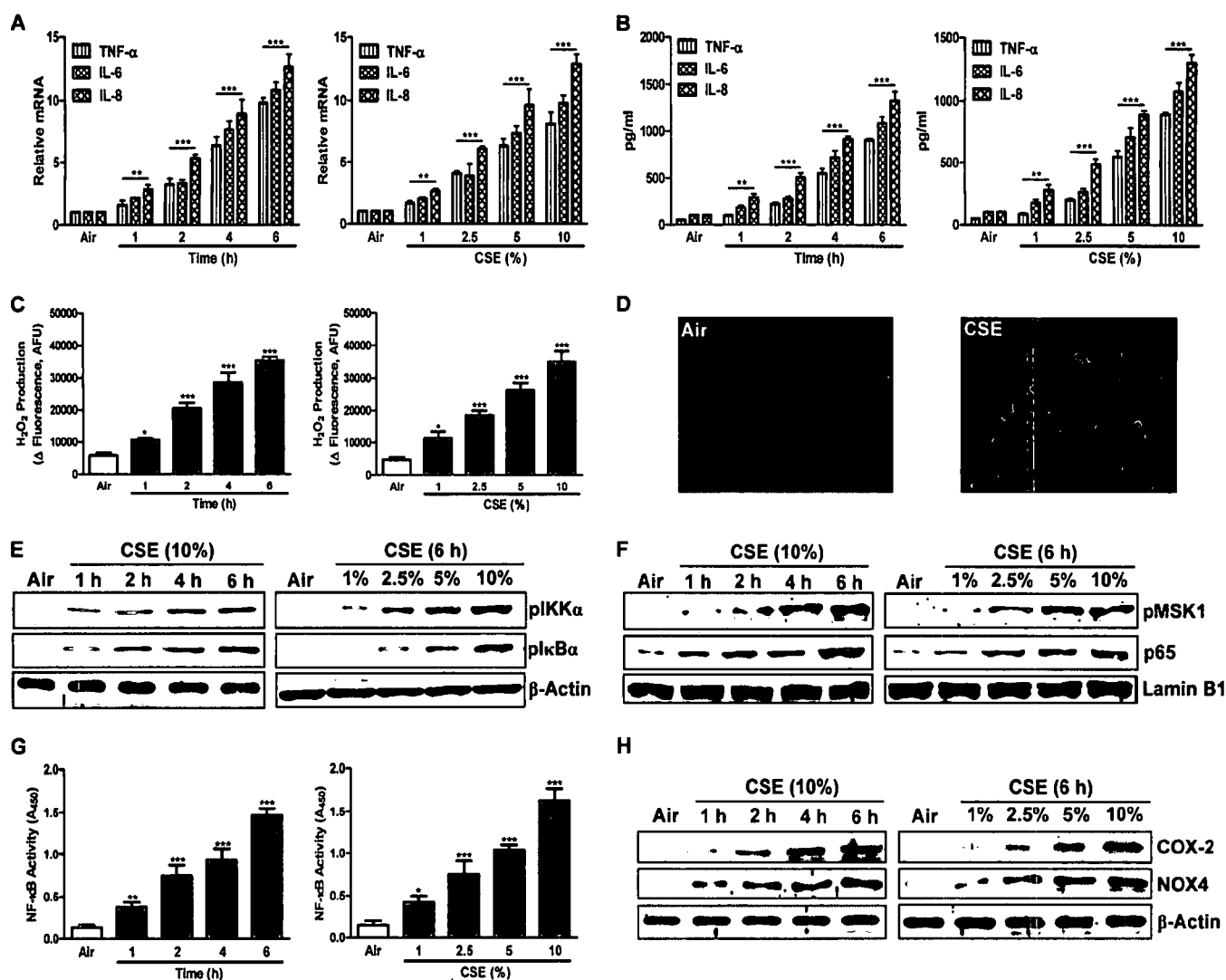


FIGURE 2. CSE induces inflammatory responses and oxidative stress via up-regulation of NF- κ B. *A* and *B*, shown are time courses and concentration-response relationships for CSE-induced cytokine/chemokine gene expression (*A*) and release (*B*). *C*, H₂O₂ production. *G*, DNA binding activity of NF- κ B p65, measured by ELISA-based assay. *E*, *F*, and *H*, p-IKK α and p-I κ B α (*E*), p-MSK1 and NF- κ B p65 (*F*), and COX-2 and NOX4 protein levels (*H*), by Western blots. *D* shows ROS immunofluorescence in H292 cells exposed for 6 h to 10% CSE or air control. H292 cells were treated with various concentrations (1–10%) of CSE for 6 h or for 1–6 h with 10% CSE, as indicated. In *A*, RNA was isolated, and gene expression levels were analyzed by real-time PCR. *B* and *C* show levels measured in culture medium. *E* and *H*, in whole-cell extracts; *F* and *G*, in nuclear extracts. Data are representative of three independent experiments, with $n = 3$. *, $p < 0.05$, **, $p < 0.01$, ***, $p < 0.001$.

each puff being of 2-s duration and 35-ml volume. The pH of CSE was adjusted to 7.4 and sterilized by filtration through a 0.22- μ m filter (EMD Millipore, Billerica, MA). The extract, defined as 100% CSE, was diluted to the indicated concentrations and used within 10 min of preparation. For control experiments, air was bubbled into 10 ml of medium, which was then treated as for CSE.

Measurement of Cytokine and Chemokine Levels in Culture Medium—Cell culture medium from different treatment groups was collected and stored at -80°C . Levels of TNF- α , IL-6, and IL-8 were measured using ELISA kits (R&D Systems, Minneapolis, MN) according to the manufacturer's instructions.

Determination of Cellular ROS—H₂O₂ production in cell culture media was determined using the Amplex Red hydrogen peroxide assay kit (Molecular Probes, Eugene, OR). Production of intracellular ROS in live cells was determined using the Cell Meter fluorimetric intracellular total ROS activity assay kit (AAT Bioquest, Sunnyvale, CA). Samples were mounted on

glass slides with VECTASHIELD mounting medium (Vector Laboratories, Burlingame, CA). The slides were viewed by an Olympus Fluoview FV1000 confocal microscope (Olympus, Center Valley, PA) using a 60 \times fluorescence lens along with Fluoview confocal software (FV10-ASW v1.7, Olympus).

HDAC Activity and Transcription Factor DNA Binding Activity Assays—Nuclear proteins were extracted using a nuclear extraction kit (Active Motif, Carlsbad, CA), and their concentrations were determined using the BCA protein assay kit (Pierce). Nuclear extracts were used to quantify HDAC activity and DNA binding activity of PPAR γ , GR- α , and the p65 subunit of NF- κ B using ELISA-based kits (56210, 40196, 45496, and 40096; Active Motif).

Western Blotting—Total protein extracts were prepared, and Western blotting was performed as described previously (11). Antibodies against PPAR γ , p65, COX-2, NOX4, GR- α , HDAC2, p300, β -actin, and lamin B1 were from Santa Cruz Biotechnology (Santa Cruz, CA). Antibodies against p-Ser,

Role of PPAR γ Down-regulation and Activation in COPD

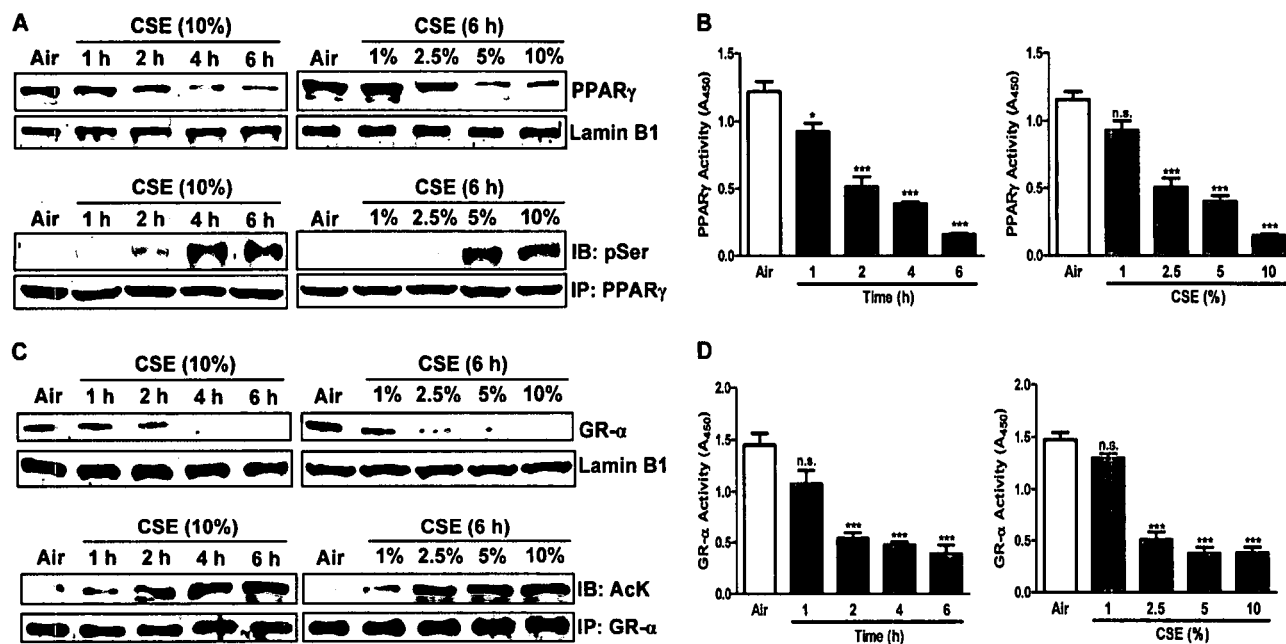


FIGURE 3. CSE down-regulates anti-inflammatory transcription factors PPAR γ and GR- α . Time courses and concentration-response relationships of transcription factor nuclear localization, modification, and activity in CSE-treated H292 cells. *A*, Western blots (*IB*) of nuclear PPAR γ (*top panel*) and phosphorylation of immunoprecipitated (*IP*) PPAR γ (*bottom panel*). *B*, PPAR γ DNA binding activity, measured using an ELISA-based assay. *C*, Western blots of nuclear GR- α (*top panel*) and acetylation of immunoprecipitated GR- α (*bottom panel*). *D*, GR- α DNA binding activity measured using an ELISA-based assay. H292 cells were treated with various concentrations (1–10%) of CSE for 6 h or for 1–6 h with 10% CSE, as indicated. Data are representative of three independent experiments, with $n = 3$ –5. *, $p < 0.05$, ***, $p < 0.001$, n.s. = nonsignificant.

p-IKK α , p-IkBa, p-MSK1, acetylated lysine (Ack), acetyl- and phospho-histone H3 (Lys-9/Ser-10), acetyl-histone H4 (Lys-12), histone H3, and histone H4 were from Cell Signaling Technology (Beverly, MA). Antibody against 4-hydroxy-2-nonenal was from Oxis International, Inc. (Beverly Hills, CA). Antibody against nitrotyrosine was from EMD Millipore. Following primary antibody reaction, the membrane was washed in Tris-buffered saline with Tween 20 (TBST) and incubated with a 1:5000 dilution of secondary antibodies consisting of donkey anti-mouse IR-680 (red) and goat anti-rabbit IR-780 (green), both from LI-COR Biosciences (Lincoln, NE), for 1 h at room temperature. The infrared signal was detected using an Odyssey infrared imager (LI-COR).

Immunoprecipitation—Nuclear extracts were prepared and were immunoprecipitated using the Dynabeads protein G immunoprecipitation kit (Invitrogen). Antibodies were bound to Dynabeads protein G, and Dynabeads-antibody complex was used to precipitate target proteins from the nuclear extracts. Unbound proteins were washed away, and complexes were eluted. All samples (20 μ g/lane) were separated by electrophoresis on SDS-polyacrylamide gels and transferred to PVDF membranes, and Western blotting was performed.

ChIP Assay—The ChIP assay was performed using the SimpleChIP enzymatic chromatin immunoprecipitation kit with magnetic beads (Cell Signaling Technology). Briefly, cellular chromatin was cross-linked with 1% formaldehyde for 10 min at room temperature, the cross-linking was stopped with 0.125 M glycine, and cells were washed twice with ice-cold PBS. Nuclei were pelleted and digested by micrococcal nuclease. Following sonication and centrifugation, equal amounts of sheared chromatin were incubated overnight at 4 $^{\circ}$ C with antibodies, IgG as negative control, and RNA polymerase II as positive

control (Cell Signaling Technology). Protein G magnetic beads were then added, and the chromatin was incubated with rotation for 2 h at 4 $^{\circ}$ C. An aliquot of chromatin that was not incubated with any antibody was used as the input control sample. Antibody-bound protein-DNA complexes were eluted and subjected to real-time PCR as described under “RNA Isolation and Quantitative Real-time RT-PCR” with specific primers for TNF- α , IL-6, IL-8, and α -satellite (supplemental Table 1).

RNA Isolation and Quantitative Real-time RT-PCR—RNA was isolated using the RNeasy mini kit (Qiagen), and cDNA was generated from 100 ng of total RNA using MultiScribe reverse transcriptase (Applied Biosystems, Foster City, CA) employing random and oligo(dT) primers. Real-time quantitative PCR was performed using 100 ng of cDNA with 2 \times SYBR Green master mix (Applied Biosystems) and specific primers for the genes of interest (supplemental Table 1). These experiments were performed on an AB 7500 fast thermal cycler using a three-step protocol employing the melting curve method. The average of each gene cycle threshold (C_t) was determined for each experiment. Relative cDNA levels ($2^{-\Delta\Delta C_t}$) for the genes of interest were determined using the comparative C_t method, which generates the $\Delta\Delta C_t$ as the difference between the gene of interest and the housekeeping genes β -actin and 9 S rRNA for each sample. Each averaged experimental gene expression sample was compared with the averaged control sample, which was set to 1.

Transfecting Small Interfering RNA into Normal HBE Cells—Normal HBE cells were incubated for 8 h with a liposome complex containing 100 nM of small interfering RNA (siRNA) targeted to PPAR γ or scrambled control (Dharmacon, Lafayette, CO; supplemental Table 2) and Lipofectamine 2000 (Invitrogen) under serum- and antibiotic-free conditions. After 8 h, fresh medium with 10% FBS was added, and the cells were incu-

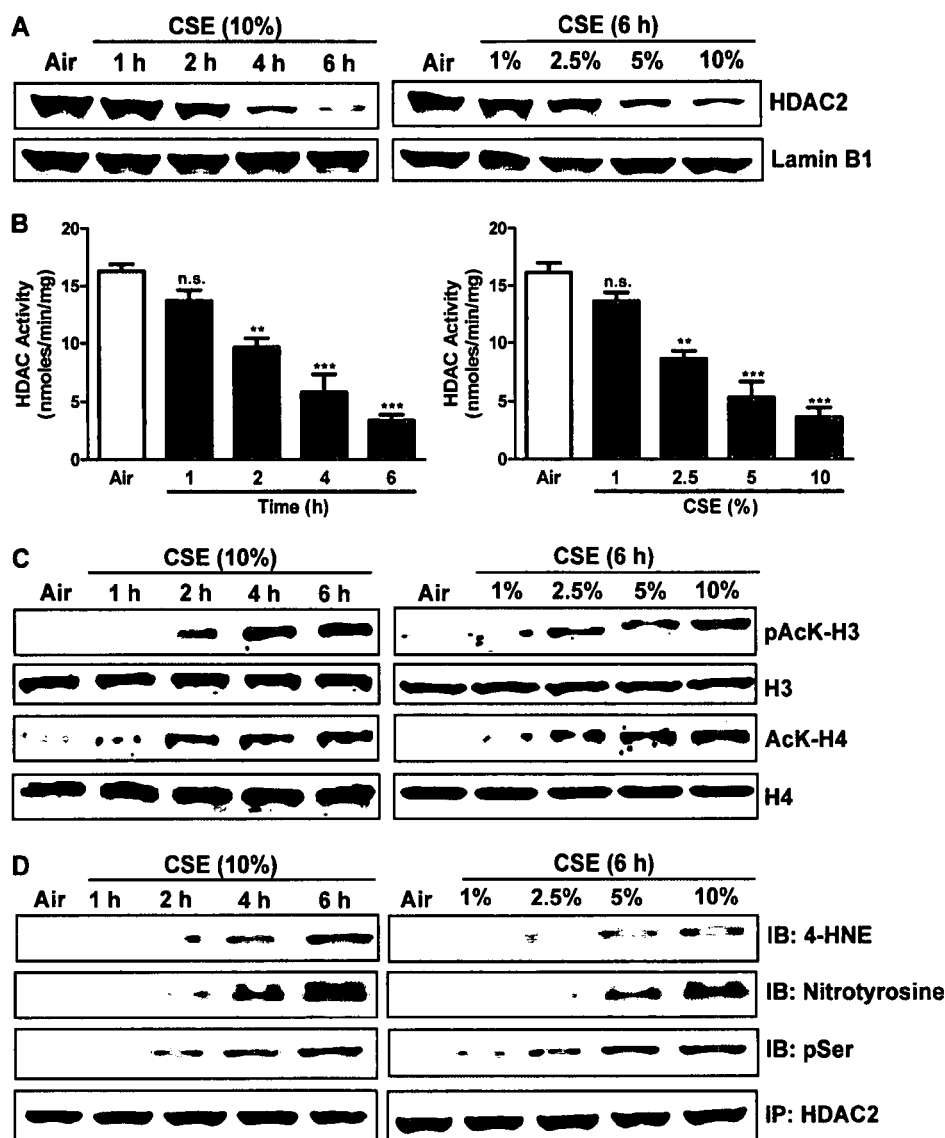


FIGURE 4. CSE down-regulates HDAC2 and increases chromatin acetylation. Shown are time courses and concentration-response relationships of effects on HDAC2 and histone acetylation in CSE-treated H292 cells. *A*, Western blots of nuclear HDAC2. *B*, deacetylation activity of HDAC measured using an ELISA-based assay. *C*, Western blots showing acetyl- and phospho-histone H3 (Lys-9/Ser-10) and total histone H3; acetylated (Lys-12) and total histone H4. *D*, Western blots showing immunoprecipitated HDAC2 alkylation with 4-hydroxy-2-nonenal (4-HNE), nitrosylation, and phosphorylation. H292 cells were treated with various concentrations (1–10%) of CSE for 6 h or for 1–6 h with 10% CSE, as indicated. Data are representative of three independent experiments, with $n = 3$. *, $p < 0.05$, ***, $p < 0.001$, n.s. = nonsignificant.

bated for a further 16 h. After a 24-h incubation, cells were treated with CSE as described.

Statistical Analysis—Data are presented as mean \pm S.D. Differences between groups were analyzed using an unpaired t test or analysis of variance followed by a Bonferroni's multiple comparison test using GraphPad Prism 5.03 (GraphPad Software, La Jolla, CA). A $p < 0.05$ was considered significant.

RESULTS

PPAR γ Down-regulation in COPD Is Associated with Reduction of HDAC2 and Activation of NF- κ B—To assess the potential pathophysiological role of PPAR γ in COPD, we tested whether PPAR γ expression and function are altered in lung tissue samples of COPD patients and in airway epithelial cells. These cells are directly smoke-exposed in cigarette smokers and are pathogenic targets and mediators in COPD (12, 13). We found

that PPAR γ protein (shown by Western blots) and DNA binding activity (Fig. 1A) were reduced in lung tissue and HBE cells of COPD patients when compared with those from individuals without COPD. This PPAR γ down-regulation was associated with the previously reported (3) up-regulated expression and activity of the pro-inflammatory transcription factor NF- κ B and down-regulation of the corepressor HDAC2 (Fig. 1B), a factor that participates in GR- α -mediated anti-inflammatory activity. HBE cells from COPD patients also exhibited oxidative stress consistent with their proinflammatory state, as shown by immunostaining for ROS followed by confocal microscopy (Fig. 1C).

CSE Induces Inflammatory Responses and Oxidative Stress in Human Epithelial Cells—Cigarette smoking, the major risk factor for COPD, produces lung inflammation and oxidative stress. To assess the mechanisms by which smoke down-regu-

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lates epithelial PPAR γ and induces inflammation, we determined the time courses and concentration-response relationships of CSE-induced proinflammatory proteins, transcriptional mediators, and ROS in H292 human lung epithelial cells. Treating cells with varying concentrations of CSE for 6 h or with 10% CSE for various times up-regulated expression and release of the inflammatory cytokines TNF- α and IL-6 and the chemokine IL-8 (Fig. 2, A and B). Production of H₂O₂ was also increased (Fig. 2C) as were intracellular ROS levels seen by immunofluorescence after a 6-h exposure to 10% CSE (Fig. 2D). CSE exposure likewise activated the proinflammatory transcription factor NF- κ B, seen via increased nuclear NF- κ B p65 levels (Fig. 2F) and DNA binding activity (Fig. 2G), and increased expressed protein levels of its transcriptional targets COX-2 and NADPH oxidase 4 (NOX4) (Fig. 2H).

We also measured changes in inhibitor of NF- κ B (I κ B), which down-regulates activity of NF- κ B by preventing its translocation to the nucleus, and in I κ B kinase (IKK), which drives ubiquitination and degradation of I κ B, thereby increasing NF- κ B activity (14). CSE treatment increased the levels of phosphorylated I κ B and phosphorylated (activated) IKK (Fig. 2E) and those of the activated form of mitogen- and stress-activated protein kinase 1 (MSK1), which phosphorylates IKK (Fig. 2F). MSK1 also promotes inflammatory gene transcription by phosphorylating NF- κ B itself, allowing it to recruit coactivators, and by phosphorylating histone H3, allowing it to induce chromatin loosening (15). The time courses and concentration-response relationships of all these CSE-induced responses were very similar, pointing to a broadly coordinated proinflammatory program in lung epithelial cells.

CSE Down-regulates PPAR γ , GR- α , and HDAC2 while Enhancing Chromatin Acetylation—Based on the CSE-induced proinflammatory profile we saw in H292 cells and the suppression of PPAR γ seen in HBE cells of COPD patients, we tested whether CSE influences PPAR γ function in H292 cells. CSE induced time- and concentration-dependent decreases in nuclear levels (Fig. 3A, top panel) and DNA binding activity (Fig. 3B) of PPAR γ that were accompanied by increased phosphorylation, an inhibitory post-translational modification (Fig. 3A, bottom panel). To test the idea that CSE-induced down-regulation of GR- α might contribute to the ineffectiveness of glucocorticoids in COPD, we tested the effects of CSE on GR- α . Supporting our hypothesis, exposing H292 cells to CSE down-regulated both expression and activity of GR- α and also induced its lysine acetylation (Fig. 3, C and D), an inhibitory post-translational modification.

Transcription factors attract coactivators with histone acetyltransferase activity, which acetylates specific lysines in histones H3 and H4 and thereby loosens chromatin structure so as to allow RNA polymerase to bind and initiate transcription. GR- α suppresses proinflammatory gene expression in part by associating with NF- κ B and attracting the corepressor HDAC2, which inhibits transcriptional activation by deacetylating histones (16). We tested the influence of CSE on this system. CSE decreased the nuclear localization and activity of HDAC2 (Fig. 4, A and B) and thus increased the acetylation of histones H3 and H4, in a time- and concentration-dependent manner (Fig. 4C). CSE-induced suppression of HDAC activity reflected not

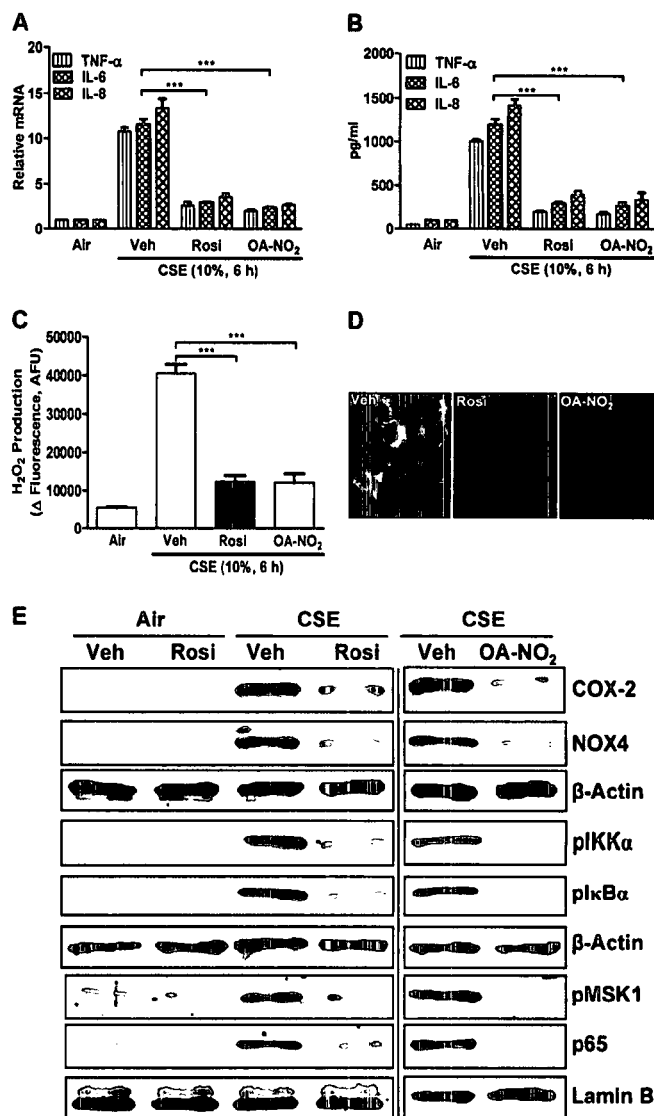


FIGURE 5. PPAR γ activation decreases CSE-induced cytokine production and oxidative stress by modulating NF- κ B. Shown are effects of treatment with Rosi (1 μ M) or OA-NO₂ (100 nM) followed by CSE treatment (10%, 6 h) of H292 cells. A and B, cytokine/chemokine gene expression (A) and release (B) of H292 cells. Veh, vehicle. C, H₂O₂ production. D, intracellular ROS levels. E, Western blots showing levels of COX-2, NOX4, p-IKK α , p-I κ B α , p-MSK1, and NF- κ B p65. In A, RNA was isolated, and gene expression levels were analyzed by real-time PCR. B and C show levels measured in culture medium. AFU, arbitrary fluorescence units. D was assessed by confocal microscopy. E, in whole-cell and nuclear extracts, as indicated by β -actin or lamin B1, respectively. Data are representative of three independent experiments with $n = 3-5$. ***, $p < 0.001$.

only its down-regulated expression, but also induction of multiple concentration- and time-dependent post-translational modifications including serine phosphorylation, tyrosine nitrosylation, and cysteine alkylation by 4-hydroxy-2-nonenal, a specific marker of oxidative stress (Fig. 4D).

PPAR γ Activation Reduces CSE-induced Inflammation and Oxidative Stress while Up-regulating GR- α and HDAC2—To determine whether PPAR γ activation can suppress the CSE-induced proinflammatory profile and resulting oxidative stress in epithelial cells, we treated H292 cells with either the synthetic agonist Rosi (1 μ M) or the endogenous agonist OA-NO₂ (100 nM) for the 30 min preceding a 6-h exposure to 10% CSE. Both PPAR γ agonists reduced the CSE-induced increases in

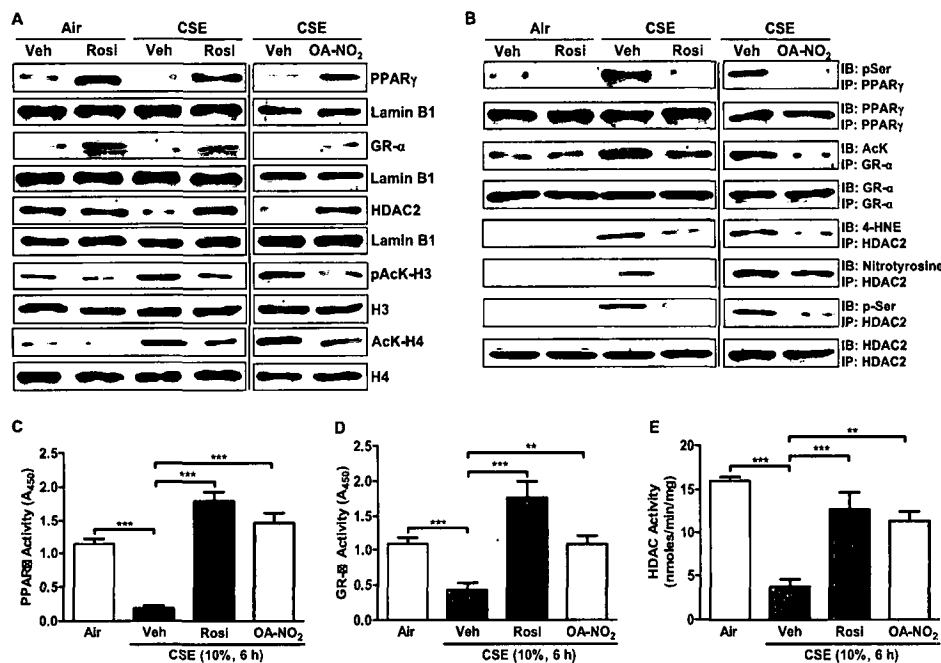


FIGURE 6. PPAR γ activation reverses CSE-induced changes in PPAR γ , GR- α , and HDAC2 and in chromatin acetylation. Shown are effects of treatment with Rosi (1 μ M) or OA-NO₂ (100 nM) followed by CSE treatment (10%, 6 h) of H292 cells. *A*, Western blots showing nuclear levels of PPAR γ , GR- α , and HDAC2, as well as showing acetyl- and phospho-histone H3 (Lys-9/Ser-10) and total histone H3; acetylated (Lys-12) and total histone H4. *Veh*, vehicle. *B*, Western blots (*IB*) showing phosphorylation in immunoprecipitated (*IP*) PPAR γ , acetylation in immunoprecipitated GR- α , and 4-hydroxy-2-nonenal (4-HNE) alkylation, nitrosylation, and phosphorylation in immunoprecipitated HDAC2. *C*, DNA binding activity of PPAR γ . *D*, DNA binding activity of GR- α . *E*, deacetylation activity of HDAC. All activities were measured using ELISA-based assays. Data are representative of three independent experiments with $n = 3-5$. **, $p < 0.01$, ***, $p < 0.001$.

cytokine gene expression (Fig. 5A) and secretion (Fig. 5B) by ~80% and similarly reduced H₂O₂ production (Fig. 5C) and intracellular ROS seen by immunostaining (Fig. 5D). Both agonists likewise markedly reduced the levels of NF- κ B and its target proteins COX-2 and NOX4, as well as the phosphorylated forms of MSK1, IKK, and I κ B (Fig. 5E). These data indicate that agonist-induced PPAR γ activation inhibits the pro-inflammatory effects of CSE.

To determine the mechanisms by which PPAR γ activation exerts its anti-inflammatory and antioxidant effects, we studied the effects of Rosi or OA-NO₂ on nuclear localization and activity of PPAR γ , GR- α , and HDAC. Treatment with Rosi or OA-NO₂ more than reversed the decreases in nuclear PPAR γ levels caused by CSE exposure, raising levels even above the air-vehicle treatment baseline (Fig. 6A). Both PPAR γ agonists likewise up-regulated DNA binding activity of PPAR γ and GR- α along with the deacetylase activity of HDAC2 (Fig. 6, C-E). These increases in activity were accompanied by decreases in PPAR γ phosphorylation, GR- α acetylation, and the levels of HDAC2 phosphorylation, nitrosylation, and alkylation (Fig. 6B). The increased HDAC2 activity was associated with decreased acetylation of histones H3 and H4 (Fig. 6A). Taken together, these data demonstrate that PPAR γ activation can reverse CSE-induced proinflammatory effects and ROS generation in epithelial cells and suggest that this is due both to direct anti-inflammatory effects of PPAR γ itself and to restoration of the HDAC2 activity required by GR- α for effective anti-inflammatory action.

Activation of PPAR γ Modifies CSE-induced Protein-protein and Protein-DNA Associations—Transcription is regulated both by direct modulation of the activities of relevant transcrip-

tion factors and their abilities to attract and bind coactivators or corepressors. Ligand-activated PPAR γ inhibits NF- κ B by direct binding, among other mechanisms (17), while GR- α links NF- κ B to the corepressor HDAC2 and blocks its recruitment of the histone acetyltransferase coactivator p300 and the coactivator MSK1. Co-immunoprecipitation experiments showed that CSE exposure greatly increased the amounts of p300 and MSK1 associated with nuclear NF- κ B. These effects were largely reversed by treatment with either Rosi or OA-NO₂ (Fig. 7A). PPAR γ activation likewise reversed the CSE-induced decrease in association between GR- α and NF- κ B, while NF- κ B was further inhibited by increased direct association with PPAR γ . Rosi or OA-NO₂ treatment also increased the association of HDAC2 and of PPAR γ with GR- α (Fig. 7B). We confirmed by ChIP that the observed agonist-induced diminution of CSE-elevated nuclear localization of NF- κ B (Fig. 7C) and MSK1 (Fig. 7D) was associated with reduced binding to the promoter regions of the NF- κ B target genes TNF- α , IL-6, and IL-8. This observation further implies that MSK1 was bound to NF- κ B.

PPAR γ Knockdown Amplifies and Activation Reverses CSE Effects in HBE cells—To test whether endogenous PPAR γ activity suppresses the CSE-induced proinflammatory and related transcriptional program in HBE cells, we used a gene silencing approach. Treating HBE cells with PPAR γ -directed siRNA abrogated PPAR γ expression to the suppressed levels seen with CSE treatment (Fig. 8A), while agonist treatment up-regulated expression in whole-cell extracts above vehicle-treated baseline (Fig. 8B). Such PPAR γ knockdown augmented CSE-induced alterations in HDAC and NF- κ B activity (Fig. 8C) and in CSE-induced stimulation of IL-8 release (Fig. 8D) versus those seen

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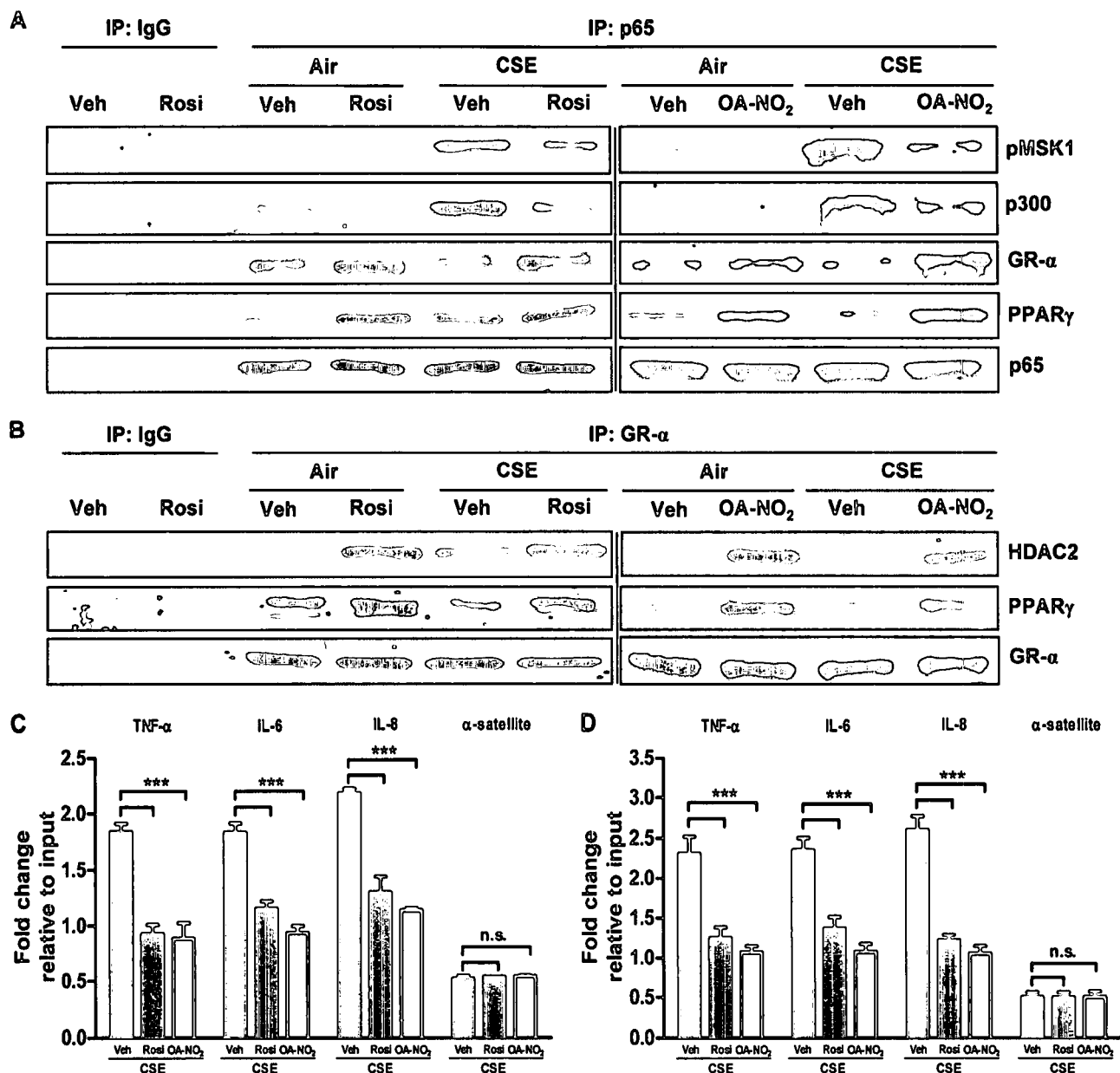


FIGURE 7. PPAR γ activation modulates CSE-induced protein-protein and protein-DNA interactions. Shown are effects of treatment with Rosi (1 μ M) or OA-NO₂ (100 nM) followed by CSE treatment (10%, 6 h) of H292 cells. *A* and *B*, nuclear extracts were immunoprecipitated (IP) for NF- κ B p65 and GR- α and Western blotted for p-MSK1, p300, GR- α , PPAR γ , and p65 (*A*) and HDAC2, PPAR γ , and GR- α (*B*). *Veh*, vehicle. *C* and *D*, chromatin was cross-linked and immunoprecipitated with antibodies against p65 (*left*) and p-MSK1 (*right*). Antibody-bound protein-DNA complexes were eluted and subjected to real-time PCR with specific primers for TNF- α , IL-6, IL-8, and α -satellite DNA. Data are representative of three independent experiments with $n = 3-5$. ***, $p < 0.001$, *n.s.* = nonsignificant.

in wild-type cells. Thus, whereas PPAR γ activation reversed the deleterious effects of CSE, reducing PPAR γ greatly exaggerated them.

To assess the potential relevance of agonist-induced PPAR γ activation to the effects of COPD we saw in HBE cells (Fig. 1), we tested the abilities of Rosi- and OA-NO₂-induced PPAR γ activation to inhibit CSE responses in HBE cells. As in H292 cells (Figs. 5-7), both agonists abrogated CSE-induced suppression of PPAR γ , GR- α , and HDAC2 levels and its up-regulation of NF- κ B (Fig. 8E). These effects of Rosi and OA-NO₂ were accompanied by reduced NF- κ B binding to the promoter region of its target gene IL-8 (Fig. 8F) and decreased CSE-stimulated IL-8 release (Fig. 8G). These effects in human lung cells

thus show that our results are generalizable beyond H292 cells and support their relevance for the smoke-exposed human airway *in vivo*.

DISCUSSION

Our studies lead to two central conclusions. First, PPAR γ expression and DNA binding activity are down-regulated in lung tissue samples and bronchial epithelial cells from COPD patients. These observations are linked to down-regulation of GR- α and its associated corepressor HDAC2, whereas the transcription factor NF- κ B is up-regulated. The net effect of these findings is the enhanced airway inflammation typically observed in COPD. CSE treatment of human lung epithelial

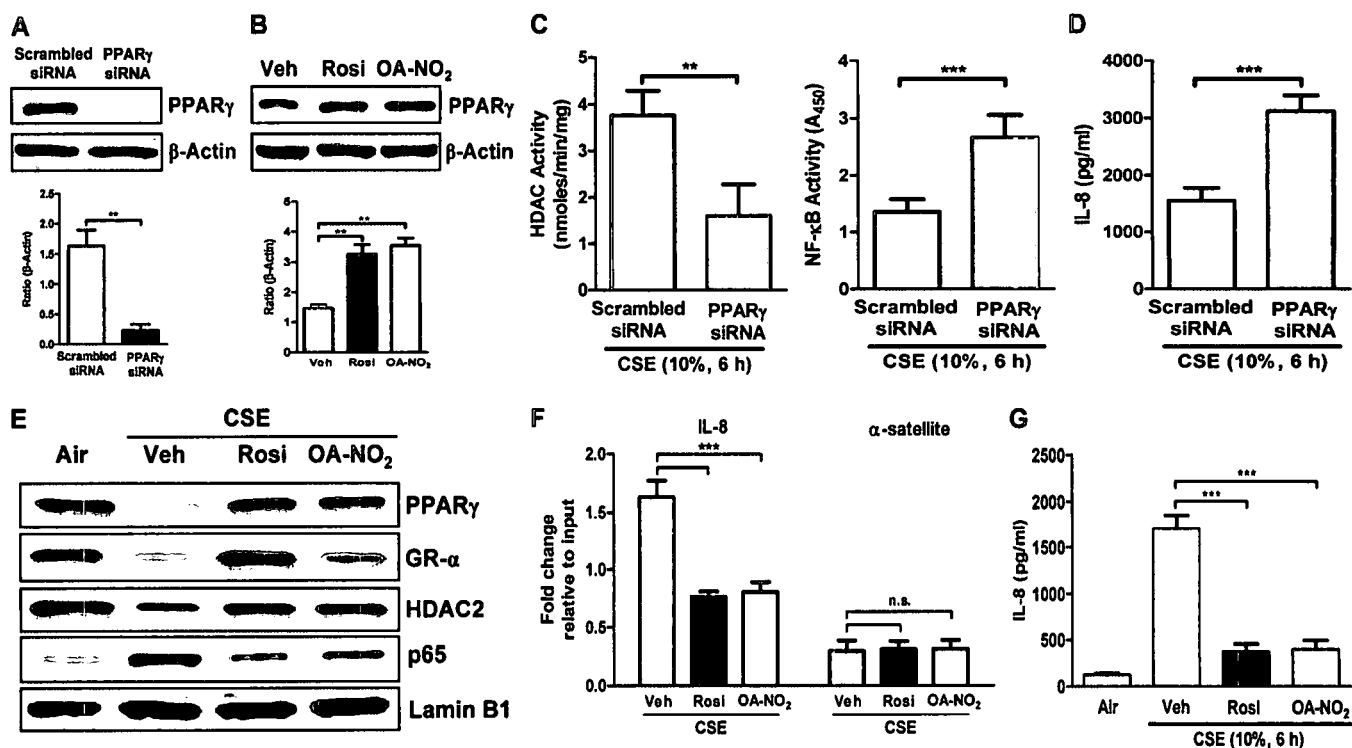


FIGURE 8. PPAR γ knockdown exaggerates whereas PPAR γ activation ameliorates CSE-induced inflammatory response in HBE cells. A–G, effects of PPAR γ knockdown with siRNA (A, C, and D) and activation with OA-NO $_2$ (100 nM) or Rosi (1 μ M) (B and E–G) followed by CSE treatment (10%, 6 h) in normal HBE cells. A and B, Western blots showing whole-cell PPAR γ levels following knockdown (A) and agonist treatment (without CSE treatment) (B). Veh, vehicle. C, deacetylase activity of HDAC (left) and DNA binding activity of NF- κ B (right) measured using ELISA-based assays. D, secretion of IL-8. E, Western blots showing nuclear localization of PPAR γ , GR- α , HDAC2, and NF- κ B p65. F, chromatin was cross-linked and immunoprecipitated with antibodies against p65. Antibody-bound protein-DNA complexes were eluted and subjected to real-time PCR with specific primers for IL-8 and α -satellite. G, secretion of IL-8. Data are representative of three independent experiments with $n = 3$ –5. **, $p < 0.01$, ***, $p < 0.001$, n.s. = nonsignificant.

cells recapitulated the effects observed in samples taken directly from COPD patients, and these effects were exaggerated by PPAR γ knockdown. Second, these deleterious effects of CSE were reversed by either of two structurally distinct PPAR γ agonists, one synthetic, the other endogenous, that each up-regulated expression and activity of the nuclear receptor. These agonists also largely or completely reversed CSE effects on other anti-inflammatory proteins, on the pro-inflammatory transcription factor NF- κ B, and on cytokine, chemokine, and ROS production. By demonstrating both PPAR γ down-regulation in COPD and the ability of PPAR γ activation to reverse all effects in a smoke-induced *in vitro* model of the disease, our findings thus support a crucial role of PPAR γ down-regulation in pathogenesis of smoking-induced COPD.

Mechanistic studies supported multiple paths through which PPAR γ activation, with consequent increases in its expression and activity, blocks the ability of cigarette smoke to up-regulate NF- κ B and thus induce inflammation. Co-immunoprecipitation demonstrated binding of PPAR γ to NF- κ B, which can inhibit that transcription factor in at least two different ways (17, 18). Furthermore, treatment with either PPAR γ agonist reversed the CSE-induced phosphorylation of IKK, thus blocking degradation of I κ B and consequent nuclear localization of NF- κ B (14). This extends to airway epithelial cells and an additional PPAR γ agonist previous observations that the thiazolidinedione pioglitazone blocks IKK activation through a PPAR γ -dependent mechanism in IL-1 β -stimulated vascular smooth muscle cells (19). The agonist-induced reduction in

IKK phosphorylation we see presumably reflects the accompanying decrease in activating phosphorylation of MSK1. The ability of PPAR γ to attack inflammation via multiple pathways thus enhances its attractiveness as a potential therapeutic target in COPD.

It is also unclear whether the PPAR γ down-regulation and inhibition we observe directly reflect inflammatory signaling, are due to inflammation-associated oxidative stress, or both. Blanquicett *et al.* (20) have reported that H $_2$ O $_2$ induces a prolonged down-regulation of PPAR γ mRNA expression in human vascular endothelial cells. The authors attributed this effect to oxidative stress activation of the transcription factor activator protein 1 (AP1). The inhibitory post-translational phosphorylation we also see appears to reflect a different mechanism, however, since it is driven by activation of mitogen-activated protein kinases (MAPKs). Previous studies have shown that such phosphorylation is mediated by members of the MAPK family (21–24) and that it occurs specifically at Ser-84 (Ser-82 in the mouse) (21, 22). There is redundancy in the pathways involved because PPAR γ can be phosphorylated by either extracellular signal-related kinase (21–23) or c-Jun N-terminal kinase (21, 24). Both are members of the MAPK family that can be activated by cigarette smoke (25).

The limited effectiveness of glucocorticoids represents a major therapeutic challenge in COPD. We demonstrated that CSE reduces nuclear localization and activity of both GR- α and the HDAC2 corepressor that it utilizes, with accompanying post-translational modifications of these proteins, and that

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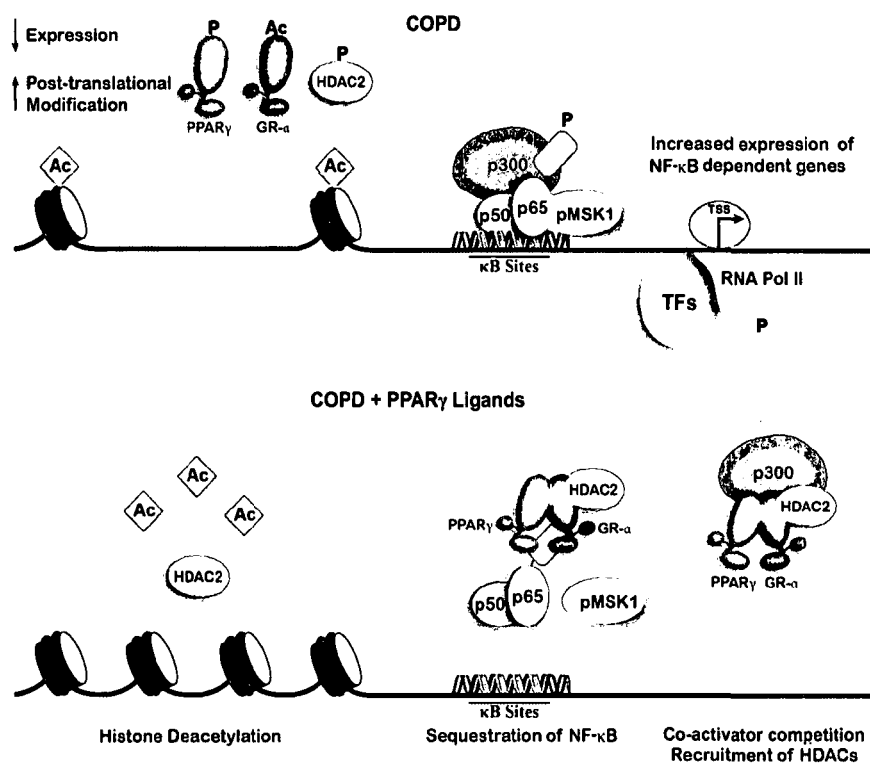


FIGURE 9. Schematic summary of how PPAR γ , GR- α , and HDAC2 affect transcription of NF- κ B target genes in COPD. *Top panel*, cigarette smoke-induced inflammatory signaling, which leads to degradation and post-translational inhibitory modifications of PPAR γ , along with HDAC2 and GR- α , results in histone acetylation and chromatin unwinding. This allows NF- κ B and its associated coactivators to bind to target promoters and stimulate transcription by RNA polymerase II (*RNA Pol II*). *Bottom panel*, activation of PPAR γ up-regulates HDAC2 and GR- α expression in addition to expression of PPAR γ itself. This results in removal of histone acetyl groups and condensation of chromatin structure, blocking NF- κ B and RNA polymerase II binding. NF- κ B activity is further reduced by binding to PPAR γ and GR- α and, through GR- α , to HDAC2, as well as by PPAR γ competition for essential coactivators.

these effects are reversed by PPAR γ activation. This observation suggests that PPAR γ activation may restore glucocorticoid sensitivity in lung epithelial cells and potentially in COPD patients, raising the possibility that joint administration of PPAR γ and GR- α agonists would be therapeutically appropriate. PPAR γ activation also increased its association with GR- α , as has been observed by others (26). Whether this PPAR γ -GR- α binding is direct or indirect remains unclear, however. It has been suggested that it may represent binding to common coactivators (26).

A prior study found that PPAR γ levels in lung tissues were up-regulated in patients with mild COPD, but in line with our present findings, were down-regulated in those with moderate or severe disease (27). The cell types involved were not identified. Because PPAR γ levels were recently found to be unaltered in alveolar macrophages of COPD patients (28), our findings clearly point to lung epithelial cells as a key locus of PPAR γ down-regulation and target for its potential therapeutic activation in COPD patients. Other previous investigations have shown that PPAR γ activation can attenuate inflammation either in animal models of COPD or following CSE exposure *in vitro*, but have not addressed the signaling pathways we investigated. Both the thiazolidinedione pioglitazone (29) and the endogenous PPAR γ agonist 15-deoxy- $\Delta^{12,14}$ -prostaglandin J₂ (15d-PGJ₂) (30) have proven effective in the LPS-induced model of COPD, while both Rosi and pioglitazone were effective in a smoke-induced model (28). *In vitro*, Lee *et al.* (31) attributed the ability of Rosi to inhibit CSE-induced TNF- α and

mucin production in H292 cells to up-regulation of phosphatase and tensin homolog deleted on chromosome 10 (PTEN), with consequent down-regulation of the Akt signaling pathway. However, Rosi did not block CSE-induced cytokine production in a monocyte-macrophage cell line in which CSE disrupts the association between PPAR γ and NF- κ B (32). Taken together with the previously mentioned study by Lea *et al.* (28), this suggests that the role of PPAR γ in COPD may differ between macrophages and epithelial cells.

Our results show that down-regulation of epithelial cell PPAR γ expression and activity plays an important role in cigarette smoke-induced inflammation and the pathophysiology of COPD (Fig. 9, *top panel*). Among its other effects, this down-regulation decreases HDAC2 expression and activity, which contributes to increased acetylation of chromatin histones and a looser, unwound chromatin conformation. This conformational change facilitates binding of NF- κ B (p50 + p65, expression and activity of which are up-regulated in COPD) and its p300 coactivator to the genes' promoter regions. Acetylation by p300 further loosens chromatin structure, allowing binding of RNA polymerase II and increased transcription of these genes. These changes are reversed by PPAR γ activation (Fig. 9, *bottom panel*). This leads to up-regulation of HDAC2 expression and activity, with removal of histone acetyl groups and rewinding of the chromatin. NF- κ B, now bound to PPAR γ , GR- α , and HDAC2, no longer binds to the promoter regions of its target proteins. Furthermore, activated PPAR γ itself attracts the coactivators that NF- κ B requires (33), limiting the activity of

any remaining promoter-bound transcription factor. We also show that PPAR γ and GR- α simultaneously bound to NF- κ B, as suggested by our finding that these two nuclear hormone receptors co-immunoprecipitate.

Our studies thus provide major new insights into the mechanisms by which COPD-induced down-regulation of PPAR γ expression and inhibition of its activity contribute to the pro-inflammatory phenotype characteristic of this disease and the ways in which PPAR γ agonists reverse these effects. They also illuminate the mechanisms underlying the glucocorticoid insensitivity seen in COPD and imply that PPAR γ agonists could restore sensitivity. Taken together, these results support the possibility that PPAR γ agonists might prove effective treatments for this common and deadly disease.

REFERENCES

- Mannino, D. M., and Buist, A. S. (2007) Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* **370**, 765–773
- Barnes, P. J. (2006) Corticosteroids: the drugs to beat. *Eur. J. Pharmacol.* **533**, 2–14
- Barnes, P. J. (2009) Histone deacetylase-2 and airway disease. *Ther. Adv. Respir. Dis.* **3**, 235–243
- Doyle, K., and Fitzpatrick, F. A. (2010) Redox signaling, alkylation (carbonylation) of conserved cysteines inactivates class I histone deacetylases 1, 2, and 3 and antagonizes their transcriptional repressor function. *J. Biol. Chem.* **285**, 17417–17424
- Ito, K., Hanazawa, T., Tomita, K., Barnes, P. J., and Adcock, I. M. (2004) Oxidative stress reduces histone deacetylase 2 activity and enhances IL-8 gene expression: role of tyrosine nitration. *Biochem. Biophys. Res. Commun.* **315**, 240–245
- Adenuga, D., Yao, H., March, T. H., Seagrave, J., and Rahman, I. (2009) Histone deacetylase 2 is phosphorylated, ubiquitinated, and degraded by cigarette smoke. *Am. J. Respir. Cell Mol. Biol.* **40**, 464–473
- Ricote, M., Li, A. C., Willson, T. M., Kelly, C. J., and Glass, C. K. (1998) The peroxisome proliferator-activated receptor- γ is a negative regulator of macrophage activation. *Nature* **391**, 79–82
- Nencioni, A., Wesselborg, S., and Brossart, P. (2003) Role of peroxisome proliferator-activated receptor γ and its ligands in the control of immune responses. *Crit. Rev. Immunol.* **23**, 1–13
- Baker, P. R. S., Schopfer, F. J., Sweeney, S., and Freeman, B. A. (2004) Red cell membrane and plasma linoleic acid nitration products: synthesis, clinical identification, and quantitation. *Proc. Natl. Acad. Sci. U.S.A.* **101**, 11577–11582
- Baker, P. R. S., Lin, Y., Schopfer, F. J., Woodcock, S. R., Groeger, A. L., Batthyany, C., Sweeney, S., Long, M. H., Iles, K. E., Baker, L. M. S., Branchaud, B. P., Chen, Y. E., and Freeman, B. A. (2005) Fatty acid transduction of nitric oxide signaling: multiple nitrated unsaturated fatty acid derivatives exist in human blood and urine and serve as endogenous peroxisome proliferator-activated receptor ligands. *J. Biol. Chem.* **280**, 42464–42475
- Reddy, A. T., Lakshmi, S. P., Kleinhenz, J. M., Sutliff, R. L., Hart, C. M., and Reddy, R. C. (2012) Endothelial cell peroxisome proliferator-activated receptor γ reduces endotoxemic pulmonary inflammation and injury. *J. Immunol.* **189**, 5411–5420
- DiStefano, A., Caramori, G., Oates, T., Capelli, A., Lusuardi, M., Gnemm, I., Ioli, F., Chung, K. F., Donner, C. F., Barnes, P. J., and Adcock, I. M. (2002) Increased expression of nuclear factor- κ B in bronchial biopsies from smokers and patients with COPD. *Eur. Respir. J.* **20**, 556–563
- Jeffery, P. K. (2004) Remodeling and inflammation of bronchi in asthma and chronic obstructive pulmonary disease. *Proc. Am. Thorac. Soc.* **1**, 176–183
- Alkalay, I., Yaron, A., Hatzubai, A., Orian, A., Ciechanover, A., and Ben-Neriah, Y. (1995) Stimulation-dependent I κ B α phosphorylation marks the NF- κ B inhibitor for degradation via the ubiquitin-proteasome pathway. *Proc. Natl. Acad. Sci. U.S.A.* **92**, 10599–10603
- Beck, I. M., Vanden Berghe, W., Vermeulen, L., Bougarne, N., Vander Cruyssen, B., Haegeman, G., and De Bosscher, K. (2008) Altered subcellular distribution of MSK1 induced by glucocorticoids contributes to NF- κ B inhibition. *EMBO J.* **27**, 1682–1693
- Ito, K., Barnes, P. J., and Adcock, I. M. (2000) Glucocorticoid receptor recruitment of histone deacetylase 2 inhibits interleukin-1 β -induced histone H4 acetylation on lysines 8 and 12. *Mol. Cell. Biol.* **20**, 6891–6903
- Hou, Y., Moreau, F., and Chadee, K. (2012) PPAR γ is an E3 ligase that induces the degradation of NF κ B/p65. *Nat. Commun.* **3**, 1300
- Pascual, G., Fong, A. L., Ogawa, S., Gamliel, A., Li, A. C., Perissi, V., Rose, D. W., Willson, T. M., Rosenfeld, M. G., and Glass, C. K. (2005) A SUMOylation-dependent pathway mediates transrepression of inflammatory response genes by PPAR- γ . *Nature* **437**, 759–763
- Martín, A., Pérez-Girón, J. V., Hernanz, R., Palacios, R., Briones, A. M., Fortuño, A., Zalba, G., Salices, M., and Alonso, M. J. (2012) Peroxisome proliferator-activated receptor- γ activation reduces cyclooxygenase-2 expression in vascular smooth muscle cells from hypertensive rats by interfering with oxidative stress. *J. Hypertens.* **30**, 315–326
- Blanquicett, C., Kang, B. Y., Ritzenthaler, J. D., Jones, D. P., and Hart, C. M. (2010) Oxidative stress modulates PPAR γ in vascular endothelial cells. *Free Radic. Biol. Med.* **48**, 1618–1625
- Adams, M., Reginato, M. J., Shao, D., Lazar, M. A., and Chatterjee, V. K. (1997) Transcriptional activation by peroxisome proliferator-activated receptor γ is inhibited by phosphorylation at a consensus mitogen-activated protein kinase site. *J. Biol. Chem.* **272**, 5128–5132
- Camp, H. S., and Tafuri, S. R. (1997) Regulation of peroxisome proliferator-activated receptor γ activity by mitogen-activated protein kinase. *J. Biol. Chem.* **272**, 10811–10816
- Hu, E., Kim, J. B., Sarraf, P., and Spiegelman, B. M. (1996) Inhibition of adipogenesis through MAP kinase-mediated phosphorylation of PPAR γ . *Science* **274**, 2100–2103
- Camp, H. S., Tafuri, S. R., and Leff, T. (1999) c-Jun N-terminal kinase phosphorylates peroxisome proliferator-activated receptor- γ 1 and negatively regulates its transcriptional activity. *Endocrinology* **140**, 392–397
- Mercer, B. A., and D'Armiento, J. M. (2006) Emerging role of MAP kinase pathways as therapeutic targets in COPD. *Int. J. Chron. Obstruct. Pulmon. Dis.* **1**, 137–150
- Lahiri, S., Sen, T., and Palit, G. (2009) Involvement of glucocorticoid receptor and peroxisome proliferator activated receptor- γ in pioglitazone mediated chronic gastric ulcer healing in rats. *Eur. J. Pharmacol.* **609**, 118–125
- Li, J., Dai, A., Hu, R., Zhu, L., and Tan, S. (2010) Positive correlation between PPAR γ /PGC-1 α and γ -GCS in lungs of rats and patients with chronic obstructive pulmonary disease. *Acta Biochim. Biophys. Sin.* **42**, 603–614
- Lea, S., Plumb, J., Metcalfe, H., Spicer, D., Woodman, P., Fox, J. C., and Singh, D. (2013) The effect of PPAR- γ ligands on *in vitro* and *in vivo* models of COPD. *Eur. Respir. J.* **41**, 1183/09031936.00187812
- Sharma, R., Kaundal, R. K., and Sharma, S. S. (2009) Amelioration of pulmonary dysfunction and neutrophilic inflammation by PPAR γ agonist in LPS-exposed guinea pigs. *Pulm. Pharmacol. Ther.* **22**, 183–189
- Wang, X., Wang, Y., Zhao, X., Andersson, R., Song, Z., and Yang, D. (2009) Potential effects of peroxisome proliferator-activated receptor activator on LPS-induced lung injury in rats. *Pulm. Pharmacol. Ther.* **22**, 318–325
- Lee, S. Y., Kang, E. J., Hur, G. Y., Jung, K. H., Jung, H. C., Lee, S. Y., Kim, J. H., Shin, C., In, K. H., Kang, K. H., Yoo, S. H., and Shim, J. J. (2006) Peroxisome proliferator-activated receptor- γ inhibits cigarette smoke solution-induced mucin production in human airway epithelial (NCI-H292) cells. *Am. J. Physiol. Lung Cell Mol. Physiol.* **291**, L84–90
- Caito, S., Yang, S. R., Kode, A., Edirisinghe, I., Rajendrasozhan, S., Phipps, R. P., and Rahman, I. (2008) Rosiglitazone and 15-deoxy-Delta12,14-prostaglandin J2, PPAR γ agonists, differentially regulate cigarette smoke-mediated pro-inflammatory cytokine release in monocytes/macrophages. *Antioxid. Redox. Signal.* **10**, 253–260
- Li, M., Pascual, G., and Glass, C. K. (2000) Peroxisome proliferator-activated receptor γ -dependent repression of the inducible nitric oxide synthase gene. *Mol. Cell. Biol.* **20**, 4699–4707

Down-regulated Peroxisome Proliferator-activated Receptor γ (PPAR γ) in Lung Epithelial Cells Promotes a PPAR γ Agonist-reversible Proinflammatory Phenotype in Chronic Obstructive Pulmonary Disease (COPD)

Sowmya P. Lakshmi, Aravind T. Reddy, Yingze Zhang, Frank C. Scirba, Rama K. Mallampalli, Steven R. Duncan and Raju C. Reddy

J. Biol. Chem. 2014, 289:6383-6393.

doi: 10.1074/jbc.M113.536805 originally published online December 24, 2013

Access the most updated version of this article at doi: 10.1074/jbc.M113.536805

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August 10, 2018

VIA ELECTRONIC MAIL

ksakabe@asbmb.org

Kaoru Sakabe, Ph.D.

Data Integrity Manager

American Society for Biochemistry and Molecular Biology

11200 Rockville Pike

Suite 302

Rockville, MD 20852

**Re: *Journal of Biological Chemistry* Publication
*Lakshmi, et al. 2014 Article***

Dear Dr. Sakabe:

We represent Mr. Aravind Reddy Tarugu, a co-author of Lakshmi SP, Reddy AT, Zhang Y, Scirba FC, Mallampalli RK, Duncan SR, and Reddy RC, *The Journal of Biological Chemistry* 289(10):6383-6393 (2014), "Down-regulated peroxisome proliferator-activated receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)" (the "Paper"). Mr. Tarugu was notified in January 2016 of an allegation that "the left band in the left panel in the β -actin plot appears to be the same as the left band in the right panel of the pMSK1 blot, flipped by 180°." A joint inquiry on this matter by the University of Pittsburgh (the "University") and the Department of Veterans Affairs ("VA"), led by the University of Pittsburgh, resulted in dismissal of this matter on February 2016. In a follow up by the VA to this dismissal, the VA requested that the University initiate a joint investigation by the University and the VA led by the University, which resulted in a finding that Mr. Reddy falsified Figure 5E.

After receiving the final investigation report, the University and the VA made separate determinations to which we appealed. After the appeals, the University reversed its decision while the VA affirmed the findings of the University investigation report. Dr. Steven Graham, the Research Integrity Officer for the VA, implemented a corrective action plan for Mr. Reddy which requires him to notify JBC not later than August 10, 2018 of the VA's finding against him. This letter constitutes that notice.

Notwithstanding the VA's finding, Mr. Reddy submits that no action should be taken by JBC with regard to the Paper. With all due respect to the VA, its conclusion that the left band in the right panel of the pMSK1 blot was falsified is wrong and without any preponderance of evidence. In fact, in direct contrast to the VA's decision, the University (the lead institute that

Dr. Sakabe
August 10, 2018
Page 2

conducted the investigation), after an appeal to the Provost and a review by an Appeal Panel consisting of five Professors, *unanimously reversed* the finding against Mr. Reddy that had been made by the joint investigation committee. See Attachment No. 1 (redacted copy of Provost Patricia Beeson's April 4, 2018 final decision after appeal) and Attachment No. 2 (redacted copy of the March 27, 2018 recommendation of the University's appeal panel). The Appeal Panel's recommendation for reversing states in pertinent part:

There was disagreement between the two experts who examined the image evidence [as to whether the bands are identical], and that disagreement was not fully addressed and resolved by the Investigative Board. . . [T]he figure panel at the center of the investigation was not essential for the paper's conclusions.

A finding of no misconduct on your part will be reported.

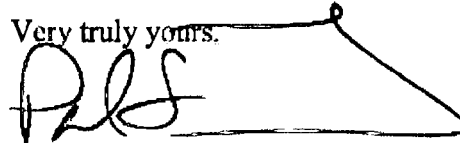
Attachment No. 2 at p.3. In reversing, Provost Beeson expressly withdrew the sanction issued by Assistant Dean Saleem Khan (following the investigation) which would have required Mr. Reddy to retract the Paper – the same sanction being upheld by VA.

The decision of Provost Beeson and the recommendation of the Appeal Panel reversing the finding is supported by two experts in the field, Dr. Alan Price and Dr. John Dahlberg whose opinions are attached as Attachment Nos. 3 and 4, respectively. Dr. Price spent 17 years working with ORI, having served in the latter years as the Associate Director for Investigative Oversight for ORI. During that time, his group was involved with over 3,000 allegations/queries and over 700 formal inquiries or investigations, and they made more than 175 findings of scientific/research misconduct. During his last decade in ORI, Dr. Price reviewed and handled all of the allegations received by ORI from individuals, institutions, and the National Institutes of Health (NIH). Dr. Dahlberg spent 23 years at ORI. In 2006, he became the Director of the Division of Investigational Oversight (DIO), the division within ORI responsible for conducting oversight review of institutional inquiries and investigations involving questioned research funded by the Public Health Service. In mid-2013, he became Deputy Director of ORI where he remained until his retirement in April 2015. During his tenure at ORI, Dr. Dahlberg handled thousands of allegations and dealt with hundreds of cases. Both Dr. Price and Dr. Dahlberg have reviewed the pertinent documents and data, and they agree that a preponderance of the evidence does not establish that the two images are identical. They agree with the University's decision to reverse the finding against Mr. Reddy.

The VA stands alone in its conclusion that the image in Figure 5E was falsified without exhibiting any preponderance of evidence. Neither Provost Beeson, the University's Appeal Panel, Dr. Price or Dr. Dahlberg agree. While we have brought the VA's decision to your attention as directed by Dr. Graham, we respectfully submit that the VA's decision does not warrant that any action be taken with respect to the Paper.

Dr. Sakabe
August 10, 2018
Page 3

Should you or the Publications Committee have any questions or need further information, please do not hesitate to contact me.

Very truly yours.


Paul S. Thaler

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Steven Graham



University of Pittsburgh

Office of the Provost and Senior Vice Chancellor

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4200 Fifth Avenue
Pittsburgh, PA 15260
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Patricia E. Beason
Provost
Senior Vice Chancellor

April 4, 2018

Aravind Tarugu
Senior Research Associate
Department of Medicine
Montefiore NW 628

Dear Mr. Tarugu:

In response to your appeal from the decisions of School of Medicine Assistant Dean for Faculty Affairs Saleem Khan following his receipt of the report of the Investigative Board, an Appeal Panel was appointed. Your appeal requested review of the research misconduct finding [REDACTED]. I have reviewed the Panel's recommendations sent to me in late March, which I am attaching to this letter.

My decision is to accept the recommendation of the Panel that Dr. Khan's finding of research misconduct on your part be reversed [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

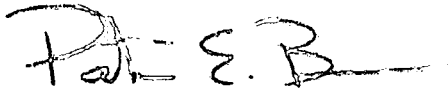
[REDACTED]

Public Health Service Policy requires the University to report the result of the investigation to the Office of Research Integrity, US Department of Health and Human Services. A finding of no research misconduct on your part will be reported.

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED] Therefore this decision

shall be the final disposition of this matter on behalf of the University.

Sincerely,



Patricia E. Beeson

REPORT OF THE APPEAL PANEL

IN THE MATTER OF

████████████████████ ARAVIND REDDY TARUGU

Yuan Chang, MD

Distinguished Professor & American Cancer Society Professor of Pathology

Mary Ganguli, MD

Professor of Psychiatry

Penelope A. Morel, MD

Professor of Immunology

Yoel Sadovsky, MD (Appeal Panel Chair)

Distinguished Professor of Obstetrics, Gynecology & Reproductive Services

John V. Williams, MD

Professor of Pediatrics

March xx, 2018

Introduction

This matter has its origin in a joint Inquiry to assess allegations regarding publications of the Respondent [REDACTED]

[REDACTED] Mr. Aravind Reddy Tarugu, Research Associate, Department of Medicine. The Inquiry was started on January 5, 2016 and involved both the University of Pittsburgh and the VA Pittsburgh Healthcare System (VAPHS), with the University serving as the lead institution at the request of VAPHS. The Inquiry Panel recommended the matter be closed without further investigation and the University accepted the recommendation. However, VAPHS asked that an Investigation be conducted. The University agreed to lead a joint Investigation. An Investigative Board considered this matter and based upon their report School of Medicine Assistant Dean for Faculty Affairs Saleem Khan, PhD, found that Mr. Aravind Reddy Tarugu had committed research misconduct through falsification by publishing the same image twice (as mirror images), but with different descriptions. [REDACTED]

The publication containing the alleged falsification is:

Lakshmi SP, Reddy AT, Zhang Y, Scirba FC, Mallampalli RK, Duncan SR, and Reddy RC. *The Journal of Biological Chemistry* 289(10): 6383-6393 (2014). "Down-regulated Peroxisome Proliferator-Activated Receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)".

On November 27, 2017 Mr. Paul Thaler, on behalf of the Respondent [REDACTED], filed an appeal of these findings and asked that the findings be reversed. On February 9, 2018 the members of the Appeal Panel convened with Dr. Craig Wilcox, Research Integrity Officer of the University of Pittsburgh and Dr. Mara Horwitz, Associate Research Integrity Officer, to discuss the charge to the Appeal Panel and procedures relevant to that charge. The Appeal Panel met again on March 16, 2018.

Grounds for the Appeal of the Finding of Research Misconduct

The University of Pittsburgh 2008 Research Integrity Policy (Policy #11-01-01) states that grounds for an appeal are limited to (1) failure to follow appropriate procedures; (2) insufficiency of evidence; or (3) arbitrary and capricious decision making.

The relevant grounds of the Respondent [REDACTED]' appeal are as follows: (1) There was a failure to follow standard procedures resulting in (a) failure to secure evidence, (b) failure to provide proper notification to the Respondent [REDACTED] prior to the appearance of the witness, and (c) failure to provide for impartial committees during the Inquiry and Investigation. (2) The research misconduct [REDACTED] not demonstrated by a preponderance of the evidence, and the Respondent [REDACTED]' conduct of research is not a "significant departure from accepted practices" and therefore can constitute neither research misconduct [REDACTED].

Appeal Panel Activity

The Appeal Panel convened on February 9, 2018 for initial discussion and to receive evidence considered by the Investigative Board. The Panel also received records of the investigative process, the transcript of the Investigative Board hearing, and correspondence in the record including the June 5, 2017 response from Mr. Thaler and the Respondent [REDACTED] regarding the draft investigative report, the August 2, 2017 additional comments from Mr. Thaler on behalf of the Respondent [REDACTED], the November 27, 2017

communication of the grounds for appeal, and a January 31, 2018 communication from Mr. Thaler regarding supplemental information pertaining to a desktop computer discussed in the report of the Investigative Board. The grounds for an appeal as described by the University of Pittsburgh Research Integrity Policy (cited above) were reviewed. The appeal filed on behalf of the Respondent was discussed and each of the specific grounds for an appeal of the findings of Research Misconduct was discussed.

Following the February 9, 2018 meeting the Appeal Panel considered the record and the documents received in support of the appeal and then reconvened on March 16, 2018.

Appeal Panel Recommendations

The Appeal Panel agreed unanimously to recommend reversal of the finding of Research Misconduct on the part of Mr. Aravind Reddy Tarugu.

[REDACTED]

Appeal Panel Advice Regarding the Grounds for the Appeal

Research Misconduct Finding

The Panel offers the following comments regarding the claims made by the Respondent in the appeal of the research misconduct finding:

The misconduct is based solely on the apparent match of the images. The issue of the bands being identical is not conclusively resolved. There is insufficient evidence of intentionality.

Agreed. There was disagreement between the two experts who examined the image evidence, and that disagreement was not fully addressed and resolved by the Investigative Board.

[REDACTED]

[REDACTED] The Panel also determined that intention was not proven by a preponderance of evidence, including a lack of proof for purposeful image manipulation. The Panel also noted the lack of a motive, as the figure panel at the center of the investigation was not essential for the paper's conclusions.

The investigation was infected with irregularities. Witness procedures were not followed.

Agreed with qualifications. The sequestration process was deficient. The Panel felt the University made the appropriate attempts to sequester the relevant information but the usual procedures were hampered by issues that arose due to VAPHS imposed data security rules and technical capabilities.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

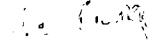
[REDACTED]

[REDACTED]

Signature Page

Panel Member

Date



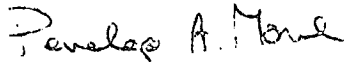
March 28, 2018

Yuan Chang, MD
Distinguished Professor &
American Cancer Society Professor of Pathology



March 29, 2018

Mary Ganguli, MD
Professor of Psychiatry



March 28, 2018

Penelope A. Morel, MD
Professor of Immunology



March 26, 2018

Yoel Sadovsky, MD (Appeal Panel Chair)
Distinguished Professor of Obstetrics, Gynecology & Reproductive Sciences



March 25, 2018

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Paul Thaler and Karen S. Karas, Counsels
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705
Washington, DC 20036

August 10, 2018

RE: Opinion on DVA-required notice to *JBC* Editor by Aravind Reddy on 2014 paper finding

You requested my expert opinion, regarding a Department of Veterans Affairs (DVA) remedial action plan for Mr. Aravind Reddy ("Mr. Reddy"), requiring notification of the *Journal of Biological Chemistry* (*JBC*), following a University of Pittsburgh (UPitt) Appeal Panel Report of March 27, 2018, and the UPitt Provost's acceptance letter of April 4, 2018, reversing the finding of an earlier joint UPitt/Veterans Administration Pittsburgh Health Care System (VAPitt) investigation of research involving two western blot β -actin bands, published in Figure 5E in *JBC* 289(10):6383 (2014), with technical assistance from Mr. Reddy as the second author. You previously provided me with the UPitt/VAPitt inquiry and investigation reports and exhibits, which I reviewed in October 2017 for my expert opinion on the case process and initial findings.

I understand that, given the recent reversal of the UPitt findings, UPitt officials also reversed the proposed sanction that would have required Mr. Reddy to request *JBC* retract this publication. However, I understand that DVA has affirmed its own finding against Mr. Reddy, and DVA is requiring him to notify *JBC* about that finding for this publication.

As background, I was a faculty member at the University of Michigan from 1970-1987. I retired from the federal Office of Research Integrity (ORI) after 17 years in 2006, serving the last six years as ORI Associate Director for Investigative Oversight. We handled over 3,000 allegations/queries and over 700 formal inquiries/investigations and made over 175 findings of scientific/research misconduct. During my last decade there, I reviewed and handled all of the allegations received from individuals, institutions, and the National Institutes of Health (NIH). We also reviewed and analyzed all of the reports of inquiries/investigations by universities, hospitals, and other research institutions funded by NIH research grants. I believe that no one person has seen, handled, and resolved more allegations, investigations, and oversight cases of scientific/research misconduct than I have. I also communicated with many journal editors, including at *JBC*, on correction or retraction of publications with allegedly falsified images or other data. I was a biochemist and member of FASEB's Biochemistry Society which hosts *JBC*. For the past twelve years, I have been consulting formally with individuals and institutional officials on such matters, as Price Research Integrity Consultant Experts (P.R.I.C.E.).

DVA notice to Mr. Reddy on notifying the *JBC* of the DVA's finding

On July 9, 2018, the Research Integrity Officer (RIO) and Associate Chief of Staff, Research and Development at VAPitt, sent a memo to Mr. Reddy, outlining a remedial action plan for him to follow, specifically stating:

You must notify the Journal of Biological Chemistry (*JBC*) of the VA's finding of research misconduct regarding the data published in the *JBC* 289(10):6383-6393 (2014)... [which requires] each author is required to provide details of the finding.

My opinion on Mr. Reddy notifying the *JBC* of DVA's finding of research misconduct

In notifying the Editor of *JBC* of the finding as required in the remedial action plan memo by the VAPitt RIO, I believe Mr. Reddy should quote the research misconduct finding in the joint UPitt/VAPitt investigation committee report:

Statement of Findings - Research Misconduct

We find the allegation stated in the charge to our committee to be true. In Figure 5E of the *JBC* 2014 paper referenced above, the first band in the left panel in the β -actin blot (lane 6) is indeed sufficiently identical to the first band in the right panel of the pMSK1 blot (when reflected across a vertical line) to support the allegation...

We find that the creation and publication of these two images, one derived from the other through digital manipulation, is falsification and that the falsification was intentional. The evidence of intent is that the same image was chosen twice (an action very unlikely to occur by accident) and a mirror image of one of the images was created (a second action very unlikely to occur by accident). We find research misconduct...

I believe Mr. Reddy should also quote the statement in the VAPitt RIO's July 9, 2018, remedial action memo above, that the Network Director of VA Healthcare-VISN 4 had concluded that he:

... committed research misconduct by falsifying data with 2 blots being the mirror image of each other and represented as different blots in a publication.

In addition, I believe Mr. Reddy should quote the conclusions in the March 27, 2018, UPitt Appeal Panel Report (p. 3), with which I very strongly concur:

The Appeal Panel agreed unanimously to recommend reversal of the finding of Research Misconduct on the part of Mr. Aravind Reddy Tarugu....

The Panel offers the following comments regarding the claims made by the Respondent in the appeal of the research misconduct finding:

The misconduct is based solely on the apparent match of the images. The issue of the bands being identical is not conclusively resolved. There is insufficient evidence of intentionality.

Agreed. There was disagreement between the two experts who examined the image evidence, and that disagreement was not fully addressed and resolved by the Investigative Board.... The Panel also determined that intention was not proven by a preponderance of evidence, including a lack of proof for purposeful image manipulation. The Panel also noted the lack of a motive, as the figure panel at the center of the investigation was not essential for the paper's conclusions.

The investigation was infected with irregularities. Witness procedures were not followed.

Agreed with qualifications. The sequestration process was deficient. The Panel felt the University made the appropriate attempts to sequester the relevant information but the usual procedures were hampered by issues that arose due to VAPHS imposed data security rules and technical capabilities.

My opinion on the lack of justification for a retraction of the 2014 *JBC* paper

Based on my almost three decades of reviewing over 800 investigation reports, I strongly agree with the Appeal Panel that intentional falsification by Mr. Reddy, with manipulation of the control blot data in Figure 5E, was not proven by a preponderance of evidence. Therefore, as the Appeal Panel concluded, a research misconduct finding against Mr. Reddy is unwarranted.

I recommend that Mr. Reddy notify the Editor of *JBC*, about the VAPitt finding, supplying the above information, and arguing strongly, as I have, that no retraction of the 2014 *JBC* paper is warranted.

Sincerely,



Alan R. Price, Ph.D.
Price Research Integrity Consultant Experts
Former Associate Director of the U.S. Office of Research Integrity

TO: Paul Thaler, Karen Karas

FROM: John Dahlberg, PhD

DATE: August 10, 2018

SUBJECT: Request of the Department of Veterans Affairs (VA) that Mr. Aravind Reddy notify Journal of Biological Chemistry (JBC) regarding the finding made against him in the matter of JBC paper 289:10, pp. 6383–6393, March 7, 2014 (“the JBC paper”)

I have been asked to opine on the appropriateness of the VA’s adherence to the University of Pittsburgh Investigative Committee’s recommendation that the referenced published paper be retracted by one of the co-authors. By way of background, after twenty five years as a bench scientist, I joined the Office of Research Integrity (ORI) within the Department of Health and Human Services, where I spent an additional twenty three years as a scientist/investigator in the Division of Investigative Oversight (DIO). From 2006-2013 I was the Director of DIO, and from 2013-2015 I served as the Deputy Director of ORI, at which time I retired from federal service. While at ORI, I evaluated thousands of allegations of possible research misconduct, and conducted oversight review and analyzed hundreds of inquiries and investigations of cases of alleged research misconduct involving individuals and institutions from all regions of the United States.

One of the principal objectives of ORI was to help ensure the accuracy of the scientific literature, and when we concurred with institutional findings of research misconduct and made separate findings of misconduct on behalf of the federal government, we typically requested correction or retraction of articles when the scope of the findings warranted such an action. Of course, ORI realized that neither we nor the respondents who agreed to voluntary settlements with ORI could demand that editors retract a paper, as that determination more appropriately rests with the journal’s editors who are more qualified to judge the impact of the misconduct on the overall accuracy of the published manuscript and the impact of the fabrications, falsifications, and/or plagiarism on the scientific community.

I have reviewed the single issue on which the VA determined, based on the Investigative Report made by the University of Pittsburgh and VAPHS’s joint investigation led by the University, that Mr. Reddy had committed research misconduct, thereby warranting, in its view, retraction of the referenced JBC paper. I note that the alleged infraction involves a claim that two bands in Figure 5E appear to be the same.¹ After careful consideration of the appeal to the Provost, the University of Pittsburgh found that there was insufficient evidence to prove that these two bands were identical (or as ORI would phrase it, had a common origin), and did not find that Mr. Reddy had committed research misconduct.

¹ “the first band in the left panel in the β -actin blot appears to be the same as the first band in the right panel of the pMSK1 blot, if one or the other was reflected across a vertical reference line” (University of Pittsburgh Investigation Report, page 5)

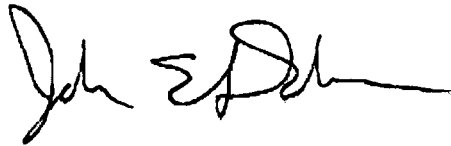
ORI dealt with similar claims on many occasions and nearly always determined that forensic comparison of two bands might show that they appeared very similar or perhaps identical, but that in the absence of additional evidence of possible misconduct, it would be inappropriate to make a finding of research misconduct based on a single possibly duplicated band. In this case, the JBC paper contains multiple figures with western blots containing approximately 150 lanes of blots with approximately 650 separate bands. None of the remaining bands were alleged to have been duplicated. ORI never made findings of research misconduct based on such a flimsy evidentiary basis.

The University Appeal Panel also noted in their response to the UP-investigation report that the figure in question was of marginal significance. The panel also noted that because the questioned panel was not essential to the paper's conclusions, it could not determine that anyone would have had a motive to falsify the figure.

It should also be noted that the questioned images are control blots, and that the research record described two separate experiments containing corresponding blot images.

For these reasons, I respectfully recommend that the editors of JBC agree with UP and Mr. Aravind Reddy to not retract the referenced paper. I am proud of the efforts made by ORI during my tenure to be cognizant of the adverse consequences of a finding of research misconduct to the reputation of a scientist; in cases such as this ORI would not have concurred with the VA's findings or recommendations.

John Dahlberg

A handwritten signature in black ink, appearing to read "John Dahlberg", written in a cursive style.

From: Paul S. Thaler <pthaler@cohenseglias.com>
Sent: Wednesday, August 22, 2018 4:56 PM
To: 'Kaoru Sakabe'
Cc: Karen S. Karas
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Here is the response I received from my clients:

"No one has access to these files.

The LiCor that was used to generate these images was located in a common facility, used by multiple users.

This instrument and its associated computer are no longer operational and were replaced by an upgraded system."

Please let me know if there is anything else I can do to assist you.

Sincerely,

Paul

Paul S. Thaler ■ Partner

Cohen Seglias Pallas Greenhall & Furman PC

1828 L Street, NW, Suite 705 ■ Washington, DC 20036

P: 202.466.4110 ■ F: 202.380.0218

[website](#) | [vCard](#) | [offices](#) | [email](#)



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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Tuesday, August 21, 2018 10:29 AM
To: Paul S. Thaler

Cc: Karen S. Karas

Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for providing these data. It seems the authors used a LICOR imaging system to obtain these data. Do the authors have access to the LICOR acquisition zip files? If so, would they be able to provide these data?

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Paul S. Thaler" <pthaler@cohenseglias.com>

Date: Monday, August 20, 2018 at 2:48 PM

To: Kaoru Sakabe <ksakabe@asbmb.org>

Cc: "Karen S. Karas" <kkaras@cohenseglias.com>

Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Please find attached the files you requested.

Thank you for your attention to this.

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From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Thursday, August 16, 2018 at 2:26 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

This will confirm that we also represent Dr. Raju Reddy. We are happy to help get your questions answered.

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Sent: Thursday, August 16, 2018 2:01 PM
To: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for your patience. From your letter, it sounds like you represent only Mr. Aravind Reddy and not Dr. Raju Reddy, the corresponding author. Please confirm as we have questions for the authors.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
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ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Saturday, August 11, 2018 at 7:19 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Thank you, Dr. Sakabe. We look forward to hearing from you.

Sincerely,

Paul S. Thaler, Esq.
Cohen Seglias Pallas Greenhall & Furman PC
(202) 587-4750

Sent from my iPad

On Aug 10, 2018, at 2:58 PM, Kaoru Sakabe <ksakabe@asbmb.org> wrote:

Dear Mr. Thaler,

Thank you for your letter. Please allow us some time to review the information.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org


[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: Cynthia Roberson <croberson@cohenseglias.com>
Date: Friday, August 10, 2018 at 11:54 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Good afternoon Dr. Sakabe.

Please see attached letter on behalf of Paul S. Thaler regarding the above reference matter. Should you have any questions or concerns, please do not hesitate to contact Mr. Thaler.

Thank you
Cynthia

Cynthia Roberson <Administrative Assistant
Cohen Seglias Pallas Greenhall & Furman PC

1828 L Street, NW, Suite 705<image001.gif>Washington, DC 20036
P: 202.466.4110<image001.gif>F: 202.466.2693

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<image002.png>
<image003.gif><image004.gif>

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From: Paul S. Thaler <pthaler@cohenseglias.com>
Sent: Thursday, August 30, 2018 3:10 PM
To: 'Kaoru Sakabe'
Cc: Karen S. Karas
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]
Attachments: 2018-07-24 & 25 Emails between Aravind and Khan_Redacted.pdf

Dear Dr. Sakabe:

This email responds to (1) your August 23, 2018 email requesting a copy of the report from the VA as well as unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter and (2) your August 29, 2018 email requesting original data to Figs 1A and 6A.

Regarding the requests in your August 23, 2018 email – we decline to provide unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter. Those documents contain confidential information and were redacted at the suggestion of Dean Saleem Khan. A redacted copy of Mr. Aravind Tarugu's email exchange with Dean Khan is attached. We also decline to provide a copy of the VA's report. We have been informed by the VA that the finding against Mr. Tarugu will not be published. Therefore, Mr. Tarugu is entitled to maintain the report's confidentiality.

Regarding the requests in your August 29, 2018 email - we decline to provide the requested data. As you know, my clients have been fully cooperative and have thus far provided you the all the data and information you have requested, even the data requested in your August 16, 2018 that is not relevant to the subject matter (β -actin blot and the pMSK1 blot in Figure 5E). Your August 29, 2018 email requests additional data that is not relevant to the scope of our initial communication to you (our August 10, 2018 letter) or to Mr. Tarugu's obligation to notify you regarding the VA's finding with respect to Figure 5E.

My clients will continue to cooperate in any way they can with respect to any additional questions you may have regarding the β -actin blot and the pMSK1 blot in Figure 5E.

Thank you for your attention to this.

Sincerely,

Paul S. Thaler ■ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ■ Washington, DC 20036
P: 202.466.4110 ■ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Wednesday, August 29, 2018 3:15 PM
To: Paul S. Thaler .
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

In addition to the below documents, we would like to review the original data to Figs 1A and 6A.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: Kaoru Sakabe <ksakabe@asbmb.org>
Date: Thursday, August 23, 2018 at 3:19 PM
To: "Paul S. Thaler" <pthaler@cohenseglia.com>
Cc: "Karen S. Karas" <kkaras@cohenseglia.com>
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for this information. Would you be able to provide a non-redacted version of attachments 1 and 2 from your letter? Additionally, we would like to review the report from the VA.

Sincerely,
Kaoru Sakabe, PhD
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From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Wednesday, August 22, 2018 at 4:56 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Here is the response I received from my clients:

"No one has access to these files.
The LiCor that was used to generate these images was located in a common facility, used by multiple users.
This instrument and its associated computer are no longer operational and were replaced by an upgraded system."

Please let me know if there is anything else I can do to assist you.

Sincerely,

Paul
Paul S. Thaler ▪ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ▪ Washington, DC 20036
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From: Cynthia Roberson <croberson@cohenseglias.com>

Date: Friday, August 10, 2018 at 11:54 AM

To: Kaoru Sakabe <ksakabe@asbmb.org>

Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>

Subject: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

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Thank you
Cynthia

Cynthia Roberson<image001.gif>Administrative Assistant
Cohen Seglias Pallas Greenhall & Furman PC
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Tarugu, Aravind Reddy

From: Khan, Saleem A
Sent: Wednesday, July 25, 2018 11:57 AM
To: Tarugu, Aravind Reddy
[REDACTED]
Subject: RE: Request

Dear Aravind:

The April 4, 2018 letter from Provost Beeson is the official notification from the University regarding the disposition of your appeal, as the Provost is the highest ranking academic officer. It would be inappropriate for an additional letter to be generated. If there is information included in the notification that you do not wish to share with the JBC, I would suggest considering a redaction. Sorry I could not be of further assistance.

Sincerely,

Saleem A. Khan, Ph.D.
Associate Dean for Academic Affairs
Professor
Department of Microbiology and Molecular Genetics
University of Pittsburgh School of Medicine
S527 Scaife Hall
Pittsburgh, PA 15261
Office (412) 648 – 3911
E-mail: khan@pitt.edu

From: Tarugu, Aravind Reddy
Sent: Tuesday, July 24, 2018 11:56 AM
To: Khan, Saleem A <khan@pitt.edu>
[REDACTED]
Subject: Request

Dear Dean Khan,

As you may be aware, the VA Undersecretary upheld the decision made by ORO [REDACTED]. I was contacted by the VA to send a notification of this VA finding to JBC. As the University of Pittsburgh, the lead institute of this investigation overturned this decision, I would like to send this response letter to JBC along with the VA ORO letter. As the letter from the Provost (dated April 4, 2018) includes confidential information and internal findings, I cannot use it in the current format.

I request that you provide me with a letter stating a finding of no research misconduct on my part, [REDACTED]
[REDACTED]

I have a deadline for sending this notification (August 10, 2018), hence I kindly request your immediate attention to this matter.

Thank you in advance for your help. I appreciate it.



Paul S. Thaler
Attorney At Law

1828 L Street, NW
Suite 705
Washington, DC 20036

T: 202.466.4110 | F: 202.380.0218
pthaler@cohenseglias.com
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September 12, 2018

VIA ELECTRONIC MAIL

ksakabe@asbmb.org

Kaoru Sakabe, Ph.D.

Data Integrity Manager

American Society for Biochemistry
and Molecular Biology

11200 Rockville Pike

Suite 302

Rockville, MD 20852

***Re: Journal of Biological Chemistry Publication
Lakshmi, et al. 2014 Article***

Dear Dr. Sakabe:

I write to follow up on our continuing dialogue regarding the above-referenced paper. First, I want to let you know that neither we nor our clients realized that the document attached to your August 31, 2018 email constituted the totality of JBC's analysis of the images, so we appreciate your having confirmed that fact in your September 7, 2018 email. Second, we want to address any misunderstanding that you or any of JBC's Editors might have had in response to our August 30, 2018 email (objecting to providing data for additional figures). Third, we want to share with you and the JBC Editors the original images and their forensic analyses undertaken by our clients, which is attached and discussed below, and which we hope the JBC editors will find helpful.

As you know, the reason we contacted you in August was because Mr. Aravind R. Tarugu was directed to do so by Dr. Steven Graham, the research integrity officer of the Department of Veteran Affairs' ("VA"). The only figure about which the VA is concerned (and thus the narrow focus of our initial communication to you) is Figure 5E (specifically, two panels in Figure 5E, beta actin and pMsk1). However, in response to our initial August letter, you requested original data not only for Figure 5E, but Figures 3C and 4C as well. Even though JBC's request went beyond the concern of the VA, my clients provided all of the requested data. They also answered your follow-up inquiry regarding the LICOR imaging system. When, however, JBC further expanded its inquiry to include Figures 1A and 6A, it was, in our opinion, appropriate to set limits on what seemed to us to be an ever expanding inquiry that was getting

Dr. Sakabe
September 12, 2018
Page 2

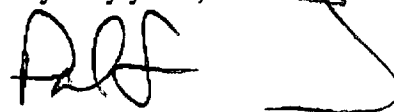
further and further away from the concern of the VA (two panels in Figure 5E). That is what lead to our August 30, 2018 email to you objecting to JBC's request for data related to Figures 1A and 6A. We were surprised to then receive your August 31, 2018 email advising us of the decision of JBC's Editors that Figures 1A and 6A, and Figures 3C and 4C, contained duplications and that they had decided the article should be withdrawn.

Our clients strongly disagree with the decision of the Editors that the article should be withdrawn. We request that the Editors carefully review the attachments to this letter and then reconsider and reverse their decision. Mr. Tarugu and Dr. Reddy are deeply concerned that the Editors reached their conclusions regarding the subject Figures (Figures 1A and 6A, 3C and 4C, and 5E) without reviewing the *original images* and without completing a proper *forensic* analysis. The pdf attachment to your August 31, 2018 email does not reveal that any such forensic analysis of any of the images was undertaken.

As shown in Attachment No.2 to this letter, when the original images are reviewed or forensically analyzed as instructed by the Department of Health and Human Service's Office of Research Integrity, it is apparent that there is *no* duplication of images in Figures 1A, 6A, 3C, 4C and 5E. Attachment No. 1 is a letter from Dr. Reddy and Mr. Tarugu explaining the forensic analyses they undertook and the tools they employed. The results of the forensic analyses regarding Figure 5E are further supported by lab notebook pages (included as part of Attachment No. 2 at p. 7) as well as the expert opinion of Dr. John C. Russ (included as part of Attachment No. 2 at p.6).

On behalf of Mr. Tarugu and Dr. Reddy, we thank you and the Editors for considering these additional materials. For all these reasons, and those stated in the attached letter and analyses, we request that JBC's Editors reconsider their decision and conclude instead that withdrawal of the article is not necessary. Dr. Reddy and Mr. Tarugu will continue to cooperate and will answer any questions that the Editors may have regarding the attached letter and analyses. Our clients are willing to provide additional information consistent with the positions we have taken in our prior communications .

Very truly yours,



Paul S. Thaler

Attachments

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Raju C. Reddy

September 11, 2018

Dear Dr. Sakabe:

On August 10, 2018, Mr. Thaler, on behalf of Mr. Tarugu, sent you a letter as notification to the Journal of Biological Chemistry (hereafter “JBC”) (hereafter “*Notice to JBC*”), as required by the Department of Veterans Affairs (“VA”), regarding the VA’s finding made related to Figure 5E beta actin and pMsk1 in the Lakshmi et al. 2014 article. In response to the *Notice to JBC*, JBC requested that we provide data for additional images. Even though that request went beyond the scope of the initial *Notice to JBC*, in the spirit of cooperation and disclosure, we provided the data as requested. We then received a further request, on August 29, to provide additional images not related to the image in question as outlined in the *Notice to JBC*. As we had not received an explanation for this request and the requested images were beyond the scope of the *Notice to JBC*, we respectfully declined to provide this data, yet indicated our full cooperation to provide any additional information related to Figure 5E beta actin and pMsk1.

On August 31st, 2018, we were notified by JBC via our attorney Mr. Thaler that “*the Editors are requesting that the authors withdraw this article*” adding “*In addition to the duplication in Fig 5E, we determined the following:*”

- *The PPAR γ blot from Fig 1A was reused in Fig 6A as pAcK-H3 and H3*
- *The Lamin B1 blot from Fig 3C was reused in Fig 4C as H3*”

Attached to JBC’s August 31, 2018 email was a PDF attachment (hereafter “*JBC Analysis*”) providing pictorial information as a basis for the above determination. Since we did not receive any additional information regarding this analysis, such as the source of images, software tools used, and interpretations made based on such analysis, we are not able to understand from the *JBC Analysis* how JBC reached its conclusions regarding image duplication. However, after reviewing the images in the *JBC Analysis*, it appears that JBC used snapshots of images from the Lakshmi et al. 2014 article to perform an image analysis to which a color gradient was applied on figure 1A, 6A and 5E to determine if reuse of the images occurred. Our understanding that JBC used snapshots comes from the existence of border lines below and above the images of interest as we prepared the figures with the outlines for publication. The *JBC Analysis* does not reveal any analysis performed on figures 3C and 4C, and, thus, JBC’s conclusion regarding those figures seems to be based entirely on a naked eye comparison. Additionally, no information on histogram equalization was provided in the *JBC Analysis*. As we believe that snapshots were used and no histogram equalization was performed prior to JBC’s image analysis, these factors may have resulted in some of the inaccuracies with the *JBC Analysis*.

In light of our concern about the *JBC Analysis* and the fact that JBC’s inquiries have now surpassed the original scope of both the *Notice to JBC* and the VA’s concern, we are attaching to Mr. Thaler’s letter (as Attachment No. 2) the images for the above-mentioned figures and detailed forensic image analyses performed with these images. As you can see, the images themselves, when evaluated in their proper context, ***provide conclusive evidence*** that no images were reused. In addition, however, we are providing additional incontrovertible image analysis to further demonstrate lack of reuse. The tools and procedures we used for analyzing these images

are provided below. We used two different advanced approaches to perform forensics image analysis. The availability and application of these tools is well documented in the literature and in the relevant online sections. We are able to provide any additional details regarding these tools as necessary.

1. Using NIH Office of Research Integrity (ORI) Advanced Forensic Actions tools in Adobe Photoshop: In this process histogram equalized images were applied with advanced dark or light areas and advanced gradient map to determine the similarities or differences (in our case) between images. The preset actions will allow the user to limit personal biases.
2. Using image segmentation, thresholding, and sobel gradient in MATLAB Image Processing Toolbox: In this process histogram equalized image is portioned into regions based on the pixel characteristics of the image. This will find the discontinuities in pixel values and indicated edges. This process eliminates biases as the process is performed as a coded program.
3. Use of notebook entries: Along with image analysis and original images, we also provided lab notebook entries related to Figure 5E beta actin and pMsk1 performed ~6 months apart by two different researchers.

Forensic analysis of our images clearly shows the differences between each allegedly duplicated image. These differences include:

- a) Several differences in excised borders of membrane and its size.
- b) Presence of protein marker lanes in the blots.
- c) Several differences in heatmaps and gradient maps of images and bands.
- d) Several differences in backgrounds of the images.

All of the above differences reflect very clear and conclusive results from rigorous analysis versus analysis performed in a non-rigorous manner (using the naked eye, or focusing on singular images or general visual effects).

Along with these analyses, we provide the forensics image analysis performed by Dr. John Russ (included in Attachment No. 2 to Mr. Thaler's September 11, 2018 letter). Dr. Russ has authored several highly regarded and cited works on image processing. His book "The Image Processing Handbook" has been consistently rated as the best overall introduction to computer-based image processing and has been cited >4,000 times according to Google citations. He has also been awarded the Ernst Abbe Memorial Award for his contributions to the field.

In our *Notice to JBC*, we also provided evaluations from Dr. Alan Price and Dr. John Dahlberg, two highly respected, independent experts who retired after long careers in senior level positions at NIH's ORI and have extensive experience reviewing thousands of allegations and misconduct/data manipulation cases. Both experts independently agreed with us and explained why the paper should not be retracted. We also emphasize that the University of

Pittsburgh was the lead institute of this investigation and *concluded that there was no misconduct and that there was no evidence of image reuse.*

With all the above factual evidence, we respectfully decline to withdraw our article.

Sincerely,

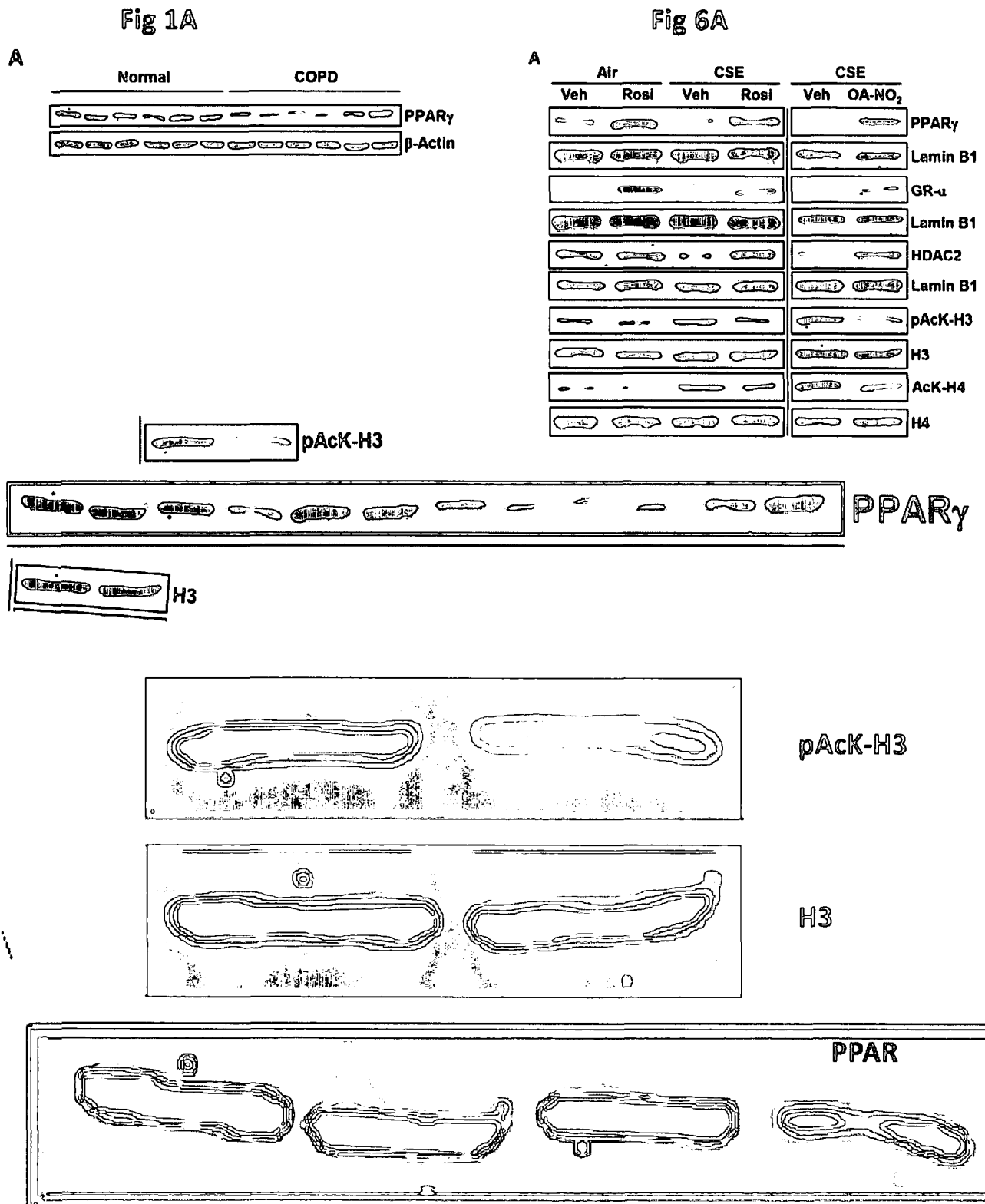
Aravind T. Reddy
Aravind Reddy Tarugu

Raju Reddy
Raju C. Reddy

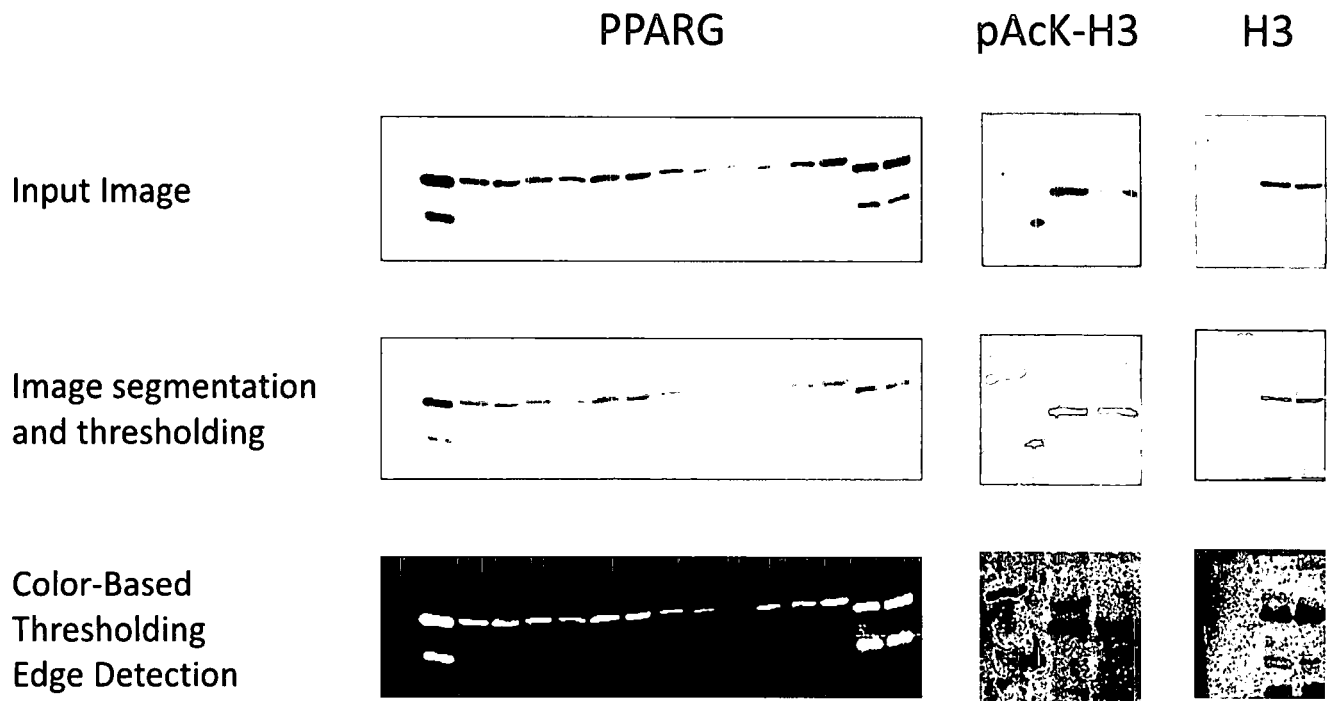
JBC: Figure 1A (PPAR gamma) and 6A (pAckH3; H3).

Same data used to represent different experimental conditions

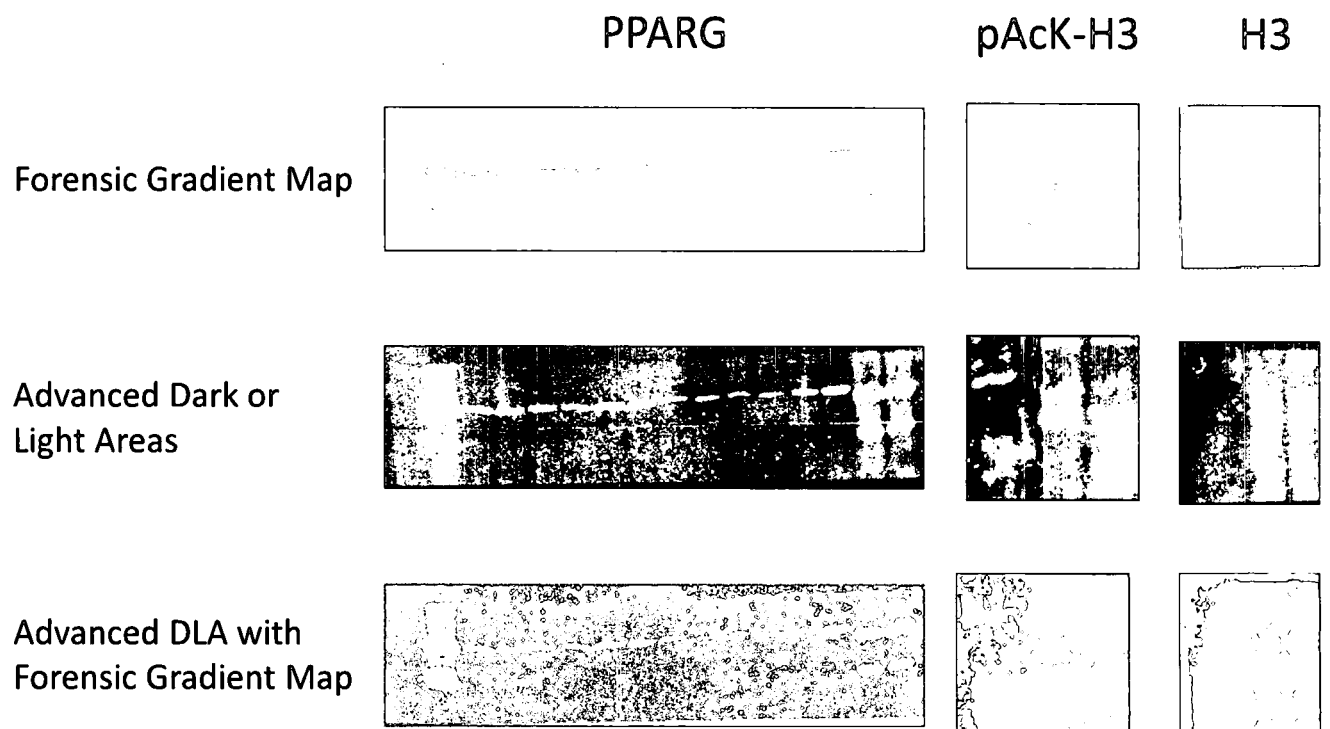
Reddy RC
JBC/2013/536805
Figs 1A and 6A



Forensic Image analysis was performed with
MATLAB (The Image Processing Toolbox)



Forensic Image analysis performed with Adobe Photoshop using
NIH Office of Research Integrity (ORI) Advanced Forensic Actions



JBC: Figure 3C (Lamin B1) and 4C (H3).

Same data used to represent different experimental conditions

Reddy RC
JBC/2013/536805
Figs 3C and 4C

Fig 3C

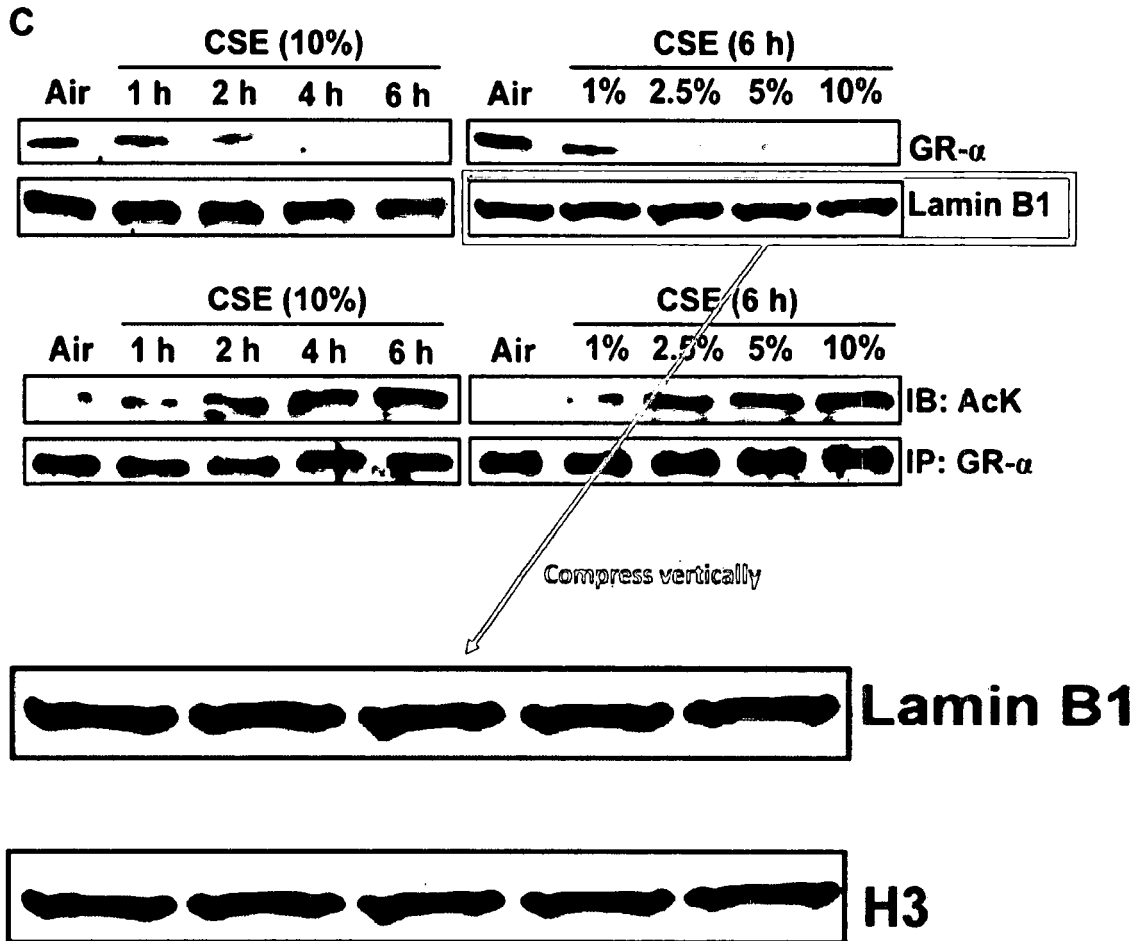
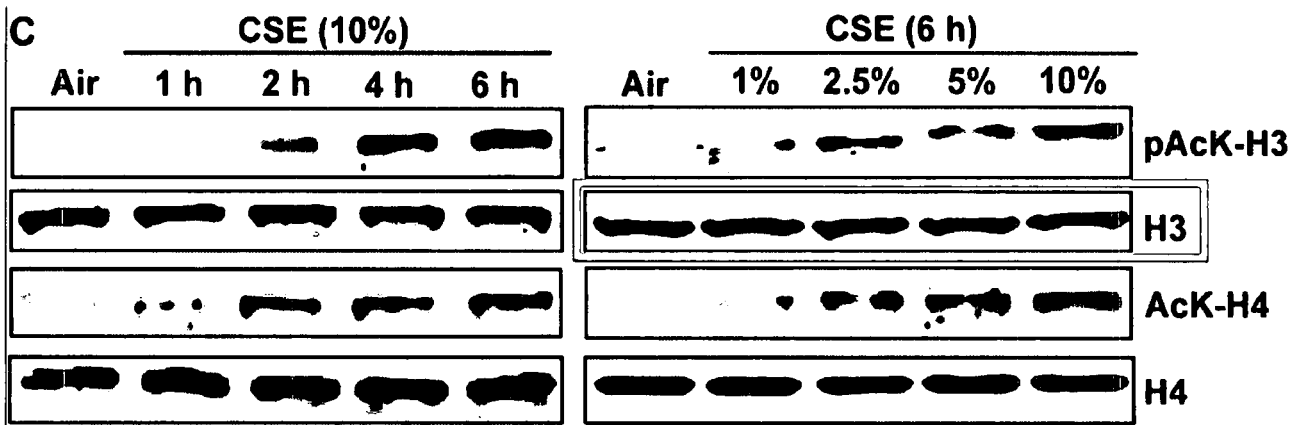
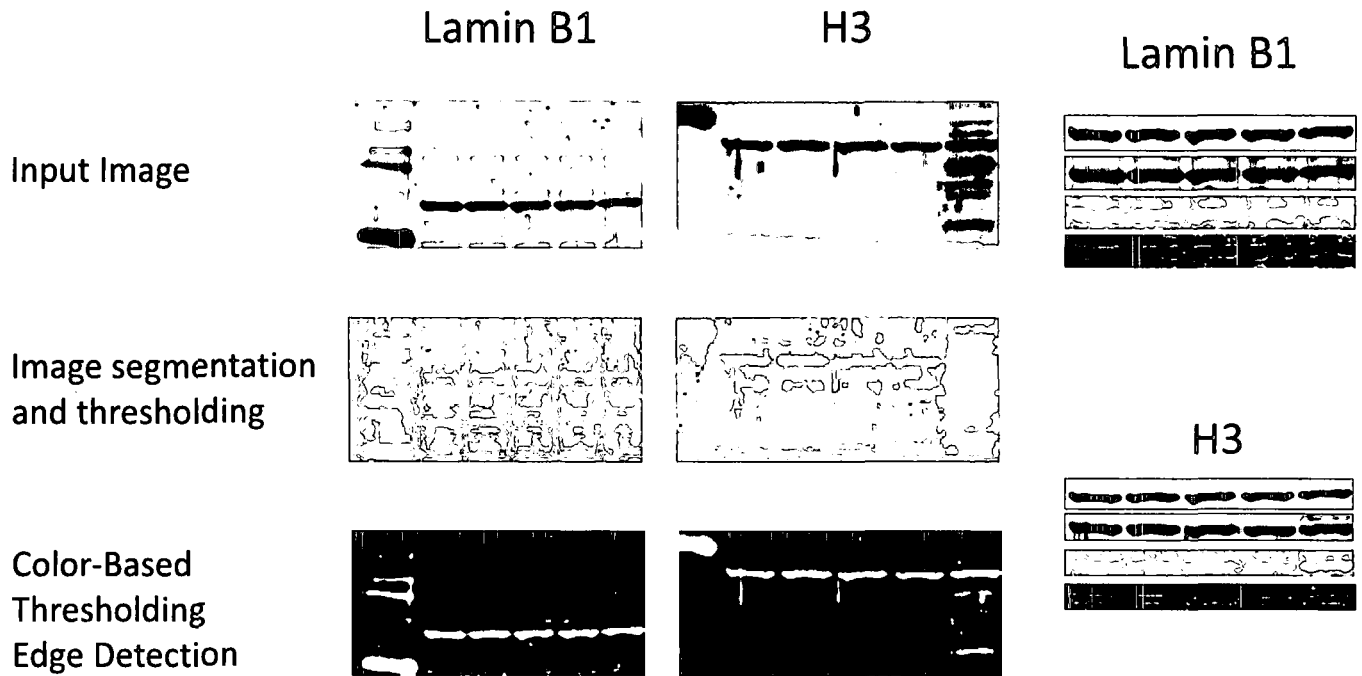


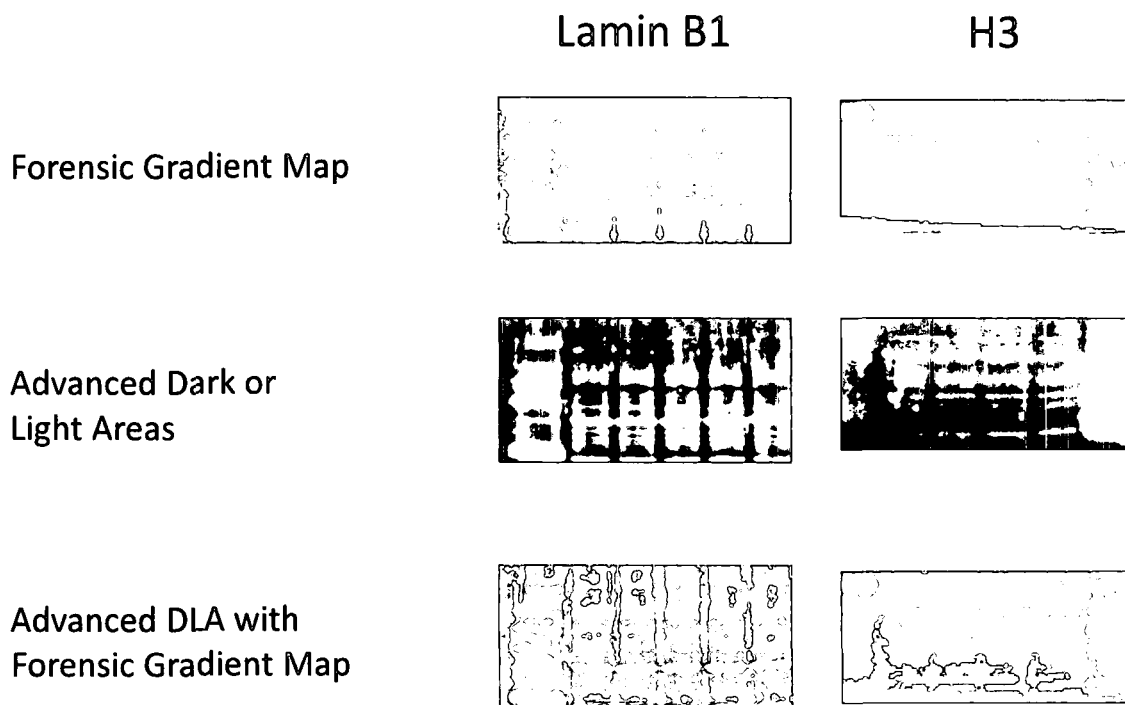
Fig 4C



Forensic Image analysis was performed with
MATLAB (The Image Processing Toolbox)



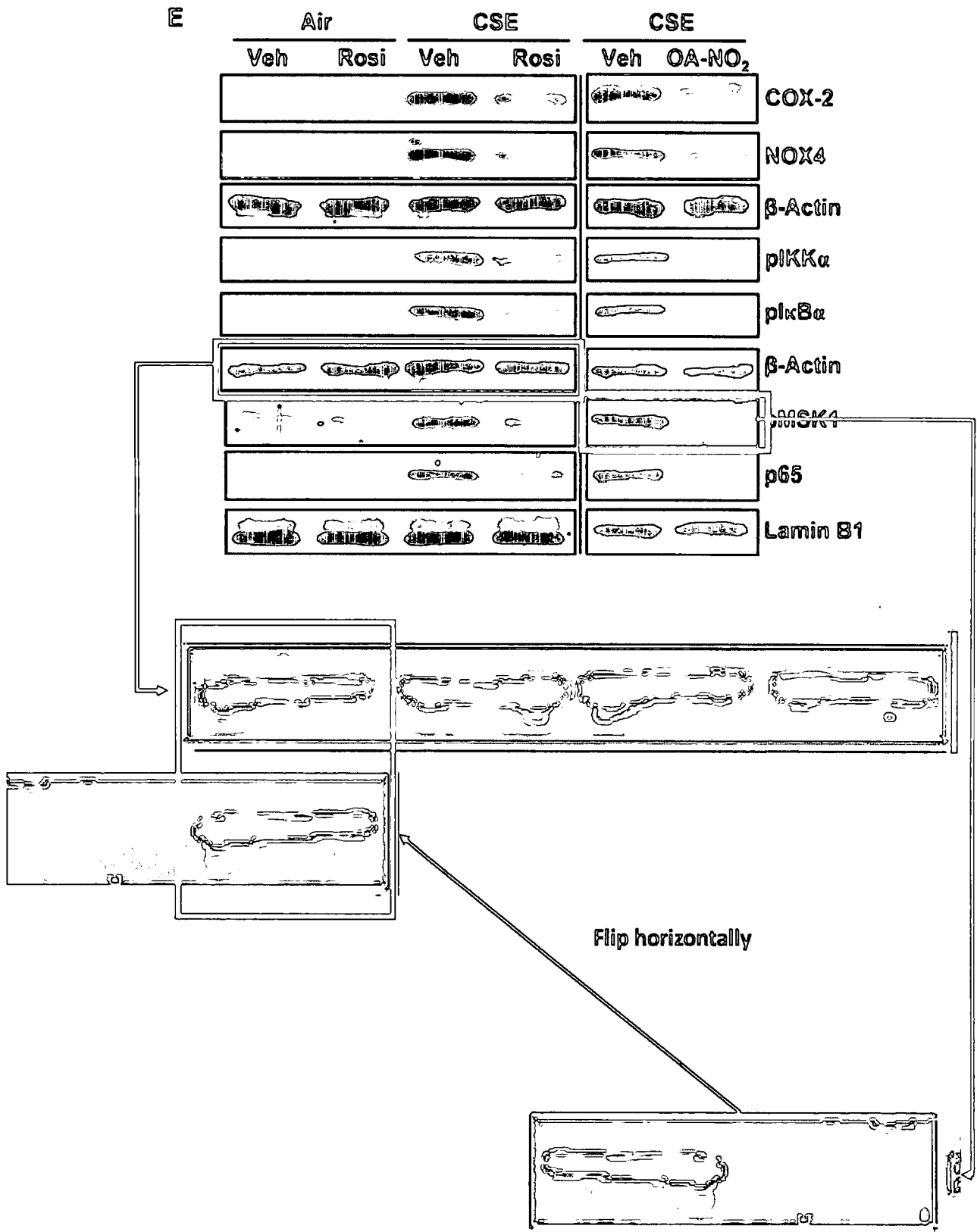
Forensic Image analysis performed with Adobe Photoshop using
NIH Office of Research Integrity (ORI) Advanced Forensic Actions



JBC: Figure 5E (bActin and pMsk1).

Same data used to represent different experimental conditions

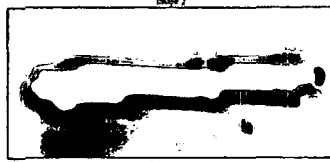
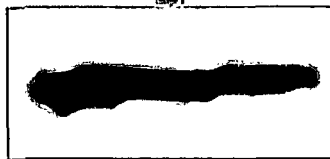
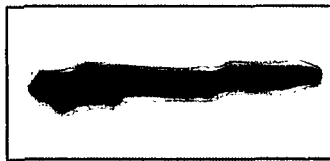
Reddy RC
JBC/2013/536805
Fig 5E



Forensic Image analysis performed by Dr. John C. Russ

Several important differences are noteworthy.

First, nearly the entire border of the difference image is dark, indicating that one blot image is definitely larger than the other.



Second, along the border there are variations in the density difference that are not uniform. In other words, one image could not be generated by simply enlarging the other or applying an overall brightness adjustment, which would have produced the same density all along the border. This is especially marked at the right edge, where an entirely different shape is revealed.

Third, there are several locations within the dense region (bright in the image shown) where pixels are slightly darkened indicating different densities in the original images.

Fourth, there are numerous regions in the surrounding areas that do not match, producing various darkened or lightened regions. That indicates that the images of the substrates are different.

From these differences, there is no doubt in my mind that the two original images are distinct.

Forensic Image analysis was performed with
MATLAB (The Image Processing Toolbox)

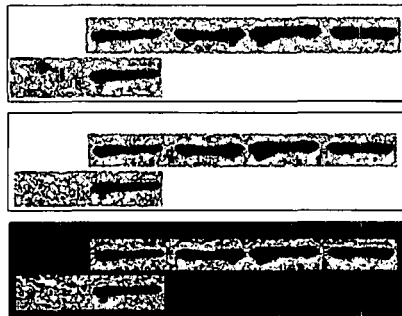
Forensic Image analysis performed with Adobe
Photoshop using
NIH Office of Research Integrity (ORI)
Advanced Forensic Actions

Input Image
Histogram Equalized

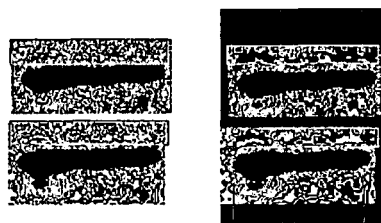


Beta Actin
pMsk1 (Flipped for Analysis)

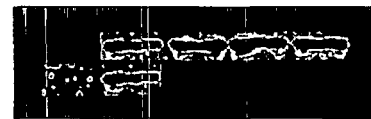
Image segmentation and thresholding to detect edges



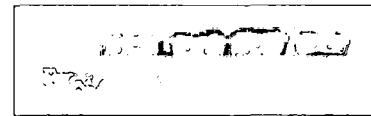
Key differences between two images in terms of band shape threshold and background



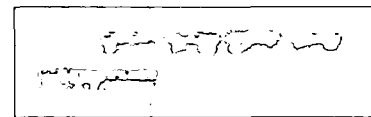
Advanced Dark or Light Areas (Gray)



Forensic Gradient Map 1



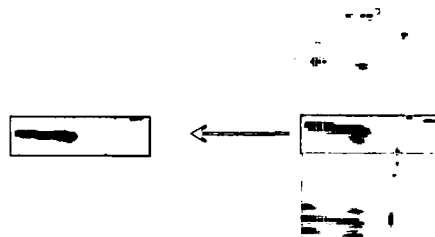
Forensic Gradient Map 2



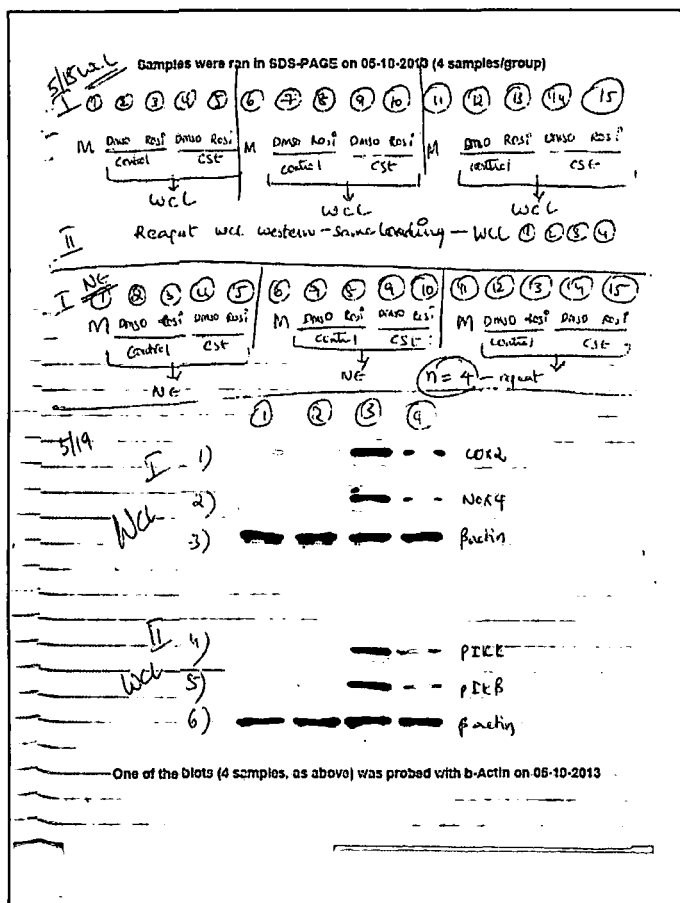
Other Evidence

- 1) Full blot of pMsk1 showing a two lane small blot.
- 2) Experimental details of Beta Actin ran on 05-18-2013 to 05-19-2013
- 3) Experimental details of pMsk1 ran on 10-05-2013 to 10-06-2013

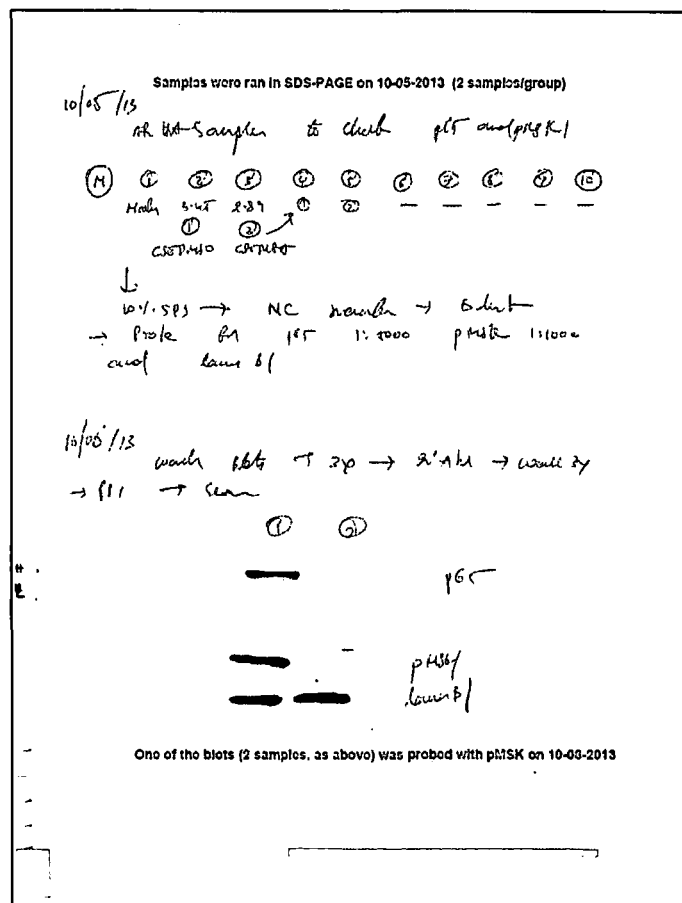
1



2



3



From: Kaoru Sakabe <ksakabe@asbmb.org>
Sent: Friday, August 31, 2018 8:41 AM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]
Attachments: Reddy 536805.pdf

Dear Mr. Thaler,

Thank you for your message. In addition to the duplication in Fig 5E, we determined the following:

- The PPAR γ blot from Fig 1A was reused in Fig 6A as pAcK-H3 and H3
- The Lamin B1 blot from Fig 3C was reused in Fig 4C as H3

In light of these issues, the Editors are requesting that the authors withdraw this article. Please communicate this decision to all authors. Please request withdrawal by September 14, 2018. If the authors choose to withdraw the article, we will work with them to draft a mutually agreeable withdrawal notice. If the authors do not withdraw the article, then we will forward this matter to the ASBMB Publications Committee. The Committee may request more information, request a draft of a correction notice for editorial approval, or determine that the article is to be retracted. If the Committee determines that retraction is warranted, no further appeals will be considered and ASBMB will draft and publish a retraction notice.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Thursday, August 30, 2018 at 3:09 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe:

This email responds to (1) your August 23, 2018 email requesting a copy of the report from the VA as well as unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter and (2) your August 29, 2018 email requesting original data to Figs 1A and 6A.

Regarding the requests in your August 23, 2018 email – we decline to provide unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter. Those documents contain confidential information and were redacted at the suggestion of Dean Saleem Khan. A redacted copy of Mr. Aravind Tarugu's email exchange with Dean Khan is attached. We also decline to provide a copy of the VA's report. We have been informed by the VA that the finding against Mr. Tarugu will not be published. Therefore, Mr. Tarugu is entitled to maintain the report's confidentiality.

Regarding the requests in your August 29, 2018 email - we decline to provide the requested data. As you know, my clients have been fully cooperative and have thus far provided you the all the data and information you have requested, even the data requested in your August 16, 2018 that is not relevant to the subject matter (β -actin blot and the pMSK1 blot in Figure 5E). Your August 29, 2018 email requests additional data that is not relevant to the scope of our initial communication to you (our August 10, 2018 letter) or to Mr. Tarugu's obligation to notify you regarding the VA's finding with respect to Figure 5E.

My clients will continue to cooperate in any way they can with respect to any additional questions you may have regarding the β -actin blot and the pMSK1 blot in Figure 5E.

Thank you for your attention to this.

Sincerely,

Paul S. Thaler ◻ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Wednesday, August 29, 2018 3:15 PM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

In addition to the below documents, we would like to review the original data to Figs 1A and 6A.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: Kaoru Sakabe <ksakabe@asbmb.org>
Date: Thursday, August 23, 2018 at 3:19 PM
To: "Paul S. Thaler" <pthaler@cohenseglias.com>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for this information. Would you be able to provide a non-redacted version of attachments 1 and 2 from your letter? Additionally, we would like to review the report from the VA.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Wednesday, August 22, 2018 at 4:56 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Here is the response I received from my clients:

"No one has access to these files.

The LiCor that was used to generate these images was located in a common facility, used by multiple users.

This instrument and its associated computer are no longer operational and were replaced by an upgraded system."

Please let me know if there is anything else I can do to assist you.

Sincerely,

Paul

Paul S. Thaler ◻ Partner

Cohen Seglias Pallas Greenhall & Furman PC

1828 L Street, NW, Suite 705 ◻ Washington, DC 20036

P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]

Sent: Tuesday, August 21, 2018 10:29 AM

To: Paul S. Thaler

Cc: Karen S. Karas

Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for providing these data. It seems the authors used a LICOR imaging system to obtain these data. Do the authors have access to the LICOR acquisition zip files? If so, would they be able to provide these data?

Sincerely,

Kaoru Sakabe, PhD

Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Monday, August 20, 2018 at 2:48 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Please find attached the files you requested.

Thank you for your attention to this.

Sincerely,

Paul
Paul S. Thaler ◻ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [<mailto:ksakabe@asbmb.org>]
Sent: Thursday, August 16, 2018 2:29 PM

To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for the quick response. We would be interested in reviewing the original data for Figs 3C, 4C, and 5E. We would prefer that these images be provided uncropped and minimally processed.

Thank you in advance for your help.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
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[Journal of Lipid Research](#)

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Thursday, August 16, 2018 at 2:26 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

This will confirm that we also represent Dr. Raju Reddy. We are happy to help get your questions answered.

Sincerely,

Paul S. Thaler ◻ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0218

[website](#) | [vCard](#) | [offices](#) | [email](#)



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message, please reply to the sender that you received the message in error and delete all copies of the message from your computer and network. Dissemination, copying, or other use of this message by any person or entity other than the intended recipient is strictly prohibited.

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Thursday, August 16, 2018 2:01 PM
To: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for your patience. From your letter, it sounds like you represent only Mr. Aravind Reddy and not Dr. Raju Reddy, the corresponding author. Please confirm as we have questions for the authors.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Saturday, August 11, 2018 at 7:19 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Thank you, Dr. Sakabe. We look forward to hearing from you.

Sincerely,

Paul S. Thaler, Esq.
Cohen Seglias Pallas Greenhall & Furman PC
(202) 587-4750

Sent from my iPad

On Aug 10, 2018, at 2:58 PM, Kaoru Sakabe <ksakabe@asbmb.org> wrote:

Dear Mr. Thaler,

Thank you for your letter. Please allow us some time to review the information.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: Cynthia Roberson <croberson@cohenseglia.com>
Date: Friday, August 10, 2018 at 11:54 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglia.com>
Subject: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Good afternoon Dr. Sakabe.

Please see attached letter on behalf of Paul S. Thaler regarding the above reference matter. Should you have any questions or concerns, please do not hesitate to contact Mr. Thaler.

Thank you
Cynthia

Cynthia Roberson<image001.gif>Administrative Assistant
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705<image001.gif>Washington, DC 20036
P: 202.466.4110<image001.gif>F: 202.466.2693

website | offices | email
<image002.png>
<image003.gif><image004.gif>

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Same data used to represent different experimental conditions

Reddy RC
JBC/2013/536805
Figs 1A and 6A

Fig 1A

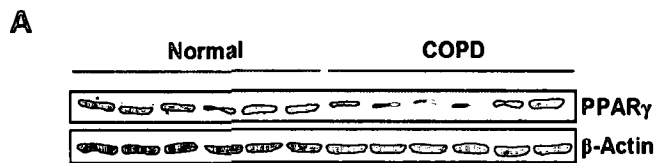


Fig 6A

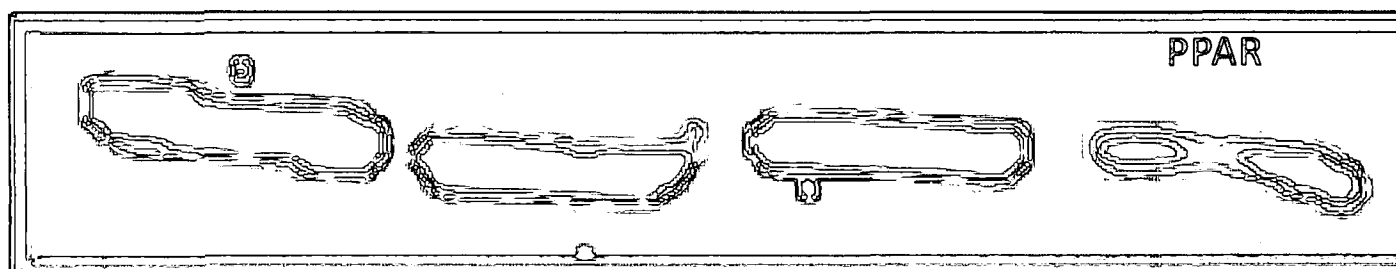
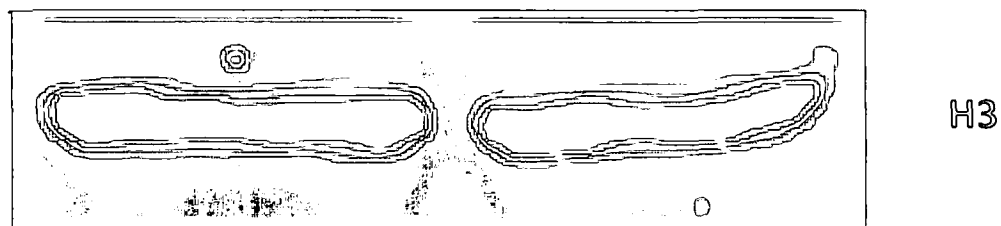
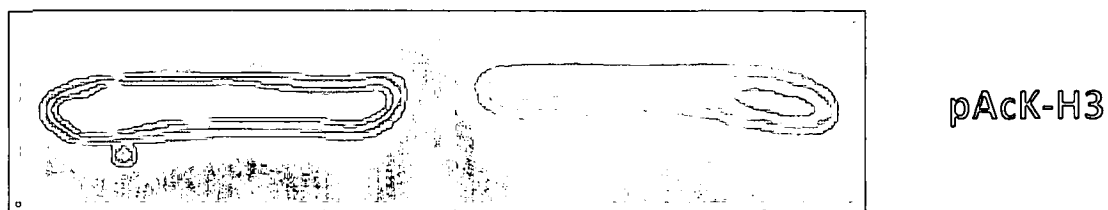
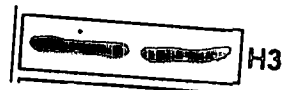
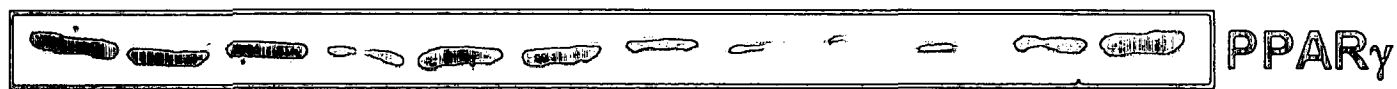
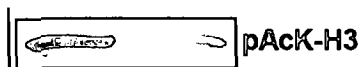
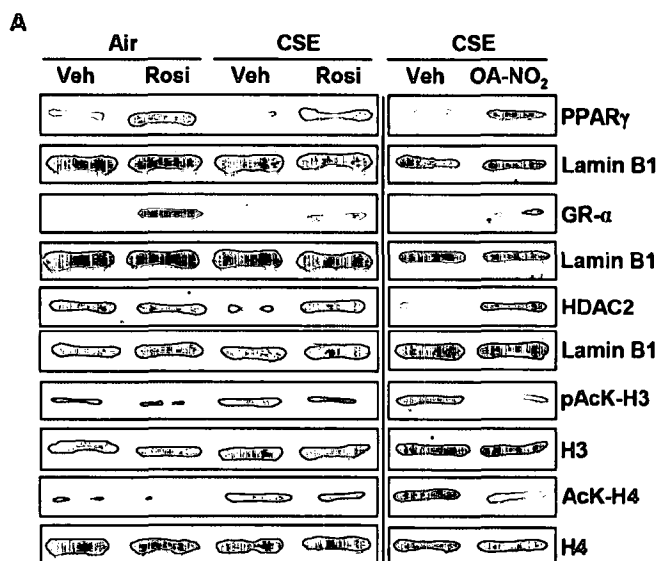


Fig 3C

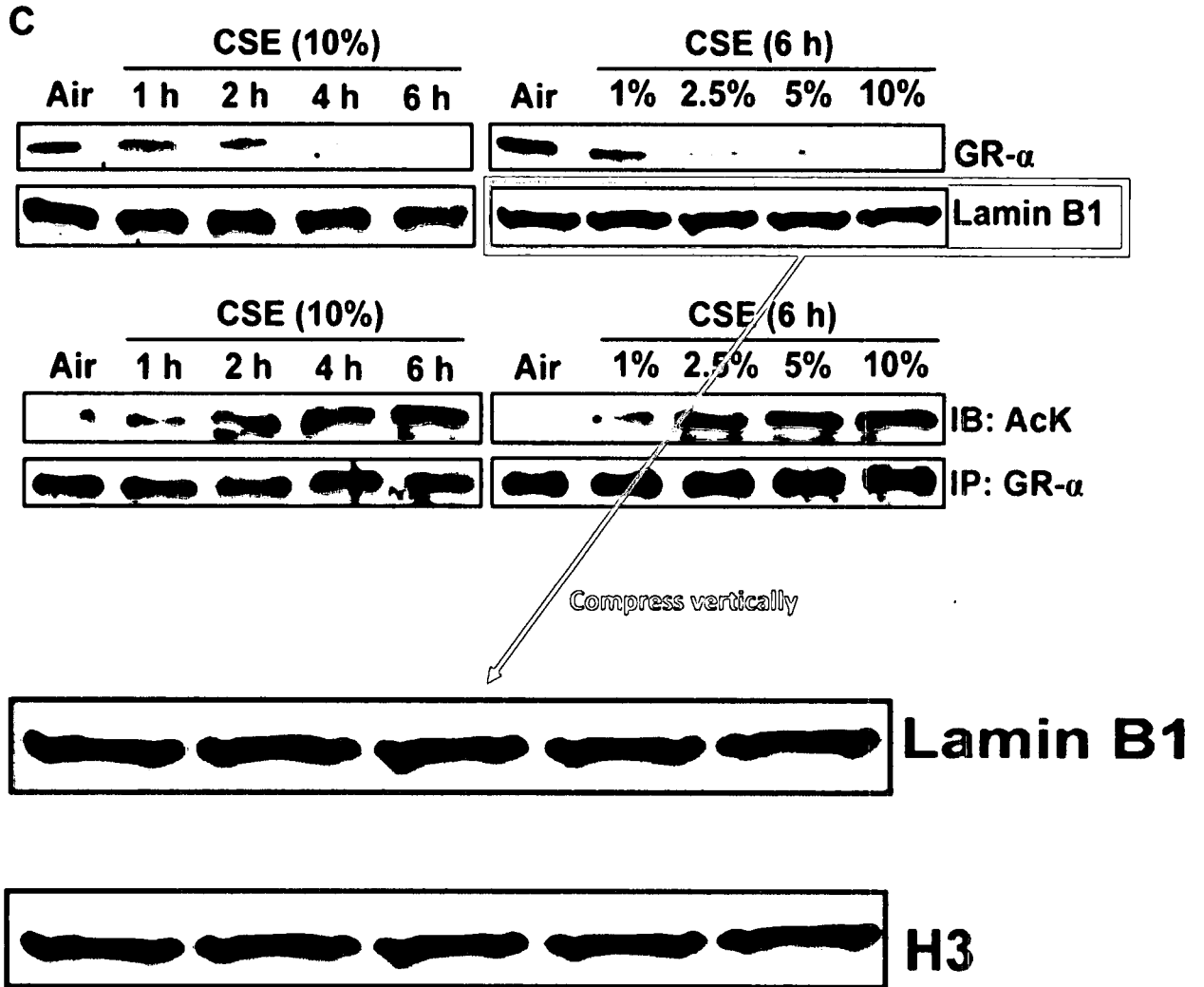
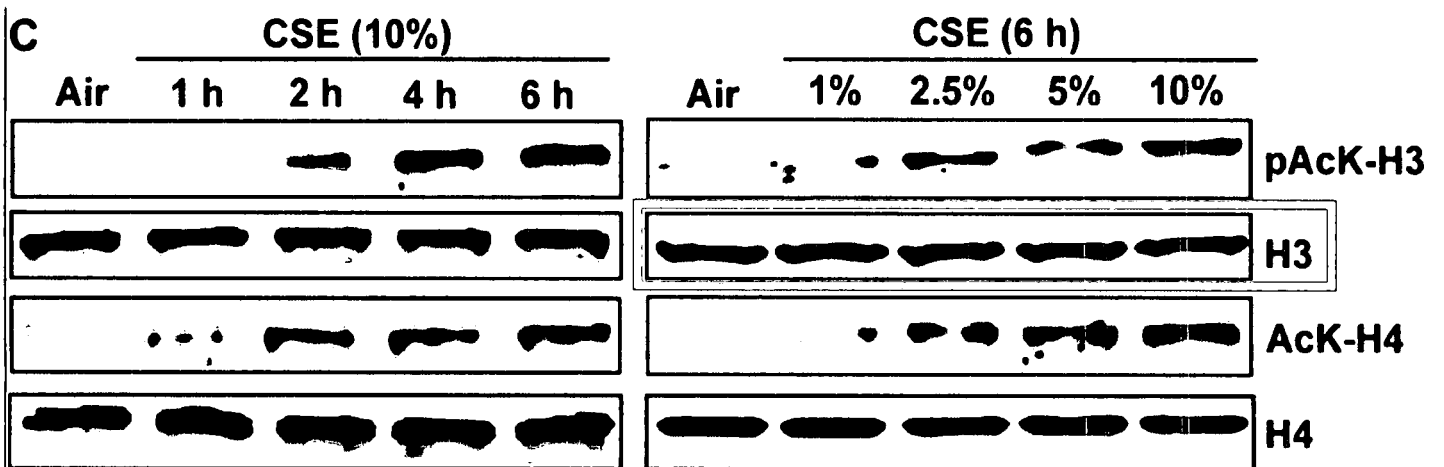
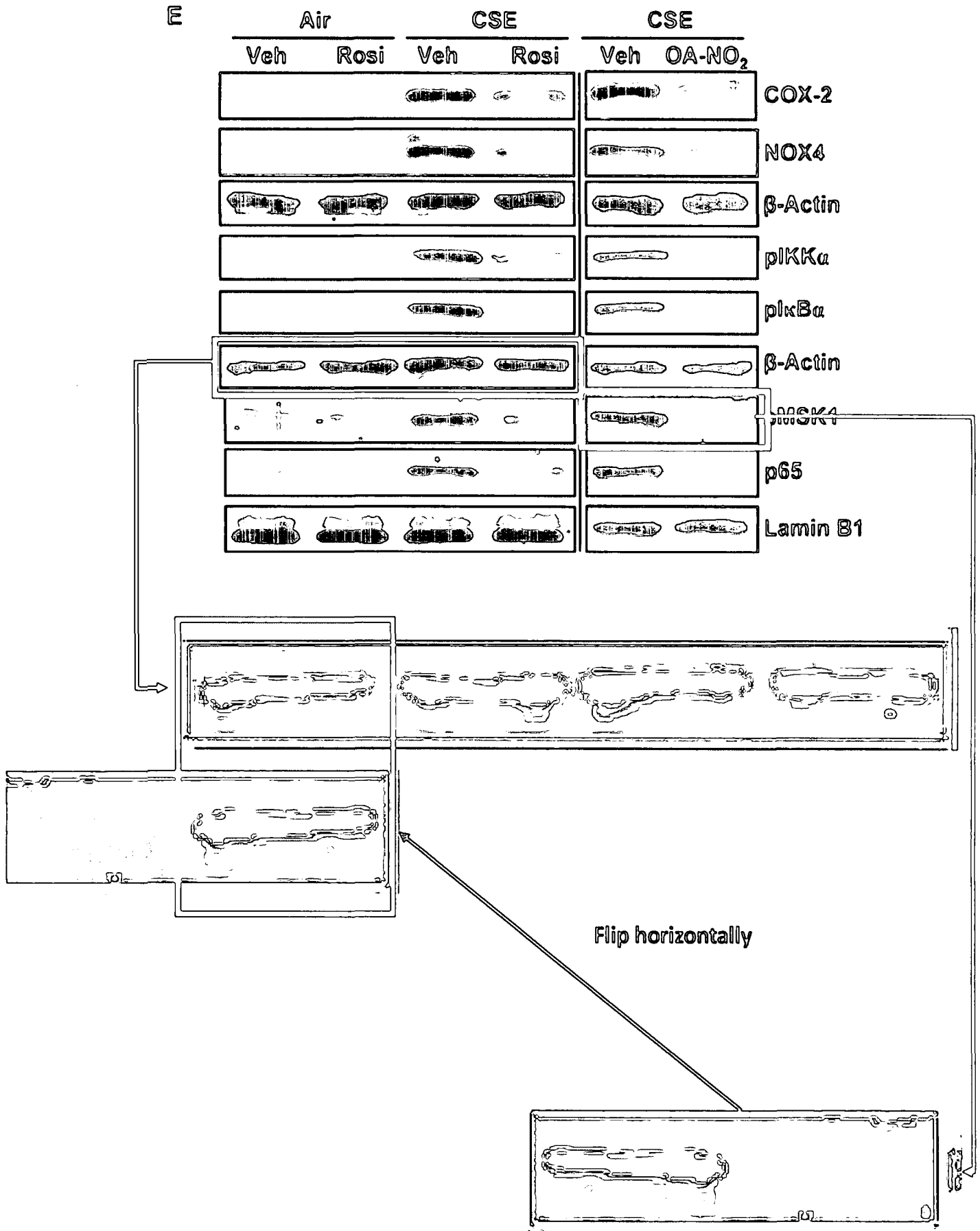


Fig 4C



Same data used to represent different experimental conditions

Reddy RC
JBC/2013/536805
Fig 5E



From: Kaoru Sakabe <ksakabe@asbmb.org>
Sent: Wednesday, September 12, 2018 4:36 PM
To: Karen S. Karas; Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler:

Because your client refused to provide the original data and images for figures 1A and 6A, any criticism of the JBC processes are the result of your clients' failure to provide requested and required information. The images in the PDF provided are of too poor quality for JBC to analyze. The data shown in the attachment for figures 3C and 4C do not appear to correspond with what is presented in the publication. The quality of the data provided on August 20 was of such poor quality that we requested the native files, but none were provided. Finally, we requested full copies of the investigation reports to determine the rigor and completeness of the committee's investigation. Your client has failed to provide the requested information to ensure the integrity of the article. Accordingly, we renew our request that the authors withdraw the paper by September 14.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Wednesday, September 12, 2018 at 9:30 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>, "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Please see the attached correspondence.

Thank you,
Karen Karas

Karen S. Karas ▪ Senior Counsel
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ▪ Washington, DC 20036

P: 202.466.4110 ▪ D: 202-587-4745 ▪ F: 202.380.0514

From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Friday, September 7, 2018 7:21 AM
To: Karen S. Karas; Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Ms. Karas,

Thank you for your message. The information you requested in your message from yesterday was provided to you and Mr. Thaler on August 31. Please let me know by September 14th if the authors will withdraw the article.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Karen S. Karas" <kkaras@cohenseglia.com>
Date: Thursday, September 6, 2018 at 4:06 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>, "Paul S. Thaler" <pthaler@cohenseglia.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe:

Thank you for your August 31, 2018 email giving us the reasons for the journal's interest in reviewing the data for the additional images. There was no explanation in your August 29, 2018 email as to why the journal was seeking data about yet more images, and that is why we objected to the request. Please send us the journal's basis/analysis for determining that the images were reused (Figs. 1a and 6a; Figs. 3c and 4c; and 5E). We will review the journal's analysis with our clients once we receive it, and we will provide you with the original data for the additional images.

Thank you,
Karen Karas

Karen S. Karas ▪ Senior Counsel
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ▪ Washington, DC 20036
P: 202.466.4110 ▪ D: 202-587-4745 ▪ F: 202.380.0514

From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Friday, August 31, 2018 8:41 AM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for your message. In addition to the duplication in Fig 5E, we determined the following:

- The PPAR γ blot from Fig 1A was reused in Fig 6A as pAcK-H3 and H3
- The Lamin B1 blot from Fig 3C was reused in Fig 4C as H3

In light of these issues, the Editors are requesting that the authors withdraw this article. Please communicate this decision to all authors. Please request withdrawal by September 14, 2018. If the authors choose to withdraw the article, we will work with them to draft a mutually agreeable withdrawal notice. If the authors do not withdraw the article, then we will forward this matter to the ASBMB Publications Committee. The Committee may request more information, request a draft of a correction notice for editorial approval, or determine that the article is to be retracted. If the Committee determines that retraction is warranted, no further appeals will be considered and ASBMB will draft and publish a retraction notice.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Paul S. Thaler" <pthaler@cohenseglia.com>
Date: Thursday, August 30, 2018 at 3:09 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglia.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe:

This email responds to (1) your August 23, 2018 email requesting a copy of the report from the VA as well as unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter and (2) your August 29, 2018 email requesting original data to Figs 1A and 6A.

Regarding the requests in your August 23, 2018 email – we decline to provide unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter. Those documents contain confidential information and were redacted at the suggestion of Dean Saleem Khan. A redacted copy of Mr. Aravind Tarugu's email exchange with Dean Khan is

attached. We also decline to provide a copy of the VA's report. We have been informed by the VA that the finding against Mr. Tarugu will not be published. Therefore, Mr. Tarugu is entitled to maintain the report's confidentiality.

Regarding the requests in your August 29, 2018 email - we decline to provide the requested data. As you know, my clients have been fully cooperative and have thus far provided you the all the data and information you have requested, even the data requested in your August 16, 2018 that is not relevant to the subject matter (β -actin blot and the pMSK1 blot in Figure 5E). Your August 29, 2018 email requests additional data that is not relevant to the scope of our initial communication to you (our August 10, 2018 letter) or to Mr. Tarugu's obligation to notify you regarding the VA's finding with respect to Figure 5E.

My clients will continue to cooperate in any way they can with respect to any additional questions you may have regarding the β -actin blot and the pMSK1 blot in Figure 5E.

Thank you for your attention to this.

Sincerely,

Paul S. Thaler ■ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ■ Washington, DC 20036
P: 202.466.4110 ■ F: 202.380.0218

[website](#) | [vCard](#) | [offices](#) | [email](#)



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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Wednesday, August 29, 2018 3:15 PM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

In addition to the below documents, we would like to review the original data to Figs 1A and 6A.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: Kaoru Sakabe <ksakabe@asbmb.org>
Date: Thursday, August 23, 2018 at 3:19 PM
To: "Paul S. Thaler" <pthaler@cohenseglias.com>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for this information. Would you be able to provide a non-redacted version of attachments 1 and 2 from your letter? Additionally, we would like to review the report from the VA.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Wednesday, August 22, 2018 at 4:56 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Here is the response I received from my clients:

"No one has access to these files.

The LiCor that was used to generate these images was located in a common facility, used by multiple users.

This instrument and its associated computer are no longer operational and were replaced by an upgraded system."

Please let me know if there is anything else I can do to assist you.

Sincerely,

Paul

Paul S. Thaler ▪ Partner

Cohen Seglias Pallas Greenhall & Furman PC

1828 L Street, NW, Suite 705 ▪ Washington, DC 20036

P: 202.466.4110 ▪ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]

Sent: Tuesday, August 21, 2018 10:29 AM

To: Paul S. Thaler

Cc: Karen S. Karas

Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for providing these data. It seems the authors used a LICOR imaging system to obtain these data. Do the authors have access to the LICOR acquisition zip files? If so, would they be able to provide these data?

Sincerely,

Kaoru Sakabe, PhD

Data Integrity Manager

American Society for Biochemistry and Molecular Biology

11200 Rockville Pike, Suite 302, Rockville, MD 20852

ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Monday, August 20, 2018 at 2:48 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Please find attached the files you requested.

Thank you for your attention to this.

Sincerely,

Paul
Paul S. Thaler ■ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ■ Washington, DC 20036
P: 202.466.4110 ■ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Thursday, August 16, 2018 2:29 PM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for the quick response. We would be interested in reviewing the original data for Figs 3C, 4C, and 5E. We would prefer that these images be provided uncropped and minimally processed.

Thank you in advance for your help.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Paul S. Thaler" <pthaler@cohenseglias.com>

Date: Thursday, August 16, 2018 at 2:26 PM

To: Kaoru Sakabe <ksakabe@asbmb.org>

Cc: "Karen S. Karas" <kkaras@cohenseglias.com>

Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

This will confirm that we also represent Dr. Raju Reddy. We are happy to help get your questions answered.

Sincerely,

Paul S. Thaler ■ Partner

Cohen Seglias Pallas Greenhall & Furman PC

1828 L Street, NW, Suite 705 ■ Washington, DC 20036

P: 202.466.4110 ■ F: 202.380.0218

[website](#) | [vCard](#) | [offices](#) | [email](#)



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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Thursday, August 16, 2018 2:01 PM
To: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for your patience. From your letter, it sounds like you represent only Mr. Aravind Reddy and not Dr. Raju Reddy, the corresponding author. Please confirm as we have questions for the authors.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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[Journal of Lipid Research](#)

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Saturday, August 11, 2018 at 7:19 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Thank you, Dr. Sakabe. We look forward to hearing from you.

Sincerely,

Paul S. Thaler, Esq.
Cohen Seglias Pallas Greenhall & Furman PC
(202) 587-4750

Sent from my iPad

On Aug 10, 2018, at 2:58 PM, Kaoru Sakabe <ksakabe@asbmb.org> wrote:

Dear Mr. Thaler,

Thank you for your letter. Please allow us some time to review the information.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
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

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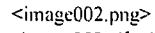
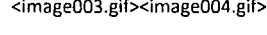

From: Cynthia Roberson <croberson@cohenseglia.com>
Date: Friday, August 10, 2018 at 11:54 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglia.com>
Subject: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Good afternoon Dr. Sakabe.

Please see attached letter on behalf of Paul S. Thaler regarding the above reference matter. Should you have any questions or concerns, please do not hesitate to contact Mr. Thaler.

Thank you
Cynthia

Cynthia Roberson<Administrative Assistant
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705<Washington, DC 20036
P: 202.466.4110<F: 202.466.2693

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<>
<><>

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Paul S. Thaler
Attorney At Law

1828 L Street, NW
Suite 705
Washington, DC 20036

T: 202.466.4110 | F: 202.466.2693
pthaler@cohenseglias.com
www.cohenseglias.com

September 14, 2018

VIA ELECTRONIC MAIL

ksakabe@asbmb.org

Kaoru Sakabe, Ph.D.
Data Integrity Manager
American Society for Biochemistry
and Molecular Biology
11200 Rockville Pike
Suite 302
Rockville, MD 20852

***Re: Journal of Biological Chemistry Publication
Lakshmi, et al. 2014 Article***

Dear Dr. Sakabe:

I am in receipt of your September 12, 2018 email. With all due respect, your email does not fairly characterize the communications we have had over the last several weeks, nor does it reflect the spirit of cooperation or good faith with which my clients have acted. Until receiving your email yesterday, we did not know that JBC was dissatisfied with the data/images they had already been provided. I have gone back through your earlier emails to make sure we did not overlook something, but I can find no email in which you advised, for example, that the quality of the data provided on August 20 was "of such poor quality that [JBC] requested the native files" or that the images provided in the pdf "are of too poor quality for JBC to analyze." None of your prior emails, before yesterday, noted any concern about the quality of the data/images my clients have provided, nor did you make any follow-up requests after receiving the files, by notifying us of the concern(s) that you had. Our communications (and my clients' efforts to respond to JBC's concerns) would have benefited from more transparency by JBC about its concerns. My clients are understandably frustrated and perceive that they are being blamed for not responding to JBC's concerns that they did not even know existed about data/image quality. This was the same frustration we had over JBC's request for the data for Figures Figs 1A and 6A. The request itself did not explain why the data was being requested and did not disclose what concerns JBC had about those figures. Also note that your request was not limited to the PPAR gamma, AckH3 and H3 blots, the specific blots on which you raised concerns, but it goes well beyond, requesting 24 images. It was not until we said we would not provide the data, as your request was beyond the scope of our notification, that you then informed us as to the reason behind the request. JBC's own policy and policies by the Council of Science Editors provide

that if there is a concern about an image, JBC should notify the author as to what the concern is, ask for an explanation, and then request that data be provided. It seems that JBC has not followed its own policy. As my clients were neither notified of any concerns, nor provided an opportunity to respond/provide an explanation, they are clearly not at fault as you have stated. If you have access to a policy allowing JBC to ask for any data without first (or concurrently) notifying an author about JBC's concerns, and allowing JBC to make a determination without providing an opportunity for explanation, please do provide us with a copy of that policy.

With respect to the new concerns you raised for the first time in Wednesday's email, we address them below. Had you shared those concerns with us previously, as required by JBC's or the Council of Science Editors policies, we could have addressed them sooner.

- The reason my clients did not initially provide images for figures 1A and 6A was that they were not notified of any concerns regarding these images. Thus, it is not fair to put them at fault. Additionally, they did not "criticize" JBC's analysis; they simply stated that their understanding of the image analysis provided by you was limited, as you did not provide them with any specific information on the image analysis. We twice requested that you provide the details, but never got any response from you. Also, JBC did not contest our clients' claim that it was their understanding that snapshots from the PDF file were used by JBC for its image analysis. Using snapshots does not comport with the Department of Health and Human Services' Office of Research Integrity guidelines for image analysis. If JBC has separate guidelines for performing image analysis, please provide us with a copy. The use of the PDF file for image analysis by JBC did not result from our clients' not providing the requested information, rather it resulted because of JBC's decision to use such files to perform an image analysis on PDF snapshots. My clients are not responsible for how JBC does its image analysis.
- Regarding figures 1A and 6A – your email states that Dr. Reddy and Mr. Tarugu "refused to provide the original data and images for figures 1A and 6A" and "the images in the PDF provided are of too poor quality for JBC to analyze." They did not "refuse" to provide the original data. We clearly stated in our September 6, 2018 that we would provide the original data but asked to first see JBC's analysis. In response, you told us that the attachment to your August 31, 2018 email was the analysis (which we could not have known as it does not contain any information on how the analysis was performed and how the conclusions were drawn) and you inexplicably directed my clients to withdraw the article. Notwithstanding our disagreement with JBC as to whether the August 31, 2018 attachment is an "analysis," and whether JBC requested these images with appropriate notification, following its own policies, we are now providing the requested original data files (PPT files and .tiff file) to the email transmitting this letter. The .tiff file contain the original data for not only Figures 1A and 6A, but also Figures 3, 4 and 5.


- Your email states that “the images in the PDF provided are of too poor quality for JBC to analyze.” *See* above response regarding PPT and .tiff files being provided. Even though the existence of these files and the fact that a rigorous analysis had been performed on these images was apparent by our letter, we did not receive any request to send the .tiff files.
- Regarding the data we sent for Figures 3C and 4C, your email states: “The data shown in the attachment for figures 3C and 4C do not appear to correspond with what is presented in the publication.” To the contrary, the tiff file “7.tiff” being sent concurrently with this letter demonstrates that figures 3C and 4C do indeed correspond with what is presented in the publication” This can be seen visually from 7.tiff as well as in the analysis of those images which we provided to you on Wednesday (September 12, 2018). JBC has provided no basis or explanation for the conclusion that the data does not correspond to the images. If the Editors have conducted an analysis of the Figure 3C and 4C data that we provided on Wednesday, or should they do so with the additional images we are providing today, please provide it to us for our review.
- Your email states that “[t]he quality of the data provided on August 20 was of such poor quality that we requested the native files, but none were provided.” When we sent the data on August 20, you did not respond to inform us that JBC considered the data to be of poor quality nor did you ask for better quality data. Indeed, the Editors appear to have considered the files to have been of sufficient quality to use for their “analysis” in concluding (albeit incorrectly) that there were duplications. In any case, we are now providing, as noted above, the original .tiff files for the five figures about which JBC has inquired. The files are: 1.tiff - 1A PPAR γ ; 2.tiff - 6A pAH3; 3.tiff - 6A H3; 4.tiff - 3C Lamin; 5.tiff - 4C H3; and 6.tiff - 5E pMsk1; 7.tiff - lamin and H3 blots.
- As we stated in our August 30, 2018 email, our clients are entitled to their rights and protection of confidentiality during the investigation process. The VAPHS notice does not require us to send any documents related to the investigation. However, we wanted to be transparent and cooperative, thus we did provide documents. The redactions we made to the documents were appropriate and necessary to protect confidential information in conformance with the fair information practice (according to PHS policy 42 CFR Parts 50 and 93 and Privacy Act, and also as suggested by the University of Pittsburgh’s Dean Kahn in his email, a copy of which was sent to you) which allows us to withhold such confidential information from JBC and any other external entity. If you or the Editors have a specific question regarding the completeness of the investigation that is relevant to JBC’s own analysis of the images and data we have provided, please do let me know, and if I can respond without violating the confidentiality limits stated above, I will do so.

Dr. Reddy and Mr. Tarugu stand by the original images and image analyses we attached to our September 12, 2018 letter and which we are providing today. These demonstrate that

Dr. Sakabe
September 14, 2018
Page 4

there was no duplication in any of the images, as the Editors should also now be able to see from the additional PPT and .tiff files we are providing. Should the Editors have any evidence, analyses and/or explanation to demonstrate why my clients image analyses are wrong, ***please share it with us***. If there is any policy that supports the Editors' decision to direct that my clients withdraw the article before there is a thorough exchange of information, disclosure by the Editors of the analysis supporting their decision, and a full and fair opportunity for my clients to respond, ***please share it with us***. With all due respect, it is unfair to expect my clients to simply withdraw the article on the sole basis that JBC says these images are duplicated when JBC has not provided any evidence or analyses substantiating its conclusion. We understand JBC's interest in resolving any concerns it has, but that resolution must come only after a fair process that is transparent and clearly communicates to my clients what the concerns are and gives them an opportunity to respond.

Very truly yours,

A handwritten signature in black ink, appearing to read 'P. S. Thaler', written over a large, irregular, hand-drawn shape that resembles a stylized arrow or a large 'P'.

Paul S. Thaler

Attachments (attached to 9/14/18 transmittal email)

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Raju C. Reddy

From: Kaoru Sakabe <ksakabe@asbmb.org>
Sent: Tuesday, September 18, 2018 9:23 AM
To: Karen S. Karas
Cc: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler and Ms. Karas:

We are in receipt of all 5 files. As your clients do not agree to withdraw, we will be forwarding this matter to the ASBMB Publications Committee. I will inform you of their decision.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Karen S. Karas" <kkaras@cohenseglia.com>
Date: Friday, September 14, 2018 at 1:41 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglia.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

I have just finished sending all five emails. Please confirm receipt.

Thank you,
Karen Karas

Karen S. Karas ▪ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ▪ Washington, DC 20036
P: 202.466.4110 ▪ F: 202.380.0514

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From: Karen S. Karas <kkaras@cohenseglias.com>
Sent: Wednesday, September 19, 2018 9:12 AM
To: 'Kaoru Sakabe'
Cc: Paul S. Thaler
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Thank you for email. As this process moves forward to the next step, we would appreciate your answering the following questions and providing the information requested by close of business, September 20th, 2018, so that we have a better understanding of how the Editors reached their decision, and so that we can make plans going forward:

1. As we asked previously in our September 14 email, provide a copy of the Editors' analyses and reports describing the techniques they used to review the data/images we provided from August 10, 2018 through September 14, 2018.
2. Confirm that our September 14 emails (and all attachments) were shared with the Editors.
3. Forward the guidelines/policies which will apply to and govern the ASBMB Publications Committee's consideration of this matter.
4. Confirm that all of our communications with you, beginning with our August 10, 2018 letter, will be made available to the ASBMB Publications Committee.

Thank you,
Karen Karas

Karen S. Karas ▪ Senior Counsel
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ▪ Washington, DC 20036
P: 202.466.4110 ▪ D: 202-587-4745 ▪ F: 202.380.0514

From: Kaoru Sakabe [<mailto:ksakabe@asbmb.org>]
Sent: Tuesday, September 18, 2018 9:23 AM
To: Karen S. Karas
Cc: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler and Ms. Karas:

We are in receipt of all 5 files. As your clients do not agree to withdraw, we will be forwarding this matter to the ASBMB Publications Committee. I will inform you of their decision.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology

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ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
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[Journal of Lipid Research](#)

From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Friday, September 14, 2018 at 1:41 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

I have just finished sending all five emails. Please confirm receipt.

Thank you,
Karen Karas

Karen S. Karas ■ Attorney At Law
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September 21, 2018

VIA ELECTRONIC MAIL

enrique.delacruz@yale.edu

Dr. Enrique M. De La Cruz
Chair, ASBMB Publications Committee
American Society for Biochemistry
and Molecular Biology
11200 Rockville Pike
Suite 302
Rockville, MD 20852

**Re: *Journal of Biological Chemistry Publication*
*Lakshmi, et al. 2014 Article***

Dear Dr. De La Cruz:

We represent Mr. Aravind R. Tarugu and Dr. Raju C. Reddy, two of the co-authors of Lakshmi SP, Reddy AT, Zhang Y, Sciurba FC, Mallampalli RK, Duncan SR, and Reddy RC, *The Journal of Biological Chemistry* 289(10):6383-6393 (2014), "Down-regulated peroxisome proliferator-activated receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)" ("Article").

On August 10, 2018, we wrote to Dr. Kaoru Sakabe in her capacity as the Data Integrity Manager for the American Society for Biochemistry and Molecular Biology ("ASBMB") to advise her that concerns had been raised about two panels in *one* figure (Figure 5E) in the Article. See Appendix A (8/10/18 Thaler letter to Sakabe ("Notification to JBC")). Specifically, it was asserted that the first band in the left panel in the β -actin blot appears to be the same as the first band in the right panel of the pMSK1 blot. In sending the Notification to JBC, Mr. Tarugu was complying with a directive from the Department of Veterans Affairs ("VA") which had concluded (incorrectly and without a preponderance of evidence) that the two bands were duplicates. We have been corresponding with Dr. Sakabe for more than a month and have provided her (and the JBC editors) with substantial documentation (including data and images) demonstrating that *there is no duplication*.

After a process that was not only expanded to include images that were not the subject of any concern by the VA, but also completely lacking in transparency from ASBMB and JBC, Dr. Sakabe advised me by email on September 18, 2018 that because my clients had not agreed to voluntarily withdraw the Article, the matter would be forwarded to the ASBMB Publications

Committee for its consideration. *See* Appendix B at Attachment 1 (at 9/18/18 Sakabe email to Thaler and Karas). Mr. Tarugu and Dr. Reddy did not agree to withdraw the Article because there is no reason to withdraw it. For the reasons explained below (as supported by the accompanying Appendices), Mr. Tarugu and Dr. Reddy request that the Publications Committee conclude that withdrawal of the article is not warranted. We would appreciate your forwarding this letter (and Appendices) to the other members of the Publications Committee.

I. BACKGROUND

As we explained in the August 10, 2018 Notification to JBC, an allegation was made against Mr. Tarugu that Figure 5E contains a duplication. A joint inquiry on this matter by the University of Pittsburgh (the "University") and the Department of Veterans Affairs ("VA"), led by the University of Pittsburgh, resulted in *dismissal of this matter* on February 2016. In a follow up by the VA to this dismissal, the VA requested that the University initiate a joint investigation by the University and the VA led by the University. After the joint investigation was concluded, the matter took separate tracks. On the University track, we successfully appealed the joint finding that had been made against Mr. Tarugu. *See* Appendix A at Attachment 1 (redacted copy of the University's final decision after appeal). Because there was a lack of proof that the images were identical, *the University unanimously agreed to reverse both the finding against Mr. Tarugu and the recommended sanction that the Article be retracted*. *See* Appendix A at Attachment 2 (redacted copy of the Report of the University's Appeal Panel, at p.3). Unlike the University, however, the VA affirmed its incorrect finding that Figure 5E contains a duplication. As a result, Dr. Steven Graham, the VA's Research Integrity Officer, implemented a corrective action plan which required Mr. Tarugu to notify JBC by August 10, 2018 of the VA's finding against him. Mr. Tarugu timely did so. *See* Notification to JBC (Appendix A hereto).

As the August 10, 2018 Notification to JBC explains, the VA erred in determining that the left band in the right side panel of the pMSK1 blot in Figure 5E was a duplicate of a band in the β -actin blot. Mr. Reddy's explanation in the Notice to JBC was supported by the opinions of two experts in the field who are former senior officials at the Department of Health and Human Services Office of Research Integrity, Dr. Alan Price and Dr. John Dahlberg (*see* Appendix A at Attachments 3 and 4) as well as by expert Dr. John Russ (*see* Appendix C (9/12/18 letter from Mr. Thaler) at Attachment 2). That Figure 5E contains no duplications is also demonstrated by the additional data we have provided Dr. Sakabe, as discussed below. Importantly, on September 12, 2018, the University transmitted to Mr. Tarugu a notification from the Department of Health and Human Services' *Office of Research Integrity ("ORI") that it was "clos[ing] this case without further action"* after and as a result of "a complex and thorough review by the [ORI] Director, a review panel of scientist-investigators, and legal counsel."

II. COMMUNICATIONS WITH DR. SAKABE

In response to our Notification to JBC, Dr. Sakabe sent an email stating: "We would be interested in reviewing the original data for Figs 3C, 4C, and 5E. We would prefer that these

images be provided uncropped and minimally processed.” See Appendix B at 8/16/18 email from Dr. Sakabe. There were two things notably absent from Dr. Sakabe’s email - any comment on the information we provided in the Notice to JBC and any explanation supporting her request for data for figures *other than* Figure 5E. Even though Dr. Sakabe did not explain why she was asking for data for additional figures, Mr. Tarugu and Dr. Reddy raised no objection and provided the additional data (a total of 34 blots) as requested – including the data for Figures 3C and 4C. See Appendix B at 8/20/18 Thaler email to Sakabe.¹

Dr. Sakabe responded to our August 20, 2018 email (and its attached zip file) with an email dated August 21, 2018 in which she thanked me for the data I had sent on August 20, 2018. In addition, she asked for information about the LICOR imaging system that the authors had used: “It seems the authors used a LICOR imaging system to obtain these data. Do the authors have access to the LICOR acquisition zip files? If so, would they be able to provide these data?” See Appendix B at 8/21/18 Sakabe email to Thaler. Notably absent from Dr. Sakabe’s August 21, 2018 email was *any* mention of the data we provided on August 20, 2018 (other than her thanking me for sending it). Pertinent to later developments in this matter (discussed below), it is especially noteworthy that in her August 21, 2018 email, Dr. Sakabe did not mention any problems with the quality of the images contained in the zip file we provided on August 20, 2018.

I forwarded Dr. Sakabe’s August 21, 2018 email inquiring about the LICOR imaging system to my clients, who promptly responded. I forwarded their response to Dr. Sakabe on August 22, 2018. See Appendix B at 8/22/18 Thaler email to Sakabe. As my clients explained in the August 22, 2018 email, no one has access to the images on the LICOR system because the instrument and its associated computer are no longer operational and were replaced by an upgraded system. *Id.* At the end of my email, I stated: “Please let me know if there is anything else I can do to assist you.” In response, Dr. Sakabe emailed again. She thanked me for the information I had sent regarding the LICOR imaging system and asked whether I could send her the report from the VA and the unredacted versions of the University’s final decision after appeal and the Report of the University’s Appeal Panel (the versions attached to the Notice to JBC were redacted). See Appendix B at 8/23/18 Sakabe email to Thaler. Dr. Sakabe did not explain why she was asking for the VA report and the unredacted versions of the other documents. Several days later, she sent an email asking my clients to also provide the original data to Figures 1A and 6A. See Appendix B at 8/29/18 Sakabe email to Thaler. Notably absent from Dr. Sakabe’s August 29, 2018 email was any explanation as to why she or the JBC editors wanted to see data for the additional Figures, neither of which had anything to do with the Notice to JBC.

Although my clients had fully cooperated and responded to *all* of Dr. Sakabe’s requests for information, even as those requests sought information beyond the scope of the Notice to

¹ Attached to my August 20, 2018 email to Dr. Sakabe was a zip file containing thirty-four .tiff files and one pdf file. I assume that Dr. Sakabe has made that zip file available to the Publications Committee. If she has not, and if you cannot obtain it from her, please let me know.

JBC, they declined to respond to her requests in her August 23 and August 29 emails for the VA report, unredacted documents and data for additional figures beyond the scope of the Notice to JBC. As we explained in our August 30, 2018 response, the University documents were redacted at the suggestion of the University's Dean Kahn to protect confidential information. *See* Appendix B at 8/30/18 Thaler email to Sakabe; Appendix B at and at 7/24/18 and 7/25/18 email exchange between Mr. Tarugu and Dean Saleem Khan. My clients declined to provide the VA report because, as I explained to Dr. Sakabe, we have been informed by the VA that the finding against Mr. Tarugu will not be published. *See* Appendix B at 8/30/18 Thaler email to Sakabe. My clients declined to provide the data for Figures 1A and 6A because the request was a further deviation from the scope of the subject matter of the Notice to JBC and of Mr. Tarugu's obligation to notify JBC of the VA's finding with respect to Figure 5E. *Id.* However, I reaffirmed in my August 30, 2018 email my clients' willingness to continue to cooperate "in any way they can with respect to any additional questions [that Dr. Sakabe] may have regarding the β -actin blot and pMSK1 blot in Figure 5E." *Id.*

We reasonably expected that communications with Dr. Sakabe might continue with respect to the data and images at issue – the two bands in Figure 5E. My clients looked forward to a continuing dialogue with Dr. Sakabe about the data they had provided and remained willing to answer any questions that Dr. Sakabe or JBC's editors might have. Thus, my clients and I were shocked to receive Dr. Sakabe's next email, on August 31, 2018, in which she stated, in pertinent part:

Thank you for your [August 30, 2018 email]. In addition to the duplication in Fig 5E, we determined the following:

- The PPARy blot from Fig 1A was reused in Fig 6A as pAcK-H3 and H3
- The Lamin B1 blot from Fig 3C was reused in Fig 4C as H3

In light of these issues, the Editors are requesting that the authors withdraw the article. . . . Please request withdrawal by September 14, 2018.

See Appendix B at 8/31/18 email from Dr. Sakabe. No prior email from Dr. Sakabe had alerted us to any concerns the Editors had as to whether there were duplications in Figures 1A/6A and 3C/4C. When we declined (in our August 30, 2018 email) to provide the data for Figures 1A and 6A on the basis that Dr. Sakabe's August 29, 2018 request was beyond the scope of the VA's concern, Dr. Sakabe did not respond to inform us that there was a concern about those figures and the nature of the concern, as we noted in our September 6, 2018 response to Dr. Sakabe's August 31, 2018 email. *See* Appendix B at 9/6/18 Karas email to Sakabe. Also troubling about Dr. Sakabe's August 31, 2018 email is that it was not accompanied by any explanation or analysis demonstrating the basis for the Editors' conclusions. Thus, we asked Dr. Sakabe to "send us the journal's basis/analysis for determining that the images were reused (Figs. 1a and 6a; Figs 3c and 4c; and 5E)," and we told her that we would "review the journal's analysis with

our clients once we receive it, and we will provide you with the original data for the additional images.” *Id.*

Instead of sending the analysis we requested, Dr. Sakabe told us that the information we requested in our September 6, 2018 email was provided to us in the attachment to her August 31, 2018. *See Appendix B at 9/7/18 Sakabe email to Karas.* The attachment to Dr. Sakabe’s August 31, 2018 email (which we assume she has provided the Publications Committee) provides pictorial information but does not reveal any forensic analysis, as we pointed out in our September 12, 2018 letter responding to her September 7, 2018 email. *See Appendix C (9/12/18 Thaler letter to Sakabe) at Attachment 1.* It is a pdf showing where the Editors think they see a duplication.

Attached to our September 12, 2018 letter responding to Dr. Sakabe’s September 7, 2018 email was a separate letter to Dr. Sakabe from Mr. Tarugu and Dr. Reddy. *See Appendix C at Attachment 1.* In their letter, Mr. Tarugu and Dr. Reddy explained why the “analysis” undertaken by the Editors and Dr. Sakabe (reflected in the pdf attachment to Dr. Sakabe’s August 31, 2018 email) was deficient and does not support JBC’s conclusion of duplications. They also provided the images for all five figures and a detailed forensic image analyses performed on the images. *See Appendix C at Attachment 2.* As Dr. Reddy and Mr. Tarugu noted, the “images themselves, when evaluated in their proper context, **provide conclusive evidence** that no images were reused.” *Id.* at p. 1 (emphasis in original). My clients also described the tools they used to perform their analyses. *Id.* at p. 3. Finally, Attachment 2 to my September 12, 2018 letter also included the forensics image analysis performed by expert Dr. John Russ demonstrating that the two panels in Figure 5E are not identical.

Dr. Sakabe responded by email to my September 12, 2018 email the same day. *See Appendix B at 9/12/18 Sakabe email to Thaler.* Dr. Sakabe’s email unfairly and/or inaccurately characterized our month long communications and the data we had provided, in the following ways:

- “Because your client refused to provide the original data and images for figures 1A and 6A, any criticism of the JBC processes are the result of your clients’ failure to provide requested and required information.” My clients did not “refuse” to provide this data. They did not initially provide images for figures 1A and 6A because Dr. Sakabe failed to notify them of any concerns regarding these images. Moreover, they did offer on September 6, 2018 to provide the data but asked to first see JBC’s analysis. They did not “criticize” JBC’s analysis; they simply stated that their understanding of the image analysis provided by Dr. Sakabe was limited, as they were not provided with any specific information on the image analysis.
- “The images in the PDF provided are of too poor quality for JBC to analyze.” We did not receive any follow up request to provide .tiff files and thus had no prior notice that JBC considered the quality of the pdf “too poor” to analyze.

- “The data shown in the attachment for figures 3C and 4C do not appear to correspond with what is presented in the publication.” The data does correspond, as can be seen in the image analysis we sent with our September 12, 2018 letter.
- “The quality of the data provided on August 20 was of such poor quality that we requested the native files, but none were provided.” When we sent the data on August 20, Dr. Sakabe did not respond to inform us that JBC considered the data to be of poor quality nor did she ask for better quality data. Indeed, the Editors appear to have considered the files to have been of sufficient quality to use for their “analysis” in concluding (albeit incorrectly) that there were duplications.
- “Finally, we requested full copies of the investigation reports to determine the rigor and completeness of the committee’s investigation.” This was the first time that Dr. Sakabe offered a reason for having previously requested these documents. As we explained in our earlier correspondence to Dr. Sakabe, we redacted the documents and did not provide the VA report out of confidentiality concerns.

The foregoing is merely a summary of our detailed response, set forth in our September 14, 2018 letter (*see* Appendix D), to Dr. Sakabe’s September 12, 2018 email. The letter also expresses my clients’ understandable frustration at the utter lack of transparency that has plagued this process. In addition, accompanying our letter, we sent Dr. Sakabe the original data for *all* of the images she had requested. We sent three Power Point files and seven .tif images.²

In addition to the data and explanations we provided in our September 14, 2018 letter, we specifically requested Dr. Sakabe to provide us with the following, to help us better understand the policies and procedures which Dr. Sakabe and the Editors had followed and the analyses they used to reach their conclusions. We requested Dr. Sakabe to provide:

- “If you have access to a policy allowing JBC to ask for any data without first (or concurrently notifying an author about JBC’s concerns, and allowing JBC to make a determination without providing an opportunity for explanation, please do provide us with a copy of that policy.” Appendix D at p. 2.
- “If JBC has separate guidelines for performing image analysis [that are different from ORI’s], please provide us with a copy.” Appendix D at p. 2. We twice requested that Dr. Sakabe provide the details of JBC’s analysis, but never received a response from her. Also, JBC did not contest our clients’ claim that it was their understanding that snapshots from the PDF file were used by JBC for

² Because the files accompanying our September 14, 2018 letter are quite large and we assume that Dr. Sakabe has made, or will make, those files available to the Publications Committee, we are not providing them again with this correspondence. If you are not provided with these files, please let me know.

its image analysis. Using snapshots does not comport with ORI's guidelines for image analysis.

- "If the Editors have conducted an analysis of the Figure 3C and 4C data that we provided on Wednesday, or should they do so with the additional images we are providing today, please provide it to us for our review." Appendix D at p. 3.
- Because we had declined to provide unredacted copies of the documents related to the investigation, we offered as follows: "If you or the Editors have a specific question regarding the completeness of the investigation that is relevant to JBC's own analysis of the images and data we have provided, please do let me know, and if I can respond without violating the confidentiality limits stated above, I will do so." Appendix D at p. 3.
- "Should the Editors have any evidence, analyses and/or explanation to demonstrate why my clients image analyses are wrong, *please share it with us.*" Appendix D at p. 4 (emphasis in original).
- "If there is any policy that supports the Editors' decision to direct that my clients withdraw the article before there is a thorough exchange of information, disclosure by the Editors of the analysis supporting their decision, and a full and fair opportunity for my clients to respond, *please share it with us.*" Appendix D at p. 4 (emphasis in original).

In response to our September 14, 2018 letter and accompanying files, we received a rather curt response from Dr. Sakabe on September 18, 2018 which reads, in full:

We are in receipt of all 5 files [accompanying your September 14, 2018 letter]. As your clients do not agree to withdraw, we will be forwarding this matter to the ASBMB Publications Committee. I will inform you of their decision.

See Appendix B at 9/18/18 email from Dr. Sakabe. We received no substantive response to our September 14, 2018 letter; we received no response to our requests made in the letter for applicable procedures and policies; we received no response made in the letter for the analysis conducted by JBC; we received no response to the data we provided with our letter.

We made one last attempt with Dr. Sakabe to better understand how Dr. Sakabe and the Editors reached their conclusion that the Article should be withdrawn, but none was forthcoming. We could not even succeed in getting a response to a simple request that Dr. Sakabe confirm that all of our emails and data would be forwarded to the Publications Committee. That final communication to Dr. Sakabe was emailed on September 19, 2018 and reads, in full, as follows:

Dear Dr. Sakabe,

Thank you for [your] email. As this process moves forward to the next step, we would appreciate your answering the following questions and providing the information requested by close of business, September 20th, 2018, so that we have a better understanding of how the Editors reached their decision, and so that we can make plans going forward:

1. As we asked previously in our September 14 email, provide a copy of the Editors' analyses and reports describing the techniques they used to review the data/images we provided from August 10, 2018 through September 14, 2018.

2. Confirm that our September 14 emails (and all attachments) were shared with the Editors.

3. Forward the guidelines/policies which will apply to and govern the ASBMB Publications Committee's consideration of this matter.

4. Confirm that all of our communications with you, beginning with our August 10, 2018 letter, will be made available to the ASBMB Publications Committee.

See Appendix B at 9/19/18 Karas email to Sakabe. Dr. Sakabe responded later that same day in an email which reads, in full, as follows:

Our policies may be found here:
http://www.jbc.org/site/misc/edpolicy.xhtml#ethics_policy. *We will not share further internal analyses/reports.*

See Appendix B at 9/19/18 email from Dr. Sakabe (emphasis added).

Thus, after more than a month of communications and transmission of extensive data, my clients have no better understanding today as why they are being asked to withdraw the Article than they had on August 31, 2018.

III. THE ARTICLE SHOULD NOT BE WITHDRAWN

Mr. Tarugu and Dr. Reddy have been fully cooperative in this process. We are bewildered at the reluctance of Dr. Sakabe and the Editors to be transparent as to the analysis they undertook and the procedures they followed to reach the conclusion that that article should be withdrawn. As we stated at the end of our September 14, 2018 letter to Dr. Sakabe:

With all due respect, it is unfair to expect my clients to simply withdraw the article on the sole basis that JBC says these images are duplicated when JBC has not provided any evidence or analyses substantiating its conclusion. We

Dr. De La Cruz
September 21, 2018
Page 9

understand JBC's interest in resolving any concerns it has, but that resolution must come only after a fair process that is transparent and clearly communicates to my clients what the concerns are and gives them an opportunity to respond.

Appendix D at p.4 (9/14/18 letter from Mr. Thaler).

Mr. Tarugu and Dr. Reddy have demonstrated through the data and analyses they provided to Dr. Sakabe and the Editors that there were no duplications in the Article and that the Article should not be withdrawn. Dr. Sakabe did not provide us with any counter-analysis or explanation that would support a contrary conclusion.

IV. CONCLUSION

We appreciate the anticipated careful consideration that you and the other members of ASBMB's Publications Committee will give to this letter, all of its attachments, and the data/images previously provided to Dr. Sakabe. We hope that there will be more transparency from ASBMB going forward. To that end, we request that you provide us with the information that we sought from Dr. Sakabe but which she refused to provide, including: (1) a copy of the Editors' analyses and reports describing the techniques they used to review the data/images we provided from August 10, 2018 through September 14, 2018; (2) confirmation that you have received from Dr. Sakabe all of the attachments to all of our emails (including all zip files, powerpoint files and .tiff files); and (3) the specific guidelines/policies which will apply to and govern the ASBMB Publications Committee's consideration of this matter. In addition, we request that if the Publications Committee undertakes its own analysis of the data and images, that any such analysis be shared with us.

My clients and I are happy to answer any questions which you or the other Committee members may have.

Very truly yours,



Paul S. Thaler

Attachments

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Raju C. Reddy

APPENDIX A

AUGUST 10, 2018 LETTER FROM PAUL THALER TO DR. KAORU SAKABE ("NOTIFICATION TO JBC")

Including the following Attachments:

ATTACHMENT 1: Redacted copy of University of Pittsburgh Provost Patricia Beeson's final decision after appeal.

ATTACHMENT 2: Redacted copy of University of Pittsburgh Report of the Appeal Panel recommending reversal.

ATTACHMENT 3: Dr. Alan Price (former Associate Director for Investigative Oversight for NIH ORI) expert opinion in support of content of Notification to JBC

ATTACHMENT 4: Dr. John Dahlberg (former Director for Investigational Oversight for NIH ORI) expert opinion in support of content of Notification to JBC.

Paul S. Thaler
Attorney At Law



1828 L Street, NW
Suite 705
Washington, DC 20036

T: 202.466.4110 | F: 202.380.0218
pthaler@cohenseglias.com
www.cohenseglias.com

August 10, 2018

VIA ELECTRONIC MAIL

ksakabe@asbmb.org

Kaoru Sakabe, Ph.D.
Data Integrity Manager
American Society for Biochemistry and Molecular Biology
11200 Rockville Pike
Suite 302
Rockville, MD 20852

***Re: Journal of Biological Chemistry Publication
Lakshmi, et al. 2014 Article***

Dear Dr. Sakabe:

We represent Mr. Aravind Reddy Tarugu, a co-author of Lakshmi SP, Reddy AT, Zhang Y, Scieurba FC, Mallampalli RK, Duncan SR, and Reddy RC, *The Journal of Biological Chemistry* 289(10):6383-6393 (2014), "Down-regulated peroxisome proliferator-activated receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)" (the "Paper"). Mr. Tarugu was notified in January 2016 of an allegation that "the left band in the left panel in the β -actin plot appears to be the same as the left band in the right panel of the pMSK1 blot, flipped by 180°." A joint inquiry on this matter by the University of Pittsburgh (the "University") and the Department of Veterans Affairs ("VA"), led by the University of Pittsburgh, resulted in dismissal of this matter on February 2016. In a follow up by the VA to this dismissal, the VA requested that the University initiate a joint investigation by the University and the VA led by the University, which resulted in a finding that Mr. Reddy falsified Figure 5E.

After receiving the final investigation report, the University and the VA made separate determinations to which we appealed. After the appeals, the University reversed its decision while the VA affirmed the findings of the University investigation report. Dr. Steven Graham, the Research Integrity Officer for the VA, implemented a corrective action plan for Mr. Reddy which requires him to notify JBC not later than August 10, 2018 of the VA's finding against him. This letter constitutes that notice.

Notwithstanding the VA's finding, Mr. Reddy submits that no action should be taken by JBC with regard to the Paper. With all due respect to the VA, its conclusion that the left band in the right panel of the pMSK1 blot was falsified is wrong and without any preponderance of evidence. In fact, in direct contrast to the VA's decision, the University (the lead institute that

Dr. Sakabe
August 10, 2018
Page 2

conducted the investigation), after an appeal to the Provost and a review by an Appeal Panel consisting of five Professors, *unanimously reversed* the finding against Mr. Reddy that had been made by the joint investigation committee. See Attachment No. 1 (redacted copy of Provost Patricia Beeson's April 4, 2018 final decision after appeal) and Attachment No. 2 (redacted copy of the March 27, 2018 recommendation of the University's appeal panel). The Appeal Panel's recommendation for reversing states in pertinent part:

There was disagreement between the two experts who examined the image evidence [as to whether the bands are identical], and that disagreement was not fully addressed and resolved by the Investigative Board. . . [T]he figure panel at the center of the investigation was not essential for the paper's conclusions.

A finding of no misconduct on your part will be reported.

Attachment No. 2 at p.3. In reversing, Provost Beeson expressly withdrew the sanction issued by Assistant Dean Saleem Khan (following the investigation) which would have required Mr. Reddy to retract the Paper – the same sanction being upheld by VA.

The decision of Provost Beeson and the recommendation of the Appeal Panel reversing the finding is supported by two experts in the field, Dr. Alan Price and Dr. John Dahlberg whose opinions are attached as Attachment Nos. 3 and 4, respectively. Dr. Price spent 17 years working with ORI, having served in the latter years as the Associate Director for Investigative Oversight for ORI. During that time, his group was involved with over 3,000 allegations/queries and over 700 formal inquiries or investigations, and they made more than 175 findings of scientific/research misconduct. During his last decade in ORI, Dr. Price reviewed and handled all of the allegations received by ORI from individuals, institutions, and the National Institutes of Health (NIH). Dr. Dahlberg spent 23 years at ORI. In 2006, he became the Director of the Division of Investigational Oversight (DIO), the division within ORI responsible for conducting oversight review of institutional inquiries and investigations involving questioned research funded by the Public Health Service. In mid-2013, he became Deputy Director of ORI where he remained until his retirement in April 2015. During his tenure at ORI, Dr. Dahlberg handled thousands of allegations and dealt with hundreds of cases. Both Dr. Price and Dr. Dahlberg have reviewed the pertinent documents and data, and they agree that a preponderance of the evidence does not establish that the two images are identical. They agree with the University's decision to reverse the finding against Mr. Reddy.

The VA stands alone in its conclusion that the image in Figure 5E was falsified without exhibiting any preponderance of evidence. Neither Provost Beeson, the University's Appeal Panel, Dr. Price or Dr. Dahlberg agree. While we have brought the VA's decision to your attention as directed by Dr. Graham, we respectfully submit that the VA's decision does not warrant that any action be taken with respect to the Paper.

Dr. Sakabe
August 10, 2018
Page 3

Should you or the Publications Committee have any questions or need further information, please do not hesitate to contact me.

Very truly yours.

A handwritten signature in black ink, appearing to read 'PST', written over a horizontal line that extends to the right and then curves upwards at the end.

Paul S. Thaler

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Steven Graham



University of Pittsburgh

Office of the Provost and Senior Vice Chancellor

801 Cathedral of Learning
4200 Fifth Avenue
Pittsburgh, PA 15260
412-624-4223
Fax: 412-383-3640
beeson@pitt.edu

Patricia E. Beeson
Provost
Senior Vice Chancellor

April 4, 2018

Aravind Tarugu
Senior Research Associate
Department of Medicine
Montefiore NW 628

Dear Mr. Tarugu:

In response to your appeal from the decisions of School of Medicine Assistant Dean for Faculty Affairs Saleem Khan following his receipt of the report of the Investigative Board, an Appeal Panel was appointed. Your appeal requested review of the research misconduct finding [REDACTED]. I have reviewed the Panel's recommendations sent to me in late March, which I am attaching to this letter.

My decision is to accept the recommendation of the Panel that Dr. Khan's finding of research misconduct on your part be reversed [REDACTED].

[REDACTED]

[REDACTED]

[REDACTED]

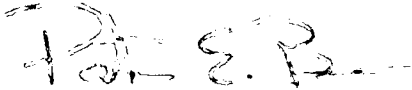
[REDACTED]

Public Health Service Policy requires the University to report the result of the investigation to the Office of Research Integrity, US Department of Health and Human Services. A finding of no research misconduct on your part will be reported.

[REDACTED]

[REDACTED] Therefore this decision shall be the final disposition of this matter on behalf of the University.

Sincerely,



Patricia E. Beeson

REPORT OF THE APPEAL PANEL

IN THE MATTER OF

████████████████████ ARAVIND REDDY TARUGU

Yuan Chang, MD
Distinguished Professor & American Cancer Society Professor of Pathology

Mary Ganguli, MD
Professor of Psychiatry

Penelope A. Morel, MD
Professor of Immunology

Yoel Sadovsky, MD (Appeal Panel Chair)
Distinguished Professor of Obstetrics, Gynecology & Reproductive Services

John V. Williams, MD
Professor of Pediatrics

March xx, 2018

Introduction

This matter has its origin in a joint Inquiry to assess allegations regarding publications of the Respondent [REDACTED]

[REDACTED] Mr. Aravind Reddy Tarugu, Research Associate, Department of Medicine. The Inquiry was started on January 5, 2016 and involved both the University of Pittsburgh and the VA Pittsburgh Healthcare System (VAPHS), with the University serving as the lead institution at the request of VAPHS. The Inquiry Panel recommended the matter be closed without further investigation and the University accepted the recommendation. However, VAPHS asked that an Investigation be conducted. The University agreed to lead a joint Investigation. An Investigative Board considered this matter and based upon their report School of Medicine Assistant Dean for Faculty Affairs Saleem Khan, PhD, found that Mr. Aravind Reddy Tarugu had committed research misconduct through falsification by publishing the same image twice (as mirror images), but with different descriptions. [REDACTED]

The publication containing the alleged falsification is:

Lakshmi SP, Reddy AT, Zhang Y, Scirba FC, Mallampalli RK, Duncan SR, and Reddy RC. *The Journal of Biological Chemistry* 289(10): 6383-6393 (2014). "Down-regulated Peroxisome Proliferator-Activated Receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)".

On November 27, 2017 Mr. Paul Thaler, on behalf of the Respondent [REDACTED], filed an appeal of these findings and asked that the findings be reversed. On February 9, 2018 the members of the Appeal Panel convened with Dr. Craig Wilcox, Research Integrity Officer of the University of Pittsburgh and Dr. Mara Horwitz, Associate Research Integrity Officer, to discuss the charge to the Appeal Panel and procedures relevant to that charge. The Appeal Panel met again on March 16, 2018.

Grounds for the Appeal of the Finding of Research Misconduct

The University of Pittsburgh 2008 Research Integrity Policy (Policy #11-01-01) states that grounds for an appeal are limited to (1) failure to follow appropriate procedures; (2) insufficiency of evidence; or (3) arbitrary and capricious decision making.

The relevant grounds of the Respondent [REDACTED]' appeal are as follows: (1) There was a failure to follow standard procedures resulting in (a) failure to secure evidence, (b) failure to provide proper notification to the Respondent [REDACTED] prior to the appearance of the witness, and (c) failure to provide for impartial committees during the Inquiry and Investigation. (2) The research misconduct [REDACTED] [REDACTED] not demonstrated by a preponderance of the evidence, and the Respondent [REDACTED]' conduct of research is not a "significant departure from accepted practices" and therefore can constitute neither research misconduct [REDACTED].

Appeal Panel Activity

The Appeal Panel convened on February 9, 2018 for initial discussion and to receive evidence considered by the Investigative Board. The Panel also received records of the investigative process, the transcript of the Investigative Board hearing, and correspondence in the record including the June 5, 2017 response from Mr. Thaler and the Respondent [REDACTED] regarding the draft investigative report, the August 2, 2017 additional comments from Mr. Thaler on behalf of the Respondent [REDACTED], the November 27, 2017

communication of the grounds for appeal, and a January 31, 2018 communication from Mr. Thaler regarding supplemental information pertaining to a desktop computer discussed in the report of the Investigative Board. The grounds for an appeal as described by the University of Pittsburgh Research Integrity Policy (cited above) were reviewed. The appeal filed on behalf of the Respondent was discussed and each of the specific grounds for an appeal of the findings of Research Misconduct was discussed.

Following the February 9, 2018 meeting the Appeal Panel considered the record and the documents received in support of the appeal and then reconvened on March 16, 2018.

Appeal Panel Recommendations

The Appeal Panel agreed unanimously to recommend reversal of the finding of Research Misconduct on the part of Mr. Aravind Reddy Tarugu.

[REDACTED]

Appeal Panel Advice Regarding the Grounds for the Appeal

Research Misconduct Finding

The Panel offers the following comments regarding the claims made by the Respondent in the appeal of the research misconduct finding:

The misconduct is based solely on the apparent match of the images. The issue of the bands being identical is not conclusively resolved. There is insufficient evidence of intentionality.

Agreed. There was disagreement between the two experts who examined the image evidence, and that disagreement was not fully addressed and resolved by the Investigative Board.

[REDACTED]

[REDACTED] The Panel also determined that intention was not proven by a preponderance of evidence, including a lack of proof for purposeful image manipulation. The Panel also noted the lack of a motive, as the figure panel at the center of the investigation was not essential for the paper's conclusions.

The investigation was infected with irregularities. Witness procedures were not followed.

Agreed with qualifications. The sequestration process was deficient. The Panel felt the University made the appropriate attempts to sequester the relevant information but the usual procedures were hampered by issues that arose due to VAPHS imposed data security rules and technical capabilities.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Signature Page

Panel Member

Date



March 28, 2018

Yuan Chang, MD
Distinguished Professor &
American Cancer Society Professor of Pathology



March 29, 2018

Mary Ganguli, MD
Professor of Psychiatry



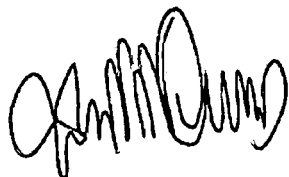
March 28, 2018

Penelope A. Morel, MD
Professor of Immunology



March 26, 2018

Yoel Sadovsky, MD (Appeal Panel Chair)
Distinguished Professor of Obstetrics, Gynecology & Reproductive Sciences



March 25, 2018

John V. Williams, MD
Professor of Pediatrics

Price Research Integrity Consultant Experts

Alan R. Price, Ph. D.

21704 Sierra Trail, Lago Vista, Texas

Cell phone 512-483-1574

Email resmiscon@researchmisconductconsultant.com

Paul Thaler and Karen S. Karas, Counsels
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705
Washington, DC 20036

August 10, 2018

RE: Opinion on DVA-required notice to *JBC* Editor by Aravind Reddy on 2014 paper finding

You requested my expert opinion, regarding a Department of Veterans Affairs (DVA) remedial action plan for Mr. Aravind Reddy ("Mr. Reddy"), requiring notification of the *Journal of Biological Chemistry (JBC)*, following a University of Pittsburgh (UPitt) Appeal Panel Report of March 27, 2018, and the UPitt Provost's acceptance letter of April 4, 2018, reversing the finding of an earlier joint UPitt/Veterans Administration Pittsburgh Health Care System (VAPitt) investigation of research involving two western blot β -actin bands, published in Figure 5E in *JBC* 289(10):6383 (2014), with technical assistance from Mr. Reddy as the second author. You previously provided me with the UPitt/VAPitt inquiry and investigation reports and exhibits, which I reviewed in October 2017 for my expert opinion on the case process and initial findings.

I understand that, given the recent reversal of the UPitt findings, UPitt officials also reversed the proposed sanction that would have required Mr. Reddy to request *JBC* retract this publication. However, I understand that DVA has affirmed its own finding against Mr. Reddy, and DVA is requiring him to notify *JBC* about that finding for this publication.

As background, I was a faculty member at the University of Michigan from 1970-1987. I retired from the federal Office of Research Integrity (ORI) after 17 years in 2006, serving the last six years as ORI Associate Director for Investigative Oversight. We handled over 3,000 allegations/queries and over 700 formal inquiries/investigations and made over 175 findings of scientific/research misconduct. During my last decade there, I reviewed and handled all of the allegations received from individuals, institutions, and the National Institutes of Health (NIH). We also reviewed and analyzed all of the reports of inquiries/investigations by universities, hospitals, and other research institutions funded by NIH research grants. I believe that no one person has seen, handled, and resolved more allegations, investigations, and oversight cases of scientific/research misconduct than I have. I also communicated with many journal editors, including at *JBC*, on correction or retraction of publications with allegedly falsified images or other data. I was a biochemist and member of FASEB's Biochemistry Society which hosts *JBC*. For the past twelve years, I have been consulting formally with individuals and institutional officials on such matters, as Price Research Integrity Consultant Experts (P.R.I.C.E.).

DVA notice to Mr. Reddy on notifying the *JBC* of the DVA's finding

On July 9, 2018, the Research Integrity Officer (RIO) and Associate Chief of Staff, Research and Development at VAPitt, sent a memo to Mr. Reddy, outlining a remedial action plan for him to follow, specifically stating:

You must notify the Journal of Biological Chemistry (*JBC*) of the VA's finding of research misconduct regarding the data published in the *JBC* 289(10):6383-6393 (2014)... [which requires] each author is required to provide details of the finding.

My opinion on Mr. Reddy notifying the *JBC* of DVA's finding of research misconduct

In notifying the Editor of *JBC* of the finding as required in the remedial action plan memo by the VAPitt RIO, I believe Mr. Reddy should quote the research misconduct finding in the joint UPitt/VAPitt investigation committee report:

Statement of Findings - Research Misconduct

We find the allegation stated in the charge to our committee to be true. In Figure 5E of the *JBC* 2014 paper referenced above, the first band in the left panel in the β -actin blot (lane 6) is indeed sufficiently identical to the first band in the right panel of the pMSK1 blot (when reflected across a vertical line) to support the allegation...

We find that the creation and publication of these two images, one derived from the other through digital manipulation, is falsification and that the falsification was intentional. The evidence of intent is that the same image was chosen twice (an action very unlikely to occur by accident) and a mirror image of one of the images was created (a second action very unlikely to occur by accident). We find research misconduct...

I believe Mr. Reddy should also quote the statement in the VAPitt RIO's July 9, 2018, remedial action memo above, that the Network Director of VA Healthcare-VISN 4 had concluded that he:

... committed research misconduct by falsifying data with 2 blots being the mirror image of each other and represented as different blots in a publication.

In addition, I believe Mr. Reddy should quote the conclusions in the March 27, 2018, UPitt Appeal Panel Report (p. 3), with which I very strongly concur:

The Appeal Panel agreed unanimously to recommend reversal of the finding of Research Misconduct on the part of Mr. Aravind Reddy Tarugu....

The Panel offers the following comments regarding the claims made by the Respondent in the appeal of the research misconduct finding:

The misconduct is based solely on the apparent match of the images. The issue of the bands being identical is not conclusively resolved. There is insufficient evidence of intentionality.

Agreed. There was disagreement between the two experts who examined the image evidence, and that disagreement was not fully addressed and resolved by the Investigative Board.... The Panel also determined that intention was not proven by a preponderance of evidence, including a lack of proof for purposeful image manipulation. The Panel also noted the lack of a motive, as the figure panel at the center of the investigation was not essential for the paper's conclusions.

The investigation was infected with irregularities. Witness procedures were not followed.

Agreed with qualifications. The sequestration process was deficient. The Panel felt the University made the appropriate attempts to sequester the relevant information but the usual procedures were hampered by issues that arose due to VAPHS imposed data security rules and technical capabilities.

My opinion on the lack of justification for a retraction of the 2014 *JBC* paper

Based on my almost three decades of reviewing over 800 investigation reports, I strongly agree with the Appeal Panel that intentional falsification by Mr. Reddy, with manipulation of the control blot data in Figure 5E, was not proven by a preponderance of evidence. Therefore, as the Appeal Panel concluded, a research misconduct finding against Mr. Reddy is unwarranted.

I recommend that Mr. Reddy notify the Editor of *JBC*, about the VAPitt finding, supplying the above information, and arguing strongly, as I have, that no retraction of the 2014 *JBC* paper is warranted.

Sincerely,



Alan R. Price, Ph.D.
Price Research Integrity Consultant Experts
Former Associate Director of the U.S. Office of Research Integrity

TO: Paul Thaler, Karen Karas

FROM: John Dahlberg, PhD

DATE: August 10, 2018

SUBJECT: Request of the Department of Veterans Affairs (VA) that Mr. Aravind Reddy notify Journal of Biological Chemistry (JBC) regarding the finding made against him in the matter of JBC paper 289:10, pp. 6383–6393, March 7, 2014 (“the JBC paper”)

I have been asked to opine on the appropriateness of the VA’s adherence to the University of Pittsburgh Investigative Committee’s recommendation that the referenced published paper be retracted by one of the co-authors. By way of background, after twenty five years as a bench scientist, I joined the Office of Research Integrity (ORI) within the Department of Health and Human Services, where I spent an additional twenty three years as a scientist/investigator in the Division of Investigative Oversight (DIO). From 2006-2013 I was the Director of DIO, and from 2013-2015 I served as the Deputy Director of ORI, at which time I retired from federal service. While at ORI, I evaluated thousands of allegations of possible research misconduct, and conducted oversight review and analyzed hundreds of inquiries and investigations of cases of alleged research misconduct involving individuals and institutions from all regions of the United States.

One of the principal objectives of ORI was to help ensure the accuracy of the scientific literature, and when we concurred with institutional findings of research misconduct and made separate findings of misconduct on behalf of the federal government, we typically requested correction or retraction of articles when the scope of the findings warranted such an action. Of course, ORI realized that neither we nor the respondents who agreed to voluntary settlements with ORI could demand that editors retract a paper, as that determination more appropriately rests with the journal’s editors who are more qualified to judge the impact of the misconduct on the overall accuracy of the published manuscript and the impact of the fabrications, falsifications, and/or plagiarism on the scientific community.

I have reviewed the single issue on which the VA determined, based on the Investigative Report made by the University of Pittsburgh and VAPHS’s joint investigation led by the University, that Mr. Reddy had committed research misconduct, thereby warranting, in its view, retraction of the referenced JBC paper. I note that the alleged infraction involves a claim that two bands in Figure 5E appear to be the same.¹ After careful consideration of the appeal to the Provost, the University of Pittsburgh found that there was insufficient evidence to prove that these two bands were identical (or as ORI would phrase it, had a common origin), and did not find that Mr. Reddy had committed research misconduct.

¹ “the first band in the left panel in the β -actin blot appears to be the same as the first band in the right panel of the pMSKI blot, if one or the other was reflected across a vertical reference line” (University of Pittsburgh Investigation Report, page 5)

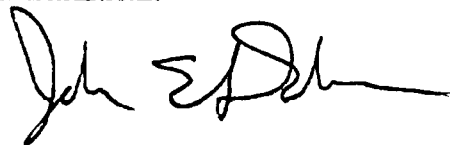
ORI dealt with similar claims on many occasions and nearly always determined that forensic comparison of two bands might show that they appeared very similar or perhaps identical, but that in the absence of additional evidence of possible misconduct, it would be inappropriate to make a finding of research misconduct based on a single possibly duplicated band. In this case, the JBC paper contains multiple figures with western blots containing approximately 150 lanes of blots with approximately 650 separate bands. None of the remaining bands were alleged to have been duplicated. ORI never made findings of research misconduct based on such a flimsy evidentiary basis.

The University Appeal Panel also noted in their response to the UP-investigation report that the figure in question was of marginal significance. The panel also noted that because the questioned panel was not essential to the paper's conclusions, it could not determine that anyone would have had a motive to falsify the figure.

It should also be noted that the questioned images are control blots, and that the research record described two separate experiments containing corresponding blot images.

For these reasons, I respectfully recommend that the editors of JBC agree with UP and Mr. Aravind Reddy to not retract the referenced paper. I am proud of the efforts made by ORI during my tenure to be cognizant of the adverse consequences of a finding of research misconduct to the reputation of a scientist; in cases such as this ORI would not have concurred with the VA's findings or recommendations.

John Dahlberg

A handwritten signature in black ink, appearing to read "John Dahlberg", written in a cursive style.

APPENDIX B

EMAIL COMMUNICATIONS

Includes:

- Email correspondence between Mr. Thaler, Ms. Karas and Dr. Sakabe from August 10, 2018 to September 19, 2018.
- Redacted copy of email communication between Mr. Tarugu and Dean Khan of University of Pittsburgh.

From: Kaoru Sakabe <ksakabe@asbmb.org>
Sent: Wednesday, September 12, 2018 4:36 PM
To: Karen S. Karas; Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler:

Because your client refused to provide the original data and images for figures 1A and 6A, any criticism of the JBC processes are the result of your clients' failure to provide requested and required information. The images in the PDF provided are of too poor quality for JBC to analyze. The data shown in the attachment for figures 3C and 4C do not appear to correspond with what is presented in the publication. The quality of the data provided on August 20 was of such poor quality that we requested the native files, but none were provided. Finally, we requested full copies of the investigation reports to determine the rigor and completeness of the committee's investigation. Your client has failed to provide the requested information to ensure the integrity of the article. Accordingly, we renew our request that the authors withdraw the paper by September 14.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Wednesday, September 12, 2018 at 9:30 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>, "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Please see the attached correspondence.

Thank you,
Karen Karas

Karen S. Karas ◻ Senior Counsel
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ D: 202-587-4745 ◻ F: 202.380.0514

From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Friday, September 7, 2018 7:21 AM
To: Karen S. Karas; Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Ms. Karas,

Thank you for your message. The information you requested in your message from yesterday was provided to you and Mr. Thaler on August 31. Please let me know by September 14th if the authors will withdraw the article.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
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From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Thursday, September 6, 2018 at 4:06 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>, "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe:

Thank you for your August 31, 2018 email giving us the reasons for the journal's interest in reviewing the data for the additional images. There was no explanation in your August 29, 2018 email as to why the journal was seeking data about yet more images, and that is why we objected to the request.

Please send us the journal's basis/analysis for determining that the images were reused (Figs. 1a and 6a; Figs. 3c and 4c; and 5E). We will review the journal's analysis with our clients once we receive it, and we will provide you with the original data for the additional images.

Thank you,
Karen Karas

Karen S. Karas ◻ Senior Counsel
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ D: 202-587-4745 ◻ F: 202.380.0514

From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Friday, August 31, 2018 8:41 AM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for your message. In addition to the duplication in Fig 5E, we determined the following:

- The PPAR γ blot from Fig 1A was reused in Fig 6A as pAck-H3 and H3
- The Lamin B1 blot from Fig 3C was reused in Fig 4C as H3

In light of these issues, the Editors are requesting that the authors withdraw this article. Please communicate this decision to all authors. Please request withdrawal by September 14, 2018. If the authors choose to withdraw the article, we will work with them to draft a mutually agreeable withdrawal notice. If the authors do not withdraw the article, then we will forward this matter to the ASBMB Publications Committee. The Committee may request more information, request a draft of a correction notice for editorial approval, or determine that the article is to be retracted. If the Committee determines that retraction is warranted, no further appeals will be considered and ASBMB will draft and publish a retraction notice.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Thursday, August 30, 2018 at 3:09 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe:

This email responds to (1) your August 23, 2018 email requesting a copy of the report from the VA as well as unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter and (2) your August 29, 2018 email requesting original data to Figs 1A and 6A.

Regarding the requests in your August 23, 2018 email – we decline to provide unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter. Those documents contain confidential information and were redacted at the suggestion of Dean Saleem Khan. A redacted copy of Mr. Aravind Tarugu's email exchange with Dean Khan is attached. We also decline to provide a copy of the VA's report. We have been informed by the VA that the finding against Mr. Tarugu will not be published. Therefore, Mr. Tarugu is entitled to maintain the report's confidentiality.

Regarding the requests in your August 29, 2018 email - we decline to provide the requested data. As you know, my clients have been fully cooperative and have thus far provided you the all the data and information you have requested, even the data requested in your August 16, 2018 that is not relevant to the subject matter (β -actin blot and the pMSK1 blot in Figure 5E). Your August 29, 2018 email requests additional data that is not relevant to the scope of our initial communication to you (our August 10, 2018 letter) or to Mr. Tarugu's obligation to notify you regarding the VA's finding with respect to Figure 5E.

My clients will continue to cooperate in any way they can with respect to any additional questions you may have regarding the β -actin blot and the pMSK1 blot in Figure 5E.

Thank you for your attention to this.

Sincerely,

Paul S. Thaler ◻ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Wednesday, August 29, 2018 3:15 PM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

In addition to the below documents, we would like to review the original data to Figs 1A and 6A.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: Kaoru Sakabe <ksakabe@asbmb.org>
Date: Thursday, August 23, 2018 at 3:19 PM
To: "Paul S. Thaler" <pthaler@cohenseglias.com>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for this information. Would you be able to provide a non-redacted version of attachments 1 and 2 from your letter? Additionally, we would like to review the report from the VA.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Wednesday, August 22, 2018 at 4:56 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Here is the response I received from my clients:

"No one has access to these files.

The LiCor that was used to generate these images was located in a common facility, used by multiple users. This instrument and its associated computer are no longer operational and were replaced by an upgraded system.”

Please let me know if there is anything else I can do to assist you.

Sincerely,

Paul

Paul S. Thaler ◻ Partner

Cohen Seglias Pallas Greenhall & Furman PC

1828 L Street, NW, Suite 705 ◻ Washington, DC 20036

P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [<mailto:ksakabe@asbmb.org>]

Sent: Tuesday, August 21, 2018 10:29 AM

To: Paul S. Thaler

Cc: Karen S. Karas

Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for providing these data. It seems the authors used a LICOR imaging system to obtain these data. Do the authors have access to the LICOR acquisition zip files? If so, would they be able to provide these data?

Sincerely,

Kaoru Sakabe, PhD

Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Monday, August 20, 2018 at 2:48 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Please find attached the files you requested.

Thank you for your attention to this.

Sincerely,

Paul
Paul S. Thaler ◻ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Thursday, August 16, 2018 2:29 PM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for the quick response. We would be interested in reviewing the original data for Figs 3C, 4C, and 5E. We would prefer that these images be provided uncropped and minimally processed.

Thank you in advance for your help.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Thursday, August 16, 2018 at 2:26 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

This will confirm that we also represent Dr. Raju Reddy. We are happy to help get your questions answered.

Sincerely,

Paul S. Thaler ◻ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]

Sent: Thursday, August 16, 2018 2:01 PM

To: Paul S. Thaler

Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for your patience. From your letter, it sounds like you represent only Mr. Aravind Reddy and not Dr. Raju Reddy, the corresponding author. Please confirm as we have questions for the authors.

Sincerely,

Kaoru Sakabe, PhD

Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: "Paul S. Thaler" <pthaler@cohenseglias.com>

Date: Saturday, August 11, 2018 at 7:19 AM

To: Kaoru Sakabe <ksakabe@asbmb.org>

Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Thank you, Dr. Sakabe. We look forward to hearing from you.

Sincerely,

Paul S. Thaler, Esq.
Cohen Seglias Pallas Greenhall & Furman PC
(202) 587-4750

Sent from my iPad

On Aug 10, 2018, at 2:58 PM, Kaoru Sakabe <ksakabe@asbmb.org> wrote:

Dear Mr. Thaler,

Thank you for your letter. Please allow us some time to review the information.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org



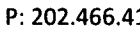
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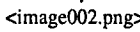
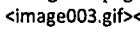
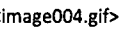
From: Cynthia Roberson <croberson@cohenseglias.com>
Date: Friday, August 10, 2018 at 11:54 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Good afternoon Dr. Sakabe.

Please see attached letter on behalf of Paul S. Thaler regarding the above reference matter. Should you have any questions or concerns, please do not hesitate to contact Mr. Thaler.

Thank you
Cynthia

Cynthia Roberson<Administrative Assistant
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705<Washington, DC 20036
P: 202.466.4110<F: 202.466.2693

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From: Kaoru Sakabe <ksakabe@asbmb.org>
Sent: Friday, September 14, 2018 1:19 PM
To: Karen S. Karas
Cc: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Ms. Karas,

I have not received an email.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Friday, September 14, 2018 at 12:25 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

I just emailed you a letter from Paul Thaler along with three Power Point files and seven .tif files. Because of the size of the attachments, I had to send the email through our firm's "Share File" site. Please send me an email to confirm receipt once you receive the email.

Thank you,

Karen Karas

Karen S. Karas ◻ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0514



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From: Karen S. Karas
Sent: Friday, September 14, 2018 1:41 PM
To: 'Kaoru Sakabe'
Cc: Paul S. Thaler
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

I have just finished sending all five emails. Please confirm receipt.

Thank you,
Karen Karas

Karen S. Karas ◻ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0514

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From: Karen S. Karas
Sent: Friday, September 14, 2018 3:54 PM
To: 'Kaoru Sakabe'
Cc: Paul S. Thaler
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

It appears that my five emails were transmitted successfully to you earlier this afternoon, as I did not receive any transmission error messages. If this is incorrect, please let me know.

Thank you,
Karen Karas

Karen S. Karas ◻ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0514

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From: Kaoru Sakabe <ksakabe@asbmb.org>
Sent: Wednesday, September 19, 2018 1:42 PM
To: Karen S. Karas
Cc: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Ms. Karas:

Our policies may be found here: http://www.jbc.org/site/misc/edpolicy.xhtml#ethics_policy. We will not share further internal analyses/reports.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Wednesday, September 19, 2018 at 9:12 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Thank you for email. As this process moves forward to the next step, we would appreciate your answering the following questions and providing the information requested by close of business, September 20th, 2018, so that we have a better understanding of how the Editors reached their decision, and so that we can make plans going forward:

1. As we asked previously in our September 14 email, provide a copy of the Editors' analyses and reports describing the techniques they used to review the data/images we provided from August 10, 2018 through September 14, 2018.
2. Confirm that our September 14 emails (and all attachments) were shared with the Editors.
3. Forward the guidelines/policies which will apply to and govern the ASBMB Publications Committee's consideration of this matter.
4. Confirm that all of our communications with you, beginning with our August 10, 2018 letter, will be made available to the ASBMB Publications Committee.

Thank you,
Karen Karas

Karen S. Karas ◻ Senior Counsel
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ D: 202-587-4745 ◻ F: 202.380.0514

From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Tuesday, September 18, 2018 9:23 AM
To: Karen S. Karas
Cc: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler and Ms. Karas:

We are in receipt of all 5 files. As your clients do not agree to withdraw, we will be forwarding this matter to the ASBMB Publications Committee. I will inform you of their decision.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Friday, September 14, 2018 at 1:41 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

I have just finished sending all five emails. Please confirm receipt.

Thank you,
Karen Karas

Karen S. Karas ◻ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC

1828 L Street, NW, Suite 705 □ Washington, DC 20036
P: 202.466.4110 □ F: 202.380.0514

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Tarugu, Aravind Reddy

From: Khan, Saleem A
Sent: Wednesday, July 25, 2018 11:57 AM
To: Tarugu, Aravind Reddy
[REDACTED]
Subject: RE: Request

Dear Aravind:

The April 4, 2018 letter from Provost Beeson is the official notification from the University regarding the disposition of your appeal, as the Provost is the highest ranking academic officer. It would be inappropriate for an additional letter to be generated. If there is information included in the notification that you do not wish to share with the JBC, I would suggest considering a redaction. Sorry I could not be of further assistance.

Sincerely,

Saleem A. Khan, Ph.D.
Associate Dean for Academic Affairs
Professor
Department of Microbiology and Molecular Genetics
University of Pittsburgh School of Medicine
S527 Scaife Hall
Pittsburgh, PA 15261
Office (412) 648 – 3911
E-mail: khan@pitt.edu

From: Tarugu, Aravind Reddy
Sent: Tuesday, July 24, 2018 11:56 AM
To: Khan, Saleem A <khan@pitt.edu>
[REDACTED]
Subject: Request

Dear Dean Khan,

As you may be aware, the VA Undersecretary upheld the decision made by ORO [REDACTED]. I was contacted by the VA to send a notification of this VA finding to JBC. As the University of Pittsburgh, the lead institute of this investigation overturned this decision, I would like to send this response letter to JBC along with the VA ORO letter. As the letter from the Provost (dated April 4, 2018) includes confidential information and internal findings, I cannot use it in the current format.

I request that you provide me with a letter stating a finding of no research misconduct on my part, [REDACTED].
[REDACTED]

I have a deadline for sending this notification (August 10, 2018), hence I kindly request your immediate attention to this matter.

Thank you in advance for your help. I appreciate it.

APPENDIX C

SEPTEMBER 12, 2018 LETTER FROM PAUL THALER TO DR. KAORU SAKABE

Including:

ATTACHMENT 1: September 11, 2018 letter from Dr. Reddy and Mr. Tarugu addressing Dr. Sakabe's comments and pdf attachment to Dr. Sakabe's August 31, 2018 email.

ATTACHMENT 2: Original data and image analysis including the complete description of techniques/tools used and observed interpretations (discussed in Dr. Reddy's and Mr. Tarugu's September 11, 2018 letter)



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September 12, 2018

VIA ELECTRONIC MAIL

ksakabe@asbmb.org

Kaoru Sakabe, Ph.D.
Data Integrity Manager
American Society for Biochemistry
and Molecular Biology
11200 Rockville Pike
Suite 302
Rockville, MD 20852

***Re: Journal of Biological Chemistry Publication
Lakshmi, et al. 2014 Article***

Dear Dr. Sakabe:

I write to follow up on our continuing dialogue regarding the above-referenced paper. First, I want to let you know that neither we nor our clients realized that the document attached to your August 31, 2018 email constituted the totality of JBC's analysis of the images, so we appreciate your having confirmed that fact in your September 7, 2018 email. Second, we want to address any misunderstanding that you or any of JBC's Editors might have had in response to our August 30, 2018 email (objecting to providing data for additional figures). Third, we want to share with you and the JBC Editors the original images and their forensic analyses undertaken by our clients, which is attached and discussed below, and which we hope the JBC editors will find helpful.

As you know, the reason we contacted you in August was because Mr. Aravind R. Tarugu was directed to do so by Dr. Steven Graham, the research integrity officer of the Department of Veteran Affairs' ("VA"). The only figure about which the VA is concerned (and thus the narrow focus of our initial communication to you) is Figure 5E (specifically, two panels in Figure 5E, beta actin and pMsk1). However, in response to our initial August letter, you requested original data not only for Figure 5E, but Figures 3C and 4C as well. Even though JBC's request went beyond the concern of the VA, my clients provided all of the requested data. They also answered your follow-up inquiry regarding the LICOR imaging system. When, however, JBC further expanded its inquiry to include Figures 1A and 6A, it was, in our opinion, appropriate to set limits on what seemed to us to be an ever expanding inquiry that was getting

Dr. Sakabe
September 12, 2018
Page 2

further and further away from the concern of the VA (two panels in Figure 5E). That is what lead to our August 30, 2018 email to you objecting to JBC's request for data related to Figures 1A and 6A. We were surprised to then receive your August 31, 2018 email advising us of the decision of JBC's Editors that Figures 1A and 6A, and Figures 3C and 4C, contained duplications and that they had decided the article should be withdrawn.

Our clients strongly disagree with the decision of the Editors that the article should be withdrawn. We request that the Editors carefully review the attachments to this letter and then reconsider and reverse their decision. Mr. Tarugu and Dr. Reddy are deeply concerned that the Editors reached their conclusions regarding the subject Figures (Figures 1A and 6A, 3C and 4C, and 5E) without reviewing the *original images* and without completing a proper *forensic* analysis. The pdf attachment to your August 31, 2018 email does not reveal that any such forensic analysis of any of the images was undertaken.

As shown in Attachment No.2 to this letter, when the original images are reviewed or forensically analyzed as instructed by the Department of Health and Human Service's Office of Research Integrity, it is apparent that there is *no* duplication of images in Figures 1A, 6A, 3C, 4C and 5E. Attachment No. 1 is a letter from Dr. Reddy and Mr. Tarugu explaining the forensic analyses they undertook and the tools they employed. The results of the forensic analyses regarding Figure 5E are further supported by lab notebook pages (included as part of Attachment No. 2 at p. 7) as well as the expert opinion of Dr. John C. Russ (included as part of Attachment No. 2 at p.6).

On behalf of Mr. Tarugu and Dr. Reddy, we thank you and the Editors for considering these additional materials. For all these reasons, and those stated in the attached letter and analyses, we request that JBC's Editors reconsider their decision and conclude instead that withdrawal of the article is not necessary. Dr. Reddy and Mr. Tarugu will continue to cooperate and will answer any questions that the Editors may have regarding the attached letter and analyses. Our clients are willing to provide additional information consistent with the positions we have taken in our prior communications .

Very truly yours,



Paul S. Thaler

Attachments

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Raju C. Reddy

September 11, 2018

Dear Dr. Sakabe:

On August 10, 2018, Mr. Thaler, on behalf of Mr. Tarugu, sent you a letter as notification to the Journal of Biological Chemistry (hereafter “JBC”) (hereafter “Notice to JBC”), as required by the Department of Veterans Affairs (“VA”), regarding the VA’s finding made related to Figure 5E beta actin and pMsk1 in the Lakshmi et al. 2014 article. In response to the *Notice to JBC*, JBC requested that we provide data for additional images. Even though that request went beyond the scope of the initial *Notice to JBC*, in the spirit of cooperation and disclosure, we provided the data as requested. We then received a further request, on August 29, to provide additional images not related to the image in question as outlined in the *Notice to JBC*. As we had not received an explanation for this request and the requested images were beyond the scope of the *Notice to JBC*, we respectfully declined to provide this data, yet indicated our full cooperation to provide any additional information related to Figure 5E beta actin and pMsk1.

On August 31st, 2018, we were notified by JBC via our attorney Mr. Thaler that “the Editors are requesting that the authors withdraw this article” adding “In addition to the duplication in Fig 5E, we determined the following:

- The PPAR γ blot from Fig 1A was reused in Fig 6A as pAcK-H3 and H3
- The Lamin B1 blot from Fig 3C was reused in Fig 4C as H3”

Attached to JBC’s August 31, 2018 email was a PDF attachment (hereafter “JBC Analysis”) providing pictorial information as a basis for the above determination. Since we did not receive any additional information regarding this analysis, such as the source of images, software tools used, and interpretations made based on such analysis, we are not able to understand from the *JBC Analysis* how JBC reached its conclusions regarding image duplication. However, after reviewing the images in the *JBC Analysis*, it appears that JBC used snapshots of images from the Lakshmi et al. 2014 article to perform an image analysis to which a color gradient was applied on figure 1A, 6A and 5E to determine if reuse of the images occurred. Our understanding that JBC used snapshots comes from the existence of border lines below and above the images of interest as we prepared the figures with the outlines for publication. The *JBC Analysis* does not reveal any analysis performed on figures 3C and 4C, and, thus, JBC’s conclusion regarding those figures seems to be based entirely on a naked eye comparison. Additionally, no information on histogram equalization was provided in the *JBC Analysis*. As we believe that snapshots were used and no histogram equalization was performed prior to JBC’s image analysis, these factors may have resulted in some of the inaccuracies with the *JBC Analysis*.

In light of our concern about the *JBC Analysis* and the fact that JBC’s inquiries have now surpassed the original scope of both the *Notice to JBC* and the VA’s concern, we are attaching to Mr. Thaler’s letter (as Attachment No. 2) the images for the above-mentioned figures and detailed forensic image analyses performed with these images. As you can see, the images themselves, when evaluated in their proper context, **provide conclusive evidence** that no images were reused. In addition, however, we are providing additional incontrovertible image analysis to further demonstrate lack of reuse. The tools and procedures we used for analyzing these images

are provided below. We used two different advanced approaches to perform forensics image analysis. The availability and application of these tools is well documented in the literature and in the relevant online sections. We are able to provide any additional details regarding these tools as necessary.

1. Using NIH Office of Research Integrity (ORI) Advanced Forensic Actions tools in Adobe Photoshop: In this process histogram equalized images were applied with advanced dark or light areas and advanced gradient map to determine the similarities or differences (in our case) between images. The preset actions will allow the user to limit personal biases.
2. Using image segmentation, thresholding, and sobel gradient in MATLAB Image Processing Toolbox: In this process histogram equalized image is portioned into regions based on the pixel characteristics of the image. This will find the discontinuities in pixel values and indicated edges. This process eliminates biases as the process is performed as a coded program.
3. Use of notebook entries: Along with image analysis and original images, we also provided lab notebook entries related to Figure 5E beta actin and pMsk1 performed ~6 months apart by two different researchers.

Forensic analysis of our images clearly shows the differences between each allegedly duplicated image. These differences include:

- a) Several differences in excised borders of membrane and its size.
- b) Presence of protein marker lanes in the blots.
- c) Several differences in heatmaps and gradient maps of images and bands.
- d) Several differences in backgrounds of the images.

All of the above differences reflect very clear and conclusive results from rigorous analysis versus analysis performed in a non-rigorous manner (using the naked eye, or focusing on singular images or general visual effects).

Along with these analyses, we provide the forensics image analysis performed by Dr. John Russ (included in Attachment No. 2 to Mr. Thaler's September 11, 2018 letter). Dr. Russ has authored several highly regarded and cited works on image processing. His book "The Image Processing Handbook" has been consistently rated as the best overall introduction to computer-based image processing and has been cited >4,000 times according to Google citations. He has also been awarded the Ernst Abbe Memorial Award for his contributions to the field.

In our *Notice to JBC*, we also provided evaluations from Dr. Alan Price and Dr. John Dahlberg, two highly respected, independent experts who retired after long careers in senior level positions at NIH's ORI and have extensive experience reviewing thousands of allegations and misconduct/data manipulation cases. Both experts independently agreed with us and explained why the paper should not be retracted. We also emphasize that the University of

Pittsburgh was the lead institute of this investigation and *concluded that there was no misconduct* and *that there was no evidence of image reuse*.

With all the above factual evidence, we respectfully decline to withdraw our article.

Sincerely,

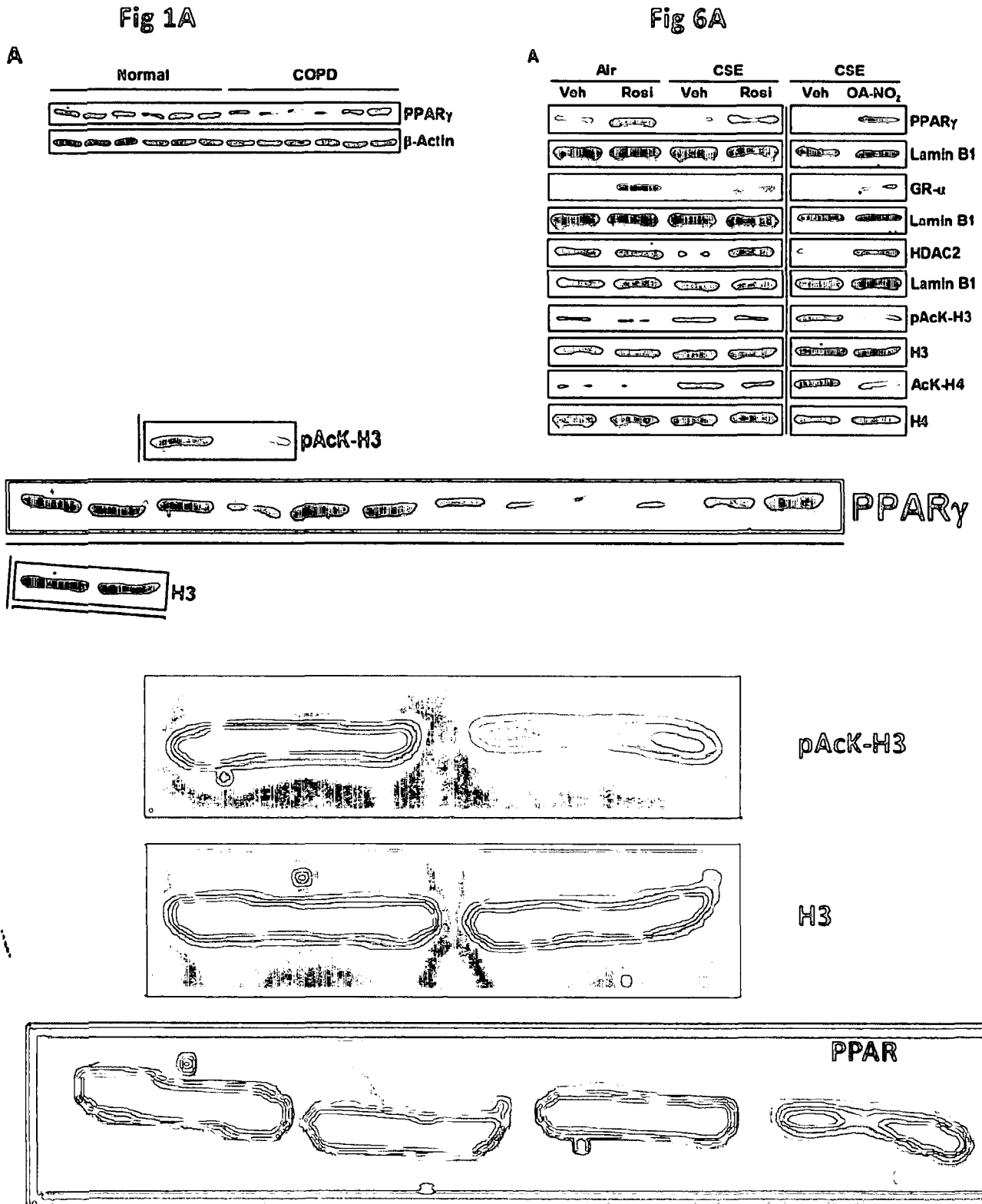
Aravind T. Reddy
Aravind Reddy Tarugu

Raju Reddy
Raju C. Reddy

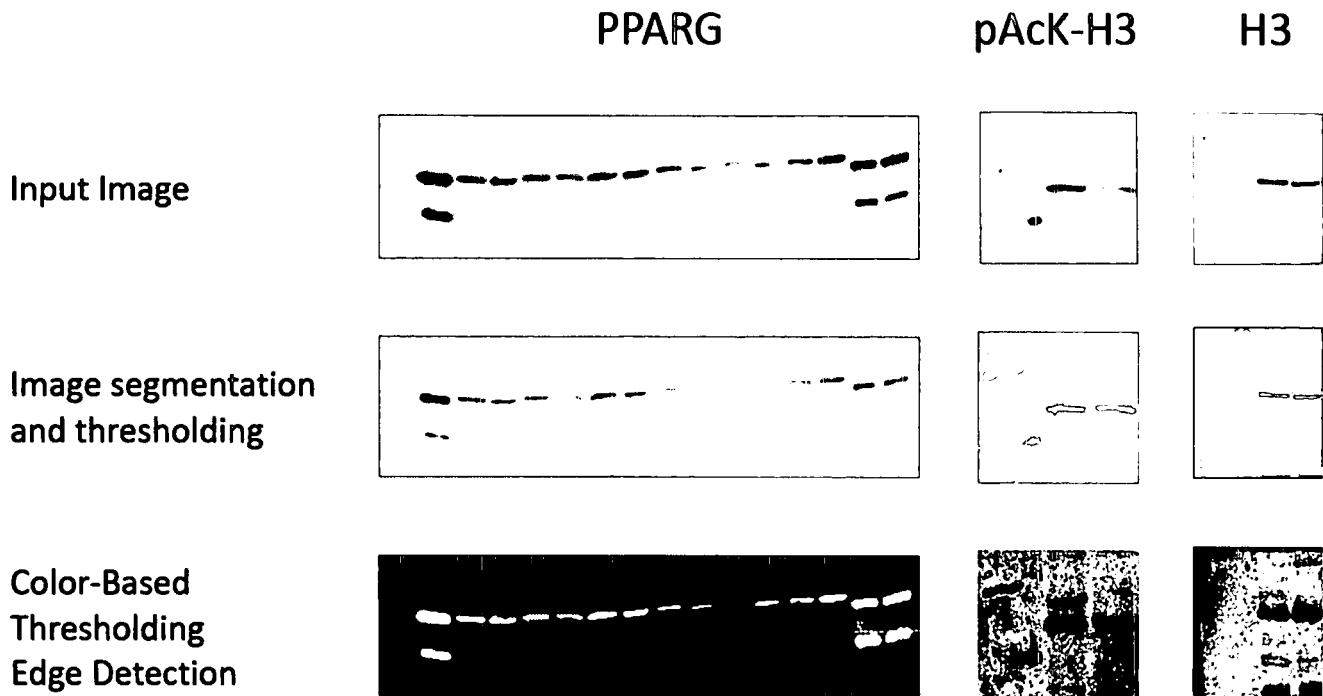
JBC: Figure 1A (PPAR gamma) and 6A (pAckH3; H3).

Same data used to represent different experimental conditions

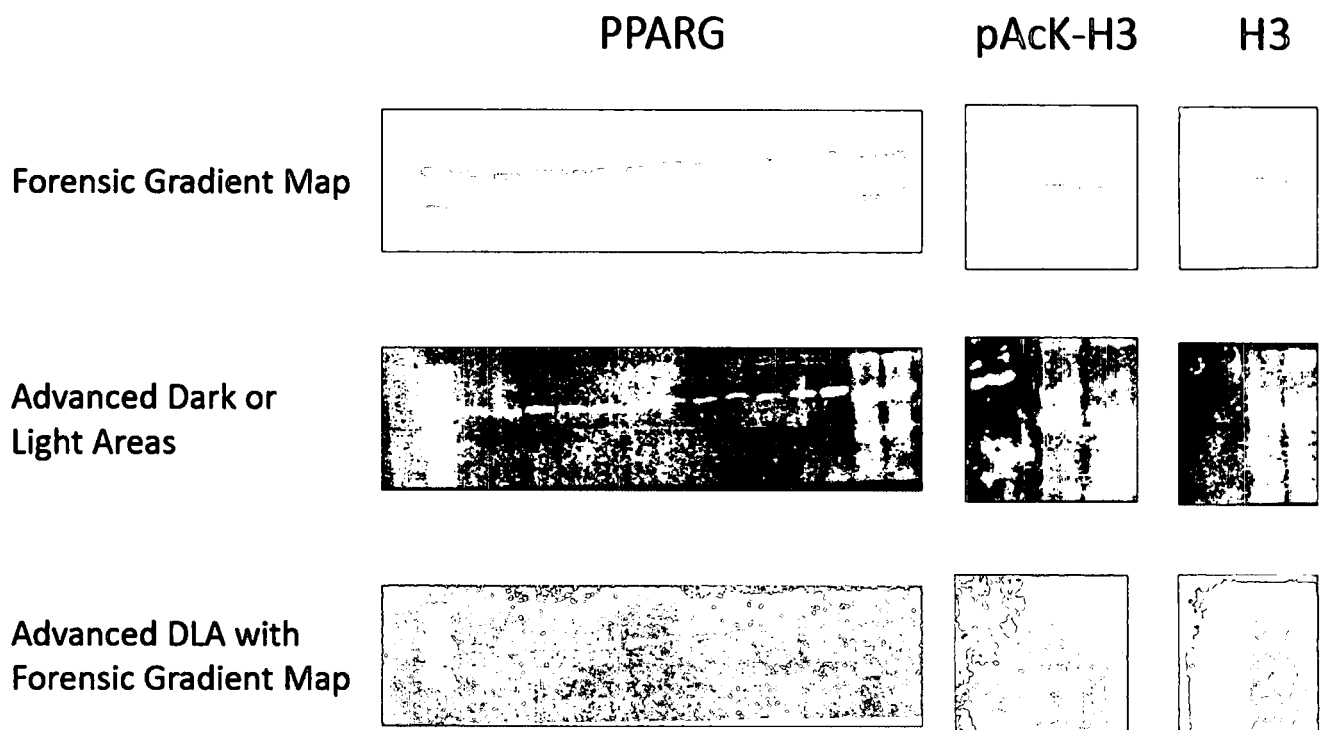
Reddy RC
JBC/2013/536805
Figs 1A and 6A



Forensic Image analysis was performed with
 MATLAB (The Image Processing Toolbox)



Forensic Image analysis performed with Adobe Photoshop using
 NIH Office of Research Integrity (ORI) Advanced Forensic Actions



JBC: Figure 3C (Lamin B1) and 4C (H3).

Same data used to represent different experimental conditions

Reddy RC
JBC/2013/536805
Figs 3C and 4C

Fig 3C

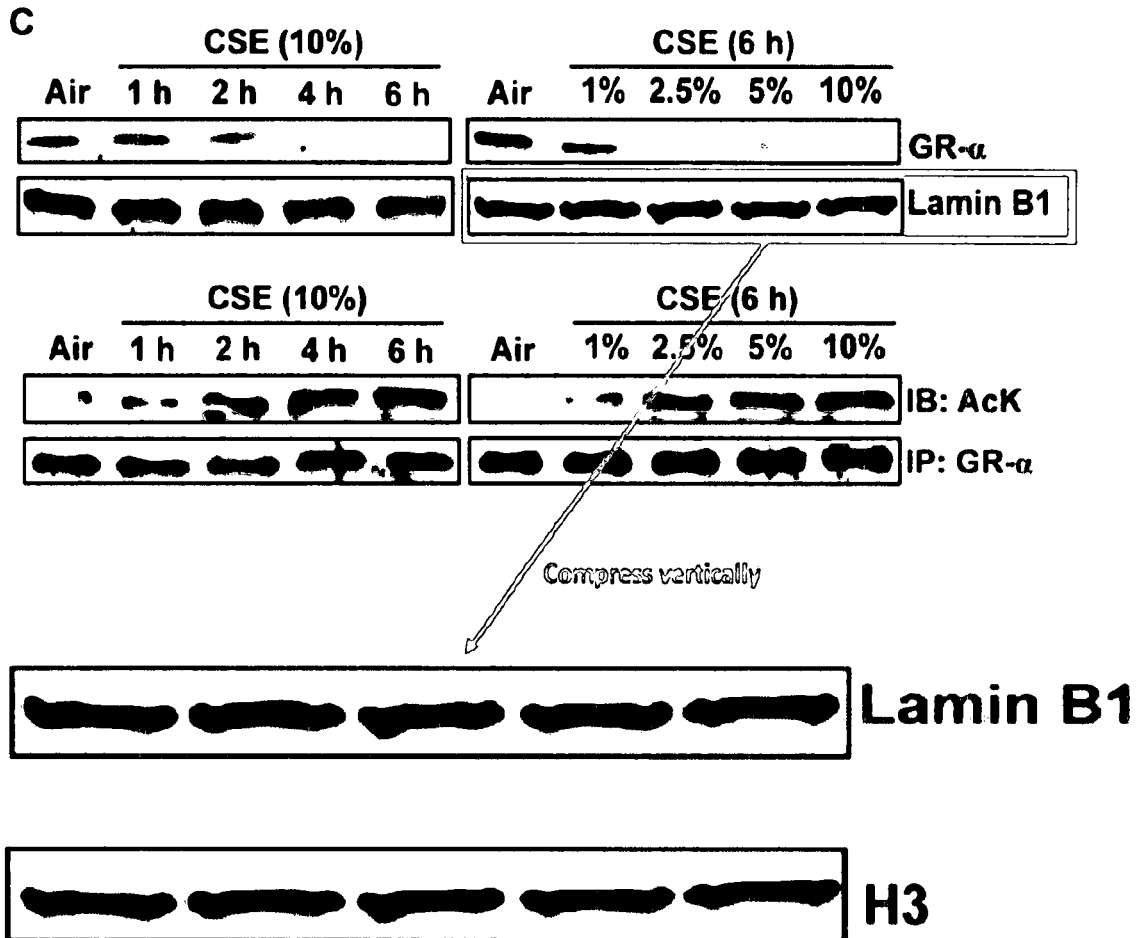
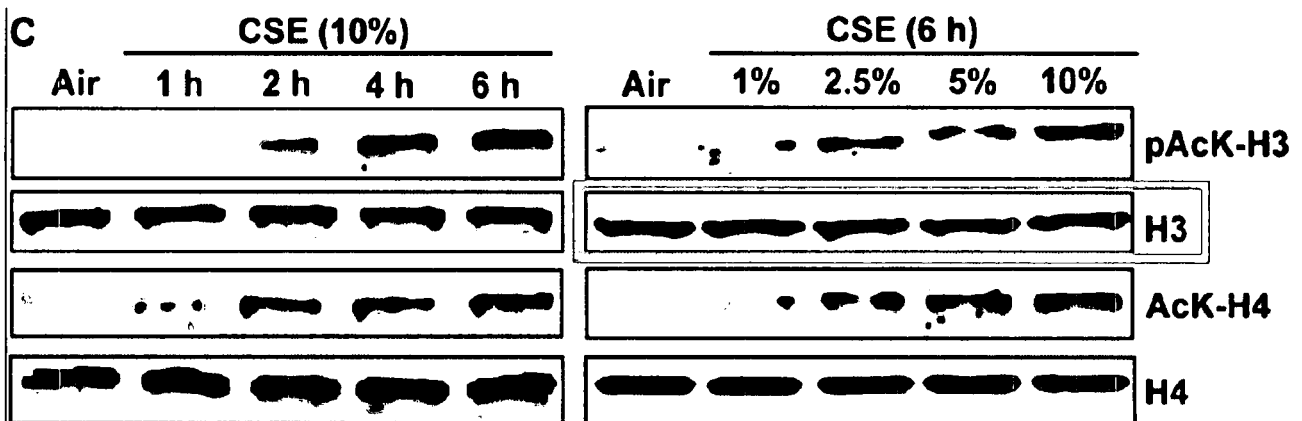
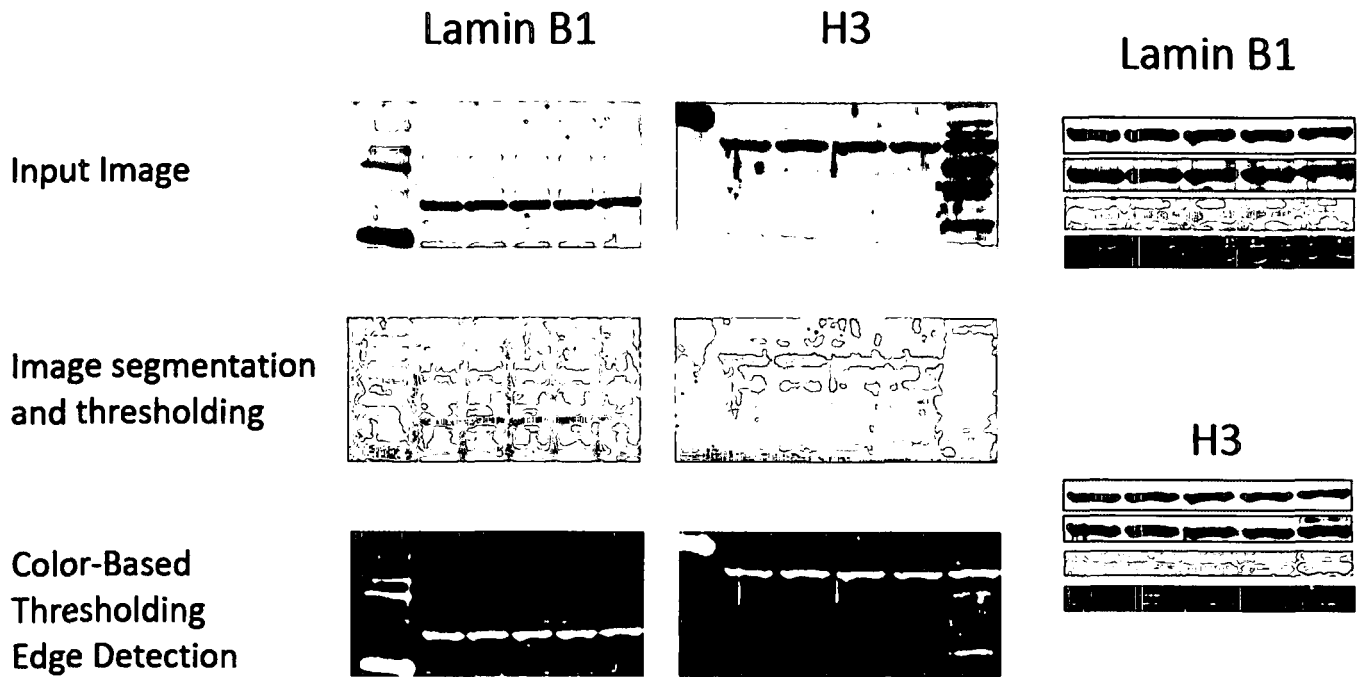


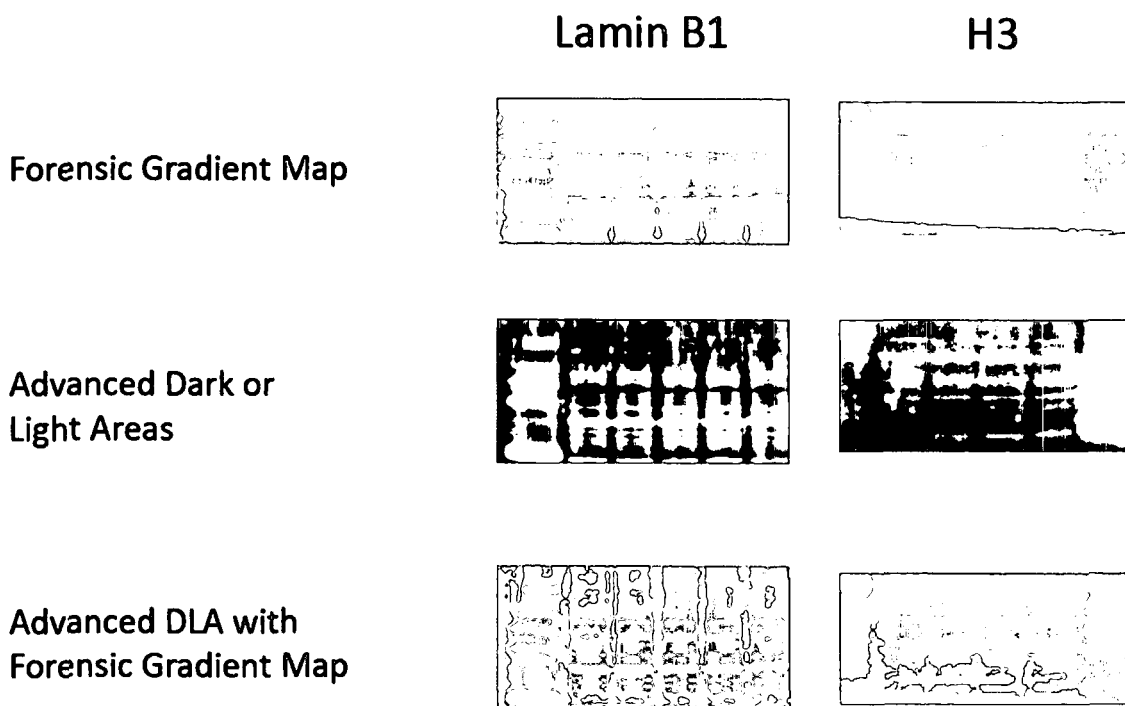
Fig 4C



Forensic Image analysis was performed with
MATLAB (The Image Processing Toolbox)



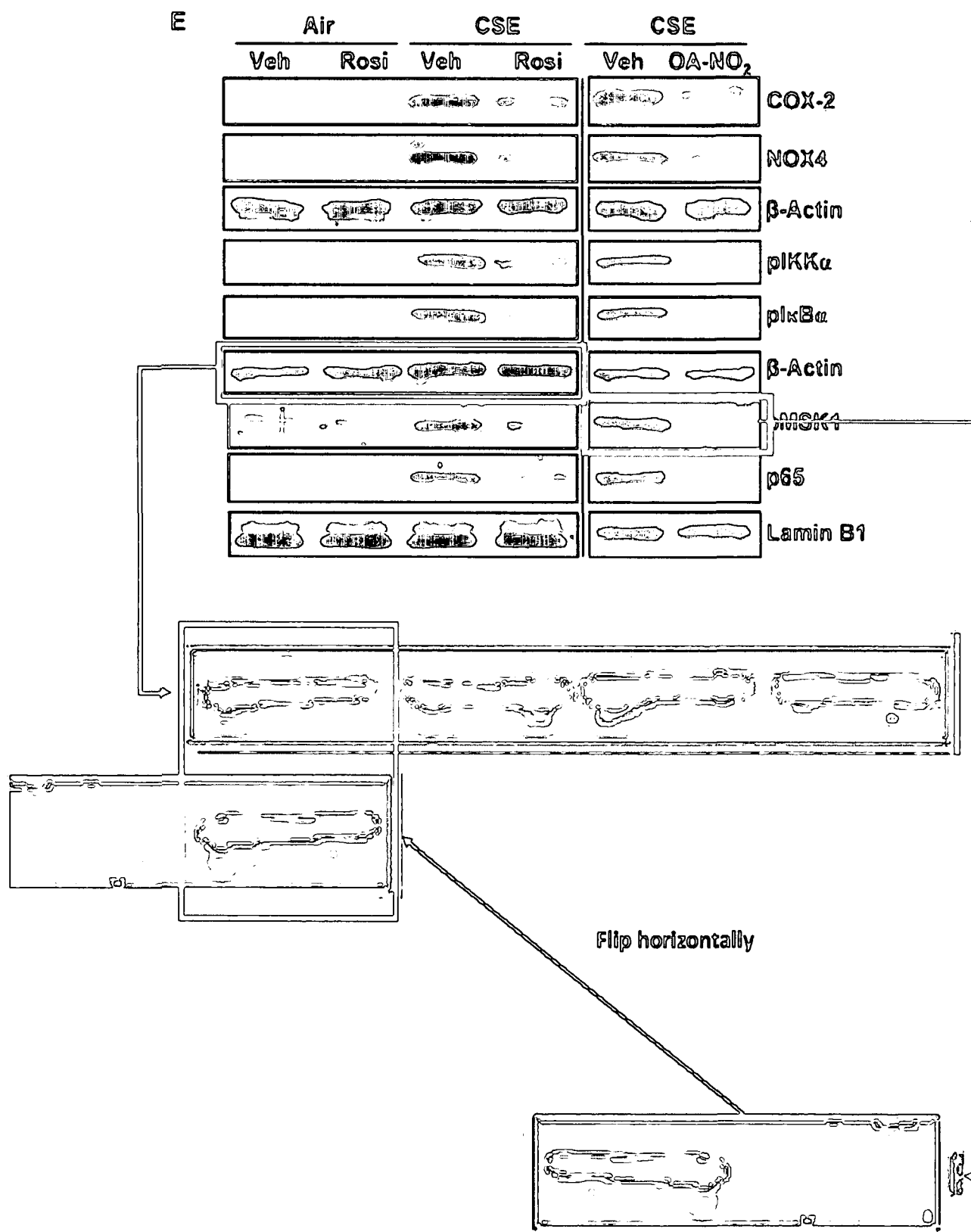
Forensic Image analysis performed with Adobe Photoshop using
NIH Office of Research Integrity (ORI) Advanced Forensic Actions



JBC: Figure 5E (bActin and pMsk1).

Same data used to represent different experimental conditions

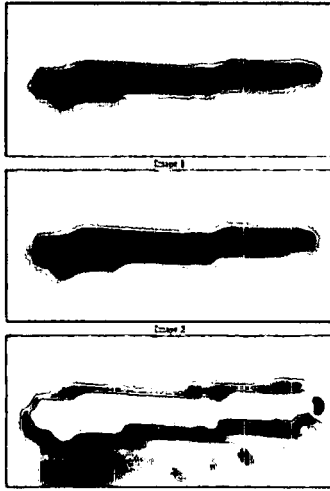
Reddy RC
JBC/2013/536805
Fig 5E



Forensic Image analysis performed by Dr. John C. Russ

Several important differences are noteworthy.

First, nearly the entire border of the difference image is dark, indicating that one blot image is definitely larger than the other.



Second, along the border there are variations in the density difference that are not uniform. In other words, one image could not be generated by simply enlarging the other or applying an overall brightness adjustment, which would have produced the same density all along the border. This is especially marked at the right edge, where an entirely different shape is revealed.

Third, there are several locations within the dense region (bright in the image shown) where pixels are slightly darkened indicating different densities in the original images.

Fourth, there are numerous regions in the surrounding areas that do not match, producing various darkened or lightened regions. That indicates that the images of the substrates are different.

From these differences, there is no doubt in my mind that the two original images are distinct.

Forensic Image analysis was performed with MATLAB (The Image Processing Toolbox)

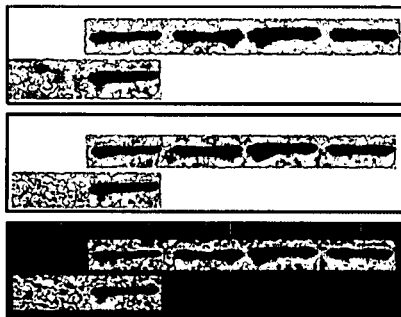
Forensic Image analysis performed with Adobe Photoshop using NIH Office of Research Integrity (ORI) Advanced Forensic Actions

Input Image
Histogram Equalized



Beta Actin
pMsk1 (Flipped for Analysis)

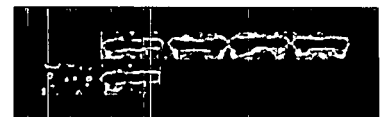
Image segmentation and thresholding to detect edges



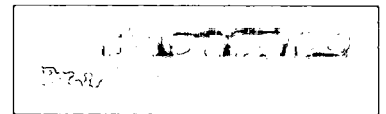
Key differences between two images in terms of band shape threshold and background



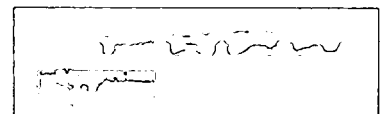
Advanced Dark or Light Areas (Gray)



Forensic Gradient Map 1



Forensic Gradient Map 2



APPENDIX D

SEPTEMBER 14, 2018 LETTER FROM PAUL THALER TO DR. KAORU SAKABE

Letter addresses Dr. Sakabe's comments, highlights the transparency and cooperation by Mr. Tarugu and Dr. Reddy, notes JBC/ASBMB's lack of transparency in this matter, and identifies Mr. Tarugu and Dr. Reddy's requests for information required for review and JBC/ASBMB's lack of response thereto.



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September 14, 2018

VIA ELECTRONIC MAIL

ksakabe@asbmb.org

Kaoru Sakabe, Ph.D.

Data Integrity Manager

American Society for Biochemistry

and Molecular Biology

11200 Rockville Pike

Suite 302

Rockville, MD 20852

***Re: Journal of Biological Chemistry Publication
Lakshmi, et al. 2014 Article***

Dear Dr. Sakabe:

I am in receipt of your September 12, 2018 email. With all due respect, your email does not fairly characterize the communications we have had over the last several weeks, nor does it reflect the spirit of cooperation or good faith with which my clients have acted. Until receiving your email yesterday, we did not know that JBC was dissatisfied with the data/images they had already been provided. I have gone back through your earlier emails to make sure we did not overlook something, but I can find no email in which you advised, for example, that the quality of the data provided on August 20 was "of such poor quality that [JBC] requested the native files" or that the images provided in the pdf "are of too poor quality for JBC to analyze." None of your prior emails, before yesterday, noted any concern about the quality of the data/images my clients have provided, nor did you make any follow-up requests after receiving the files, by notifying us of the concern(s) that you had. Our communications (and my clients' efforts to respond to JBC's concerns) would have benefited from more transparency by JBC about its concerns. My clients are understandably frustrated and perceive that they are being blamed for not responding to JBC's concerns that they did not even know existed about data/image quality. This was the same frustration we had over JBC's request for the data for Figures Figs 1A and 6A. The request itself did not explain why the data was being requested and did not disclose what concerns JBC had about those figures. Also note that your request was not limited to the PPAR gamma, AckH3 and H3 blots, the specific blots on which you raised concerns, but it goes well beyond, requesting 24 images. It was not until we said we would not provide the data, as your request was beyond the scope of our notification, that you then informed us as to the reason behind the request. JBC's own policy and policies by the Council of Science Editors provide

that if there is a concern about an image, JBC should notify the author as to what the concern is, ask for an explanation, and then request that data be provided. It seems that JBC has not followed its own policy. As my clients were neither notified of any concerns, nor provided an opportunity to respond/provide an explanation, they are clearly not at fault as you have stated. If you have access to a policy allowing JBC to ask for any data without first (or concurrently) notifying an author about JBC's concerns, and allowing JBC to make a determination without providing an opportunity for explanation, please do provide us with a copy of that policy.

With respect to the new concerns you raised for the first time in Wednesday's email, we address them below. Had you shared those concerns with us previously, as required by JBC's or the Council of Science Editors policies, we could have addressed them sooner.

- The reason my clients did not initially provide images for figures 1A and 6A was that they were not notified of any concerns regarding these images. Thus, it is not fair to put them at fault. Additionally, they did not "criticize" JBC's analysis; they simply stated that their understanding of the image analysis provided by you was limited, as you did not provide them with any specific information on the image analysis. We twice requested that you provide the details, but never got any response from you. Also, JBC did not contest our clients' claim that it was their understanding that snapshots from the PDF file were used by JBC for its image analysis. Using snapshots does not comport with the Department of Health and Human Services' Office of Research Integrity guidelines for image analysis. If JBC has separate guidelines for performing image analysis, please provide us with a copy. The use of the PDF file for image analysis by JBC did not result from our clients' not providing the requested information, rather it resulted because of JBC's decision to use such files to perform an image analysis on PDF snapshots. My clients are not responsible for how JBC does its image analysis.
- Regarding figures 1A and 6A – your email states that Dr. Reddy and Mr. Tarugu "refused to provide the original data and images for figures 1A and 6A" and "the images in the PDF provided are of too poor quality for JBC to analyze." They did not "refuse" to provide the original data. We clearly stated in our September 6, 2018 that we would provide the original data but asked to first see JBC's analysis. In response, you told us that the attachment to your August 31, 2018 email was the analysis (which we could not have known as it does not contain any information on how the analysis was performed and how the conclusions were drawn) and you inexplicably directed my clients to withdraw the article. Notwithstanding our disagreement with JBC as to whether the August 31, 2018 attachment is an "analysis," and whether JBC requested these images with appropriate notification, following its own policies, we are now providing the requested original data files (PPT files and .tiff file) to the email transmitting this letter. The .tiff file contain the original data for not only Figures 1A and 6A, but also Figures 3, 4 and 5.

Dr. Sakabe
September 14, 2018
Page 3

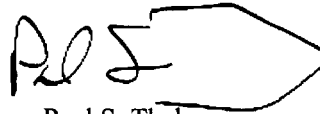
- Your email states that “the images in the PDF provided are of too poor quality for JBC to analyze.” See above response regarding PPT and .tiff files being provided. Even though the existence of these files and the fact that a rigorous analysis had been performed on these images was apparent by our letter, we did not receive any request to send the .tiff files.
- Regarding the data we sent for Figures 3C and 4C, your email states: “The data shown in the attachment for figures 3C and 4C do not appear to correspond with what is presented in the publication.” To the contrary, the tiff file “7.tiff” being sent concurrently with this letter demonstrates that figures 3C and 4C do indeed correspond with what is presented in the publication” This can be seen visually from 7.tiff as well as in the analysis of those images which we provided to you on Wednesday (September 12, 2018). JBC has provided no basis or explanation for the conclusion that the data does not correspond to the images. If the Editors have conducted an analysis of the Figure 3C and 4C data that we provided on Wednesday, or should they do so with the additional images we are providing today, please provide it to us for our review.
- Your email states that “[t]he quality of the data provided on August 20 was of such poor quality that we requested the native files, but none were provided.” When we sent the data on August 20, you did not respond to inform us that JBC considered the data to be of poor quality nor did you ask for better quality data. Indeed, the Editors appear to have considered the files to have been of sufficient quality to use for their “analysis” in concluding (albeit incorrectly) that there were duplications. In any case, we are now providing, as noted above, the original .tiff files for the five figures about which JBC has inquired. The files are: 1.tiff -1A PPARg; 2.tiff - 6A pAH3; 3.tiff - 6A H3; 4.tiff - 3C Lamin; 5.tiff - 4C H3; and 6.tiff - 5E pMsk1: 7.tiff - lamin and H3 blots.
- As we stated in our August 30, 2018 email, our clients are entitled to their rights and protection of confidentiality during the investigation process. The VAPHS notice does not require us to send any documents related to the investigation. However, we wanted to be transparent and cooperative, thus we did provide documents. The redactions we made to the documents were appropriate and necessary to protect confidential information in conformance with the fair information practice (according to PHS policy 42 CFR Parts 50 and 93 and Privacy Act, and also as suggested by the University of Pittsburgh’s Dean Kahn in his email, a copy of which was sent to you) which allows us to withhold such confidential information from JBC and any other external entity. If you or the Editors have a specific question regarding the completeness of the investigation that is relevant to JBC’s own analysis of the images and data we have provided, please do let me know, and if I can respond without violating the confidentiality limits stated above, I will do so.

Dr. Reddy and Mr. Tarugu stand by the original images and image analyses we attached to our September 12, 2018 letter and which we are providing today. These demonstrate that

Dr. Sakabe
September 14, 2018
Page 4

there was no duplication in any of the images, as the Editors should also now be able to see from the additional PPT and .tiff files we are providing. Should the Editors have any evidence, analyses and/or explanation to demonstrate why my clients image analyses are wrong, ***please share it with us***. If there is any policy that supports the Editors' decision to direct that my clients withdraw the article before there is a thorough exchange of information, disclosure by the Editors of the analysis supporting their decision, and a full and fair opportunity for my clients to respond, ***please share it with us***. With all due respect, it is unfair to expect my clients to simply withdraw the article on the sole basis that JBC says these images are duplicated when JBC has not provided any evidence or analyses substantiating its conclusion. We understand JBC's interest in resolving any concerns it has, but that resolution must come only after a fair process that is transparent and clearly communicates to my clients what the concerns are and gives them an opportunity to respond.

Very truly yours,

A handwritten signature in black ink, appearing to read 'P. S. Thaler', enclosed within a hand-drawn, irregular loop that forms a signature box.

Paul S. Thaler

Attachments (attached to 9/14/18 transmittal email)
cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Raju C. Reddy



Paul S. Thaler
Attorney At Law

1828 L Street, NW
Suite 705
Washington, DC 20036

T: 202.466.4110 | F: 202.466.2693
pthaler@cohenseglias.com
www.cohenseglias.com

November 30 , 2018

VIA ELECTRONIC MAIL

Dr. Gerald Hart, President

gwhart13@me.com

Ms. Barbara Gordon, Executive Director

bgordon@asbmb.org

Ms. Nancy Rodnan, Senior Director of Publications

nrodnan@asbmb.org

American Society for Biochemistry
and Molecular Biology

11200 Rockville Pike

Suite 302

Rockville, MD 20852

**Re: *Journal of Biological Chemistry Publication*
*Lakshmi, et al. 2014 Article***

Dear Dr. Hart, Ms. Gordon and Ms. Rodnan:

We represent Mr. Aravind R. Tarugu and Dr. Raju C. Reddy, two of the co-authors of Lakshmi SP, Reddy AT, Zhang Y, Scirba FC, Mallampalli RK, Duncan SR, and Reddy RC, The Journal of Biological Chemistry 289(10):6383-6393 (2014), "Down-regulated peroxisome proliferator-activated receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)" ("Article"). The Journal of Biological Chemistry ("JBC") and the American Society for Biochemistry and Molecular Biology ("ASBMB") have determined that the Article should be withdrawn or retracted, a decision with which our clients disagree.

Unfortunately, despite our efforts to date (which have been ongoing since August), including correspondence with Dr. Kaoru Sakabe and Dr. Enrique De La Cruz, we have not received sufficient information from JBC/ASBMB which demonstrates how JBC/ASBMB reached a conclusion that any of the images are duplicated. Thus, we are writing to you to seek your assistance in getting us the information we have requested. The lack of transparency from JBC/ASBMB is so great that we cannot even get a response to a very basic question – of the images at issue, on which images is JBC/ASBMB basing its November 21, 2018 decision that the Article should be withdrawn or retracted? Dr. Sakabe has set a deadline of Wednesday, December 5, 2018 for the authors to determine whether they will agree to voluntarily withdraw

Dr. Gerald Hart, Ms. Gordon
& Ms. Nancy Rodnan
November 30, 2018
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the Article. Without the information necessary to understand how JBC/ASBMB reached its decision, and without knowing which images were concluded to be duplicates, my clients cannot defend against retraction on the basis that there is a flaw in JBC/ASBMB's analysis (because we do not know what, if any, JBC/ASBMB actually undertook), or even make a decision as to whether to agree to a withdrawal or perhaps offer a correction.

To help you better understand the information we have requested, and to understand the nature of our communications with JBC/ASBMB, I am attaching our September 21, 2018 appeal letter to Dr. Enrique de la Cruz (Attachment A). In addition, I am attaching our November 27, 2018 email to Dr. Sakabe (Attachment B) renewing our request for information previously requested, and also requesting new information in response to Dr. Sakabe's November 21, 2018 email setting the December 5, 2018 deadline. As you will see, in our November 27, 2018 email, we requested an extension of time by which to respond to Dr. Sakabe, pending receipt of the information we have requested. We have not received a response to our November 27, 2018 email.

Our decision to send this letter to you to enlist your assistance is born of frustration in not being provided with the information we have reasonably requested from JBC/ASBMB. Our clients want to remain cooperative, but they also want to ensure that the *correct* decision is reached as a result of a *fair procedure* and *due process* with regard to their Article. We presume that JBC and ASBMB share their concern that articles that do no warrant retraction are not, in fact, retracted. Due to the fact that Dr. Sakabe's December 5, 2018 deadline is fast approaching, we hope to have a decision from you by close of business Monday, December 3, 2018, regarding whether you will agree to provide us with the information we requested in our November 27, 2018 email and whether you will agree to extend Dr. Sakabe's deadline for a reasonable period after providing that information. Our clients' goal continues to be to work with JBC/ASBMB to reach a mutually agreeable *and correct* resolution, but if JBC/ASBMB does not share that goal, then they are also prepared to consider whether some other option, including legal recourse, might be necessary.

We look forward to hearing from you.

Very truly yours,

A handwritten signature in black ink, appearing to read "P.S. Thaler", with a stylized flourish extending to the right.

Paul S. Thaler

Attachments

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Raju C. Reddy



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September 21, 2018

VIA ELECTRONIC MAIL

enrique.delacruz@yale.edu

Dr. Enrique M. De La Cruz
Chair, ASBMB Publications Committee
American Society for Biochemistry
and Molecular Biology
11200 Rockville Pike
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Rockville, MD 20852

**Re: *Journal of Biological Chemistry Publication*
*Lakshmi, et al. 2014 Article***

Dear Dr. De La Cruz:

We represent Mr. Aravind R. Tarugu and Dr. Raju C. Reddy, two of the co-authors of Lakshmi SP, Reddy AT, Zhang Y, Scieurba FC, Mallampalli RK, Duncan SR, and Reddy RC, The Journal of Biological Chemistry 289(10):6383-6393 (2014), "Down-regulated peroxisome proliferator-activated receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)" ("Article").

On August 10, 2018, we wrote to Dr. Kaoru Sakabe in her capacity as the Data Integrity Manager for the American Society for Biochemistry and Molecular Biology ("ASBMB") to advise her that concerns had been raised about two panels in *one* figure (Figure 5E) in the Article. See Appendix A (8/10/18 Thaler letter to Sakabe ("Notification to JBC")). Specifically, it was asserted that the first band in the left panel in the β -actin blot appears to be the same as the first band in the right panel of the pMSK1 blot. In sending the Notification to JBC, Mr. Tarugu was complying with a directive from the Department of Veterans Affairs ("VA") which had concluded (incorrectly and without a preponderance of evidence) that the two bands were duplicates. We have been corresponding with Dr. Sakabe for more than a month and have provided her (and the JBC editors) with substantial documentation (including data and images) demonstrating that *there is no duplication*.

After a process that was not only expanded to include images that were not the subject of any concern by the VA, but also completely lacking in transparency from ASBMB and JBC, Dr. Sakabe advised me by email on September 18, 2018 that because my clients had not agreed to voluntarily withdraw the Article, the matter would be forwarded to the ASBMB Publications

Committee for its consideration. *See* Appendix B at Attachment 1 (at 9/18/18 Sakabe email to Thaler and Karas). Mr. Tarugu and Dr. Reddy did not agree to withdraw the Article because there is no reason to withdraw it. For the reasons explained below (as supported by the accompanying Appendices), Mr. Tarugu and Dr. Reddy request that the Publications Committee conclude that withdrawal of the article is not warranted. We would appreciate your forwarding this letter (and Appendices) to the other members of the Publications Committee.

I. BACKGROUND

As we explained in the August 10, 2018 Notification to JBC, an allegation was made against Mr. Tarugu that Figure 5E contains a duplication. A joint inquiry on this matter by the University of Pittsburgh (the "University") and the Department of Veterans Affairs ("VA"), led by the University of Pittsburgh, resulted in *dismissal of this matter* on February 2016. In a follow up by the VA to this dismissal, the VA requested that the University initiate a joint investigation by the University and the VA led by the University. After the joint investigation was concluded, the matter took separate tracks. On the University track, we successfully appealed the joint finding that had been made against Mr. Tarugu. *See* Appendix A at Attachment 1 (redacted copy of the University's final decision after appeal). Because there was a lack of proof that the images were identical, *the University unanimously agreed to reverse both the finding against Mr. Tarugu and the recommended sanction that the Article be retracted*. *See* Appendix A at Attachment 2 (redacted copy of the Report of the University's Appeal Panel, at p.3). Unlike the University, however, the VA affirmed its incorrect finding that Figure 5E contains a duplication. As a result, Dr. Steven Graham, the VA's Research Integrity Officer, implemented a corrective action plan which required Mr. Tarugu to notify JBC by August 10, 2018 of the VA's finding against him. Mr. Tarugu timely did so. *See* Notification to JBC (Appendix A hereto).

As the August 10, 2018 Notification to JBC explains, the VA erred in determining that the left band in the right side panel of the pMSK1 blot in Figure 5E was a duplicate of a band in the β -actin blot. Mr. Reddy's explanation in the Notice to JBC was supported by the opinions of two experts in the field who are former senior officials at the Department of Health and Human Services Office of Research Integrity, Dr. Alan Price and Dr. John Dahlberg (*see* Appendix A at Attachments 3 and 4) as well as by expert Dr. John Russ (*see* Appendix C (9/12/18 letter from Mr. Thaler) at Attachment 2). That Figure 5E contains no duplications is also demonstrated by the additional data we have provided Dr. Sakabe, as discussed below. Importantly, on September 12, 2018, the University transmitted to Mr. Tarugu a notification from the Department of Health and Human Services' *Office of Research Integrity ("ORI") that it was "closing] this case without further action"* after and as a result of "a complex and thorough review by the [ORI] Director, a review panel of scientist-investigators, and legal counsel."

II. COMMUNICATIONS WITH DR. SAKABE

In response to our Notification to JBC, Dr. Sakabe sent an email stating: "We would be interested in reviewing the original data for Figs 3C, 4C, and 5E. We would prefer that these

images be provided uncropped and minimally processed.” See Appendix B at 8/16/18 email from Dr. Sakabe. There were two things notably absent from Dr. Sakabe’s email - any comment on the information we provided in the Notice to JBC and any explanation supporting her request for data for figures *other than* Figure 5E. Even though Dr. Sakabe did not explain why she was asking for data for additional figures, Mr. Tarugu and Dr. Reddy raised no objection and provided the additional data (a total of 34 blots) as requested – including the data for Figures 3C and 4C. See Appendix B at 8/20/18 Thaler email to Sakabe.¹

Dr. Sakabe responded to our August 20, 2018 email (and its attached zip file) with an email dated August 21, 2018 in which she thanked me for the data I had sent on August 20, 2018. In addition, she asked for information about the LICOR imaging system that the authors had used: “It seems the authors used a LICOR imaging system to obtain these data. Do the authors have access to the LICOR acquisition zip files? If so, would they be able to provide these data?” See Appendix B at 8/21/18 Sakabe email to Thaler. Notably absent from Dr. Sakabe’s August 21, 2018 email was *any* mention of the data we provided on August 20, 2018 (other than her thanking me for sending it). Pertinent to later developments in this matter (discussed below), it is especially noteworthy that in her August 21, 2018 email, Dr. Sakabe did not mention any problems with the quality of the images contained in the zip file we provided on August 20, 2018.

I forwarded Dr. Sakabe’s August 21, 2018 email inquiring about the LICOR imaging system to my clients, who promptly responded. I forwarded their response to Dr. Sakabe on August 22, 2018. See Appendix B at 8/22/18 Thaler email to Sakabe. As my clients explained in the August 22, 2018 email, no one has access to the images on the LICOR system because the instrument and its associated computer are no longer operational and were replaced by an upgraded system. *Id.* At the end of my email, I stated: “Please let me know if there is anything else I can do to assist you.” In response, Dr. Sakabe emailed again. She thanked me for the information I had sent regarding the LICOR imaging system and asked whether I could send her the report from the VA and the unredacted versions of the University’s final decision after appeal and the Report of the University’s Appeal Panel (the versions attached to the Notice to JBC were redacted). See Appendix B at 8/23/18 Sakabe email to Thaler. Dr. Sakabe did not explain why she was asking for the VA report and the unredacted versions of the other documents. Several days later, she sent an email asking my clients to also provide the original data to Figures 1A and 6A. See Appendix B at 8/29/18 Sakabe email to Thaler. Notably absent from Dr. Sakabe’s August 29, 2018 email was any explanation as to why she or the JBC editors wanted to see data for the additional Figures, neither of which had anything to do with the Notice to JBC.

Although my clients had fully cooperated and responded to *all* of Dr. Sakabe’s requests for information, even as those requests sought information beyond the scope of the Notice to

¹ Attached to my August 20, 2018 email to Dr. Sakabe was a zip file containing thirty-four .tiff files and one pdf file. I assume that Dr. Sakabe has made that zip file available to the Publications Committee. If she has not, and if you cannot obtain it from her, please let me know.

JBC, they declined to respond to her requests in her August 23 and August 29 emails for the VA report, unredacted documents and data for additional figures beyond the scope of the Notice to JBC. As we explained in our August 30, 2018 response, the University documents were redacted at the suggestion of the University's Dean Kahn to protect confidential information. *See* Appendix B at 8/30/18 Thaler email to Sakabe; Appendix B at and at 7/24/18 and 7/25/18 email exchange between Mr. Tarugu and Dean Saleem Khan. My clients declined to provide the VA report because, as I explained to Dr. Sakabe, we have been informed by the VA that the finding against Mr. Tarugu will not be published. *See* Appendix B at 8/30/18 Thaler email to Sakabe. My clients declined to provide the data for Figures 1A and 6A because the request was a further deviation from the scope of the subject matter of the Notice to JBC and of Mr. Tarugu's obligation to notify JBC of the VA's finding with respect to Figure 5E. *Id.* However, I reaffirmed in my August 30, 2018 email my clients' willingness to continue to cooperate "in any way they can with respect to any additional questions [that Dr. Sakabe] may have regarding the β -actin blot and pMSK1 blot in Figure 5E." *Id.*

We reasonably expected that communications with Dr. Sakabe might continue with respect to the data and images at issue – the two bands in Figure 5E. My clients looked forward to a continuing dialogue with Dr. Sakabe about the data they had provided and remained willing to answer any questions that Dr. Sakabe or JBC's editors might have. Thus, my clients and I were shocked to receive Dr. Sakabe's next email, on August 31, 2018, in which she stated, in pertinent part:

Thank you for your [August 30, 2018 email]. In addition to the duplication in Fig 5E, we determined the following:

- The PPARy blot from Fig 1A was reused in Fig 6A as pAcK-H3 and H3
- The Lamin B1 blot from Fig 3C was reused in Fig 4C as H3

In light of these issues, the Editors are requesting that the authors withdraw the article. . . . Please request withdrawal by September 14, 2018.

See Appendix B at 8/31/18 email from Dr. Sakabe. No prior email from Dr. Sakabe had alerted us to any concerns the Editors had as to whether there were duplications in Figures 1A/6A and 3C/4C. When we declined (in our August 30, 2018 email) to provide the data for Figures 1A and 6A on the basis that Dr. Sakabe's August 29, 2018 request was beyond the scope of the VA's concern, Dr. Sakabe did not respond to inform us that there was a concern about those figures and the nature of the concern, as we noted in our September 6, 2018 response to Dr. Sakabe's August 31, 2018 email. *See* Appendix B at 9/6/18 Karas email to Sakabe. Also troubling about Dr. Sakabe's August 31, 2018 email is that it was not accompanied by any explanation or analysis demonstrating the basis for the Editors' conclusions. Thus, we asked Dr. Sakabe to "send us the journal's basis/analysis for determining that the images were reused (Figs. 1a and 6a; Figs 3c and 4c; and 5E)," and we told her that we would "review the journal's analysis with

our clients once we receive it, and we will provide you with the original data for the additional images.” *Id.*

Instead of sending the analysis we requested, Dr. Sakabe told us that the information we requested in our September 6, 2018 email was provided to us in the attachment to her August 31, 2018. *See* Appendix B at 9/7/18 Sakabe email to Karas. The attachment to Dr. Sakabe’s August 31, 2018 email (which we assume she has provided the Publications Committee) provides pictorial information but does not reveal any forensic analysis, as we pointed out in our September 12, 2018 letter responding to her September 7, 2018 email. *See* Appendix C (9/12/18 Thaler letter to Sakabe) at Attachment 1. It is a pdf showing where the Editors think they see a duplication.

Attached to our September 12, 2018 letter responding to Dr. Sakabe’s September 7, 2018 email was a separate letter to Dr. Sakabe from Mr. Tarugu and Dr. Reddy. *See* Appendix C at Attachment 1. In their letter, Mr. Tarugu and Dr. Reddy explained why the “analysis” undertaken by the Editors and Dr. Sakabe (reflected in the pdf attachment to Dr. Sakabe’s August 31, 2018 email) was deficient and does not support JBC’s conclusion of duplications. They also provided the images for all five figures and a detailed forensic image analyses performed on the images. *See* Appendix C at Attachment 2. As Dr. Reddy and Mr. Tarugu noted, the “images themselves, when evaluated in their proper context, **provide conclusive evidence** that no images were reused.” *Id.* at p. 1 (emphasis in original). My clients also described the tools they used to perform their analyses. *Id.* at p. 3. Finally, Attachment 2 to my September 12, 2018 letter also included the forensics image analysis performed by expert Dr. John Russ demonstrating that the two panels in Figure 5E are not identical.

Dr. Sakabe responded by email to my September 12, 2018 email the same day. *See* Appendix B at 9/12/18 Sakabe email to Thaler. Dr. Sakabe’s email unfairly and/or inaccurately characterized our month long communications and the data we had provided, in the following ways:

- “Because your client refused to provide the original data and images for figures 1A and 6A, any criticism of the JBC processes are the result of your clients’ failure to provide requested and required information.” My clients did not “refuse” to provide this data. They did not initially provide images for figures 1A and 6A because Dr. Sakabe failed to notify them of any concerns regarding these images. Moreover, they did offer on September 6, 2018 to provide the data but asked to first see JBC’s analysis. They did not “criticize” JBC’s analysis; they simply stated that their understanding of the image analysis provided by Dr. Sakabe was limited, as they were not provided with any specific information on the image analysis.
- “The images in the PDF provided are of too poor quality for JBC to analyze.” We did not receive any follow up request to provide .tiff files and thus had no prior notice that JBC considered the quality of the pdf “too poor” to analyze.

- “The data shown in the attachment for figures 3C and 4C do not appear to correspond with what is presented in the publication.” The data does correspond, as can be seen in the image analysis we sent with our September 12, 2018 letter.
- “The quality of the data provided on August 20 was of such poor quality that we requested the native files, but none were provided.” When we sent the data on August 20, Dr. Sakabe did not respond to inform us that JBC considered the data to be of poor quality nor did she ask for better quality data. Indeed, the Editors appear to have considered the files to have been of sufficient quality to use for their “analysis” in concluding (albeit incorrectly) that there were duplications.
- “Finally, we requested full copies of the investigation reports to determine the rigor and completeness of the committee’s investigation.” This was the first time that Dr. Sakabe offered a reason for having previously requested these documents. As we explained in our earlier correspondence to Dr. Sakabe, we redacted the documents and did not provide the VA report out of confidentiality concerns.

The foregoing is merely a summary of our detailed response, set forth in our September 14, 2018 letter (*see* Appendix D), to Dr. Sakabe’s September 12, 2018 email. The letter also expresses my clients’ understandable frustration at the utter lack of transparency that has plagued this process. In addition, accompanying our letter, we sent Dr. Sakabe the original data for *all* of the images she had requested. We sent three Power Point files and seven .tif images.²

In addition to the data and explanations we provided in our September 14, 2018 letter, we specifically requested Dr. Sakabe to provide us with the following, to help us better understand the policies and procedures which Dr. Sakabe and the Editors had followed and the analyses they used to reach their conclusions. We requested Dr. Sakabe to provide:

- “If you have access to a policy allowing JBC to ask for any data without first (or concurrently notifying an author about JBC’s concerns, and allowing JBC to make a determination without providing an opportunity for explanation, please do provide us with a copy of that policy.” Appendix D at p. 2.
- “If JBC has separate guidelines for performing image analysis [that are different from ORI’s], please provide us with a copy.” Appendix D at p. 2. We twice requested that Dr. Sakabe provide the details of JBC’s analysis, but never received a response from her. Also, JBC did not contest our clients’ claim that it was their understanding that snapshots from the PDF file were used by JBC for

² Because the files accompanying our September 14, 2018 letter are quite large and we assume that Dr. Sakabe has made, or will make, those files available to the Publications Committee, we are not providing them again with this correspondence. If you are not provided with these files, please let me know.

its image analysis. Using snapshots does not comport with ORI's guidelines for image analysis.

- "If the Editors have conducted an analysis of the Figure 3C and 4C data that we provided on Wednesday, or should they do so with the additional images we are providing today, please provide it to us for our review." Appendix D at p. 3.
- Because we had declined to provide unredacted copies of the documents related to the investigation, we offered as follows: "If you or the Editors have a specific question regarding the completeness of the investigation that is relevant to JBC's own analysis of the images and data we have provided, please do let me know, and if I can respond without violating the confidentiality limits stated above, I will do so." Appendix D at p. 3.
- "Should the Editors have any evidence, analyses and/or explanation to demonstrate why my clients image analyses are wrong, *please share it with us.*" Appendix D at p. 4 (emphasis in original).
- "If there is any policy that supports the Editors' decision to direct that my clients withdraw the article before there is a thorough exchange of information, disclosure by the Editors of the analysis supporting their decision, and a full and fair opportunity for my clients to respond, *please share it with us.*" Appendix D at p. 4 (emphasis in original).

In response to our September 14, 2018 letter and accompanying files, we received a rather curt response from Dr. Sakabe on September 18, 2018 which reads, in full:

We are in receipt of all 5 files [accompanying your September 14, 2018 letter]. As your clients do not agree to withdraw, we will be forwarding this matter to the ASBMB Publications Committee. I will inform you of their decision.

See Appendix B at 9/18/18 email from Dr. Sakabe. We received no substantive response to our September 14, 2018 letter; we received no response to our requests made in the letter for applicable procedures and policies; we received no response made in the letter for the analysis conducted by JBC; we received no response to the data we provided with our letter.

We made one last attempt with Dr. Sakabe to better understand how Dr. Sakabe and the Editors reached their conclusion that the Article should be withdrawn, but none was forthcoming. We could not even succeed in getting a response to a simple request that Dr. Sakabe confirm that all of our emails and data would be forwarded to the Publications Committee. That final communication to Dr. Sakabe was emailed on September 19, 2018 and reads, in full, as follows:

Dear Dr. Sakabe,

Thank you for [your] email. As this process moves forward to the next step, we would appreciate your answering the following questions and providing the information requested by close of business, September 20th, 2018, so that we have a better understanding of how the Editors reached their decision, and so that we can make plans going forward:

1. As we asked previously in our September 14 email, provide a copy of the Editors' analyses and reports describing the techniques they used to review the data/images we provided from August 10, 2018 through September 14, 2018.
2. Confirm that our September 14 emails (and all attachments) were shared with the Editors.
3. Forward the guidelines/policies which will apply to and govern the ASBMB Publications Committee's consideration of this matter.
4. Confirm that all of our communications with you, beginning with our August 10, 2018 letter, will be made available to the ASBMB Publications Committee.

See Appendix B at 9/19/18 Karas email to Sakabe. Dr. Sakabe responded later that same day in an email which reads, in full, as follows:

Our policies may be found here:
http://www.jbc.org/site/misc/edpolicy.xhtml#ethics_policy. *We will not share further internal analyses/reports.*

See Appendix B at 9/19/18 email from Dr. Sakabe (emphasis added).

Thus, after more than a month of communications and transmission of extensive data, my clients have no better understanding today as why they are being asked to withdraw the Article than they had on August 31, 2018.

III. THE ARTICLE SHOULD NOT BE WITHDRAWN

Mr. Tarugu and Dr. Reddy have been fully cooperative in this process. We are bewildered at the reluctance of Dr. Sakabe and the Editors to be transparent as to the analysis they undertook and the procedures they followed to reach the conclusion that that article should be withdrawn. As we stated at the end of our September 14, 2018 letter to Dr. Sakabe:

With all due respect, it is unfair to expect my clients to simply withdraw the article on the sole basis that JBC says these images are duplicated when JBC has not provided any evidence or analyses substantiating its conclusion. We

Dr. De La Cruz
September 21, 2018
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understand JBC's interest in resolving any concerns it has, but that resolution must come only after a fair process that is transparent and clearly communicates to my clients what the concerns are and gives them an opportunity to respond.

Appendix D at p.4 (9/14/18 letter from Mr. Thaler).

Mr. Tarugu and Dr. Reddy have demonstrated through the data and analyses they provided to Dr. Sakabe and the Editors that there were no duplications in the Article and that the Article should not be withdrawn. Dr. Sakabe did not provide us with any counter-analysis or explanation that would support a contrary conclusion.

IV. CONCLUSION

We appreciate the anticipated careful consideration that you and the other members of ASBMB's Publications Committee will give to this letter, all of its attachments, and the data/images previously provided to Dr. Sakabe. We hope that there will be more transparency from ASBMB going forward. To that end, we request that you provide us with the information that we sought from Dr. Sakabe but which she refused to provide, including: (1) a copy of the Editors' analyses and reports describing the techniques they used to review the data/images we provided from August 10, 2018 through September 14, 2018; (2) confirmation that you have received from Dr. Sakabe all of the attachments to all of our emails (including all zip files, powerpoint files and .tiff files); and (3) the specific guidelines/policies which will apply to and govern the ASBMB Publications Committee's consideration of this matter. In addition, we request that if the Publications Committee undertakes its own analysis of the data and images, that any such analysis be shared with us.

My clients and I are happy to answer any questions which you or the other Committee members may have.

Very truly yours,



Paul S. Thaler

Attachments

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Raju C. Reddy

APPENDIX A

AUGUST 10, 2018 LETTER FROM PAUL THALER TO DR. KAORU SAKABE ("NOTIFICATION TO JBC")

Including the following Attachments:

ATTACHMENT 1: Redacted copy of University of Pittsburgh Provost Patricia Beeson's final decision after appeal.

ATTACHMENT 2: Redacted copy of University of Pittsburgh Report of the Appeal Panel recommending reversal.

ATTACHMENT 3: Dr. Alan Price (former Associate Director for Investigative Oversight for NIH ORI) expert opinion in support of content of Notification to JBC

ATTACHMENT 4: Dr. John Dahlberg (former Director for Investigational Oversight for NIH ORI) expert opinion in support of content of Notification to JBC.

August 10, 2018

VIA ELECTRONIC MAIL

ksakabe@asbmb.org

Kaoru Sakabe, Ph.D.

Data Integrity Manager

American Society for Biochemistry and Molecular Biology

11200 Rockville Pike

Suite 302

Rockville, MD 20852

**Re: *Journal of Biological Chemistry Publication*
*Lakshmi, et al. 2014 Article***

Dear Dr. Sakabe:

We represent Mr. Aravind Reddy Tarugu, a co-author of Lakshmi SP, Reddy AT, Zhang Y, Sciurba FC, Mallampalli RK, Duncan SR, and Reddy RC, *The Journal of Biological Chemistry* 289(10):6383-6393 (2014), "Down-regulated peroxisome proliferator-activated receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)" (the "Paper"). Mr. Tarugu was notified in January 2016 of an allegation that "the left band in the left panel in the β -actin plot appears to be the same as the left band in the right panel of the pMSK1 blot, flipped by 180°." A joint inquiry on this matter by the University of Pittsburgh (the "University") and the Department of Veterans Affairs ("VA"), led by the University of Pittsburgh, resulted in dismissal of this matter on February 2016. In a follow up by the VA to this dismissal, the VA requested that the University initiate a joint investigation by the University and the VA led by the University, which resulted in a finding that Mr. Reddy falsified Figure 5E.

After receiving the final investigation report, the University and the VA made separate determinations to which we appealed. After the appeals, the University reversed its decision while the VA affirmed the findings of the University investigation report. Dr. Steven Graham, the Research Integrity Officer for the VA, implemented a corrective action plan for Mr. Reddy which requires him to notify JBC not later than August 10, 2018 of the VA's finding against him. This letter constitutes that notice.

Notwithstanding the VA's finding, Mr. Reddy submits that no action should be taken by JBC with regard to the Paper. With all due respect to the VA, its conclusion that the left band in the right panel of the pMSK1 blot was falsified is wrong and without any preponderance of evidence. In fact, in direct contrast to the VA's decision, the University (the lead institute that

Dr. Sakabc
August 10, 2018
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conducted the investigation), after an appeal to the Provost and a review by an Appeal Panel consisting of five Professors, *unanimously reversed* the finding against Mr. Reddy that had been made by the joint investigation committee. See Attachment No. 1 (redacted copy of Provost Patricia Beeson's April 4, 2018 final decision after appeal) and Attachment No. 2 (redacted copy of the March 27, 2018 recommendation of the University's appeal panel). The Appeal Panel's recommendation for reversing states in pertinent part:

There was disagreement between the two experts who examined the image evidence [as to whether the bands are identical], and that disagreement was not fully addressed and resolved by the Investigative Board. . . [T]he figure panel at the center of the investigation was not essential for the paper's conclusions.

A finding of no misconduct on your part will be reported.

Attachment No. 2 at p.3. In reversing, Provost Beeson expressly withdrew the sanction issued by Assistant Dean Saleem Khan (following the investigation) which would have required Mr. Reddy to retract the Paper — the same sanction being upheld by VA.

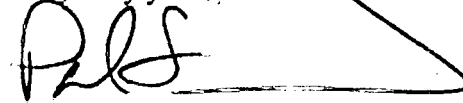
The decision of Provost Beeson and the recommendation of the Appeal Panel reversing the finding is supported by two experts in the field, Dr. Alan Price and Dr. John Dahlberg whose opinions are attached as Attachment Nos. 3 and 4, respectively. Dr. Price spent 17 years working with ORI, having served in the latter years as the Associate Director for Investigative Oversight for ORI. During that time, his group was involved with over 3,000 allegations/queries and over 700 formal inquiries or investigations, and they made more than 175 findings of scientific/research misconduct. During his last decade in ORI, Dr. Price reviewed and handled all of the allegations received by ORI from individuals, institutions, and the National Institutes of Health (NIH). Dr. Dahlberg spent 23 years at ORI. In 2006, he became the Director of the Division of Investigational Oversight (DIO), the division within ORI responsible for conducting oversight review of institutional inquiries and investigations involving questioned research funded by the Public Health Service. In mid-2013, he became Deputy Director of ORI where he remained until his retirement in April 2015. During his tenure at ORI, Dr. Dahlberg handled thousands of allegations and dealt with hundreds of cases. Both Dr. Price and Dr. Dahlberg have reviewed the pertinent documents and data, and they agree that a preponderance of the evidence does not establish that the two images are identical. They agree with the University's decision to reverse the finding against Mr. Reddy.

The VA stands alone in its conclusion that the image in Figure 5E was falsified without exhibiting any preponderance of evidence. Neither Provost Beeson, the University's Appeal Panel, Dr. Price or Dr. Dahlberg agree. While we have brought the VA's decision to your attention as directed by Dr. Graham, we respectfully submit that the VA's decision does not warrant that any action be taken with respect to the Paper.

Dr. Sakabe
August 10, 2018
Page 3

Should you or the Publications Committee have any questions or need further information, please do not hesitate to contact me.

Very truly yours,

A handwritten signature in black ink, appearing to read 'PST', enclosed within a large, irregular, hand-drawn loop that extends to the right.

Paul S. Thaler

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Steven Graham



University of Pittsburgh

Office of the Provost and Senior Vice Chancellor

801 Cathedral of Learning
4200 Fifth Avenue
Pittsburgh, PA 15260
412-624-4223
Fax: 412-3833640
beeson@pitt.edu

Patricia E. Beeson
Provost
Senior Vice Chancellor

April 4, 2018

Aravind Tarugu
Senior Research Associate
Department of Medicine
Montefiore NW 628

Dear Mr. Tarugu:

In response to your appeal from the decisions of School of Medicine Assistant Dean for Faculty Affairs Saleem Khan following his receipt of the report of the Investigative Board, an Appeal Panel was appointed. Your appeal requested review of the research misconduct finding [REDACTED]. I have reviewed the Panel's recommendations sent to me in late March, which I am attaching to this letter.

My decision is to accept the recommendation of the Panel that Dr. Khan's finding of research misconduct on your part be reversed [REDACTED].

[REDACTED]

[REDACTED]

[REDACTED]

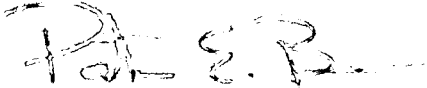
[REDACTED]

Public Health Service Policy requires the University to report the result of the investigation to the Office of Research Integrity, US Department of Health and Human Services. A finding of no research misconduct on your part will be reported.

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED] Therefore this decision

shall be the final disposition of this matter on behalf of the University.

Sincerely,



Patricia E. Beeson

REPORT OF THE APPEAL PANEL

IN THE MATTER OF

████████████████████ ARAVIND REDDY TARUGU

Yuan Chang, MD

Distinguished Professor & American Cancer Society Professor of Pathology

Mary Ganguli, MD

Professor of Psychiatry

Penelope A. Morel, MD

Professor of Immunology

Yoel Sadovsky, MD (Appeal Panel Chair)

Distinguished Professor of Obstetrics, Gynecology & Reproductive Services

John V. Williams, MD

Professor of Pediatrics

March xx, 2018

Introduction

This matter has its origin in a joint Inquiry to assess allegations regarding publications of the Respondent [REDACTED]

[REDACTED] Mr. Aravind Reddy Tarugu, Research Associate, Department of Medicine. The Inquiry was started on January 5, 2016 and involved both the University of Pittsburgh and the VA Pittsburgh Healthcare System (VAPHS), with the University serving as the lead institution at the request of VAPHS. The Inquiry Panel recommended the matter be closed without further investigation and the University accepted the recommendation. However, VAPHS asked that an Investigation be conducted. The University agreed to lead a joint Investigation. An Investigative Board considered this matter and based upon their report School of Medicine Assistant Dean for Faculty Affairs Saleem Khan, PhD, found that Mr. Aravind Reddy Tarugu had committed research misconduct through falsification by publishing the same image twice (as mirror images), but with different descriptions. [REDACTED]

The publication containing the alleged falsification is:

Lakshmi SP, Reddy AT, Zhang Y, Scirba FC, Mallampalli RK, Duncan SR, and Reddy RC. *The Journal of Biological Chemistry* 289(10): 6383-6393 (2014). "Down-regulated Peroxisome Proliferator-Activated Receptor γ (PPAR γ) in lung epithelial cells promotes a PPAR γ agonist-reversible phenotype in chronic obstructive pulmonary disease (COPD)".

On November 27, 2017 Mr. Paul Thaler, on behalf of the Respondent [REDACTED], filed an appeal of these findings and asked that the findings be reversed. On February 9, 2018 the members of the Appeal Panel convened with Dr. Craig Wilcox, Research Integrity Officer of the University of Pittsburgh and Dr. Mara Horwitz, Associate Research Integrity Officer, to discuss the charge to the Appeal Panel and procedures relevant to that charge. The Appeal Panel met again on March 16, 2018.

Grounds for the Appeal of the Finding of Research Misconduct

The University of Pittsburgh 2008 Research Integrity Policy (Policy #11-01-01) states that grounds for an appeal are limited to (1) failure to follow appropriate procedures; (2) insufficiency of evidence; or (3) arbitrary and capricious decision making.

The relevant grounds of the Respondent [REDACTED]' appeal are as follows: (1) There was a failure to follow standard procedures resulting in (a) failure to secure evidence, (b) failure to provide proper notification to the Respondent [REDACTED] prior to the appearance of the witness, and (c) failure to provide for impartial committees during the Inquiry and Investigation. (2) The research misconduct [REDACTED] not demonstrated by a preponderance of the evidence, and the Respondent [REDACTED]' conduct of research is not a "significant departure from accepted practices" and therefore can constitute neither research misconduct [REDACTED].

Appeal Panel Activity

The Appeal Panel convened on February 9, 2018 for initial discussion and to receive evidence considered by the Investigative Board. The Panel also received records of the investigative process, the transcript of the Investigative Board hearing, and correspondence in the record including the June 5, 2017 response from Mr. Thaler and the Respondent [REDACTED] regarding the draft investigative report, the August 2, 2017 additional comments from Mr. Thaler on behalf of the Respondent [REDACTED], the November 27, 2017

communication of the grounds for appeal, and a January 31, 2018 communication from Mr. Thaler regarding supplemental information pertaining to a desktop computer discussed in the report of the Investigative Board. The grounds for an appeal as described by the University of Pittsburgh Research Integrity Policy (cited above) were reviewed. The appeal filed on behalf of the Respondent was discussed and each of the specific grounds for an appeal of the findings of Research Misconduct was discussed.

Following the February 9, 2018 meeting the Appeal Panel considered the record and the documents received in support of the appeal and then reconvened on March 16, 2018.

Appeal Panel Recommendations

The Appeal Panel agreed unanimously to recommend reversal of the finding of Research Misconduct on the part of Mr. Aravind Reddy Tarugu.

[REDACTED]

Appeal Panel Advice Regarding the Grounds for the Appeal

Research Misconduct Finding

The Panel offers the following comments regarding the claims made by the Respondent in the appeal of the research misconduct finding:

The misconduct is based solely on the apparent match of the images. The issue of the bands being identical is not conclusively resolved. There is insufficient evidence of intentionality.

Agreed. There was disagreement between the two experts who examined the image evidence, and that disagreement was not fully addressed and resolved by the Investigative Board.

[REDACTED]

[REDACTED] The Panel also determined that intention was not proven by a preponderance of evidence, including a lack of proof for purposeful image manipulation. The Panel also noted the lack of a motive, as the figure panel at the center of the investigation was not essential for the paper's conclusions.

The investigation was infected with irregularities. Witness procedures were not followed.

Agreed with qualifications. The sequestration process was deficient. The Panel felt the University made the appropriate attempts to sequester the relevant information but the usual procedures were hampered by issues that arose due to VAPHS imposed data security rules and technical capabilities. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]



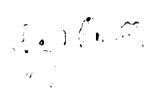
[REDACTED]

[REDACTED]

Signature Page

Panel Member

Date



March 28, 2018

Yuan Chang, MD
Distinguished Professor &
American Cancer Society Professor of Pathology



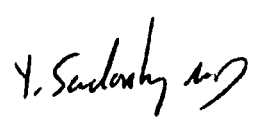
March 29, 2018

Mary Ganguli, MD
Professor of Psychiatry



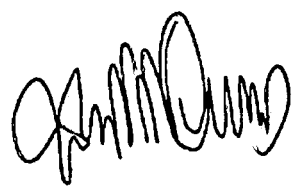
March 28, 2018

Penelope A. Morel, MD
Professor of Immunology



March 26, 2018

Yoel Sadovsky, MD (Appeal Panel Chair)
Distinguished Professor of Obstetrics, Gynecology & Reproductive Sciences



March 25, 2018

John V. Williams, MD
Professor of Pediatrics

Price Research Integrity Consultant Experts

Alan R. Price, Ph. D.

21704 Sierra Trail, Lago Vista, Texas

Cell phone 512-483-1574

Email resmiscon@researchmisconductconsultant.com

Paul Thaler and Karen S. Karas, Counsels
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705
Washington, DC 20036

August 10, 2018

RE: Opinion on DVA-required notice to *JBC* Editor by Aravind Reddy on 2014 paper finding

You requested my expert opinion, regarding a Department of Veterans Affairs (DVA) remedial action plan for Mr. Aravind Reddy ("Mr. Reddy"), requiring notification of the *Journal of Biological Chemistry (JBC)*, following a University of Pittsburgh (UPitt) Appeal Panel Report of March 27, 2018, and the UPitt Provost's acceptance letter of April 4, 2018, reversing the finding of an earlier joint UPitt/Veterans Administration Pittsburgh Health Care System (VAPitt) investigation of research involving two western blot β -actin bands, published in Figure 5E in *JBC* 289(10):6383 (2014), with technical assistance from Mr. Reddy as the second author. You previously provided me with the UPitt/VAPitt inquiry and investigation reports and exhibits, which I reviewed in October 2017 for my expert opinion on the case process and initial findings.

I understand that, given the recent reversal of the UPitt findings, UPitt officials also reversed the proposed sanction that would have required Mr. Reddy to request *JBC* retract this publication. However, I understand that DVA has affirmed its own finding against Mr. Reddy, and DVA is requiring him to notify *JBC* about that finding for this publication.

As background, I was a faculty member at the University of Michigan from 1970-1987. I retired from the federal Office of Research Integrity (ORI) after 17 years in 2006, serving the last six years as ORI Associate Director for Investigative Oversight. We handled over 3,000 allegations/queries and over 700 formal inquiries/investigations and made over 175 findings of scientific/research misconduct. During my last decade there, I reviewed and handled all of the allegations received from individuals, institutions, and the National Institutes of Health (NIH). We also reviewed and analyzed all of the reports of inquiries/investigations by universities, hospitals, and other research institutions funded by NIH research grants. I believe that no one person has seen, handled, and resolved more allegations, investigations, and oversight cases of scientific/research misconduct than I have. I also communicated with many journal editors, including at *JBC*, on correction or retraction of publications with allegedly falsified images or other data. I was a biochemist and member of FASEB's Biochemistry Society which hosts *JBC*. For the past twelve years, I have been consulting formally with individuals and institutional officials on such matters, as Price Research Integrity Consultant Experts (P.R.I.C.E.).

DVA notice to Mr. Reddy on notifying the *JBC* of the DVA's finding

On July 9, 2018, the Research Integrity Officer (RIO) and Associate Chief of Staff, Research and Development at VAPitt, sent a memo to Mr. Reddy, outlining a remedial action plan for him to follow, specifically stating:

You must notify the Journal of Biological Chemistry (*JBC*) of the VA's finding of research misconduct regarding the data published in the *JBC* 289(10):6383-6393 (2014)... [which requires] each author is required to provide details of the finding.

My opinion on Mr. Reddy notifying the *JBC* of DVA's finding of research misconduct

In notifying the Editor of *JBC* of the finding as required in the remedial action plan memo by the VAPitt RIO, I believe Mr. Reddy should quote the research misconduct finding in the joint UPitt/VAPitt investigation committee report:

Statement of Findings - Research Misconduct

We find the allegation stated in the charge to our committee to be true. In Figure 5E of the *JBC* 2014 paper referenced above, the first band in the left panel in the β -actin blot (lane 6) is indeed sufficiently identical to the first band in the right panel of the pMSK1 blot (when reflected across a vertical line) to support the allegation...

We find that the creation and publication of these two images, one derived from the other through digital manipulation, is falsification and that the falsification was intentional. The evidence of intent is that the same image was chosen twice (an action very unlikely to occur by accident) and a mirror image of one of the images was created (a second action very unlikely to occur by accident). We find research misconduct...

I believe Mr. Reddy should also quote the statement in the VAPitt RIO's July 9, 2018, remedial action memo above, that the Network Director of VA Healthcare-VISN 4 had concluded that he:

... committed research misconduct by falsifying data with 2 blots being the mirror image of each other and represented as different blots in a publication.

In addition, I believe Mr. Reddy should quote the conclusions in the March 27, 2018, UPitt Appeal Panel Report (p. 3), with which I very strongly concur:

The Appeal Panel agreed unanimously to recommend reversal of the finding of Research Misconduct on the part of Mr. Aravind Reddy Tarugu....

The Panel offers the following comments regarding the claims made by the Respondent in the appeal of the research misconduct finding:

The misconduct is based solely on the apparent match of the images. The issue of the bands being identical is not conclusively resolved. There is insufficient evidence of intentionality.

Agreed. There was disagreement between the two experts who examined the image evidence, and that disagreement was not fully addressed and resolved by the Investigative Board.... The Panel also determined that intention was not proven by a preponderance of evidence, including a lack of proof for purposeful image manipulation. The Panel also noted the lack of a motive, as the figure panel at the center of the investigation was not essential for the paper's conclusions.

The investigation was infected with irregularities. Witness procedures were not followed.

Agreed with qualifications. The sequestration process was deficient. The Panel felt the University made the appropriate attempts to sequester the relevant information but the usual procedures were hampered by issues that arose due to VAPHS imposed data security rules and technical capabilities.

My opinion on the lack of justification for a retraction of the 2014 *JBC* paper

Based on my almost three decades of reviewing over 800 investigation reports, I strongly agree with the Appeal Panel that intentional falsification by Mr. Reddy, with manipulation of the control blot data in Figure 5E, was not proven by a preponderance of evidence. Therefore, as the Appeal Panel concluded, a research misconduct finding against Mr. Reddy is unwarranted.

I recommend that Mr. Reddy notify the Editor of *JBC*, about the VAPitt finding, supplying the above information, and arguing strongly, as I have, that no retraction of the 2014 *JBC* paper is warranted.

Sincerely,



Alan R. Price, Ph.D.
Price Research Integrity Consultant Experts
Former Associate Director of the U.S. Office of Research Integrity

TO: Paul Thaler, Karen Karas

FROM: John Dahlberg, PhD

DATE: August 10, 2018

SUBJECT: Request of the Department of Veterans Affairs (VA) that Mr. Aravind Reddy notify Journal of Biological Chemistry (JBC) regarding the finding made against him in the matter of JBC paper 289:10, pp. 6383–6393, March 7, 2014 (“the JBC paper”)

I have been asked to opine on the appropriateness of the VA’s adherence to the University of Pittsburgh Investigative Committee’s recommendation that the referenced published paper be retracted by one of the co-authors. By way of background, after twenty five years as a bench scientist, I joined the Office of Research Integrity (ORI) within the Department of Health and Human Services, where I spent an additional twenty three years as a scientist/investigator in the Division of Investigative Oversight (DIO). From 2006-2013 I was the Director of DIO, and from 2013-2015 I served as the Deputy Director of ORI, at which time I retired from federal service. While at ORI, I evaluated thousands of allegations of possible research misconduct, and conducted oversight review and analyzed hundreds of inquiries and investigations of cases of alleged research misconduct involving individuals and institutions from all regions of the United States.

One of the principal objectives of ORI was to help ensure the accuracy of the scientific literature, and when we concurred with institutional findings of research misconduct and made separate findings of misconduct on behalf of the federal government, we typically requested correction or retraction of articles when the scope of the findings warranted such an action. Of course, ORI realized that neither we nor the respondents who agreed to voluntary settlements with ORI could demand that editors retract a paper, as that determination more appropriately rests with the journal’s editors who are more qualified to judge the impact of the misconduct on the overall accuracy of the published manuscript and the impact of the fabrications, falsifications, and/or plagiarism on the scientific community.

I have reviewed the single issue on which the VA determined, based on the Investigative Report made by the University of Pittsburgh and VAPHS’s joint investigation led by the University, that Mr. Reddy had committed research misconduct, thereby warranting, in its view, retraction of the referenced JBC paper. I note that the alleged infraction involves a claim that two bands in Figure 5E appear to be the same.¹ After careful consideration of the appeal to the Provost, the University of Pittsburgh found that there was insufficient evidence to prove that these two bands were identical (or as ORI would phrase it, had a common origin), and did not find that Mr. Reddy had committed research misconduct.

¹ “the first band in the left panel in the β -actin blot appears to be the same as the first band in the right panel of the pMSK1 blot, if one or the other was reflected across a vertical reference line” (University of Pittsburgh Investigation Report, page 5)


ORI dealt with similar claims on many occasions and nearly always determined that forensic comparison of two bands might show that they appeared very similar or perhaps identical, but that in the absence of additional evidence of possible misconduct, it would be inappropriate to make a finding of research misconduct based on a single possibly duplicated band. In this case, the JBC paper contains multiple figures with western blots containing approximately 150 lanes of blots with approximately 650 separate bands. None of the remaining bands were alleged to have been duplicated. ORI never made findings of research misconduct based on such a flimsy evidentiary basis.

The University Appeal Panel also noted in their response to the UP-investigation report that the figure in question was of marginal significance. The panel also noted that because the questioned panel was not essential to the paper's conclusions, it could not determine that anyone would have had a motive to falsify the figure.

It should also be noted that the questioned images are control blots, and that the research record described two separate experiments containing corresponding blot images.

For these reasons, I respectfully recommend that the editors of JBC agree with UP and Mr. Aravind Reddy to not retract the referenced paper. I am proud of the efforts made by ORI during my tenure to be cognizant of the adverse consequences of a finding of research misconduct to the reputation of a scientist; in cases such as this ORI would not have concurred with the VA's findings or recommendations.

John Dahlberg

A handwritten signature in black ink, appearing to read "John Dahlberg", written in a cursive style.

APPENDIX B

EMAIL COMMUNICATIONS

Includes:

- Email correspondence between Mr. Thaler, Ms. Karas and Dr. Sakabe from August 10, 2018 to September 19, 2018.
- Redacted copy of email communication between Mr. Tarugu and Dean Khan of University of Pittsburgh.

From: Kaoru Sakabe <ksakabe@asbmb.org>
Sent: Wednesday, September 12, 2018 4:36 PM
To: Karen S. Karas; Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler:

Because your client refused to provide the original data and images for figures 1A and 6A, any criticism of the JBC processes are the result of your clients' failure to provide requested and required information. The images in the PDF provided are of too poor quality for JBC to analyze. The data shown in the attachment for figures 3C and 4C do not appear to correspond with what is presented in the publication. The quality of the data provided on August 20 was of such poor quality that we requested the native files, but none were provided. Finally, we requested full copies of the investigation reports to determine the rigor and completeness of the committee's investigation. Your client has failed to provide the requested information to ensure the integrity of the article. Accordingly, we renew our request that the authors withdraw the paper by September 14.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Wednesday, September 12, 2018 at 9:30 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>, "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Please see the attached correspondence.

Thank you,
Karen Karas

Karen S. Karas ◻ Senior Counsel
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ D: 202-587-4745 ◻ F: 202.380.0514

From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Friday, September 7, 2018 7:21 AM
To: Karen S. Karas; Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Ms. Karas,

Thank you for your message. The information you requested in your message from yesterday was provided to you and Mr. Thaler on August 31. Please let me know by September 14th if the authors will withdraw the article.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Thursday, September 6, 2018 at 4:06 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>, "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe:

Thank you for your August 31, 2018 email giving us the reasons for the journal's interest in reviewing the data for the additional images. There was no explanation in your August 29, 2018 email as to why the journal was seeking data about yet more images, and that is why we objected to the request.

Please send us the journal's basis/analysis for determining that the images were reused (Figs. 1a and 6a; Figs. 3c and 4c; and 5E). We will review the journal's analysis with our clients once we receive it, and we will provide you with the original data for the additional images.

Thank you,
Karen Karas

Karen S. Karas ◻ Senior Counsel
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ D: 202-587-4745 ◻ F: 202.380.0514

From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Friday, August 31, 2018 8:41 AM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for your message. In addition to the duplication in Fig 5E, we determined the following:

- The PPAR γ blot from Fig 1A was reused in Fig 6A as pAcK-H3 and H3
- The Lamin B1 blot from Fig 3C was reused in Fig 4C as H3

In light of these issues, the Editors are requesting that the authors withdraw this article. Please communicate this decision to all authors. Please request withdrawal by September 14, 2018. If the authors choose to withdraw the article, we will work with them to draft a mutually agreeable withdrawal notice. If the authors do not withdraw the article, then we will forward this matter to the ASBMB Publications Committee. The Committee may request more information, request a draft of a correction notice for editorial approval, or determine that the article is to be retracted. If the Committee determines that retraction is warranted, no further appeals will be considered and ASBMB will draft and publish a retraction notice.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
[Molecular & Cellular Proteomics](#)
[Journal of Lipid Research](#)

From: "Paul S. Thaler" <pthaler@cohenseglia.com>
Date: Thursday, August 30, 2018 at 3:09 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglia.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe:

This email responds to (1) your August 23, 2018 email requesting a copy of the report from the VA as well as unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter and (2) your August 29, 2018 email requesting original data to Figs 1A and 6A.

Regarding the requests in your August 23, 2018 email – we decline to provide unredacted copies of Attachment Nos. 1 and 2 to our August 10, 2018 letter. Those documents contain confidential information and were redacted at the suggestion of Dean Saleem Khan. A redacted copy of Mr. Aravind Tarugu's email exchange with Dean Khan is attached. We also decline to provide a copy of the VA's report. We have been informed by the VA that the finding against Mr. Tarugu will not be published. Therefore, Mr. Tarugu is entitled to maintain the report's confidentiality.

Regarding the requests in your August 29, 2018 email - we decline to provide the requested data. As you know, my clients have been fully cooperative and have thus far provided you the all the data and information you have requested, even the data requested in your August 16, 2018 that is not relevant to the subject matter (β -actin blot and the pMSK1 blot in Figure 5E). Your August 29, 2018 email requests additional data that is not relevant to the scope of our initial communication to you (our August 10, 2018 letter) or to Mr. Tarugu's obligation to notify you regarding the VA's finding with respect to Figure 5E.

My clients will continue to cooperate in any way they can with respect to any additional questions you may have regarding the β -actin blot and the pMSK1 blot in Figure 5E.

Thank you for your attention to this.

Sincerely,

Paul S. Thaler ◻ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0218

[website](#) | [vCard](#) | [offices](#) | [email](#)



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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Wednesday, August 29, 2018 3:15 PM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

In addition to the below documents, we would like to review the original data to Figs 1A and 6A.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: Kaoru Sakabe <ksakabe@asbmb.org>
Date: Thursday, August 23, 2018 at 3:19 PM
To: "Paul S. Thaler" <pthaler@cohenseglias.com>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for this information. Would you be able to provide a non-redacted version of attachments 1 and 2 from your letter? Additionally, we would like to review the report from the VA.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Wednesday, August 22, 2018 at 4:56 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Here is the response I received from my clients:

"No one has access to these files.

The LiCor that was used to generate these images was located in a common facility, used by multiple users. This instrument and its associated computer are no longer operational and were replaced by an upgraded system.”

Please let me know if there is anything else I can do to assist you.

Sincerely,

Paul

Paul S. Thaler ◻ Partner

Cohen Seglias Pallas Greenhall & Furman PC

1828 L Street, NW, Suite 705 ◻ Washington, DC 20036

P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [<mailto:ksakabe@asbmb.org>]

Sent: Tuesday, August 21, 2018 10:29 AM

To: Paul S. Thaler

Cc: Karen S. Karas

Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for providing these data. It seems the authors used a LICOR imaging system to obtain these data. Do the authors have access to the LICOR acquisition zip files? If so, would they be able to provide these data?

Sincerely,

Kaoru Sakabe, PhD

Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

From: "Paul S. Thaler" <pthaler@cohenseglia.com>
Date: Monday, August 20, 2018 at 2:48 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglia.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Please find attached the files you requested.

Thank you for your attention to this.

Sincerely,

Paul
Paul S. Thaler ◻ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Thursday, August 16, 2018 2:29 PM
To: Paul S. Thaler
Cc: Karen S. Karas
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for the quick response. We would be interested in reviewing the original data for Figs 3C, 4C, and 5E. We would prefer that these images be provided uncropped and minimally processed.

Thank you in advance for your help.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

[Journal of Biological Chemistry](#)
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[Journal of Lipid Research](#)

From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Thursday, August 16, 2018 at 2:26 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Karen S. Karas" <kkaras@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

This will confirm that we also represent Dr. Raju Reddy. We are happy to help get your questions answered.

Sincerely,

Paul S. Thaler ◻ Partner
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0218

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From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Thursday, August 16, 2018 2:01 PM
To: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler,

Thank you for your patience. From your letter, it sounds like you represent only Mr. Aravind Reddy and not Dr. Raju Reddy, the corresponding author. Please confirm as we have questions for the authors.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: "Paul S. Thaler" <pthaler@cohenseglias.com>
Date: Saturday, August 11, 2018 at 7:19 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Thank you, Dr. Sakabe. We look forward to hearing from you.

Sincerely,

Paul S. Thaler, Esq.
Cohen Seglias Pallas Greenhall & Furman PC
(202) 587-4750

Sent from my iPad

On Aug 10, 2018, at 2:58 PM, Kaoru Sakabe <ksakabe@asbmb.org> wrote:

Dear Mr. Thaler,

Thank you for your letter. Please allow us some time to review the information.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: Cynthia Roberson <croberson@cohenseglia.com>
Date: Friday, August 10, 2018 at 11:54 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglia.com>
Subject: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Good afternoon Dr. Sakabe.

Please see attached letter on behalf of Paul S. Thaler regarding the above reference matter. Should you have any questions or concerns, please do not hesitate to contact Mr. Thaler.

Thank you
Cynthia

Cynthia Roberson<image001.gif>Administrative Assistant
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705<image001.gif>Washington, DC 20036
P: 202.466.4110<image001.gif>F: 202.466.2693

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<image002.png>
<image003.gif><image004.gif>

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From: Kaoru Sakabe <ksakabe@asbmb.org>
Sent: Friday, September 14, 2018 1:19 PM
To: Karen S. Karas
Cc: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Ms. Karas,

I have not received an email.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Friday, September 14, 2018 at 12:25 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

I just emailed you a letter from Paul Thaler along with three Power Point files and seven .tif files. Because of the size of the attachments, I had to send the email through our firm's "Share File" site. Please send me an email to confirm receipt once you receive the email.

Thank you,

Karen Karas

Karen S. Karas □ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 □ Washington, DC 20036
P: 202.466.4110 □ F: 202.380.0514



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From: Karen S. Karas
Sent: Friday, September 14, 2018 1:41 PM
To: 'Kaoru Sakabe'
Cc: Paul S. Thaler
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

I have just finished sending all five emails. Please confirm receipt.

Thank you,
Karen Karas

Karen S. Karas ◻ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ◻ Washington, DC 20036
P: 202.466.4110 ◻ F: 202.380.0514

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From: Karen S. Karas
Sent: Friday, September 14, 2018 3:54 PM
To: 'Kaoru Sakabe'
Cc: Paul S. Thaler
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

It appears that my five emails were transmitted successfully to you earlier this afternoon, as I did not receive any transmission error messages. If this is incorrect, please let me know.

Thank you,
Karen Karas

Karen S. Karas ▫ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ▫ Washington, DC 20036
P: 202.466.4110 ▫ F: 202.380.0514

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From: Kaoru Sakabe <ksakabe@asbmb.org>
Sent: Wednesday, September 19, 2018 1:42 PM
To: Karen S. Karas
Cc: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Ms. Karas:

Our policies may be found here: http://www.jbc.org/site/misc/edpolicy.xhtml#ethics_policy. We will not share further internal analyses/reports.

Sincerely,

Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

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From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Wednesday, September 19, 2018 at 9:12 AM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

Thank you for email. As this process moves forward to the next step, we would appreciate your answering the following questions and providing the information requested by close of business, September 20th, 2018, so that we have a better understanding of how the Editors reached their decision, and so that we can make plans going forward:

1. As we asked previously in our September 14 email, provide a copy of the Editors' analyses and reports describing the techniques they used to review the data/images we provided from August 10, 2018 through September 14, 2018.
2. Confirm that our September 14 emails (and all attachments) were shared with the Editors.
3. Forward the guidelines/policies which will apply to and govern the ASBMB Publications Committee's consideration of this matter.
4. Confirm that all of our communications with you, beginning with our August 10, 2018 letter, will be made available to the ASBMB Publications Committee.

Thank you,
Karen Karas

Karen S. Karas ▫ Senior Counsel
Cohen Seglias Pallas Greenhall & Furman PC
1828 L Street, NW, Suite 705 ▫ Washington, DC 20036
P: 202.466.4110 ▫ D: 202-587-4745 ▫ F: 202.380.0514

From: Kaoru Sakabe [mailto:ksakabe@asbmb.org]
Sent: Tuesday, September 18, 2018 9:23 AM
To: Karen S. Karas
Cc: Paul S. Thaler
Subject: Re: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Mr. Thaler and Ms. Karas:

We are in receipt of all 5 files. As your clients do not agree to withdraw, we will be forwarding this matter to the ASBMB Publications Committee. I will inform you of their decision.

Sincerely,
Kaoru Sakabe, PhD
Data Integrity Manager

American Society for Biochemistry and Molecular Biology
11200 Rockville Pike, Suite 302, Rockville, MD 20852
ksakabe@asbmb.org | www.asbmb.org

Journal of Biological Chemistry
Molecular & Cellular Proteomics
Journal of Lipid Research

From: "Karen S. Karas" <kkaras@cohenseglias.com>
Date: Friday, September 14, 2018 at 1:41 PM
To: Kaoru Sakabe <ksakabe@asbmb.org>
Cc: "Paul S. Thaler" <pthaler@cohenseglias.com>
Subject: RE: Journal of Biological Chemistry Publication Lakshmi, et al. 2014 Article [CSPGF-Active.FID483092]

Dear Dr. Sakabe,

I have just finished sending all five emails. Please confirm receipt.

Thank you,
Karen Karas

Karen S. Karas ▫ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC

1828 L Street, NW, Suite 705 □ Washington, DC 20036
P: 202.466.4110 □ F: 202.380.0514

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Tarugu, Aravind Reddy

From: Khan, Saleem A
Sent: Wednesday, July 25, 2018 11:57 AM
To: Tarugu, Aravind Reddy
[REDACTED]
Subject: RE: Request

Dear Aravind:

The April 4, 2018 letter from Provost Beeson is the official notification from the University regarding the disposition of your appeal, as the Provost is the highest ranking academic officer. It would be inappropriate for an additional letter to be generated. If there is information included in the notification that you do not wish to share with the JBC, I would suggest considering a redaction. Sorry I could not be of further assistance.

Sincerely,

Saleem A. Khan, Ph.D.
Associate Dean for Academic Affairs
Professor
Department of Microbiology and Molecular Genetics
University of Pittsburgh School of Medicine
S527 Scaife Hall
Pittsburgh, PA 15261
Office (412) 648 – 3911
E-mail: khan@pitt.edu

From: Tarugu, Aravind Reddy
Sent: Tuesday, July 24, 2018 11:56 AM
To: Khan, Saleem A <khan@pitt.edu>
[REDACTED]
Subject: Request

Dear Dean Khan,

As you may be aware, the VA Undersecretary upheld the decision made by ORO [REDACTED]. I was contacted by the VA to send a notification of this VA finding to JBC. As the University of Pittsburgh, the lead institute of this investigation overturned this decision, I would like to send this response letter to JBC along with the VA ORO letter. As the letter from the Provost (dated April 4, 2018) includes confidential information and internal findings, I cannot use it in the current format.

I request that you provide me with a letter stating a finding of no research misconduct on my part, [REDACTED].

I have a deadline for sending this notification (August 10, 2018), hence I kindly request your immediate attention to this matter.

Thank you in advance for your help. I appreciate it.

APPENDIX C

SEPTEMBER 12, 2018 LETTER FROM PAUL THALER TO DR. KAORU SAKABE

Including:

ATTACHMENT 1: September 11, 2018 letter from Dr. Reddy and Mr. Tarugu addressing Dr. Sakabe's comments and pdf attachment to Dr. Sakabe's August 31, 2018 email.

ATTACHMENT 2: Original data and image analysis including the complete description of techniques/tools used and observed interpretations (discussed in Dr. Reddy's and Mr. Tarugu's September 11, 2018 letter)



Paul S. Thaler
Attorney At Law

1828 L Street, NW
Suite 705
Washington, DC 20036

T: 202.466.4110 | F: 202.380.0218
pthaler@cohenseglias.com
www.cohenseglias.com

September 12, 2018

VIA ELECTRONIC MAIL

ksakabe@asbmb.org

Kaoru Sakabe, Ph.D.
Data Integrity Manager
American Society for Biochemistry
and Molecular Biology
11200 Rockville Pike
Suite 302
Rockville, MD 20852

***Re: Journal of Biological Chemistry Publication
Lakshmi, et al. 2014 Article***

Dear Dr. Sakabe:

I write to follow up on our continuing dialogue regarding the above-referenced paper. First, I want to let you know that neither we nor our clients realized that the document attached to your August 31, 2018 email constituted the totality of JBC's analysis of the images, so we appreciate your having confirmed that fact in your September 7, 2018 email. Second, we want to address any misunderstanding that you or any of JBC's Editors might have had in response to our August 30, 2018 email (objecting to providing data for additional figures). Third, we want to share with you and the JBC Editors the original images and their forensic analyses undertaken by our clients, which is attached and discussed below, and which we hope the JBC editors will find helpful.

As you know, the reason we contacted you in August was because Mr. Aravind R. Tarugu was directed to do so by Dr. Steven Graham, the research integrity officer of the Department of Veteran Affairs' ("VA"). The only figure about which the VA is concerned (and thus the narrow focus of our initial communication to you) is Figure 5E (specifically, two panels in Figure 5E, beta actin and pMsk1). However, in response to our initial August letter, you requested original data not only for Figure 5E, but Figures 3C and 4C as well. Even though JBC's request went beyond the concern of the VA, my clients provided all of the requested data. They also answered your follow-up inquiry regarding the LICOR imaging system. When, however, JBC further expanded its inquiry to include Figures 1A and 6A, it was, in our opinion, appropriate to set limits on what seemed to us to be an ever expanding inquiry that was getting

Dr. Sakabe
September 12, 2018
Page 2

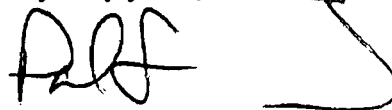
further and further away from the concern of the VA (two panels in Figure 5E). That is what lead to our August 30, 2018 email to you objecting to JBC's request for data related to Figures 1A and 6A. We were surprised to then receive your August 31, 2018 email advising us of the decision of JBC's Editors that Figures 1A and 6A, and Figures 3C and 4C, contained duplications and that they had decided the article should be withdrawn.

Our clients strongly disagree with the decision of the Editors that the article should be withdrawn. We request that the Editors carefully review the attachments to this letter and then reconsider and reverse their decision. Mr. Tarugu and Dr. Reddy are deeply concerned that the Editors reached their conclusions regarding the subject Figures (Figures 1A and 6A, 3C and 4C, and 5E) without reviewing the *original images* and without completing a proper *forensic* analysis. The pdf attachment to your August 31, 2018 email does not reveal that any such forensic analysis of any of the images was undertaken.

As shown in Attachment No.2 to this letter, when the original images are reviewed or forensically analyzed as instructed by the Department of Health and Human Service's Office of Research Integrity, it is apparent that there is *no* duplication of images in Figures 1A, 6A, 3C, 4C and 5E. Attachment No. 1 is a letter from Dr. Reddy and Mr. Tarugu explaining the forensic analyses they undertook and the tools they employed. The results of the forensic analyses regarding Figure 5E are further supported by lab notebook pages (included as part of Attachment No. 2 at p. 7) as well as the expert opinion of Dr. John C. Russ (included as part of Attachment No. 2 at p.6).

On behalf of Mr. Tarugu and Dr. Reddy, we thank you and the Editors for considering these additional materials. For all these reasons, and those stated in the attached letter and analyses, we request that JBC's Editors reconsider their decision and conclude instead that withdrawal of the article is not necessary. Dr. Reddy and Mr. Tarugu will continue to cooperate and will answer any questions that the Editors may have regarding the attached letter and analyses. Our clients are willing to provide additional information consistent with the positions we have taken in our prior communications .

Very truly yours,



Paul S. Thaler

Attachments

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Raju C. Reddy

September 11, 2018

Dear Dr. Sakabe:

On August 10, 2018, Mr. Thaler, on behalf of Mr. Tarugu, sent you a letter as notification to the Journal of Biological Chemistry (hereafter “JBC”) (hereafter “*Notice to JBC*”), as required by the Department of Veterans Affairs (“VA”), regarding the VA’s finding made related to Figure 5E beta actin and pMsk1 in the Lakshmi et al. 2014 article. In response to the *Notice to JBC*, JBC requested that we provide data for additional images. Even though that request went beyond the scope of the initial *Notice to JBC*, in the spirit of cooperation and disclosure, we provided the data as requested. We then received a further request, on August 29, to provide additional images not related to the image in question as outlined in the *Notice to JBC*. As we had not received an explanation for this request and the requested images were beyond the scope of the *Notice to JBC*, we respectfully declined to provide this data, yet indicated our full cooperation to provide any additional information related to Figure 5E beta actin and pMsk1.

On August 31st, 2018, we were notified by JBC via our attorney Mr. Thaler that “*the Editors are requesting that the authors withdraw this article*” adding “*In addition to the duplication in Fig 5E, we determined the following:*”

- *The PPAR γ blot from Fig 1A was reused in Fig 6A as pAcK-H3 and H3*
- *The Lamin B1 blot from Fig 3C was reused in Fig 4C as H3*”

Attached to JBC’s August 31, 2018 email was a PDF attachment (hereafter “*JBC Analysis*”) providing pictorial information as a basis for the above determination. Since we did not receive any additional information regarding this analysis, such as the source of images, software tools used, and interpretations made based on such analysis, we are not able to understand from the *JBC Analysis* how JBC reached its conclusions regarding image duplication. However, after reviewing the images in the *JBC Analysis*, it appears that JBC used snapshots of images from the Lakshmi et al. 2014 article to perform an image analysis to which a color gradient was applied on figure 1A, 6A and 5E to determine if reuse of the images occurred. Our understanding that JBC used snapshots comes from the existence of border lines below and above the images of interest as we prepared the figures with the outlines for publication. The *JBC Analysis* does not reveal any analysis performed on figures 3C and 4C, and, thus, JBC’s conclusion regarding those figures seems to be based entirely on a naked eye comparison. Additionally, no information on histogram equalization was provided in the *JBC Analysis*. As we believe that snapshots were used and no histogram equalization was performed prior to JBC’s image analysis, these factors may have resulted in some of the inaccuracies with the *JBC Analysis*.

In light of our concern about the *JBC Analysis* and the fact that JBC’s inquiries have now surpassed the original scope of both the *Notice to JBC* and the VA’s concern, we are attaching to Mr. Thaler’s letter (as Attachment No. 2) the images for the above-mentioned figures and detailed forensic image analyses performed with these images. As you can see, the images themselves, when evaluated in their proper context, ***provide conclusive evidence*** that no images were reused. In addition, however, we are providing additional incontrovertible image analysis to further demonstrate lack of reuse. The tools and procedures we used for analyzing these images

are provided below. We used two different advanced approaches to perform forensics image analysis. The availability and application of these tools is well documented in the literature and in the relevant online sections. We are able to provide any additional details regarding these tools as necessary.

1. Using NIH Office of Research Integrity (ORI) Advanced Forensic Actions tools in Adobe Photoshop: In this process histogram equalized images were applied with advanced dark or light areas and advanced gradient map to determine the similarities or differences (in our case) between images. The preset actions will allow the user to limit personal biases.
2. Using image segmentation, thresholding, and sobel gradient in MATLAB Image Processing Toolbox: In this process histogram equalized image is portioned into regions based on the pixel characteristics of the image. This will find the discontinuities in pixel values and indicated edges. This process eliminates biases as the process is performed as a coded program.
3. Use of notebook entries: Along with image analysis and original images, we also provided lab notebook entries related to Figure 5E beta actin and pMsk1 performed ~6 months apart by two different researchers.

Forensic analysis of our images clearly shows the differences between each allegedly duplicated image. These differences include:

- a) Several differences in excised borders of membrane and its size.
- b) Presence of protein marker lanes in the blots.
- c) Several differences in heatmaps and gradient maps of images and bands.
- d) Several differences in backgrounds of the images.

All of the above differences reflect very clear and conclusive results from rigorous analysis versus analysis performed in a non-rigorous manner (using the naked eye, or focusing on singular images or general visual effects).

Along with these analyses, we provide the forensics image analysis performed by Dr. John Russ (included in Attachment No. 2 to Mr. Thaler's September 11, 2018 letter). Dr. Russ has authored several highly regarded and cited works on image processing. His book "The Image Processing Handbook" has been consistently rated as the best overall introduction to computer-based image processing and has been cited >4,000 times according to Google citations. He has also been awarded the Ernst Abbe Memorial Award for his contributions to the field.

In our *Notice to JBC*, we also provided evaluations from Dr. Alan Price and Dr. John Dahlberg, two highly respected, independent experts who retired after long careers in senior level positions at NIH's ORI and have extensive experience reviewing thousands of allegations and misconduct/data manipulation cases. Both experts independently agreed with us and explained why the paper should not be retracted. We also emphasize that the University of

Pittsburgh was the lead institute of this investigation and *concluded that there was no misconduct and that there was no evidence of image reuse.*

With all the above factual evidence, we respectfully decline to withdraw our article.

Sincerely,

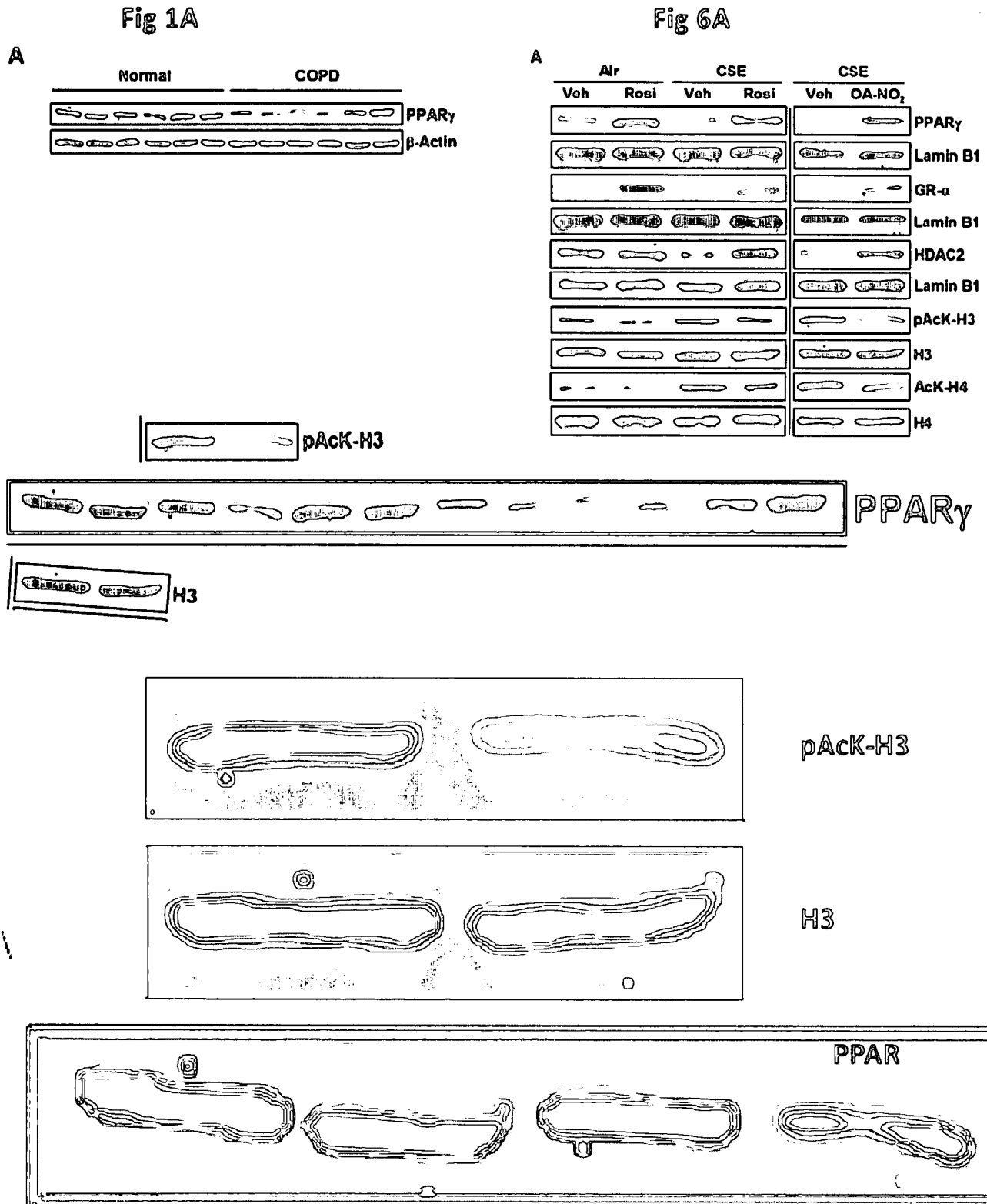
Aravind T. Reddy
Aravind Reddy Tarugu

Raju Reddy
Raju C. Reddy

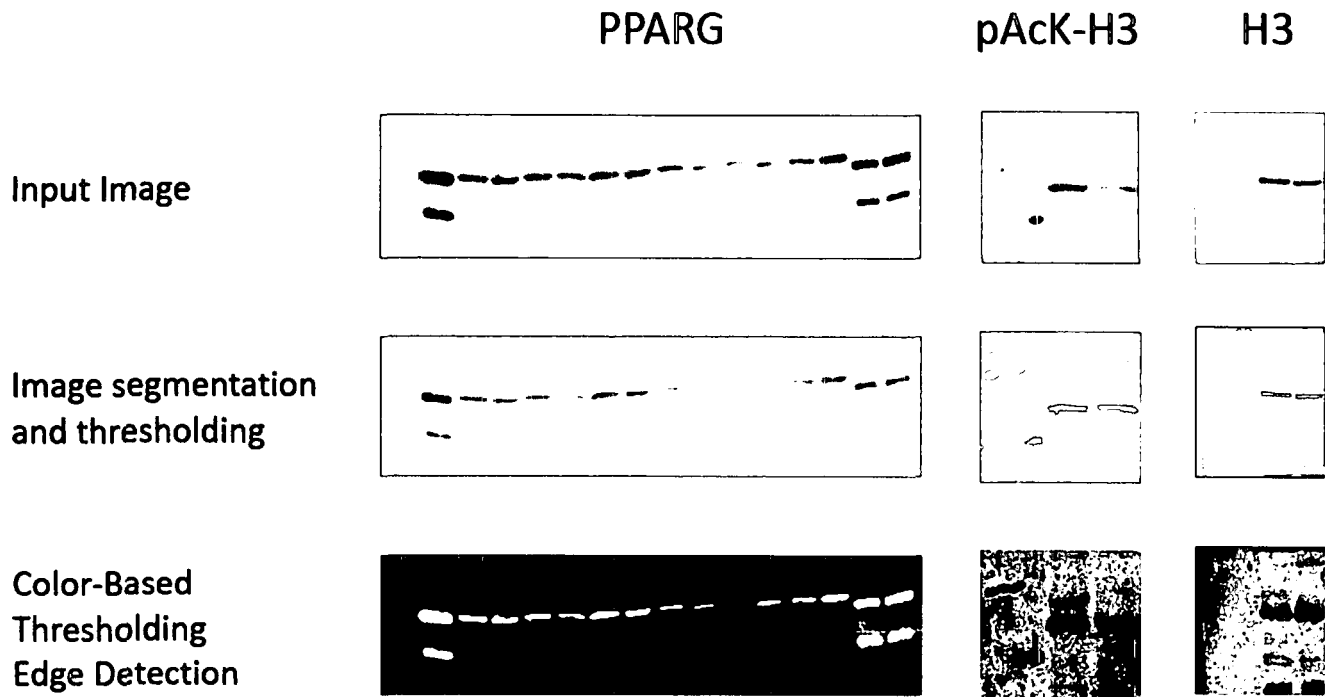
JBC: Figure 1A (PPAR gamma) and 6A (pAckH3; H3).

Same data used to represent different experimental conditions

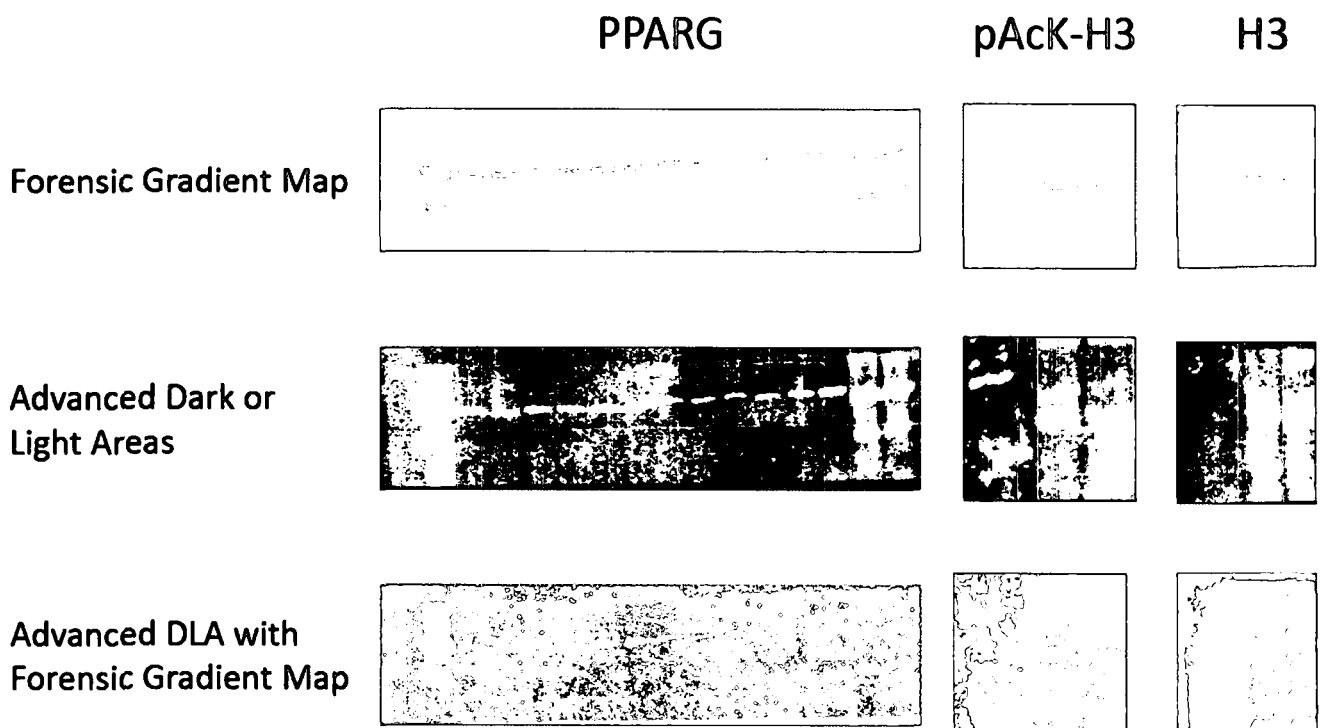
Reddy RC
JBC/2013/536805
Figs 1A and 6A



Forensic Image analysis was performed with
MATLAB (The Image Processing Toolbox)



Forensic Image analysis performed with Adobe Photoshop using
NIH Office of Research Integrity (ORI) Advanced Forensic Actions



JBC: Figure 3C (Lamin B1) and 4C (H3).

Same data used to represent different experimental conditions

Reddy RC
JBC/2013/536805
Figs 3C and 4C

Fig 3C

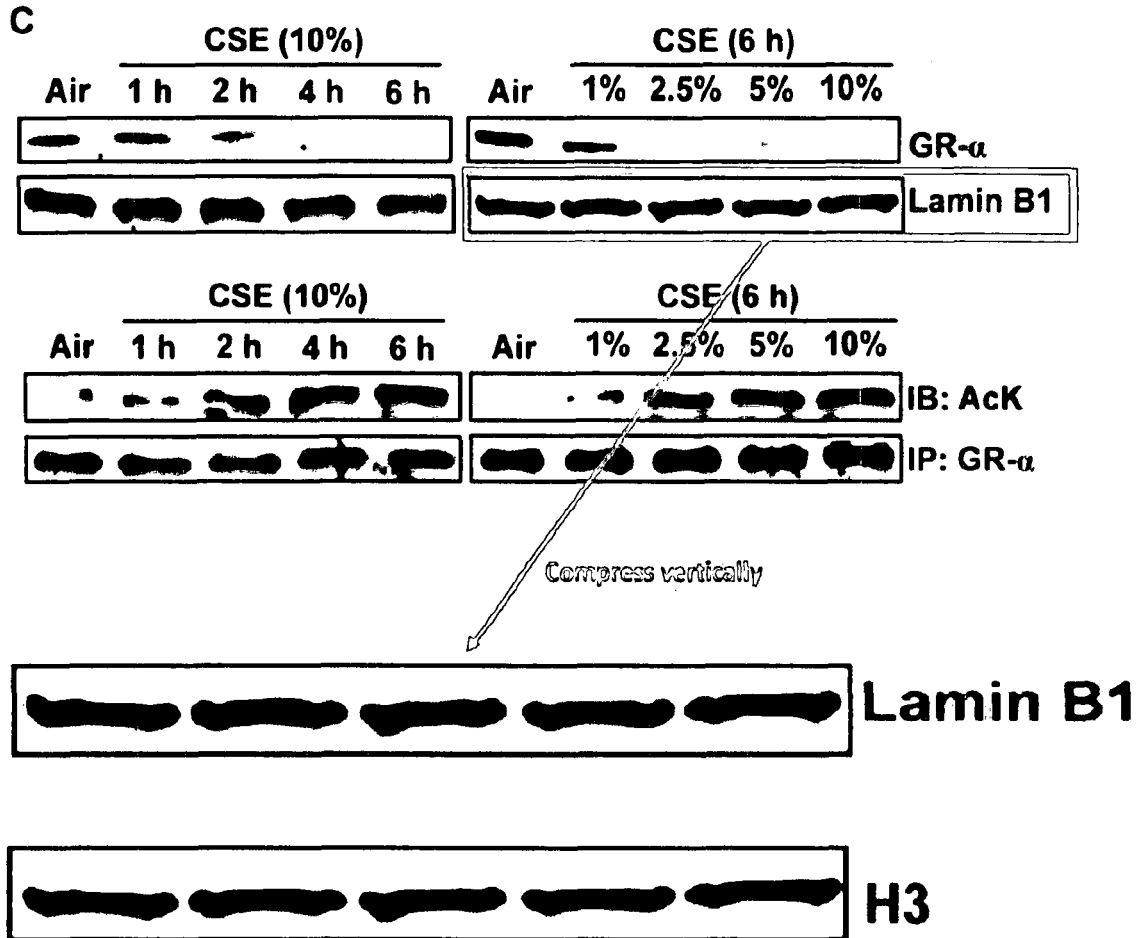
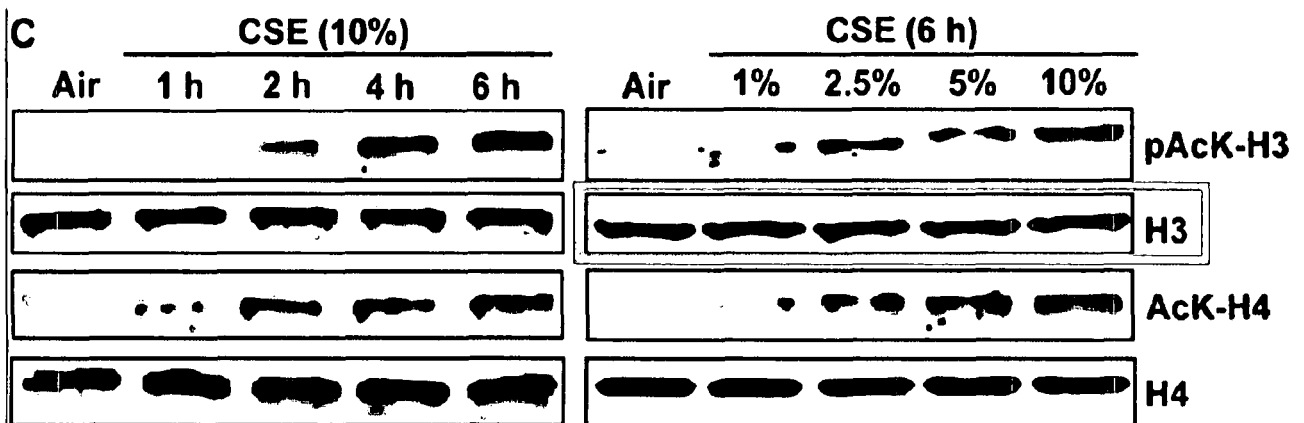
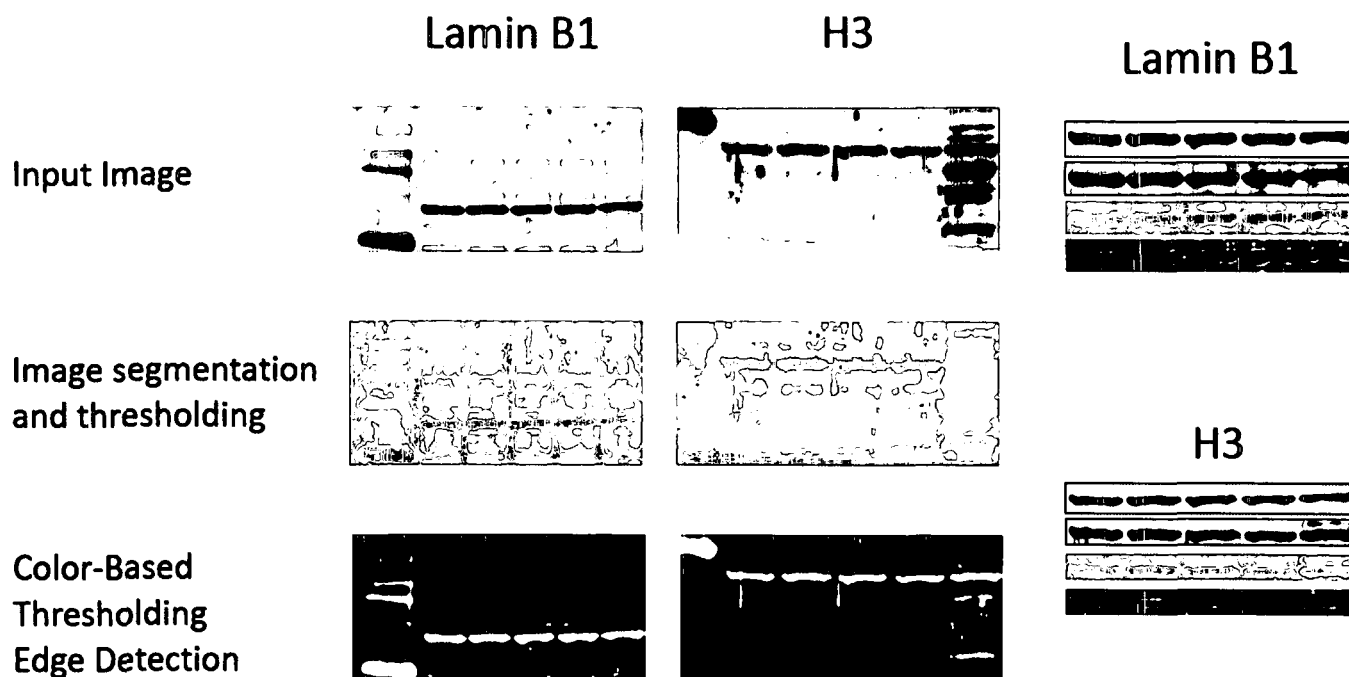


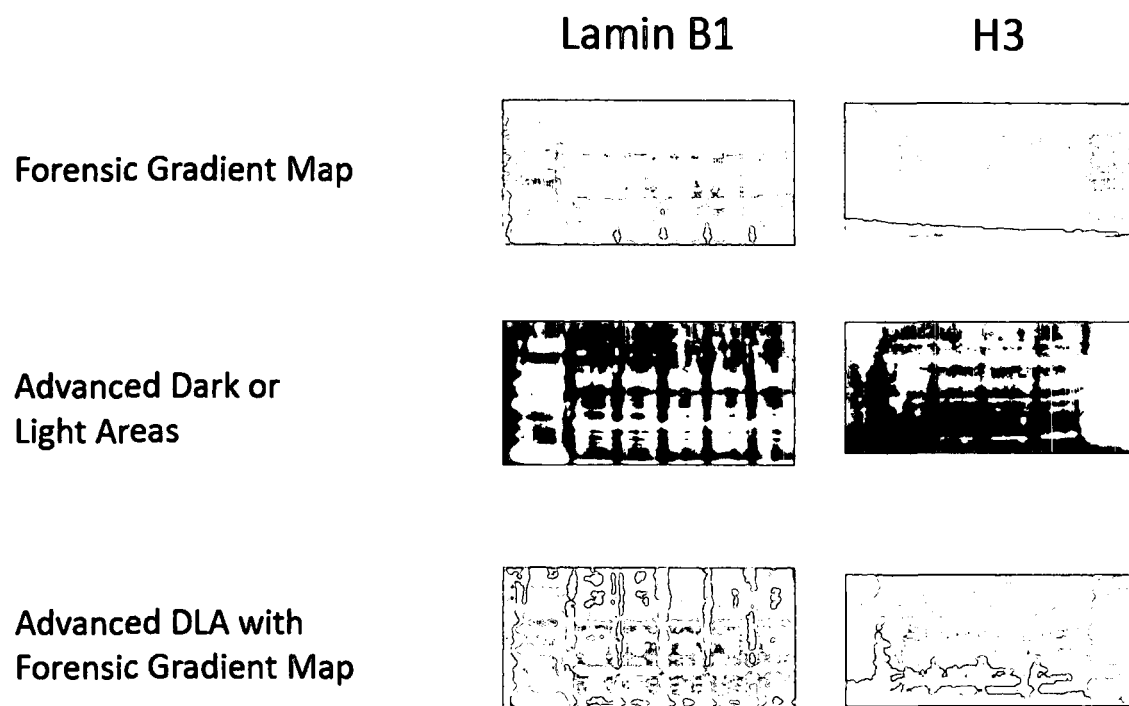
Fig 4C



Forensic Image analysis was performed with
MATLAB (The Image Processing Toolbox)



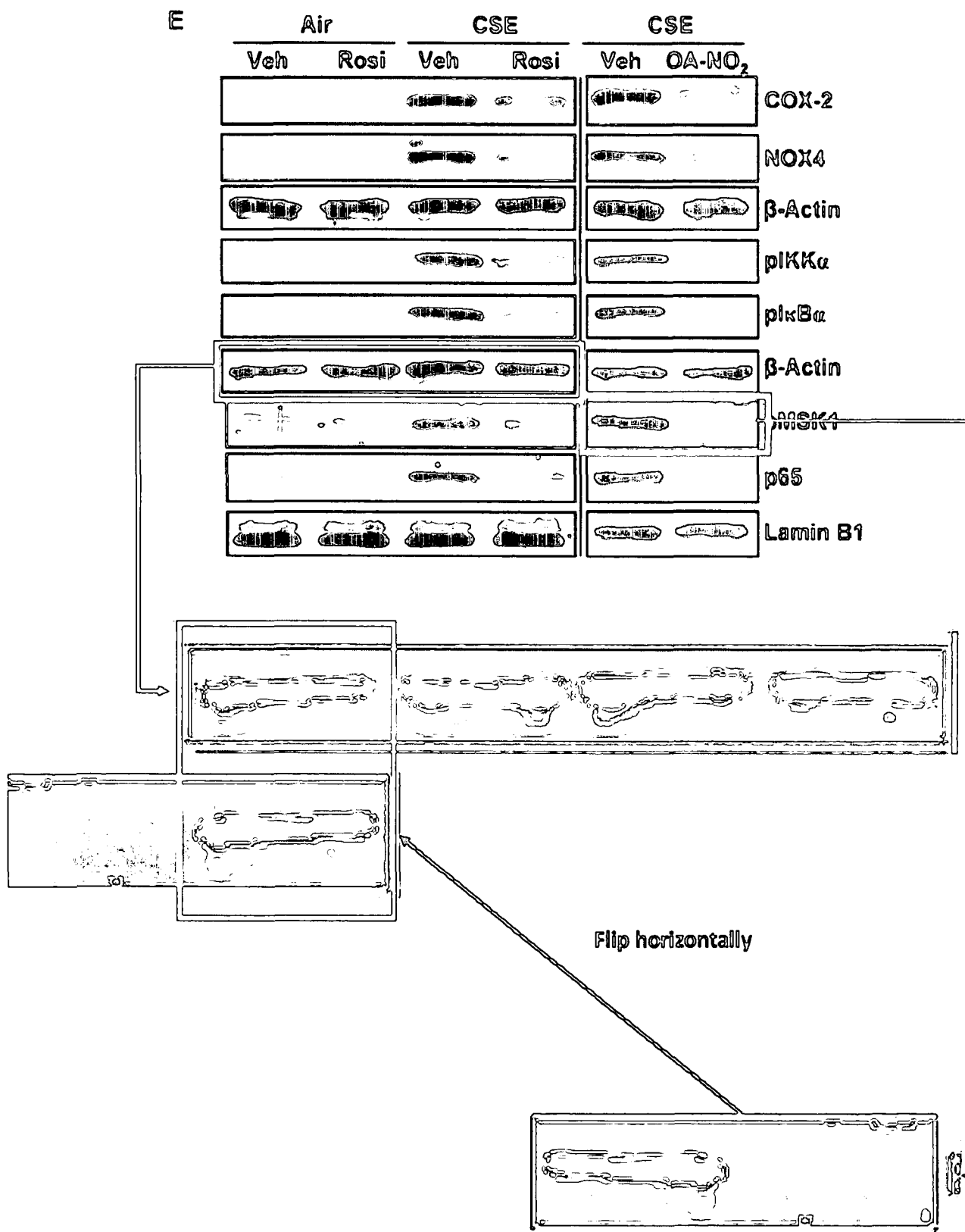
Forensic Image analysis performed with Adobe Photoshop using
NIH Office of Research Integrity (ORI) Advanced Forensic Actions



JBC: Figure 5E (bActin and pMsk1).

Same data used to represent different experimental conditions

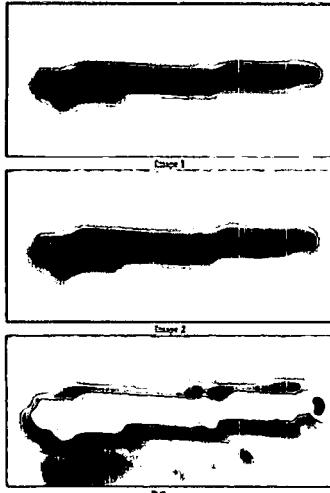
Reddy RC
JBC/2013/536805
Fig 5E



Forensic Image analysis performed by Dr. John C. Russ

Several important differences are noteworthy.

First, nearly the entire border of the difference image is dark, indicating that one blot image is definitely larger than the other.



Second, along the border there are variations in the density difference that are not uniform. In other words, one image could not be generated by simply enlarging the other or applying an overall brightness adjustment, which would have produced the same density all along the border. This is especially marked at the right edge, where an entirely different shape is revealed.

Third, there are several locations within the dense region (bright in the image shown) where pixels are slightly darkened indicating different densities in the original images.

Fourth, there are numerous regions in the surrounding areas that do not match, producing various darkened or lightened regions. That indicates that the images of the substrates are different.

From these differences, there is no doubt in my mind that the two original images are distinct.

Forensic Image analysis was performed with
MATLAB (The Image Processing Toolbox)

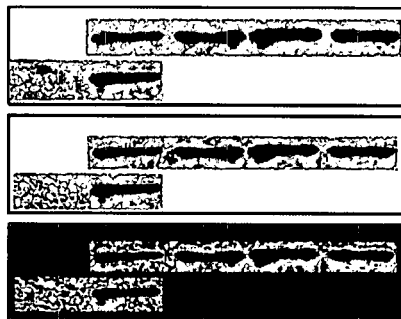
Forensic Image analysis performed with Adobe
Photoshop using
NIH Office of Research Integrity (ORI)
Advanced Forensic Actions

Input Image
Histogram Equalized



Beta Actin
pMsk1 (Flipped for Analysis)

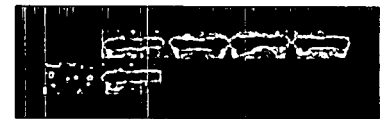
Image
segmentation
and
thresholding to
detect edges



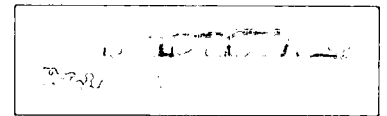
Key differences
between two
images in terms
of band shape
threshold and
background



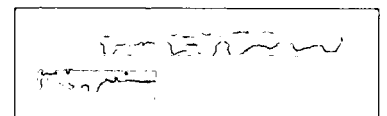
Advanced Dark or
Light Areas (Gray)



Forensic Gradient
Map 1



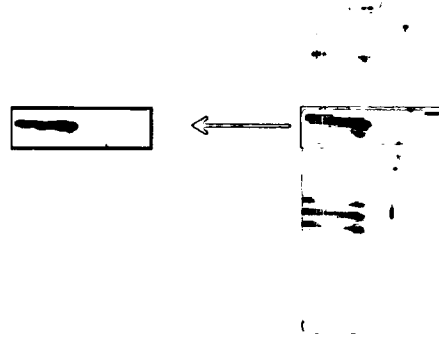
Forensic Gradient
Map 2



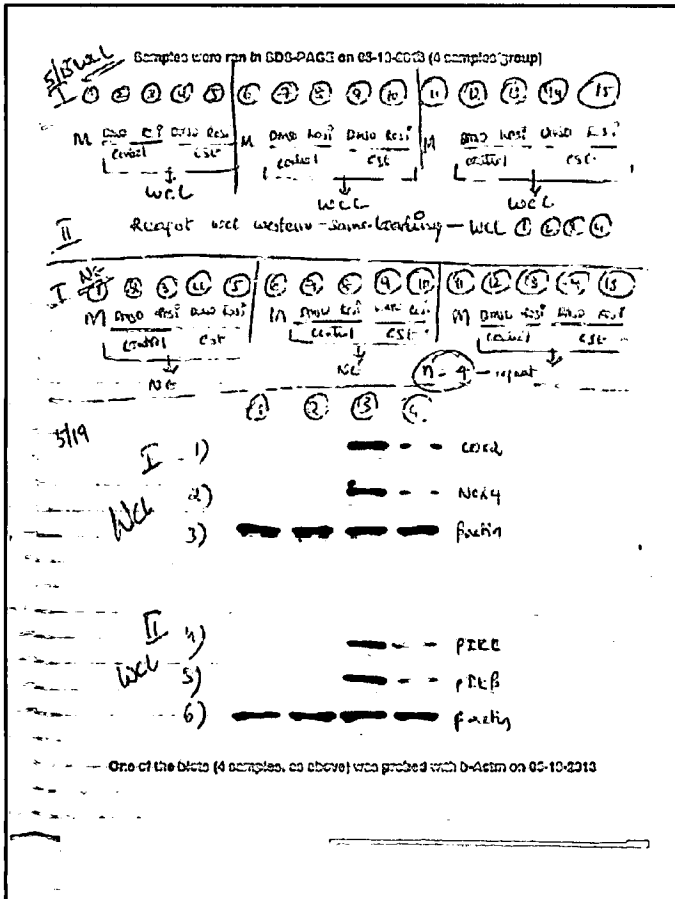
Other Evidence

- 1) Full blot of pMsk1 showing a two lane small blot.
- 2) Experimental details of Beta Actin run on 05-18-2013 to 05-19-2013
- 3) Experimental details of pMsk1 run on 10-05-2013 to 10-06-2013

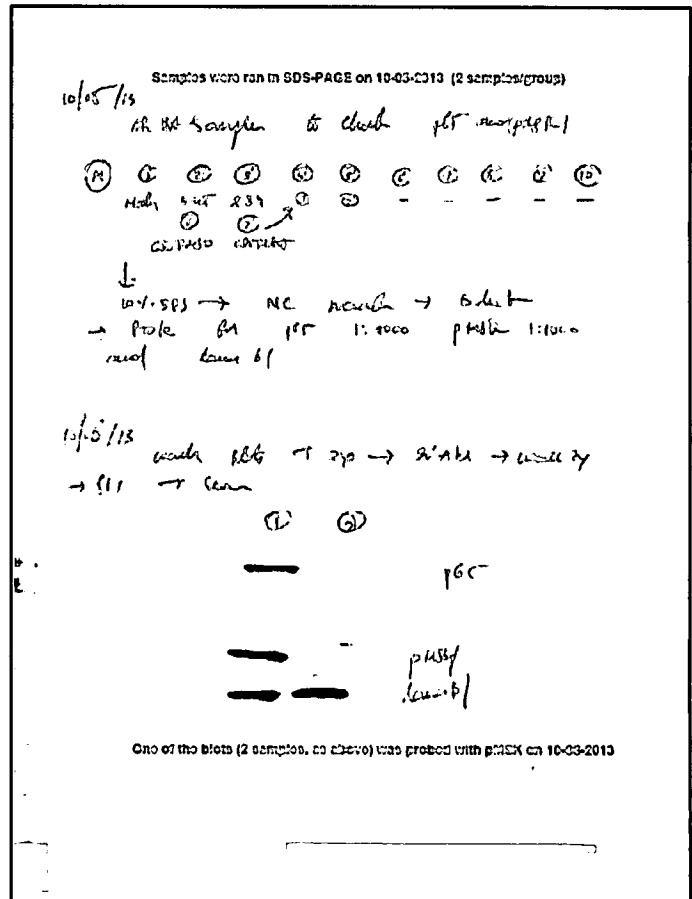
1



2



3



APPENDIX D

SEPTEMBER 14, 2018 LETTER FROM PAUL THALER TO DR. KAORU SAKABE

Letter addresses Dr. Sakabe's comments, highlights the transparency and cooperation by Mr. Tarugu and Dr. Reddy, notes JBC/ASBMB's lack of transparency in this matter, and identifies Mr. Tarugu and Dr. Reddy's requests for information required for review and JBC/ASBMB's lack of response thereto.



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www.cohenseglias.com

September 14, 2018

VIA ELECTRONIC MAIL

ksakabe@asbmb.org

Kaoru Sakabe, Ph.D.
Data Integrity Manager
American Society for Biochemistry
and Molecular Biology
11200 Rockville Pike
Suite 302
Rockville, MD 20852

***Re: Journal of Biological Chemistry Publication
Lakshmi, et al. 2014 Article***

Dear Dr. Sakabe:

I am in receipt of your September 12, 2018 email. With all due respect, your email does not fairly characterize the communications we have had over the last several weeks, nor does it reflect the spirit of cooperation or good faith with which my clients have acted. Until receiving your email yesterday, we did not know that JBC was dissatisfied with the data/images they had already been provided. I have gone back through your earlier emails to make sure we did not overlook something, but I can find no email in which you advised, for example, that the quality of the data provided on August 20 was “of such poor quality that [JBC] requested the native files” or that the images provided in the pdf “are of too poor quality for JBC to analyze.” None of your prior emails, before yesterday, noted any concern about the quality of the data/images my clients have provided, nor did you make any follow-up requests after receiving the files, by notifying us of the concern(s) that you had. Our communications (and my clients’ efforts to respond to JBC’s concerns) would have benefited from more transparency by JBC about its concerns. My clients are understandably frustrated and perceive that they are being blamed for not responding to JBC’s concerns that they did not even know existed about data/image quality. This was the same frustration we had over JBC’s request for the data for Figures Figs 1A and 6A. The request itself did not explain why the data was being requested and did not disclose what concerns JBC had about those figures. Also note that your request was not limited to the PPAR gamma, AckH3 and H3 blots, the specific blots on which you raised concerns, but it goes well beyond, requesting 24 images. It was not until we said we would not provide the data, as your request was beyond the scope of our notification, that you then informed us as to the reason behind the request. JBC’s own policy and policies by the Council of Science Editors provide

that if there is a concern about an image, JBC should notify the author as to what the concern is, ask for an explanation, and then request that data be provided. It seems that JBC has not followed its own policy. As my clients were neither notified of any concerns, nor provided an opportunity to respond/provide an explanation, they are clearly not at fault as you have stated. If you have access to a policy allowing JBC to ask for any data without first (or concurrently) notifying an author about JBC's concerns, and allowing JBC to make a determination without providing an opportunity for explanation, please do provide us with a copy of that policy.

With respect to the new concerns you raised for the first time in Wednesday's email, we address them below. Had you shared those concerns with us previously, as required by JBC's or the Council of Science Editors policies, we could have addressed them sooner.

- The reason my clients did not initially provide images for figures 1A and 6A was that they were not notified of any concerns regarding these images. Thus, it is not fair to put them at fault. Additionally, they did not "criticize" JBC's analysis; they simply stated that their understanding of the image analysis provided by you was limited, as you did not provide them with any specific information on the image analysis. We twice requested that you provide the details, but never got any response from you. Also, JBC did not contest our clients' claim that it was their understanding that snapshots from the PDF file were used by JBC for its image analysis. Using snapshots does not comport with the Department of Health and Human Services' Office of Research Integrity guidelines for image analysis. If JBC has separate guidelines for performing image analysis, please provide us with a copy. The use of the PDF file for image analysis by JBC did not result from our clients' not providing the requested information, rather it resulted because of JBC's decision to use such files to perform an image analysis on PDF snapshots. My clients are not responsible for how JBC does its image analysis.
- Regarding figures 1A and 6A – your email states that Dr. Reddy and Mr. Tarugu "refused to provide the original data and images for figures 1A and 6A" and "the images in the PDF provided are of too poor quality for JBC to analyze." They did not "refuse" to provide the original data. We clearly stated in our September 6, 2018 that we would provide the original data but asked to first see JBC's analysis. In response, you told us that the attachment to your August 31, 2018 email was the analysis (which we could not have known as it does not contain any information on how the analysis was performed and how the conclusions were drawn) and you inexplicably directed my clients to withdraw the article. Notwithstanding our disagreement with JBC as to whether the August 31, 2018 attachment is an "analysis," and whether JBC requested these images with appropriate notification, following its own policies, we are now providing the requested original data files (PPT files and .tiff file) to the email transmitting this letter. The .tiff file contain the original data for not only Figures 1A and 6A, but also Figures 3, 4 and 5.

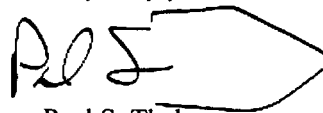
- Your email states that “the images in the PDF provided are of too poor quality for JBC to analyze.” *See* above response regarding PPT and .tiff files being provided. Even though the existence of these files and the fact that a rigorous analysis had been performed on these images was apparent by our letter, we did not receive any request to send the .tiff files.
- Regarding the data we sent for Figures 3C and 4C, your email states: “The data shown in the attachment for figures 3C and 4C do not appear to correspond with what is presented in the publication.” To the contrary, the tiff file “7.tiff” being sent concurrently with this letter demonstrates that figures 3C and 4C do indeed correspond with what is presented in the publication” This can be seen visually from 7.tiff as well as in the analysis of those images which we provided to you on Wednesday (September 12, 2018). JBC has provided no basis or explanation for the conclusion that the data does not correspond to the images. If the Editors have conducted an analysis of the Figure 3C and 4C data that we provided on Wednesday, or should they do so with the additional images we are providing today, please provide it to us for our review.
- Your email states that “[t]he quality of the data provided on August 20 was of such poor quality that we requested the native files, but none were provided.” When we sent the data on August 20, you did not respond to inform us that JBC considered the data to be of poor quality nor did you ask for better quality data. Indeed, the Editors appear to have considered the files to have been of sufficient quality to use for their “analysis” in concluding (albeit incorrectly) that there were duplications. In any case, we are now providing, as noted above, the original .tiff files for the five figures about which JBC has inquired. The files are: 1.tiff - 1A PPARg; 2.tiff - 6A pAH3; 3.tiff - 6A H3; 4.tiff - 3C Lamin; 5.tiff - 4C H3; and 6.tiff - 5E pMsk1; 7.tiff - lamin and H3 blots.
- As we stated in our August 30, 2018 email, our clients are entitled to their rights and protection of confidentiality during the investigation process. The VAPHS notice does not require us to send any documents related to the investigation. However, we wanted to be transparent and cooperative, thus we did provide documents. The redactions we made to the documents were appropriate and necessary to protect confidential information in conformance with the fair information practice (according to PHS policy 42 CFR Parts 50 and 93 and Privacy Act, and also as suggested by the University of Pittsburgh’s Dean Kahn in his email, a copy of which was sent to you) which allows us to withhold such confidential information from JBC and any other external entity. If you or the Editors have a specific question regarding the completeness of the investigation that is relevant to JBC’s own analysis of the images and data we have provided, please do let me know, and if I can respond without violating the confidentiality limits stated above, I will do so.

Dr. Reddy and Mr. Tarugu stand by the original images and image analyses we attached to our September 12, 2018 letter and which we are providing today. These demonstrate that

Dr. Sakabe
September 14, 2018
Page 4

there was no duplication in any of the images, as the Editors should also now be able to see from the additional PPT and .tiff files we are providing. Should the Editors have any evidence, analyses and/or explanation to demonstrate why my clients image analyses are wrong, ***please share it with us***. If there is any policy that supports the Editors' decision to direct that my clients withdraw the article before there is a thorough exchange of information, disclosure by the Editors of the analysis supporting their decision, and a full and fair opportunity for my clients to respond, ***please share it with us***. With all due respect, it is unfair to expect my clients to simply withdraw the article on the sole basis that JBC says these images are duplicated when JBC has not provided any evidence or analyses substantiating its conclusion. We understand JBC's interest in resolving any concerns it has, but that resolution must come only after a fair process that is transparent and clearly communicates to my clients what the concerns are and gives them an opportunity to respond.

Very truly yours,

A handwritten signature in black ink, appearing to read 'P.S. Thaler', enclosed within a hand-drawn, irregular, elongated shape that resembles a stylized arrow or a signature box.

Paul S. Thaler

Attachments (attached to 9/14/18 transmittal email)

cc: (via email)
Mr. Aravind Reddy Tarugu
Dr. Raju C. Reddy

From: Karen S. Karas
Sent: Tuesday, November 27, 2018 10:29 AM
To: 'ksakabe@asbmb.org'
Cc: Paul S. Thaler
Subject: Re: JBC/2013/536805 [CSPGF-Active.FID483092]

Dear Dr. Sakabe:

Thank you for your November 21, 2018 letter to Paul Thaler. As your letter does not contain any specific information or explanation as to how the Publications Committee reached its decision, and is not accompanied by any reports detailing the policies and review process of the ASBMB Publications Committee in this matter, our clients would like to request information and engage in discussion with the Publications Committee about the decision that has been made. Please share this email and our requests for information with Dr. Enrique De La Cruz and the other members of the Publications Committee, and please share their responses with us.

We request that the following information be provided:

- (1) The number of members of the Publications Committee who participated in the "consensus" decision and whether the decision was unanimous, and the manner by which the committee reached its final decision;
- (2) The identity of the "images" which the Committee concluded were reused (the letter simply says that "images had been reused . . .").
- (3) A specific description of the materials that the members of the Publications Committee reviewed, as the letter simply makes a general reference to "our correspondence, and the supporting information" we provided;
- (4) A disclosure as to whether any third-party analysis was obtained and considered and, if it was, a copy of that analysis along with the initial correspondence with the third-party analyst;
- (5) A response letter from the ASBMB Publications Committee providing a detailed rebuttal on why and how our clients' original data, image analysis performed by them using NIH ORI approved tools, lab notebook scans and expert analysis by Dr. Russ do not support the claim that the images were not reused; and
- (6) A statement as to whether or not the Publications Committee made a written analysis of the materials it reviewed and conclusion it reached and, if it did, a copy of that analysis.

In addition, as noted in our September 21, 2018 letter to Dr. De La Cruz, we have previously requested the following information, which has not yet been received. Please note that this information is very important for understanding the procedural regulations and "due process" governing JBC's committees, editors and the data analysis. Also note some of the policies on the current JBC site were recently updated and only effective since 2018, so they would not be relevant to this case. Thus, we continue to make requests and we hereby renew our request for the following:

- (7) Copies of bylaws/guidelines/policies which applied to and governed the ASBMB Publications Committee's consideration of this matter;
- (8) Copies of any policy which allows JBC to ask for any data without first (or concurrently) notifying an author about JBC's concerns, and allowing JBC to decide without providing an opportunity for explanation;
- (9) JBC's guidelines, if any, governing how image analysis is performed at JBC;

(10) Copies of any analyses performed by JBC on the data that we provided other than the analysis performed on PDF snapshots that we received on August 31st, 2018;

(11) JBC Editors' detailed rebuttal and reports describing the techniques they used to review and demonstrate why my clients' evidentiary materials provided from August 10, 2018 through September 14, 2018, are inconclusive of their claim that images were not reused; and

(12) Copies of any policy that supports the Editors' decision to direct that my clients withdraw the article before there is a thorough exchange of information, disclosure by the Editors (and now, the Publications Committee) of the analysis supporting their decision, and a full and fair opportunity for my clients to respond.

Please provide the requested twelve items of information as soon as possible. We anticipate that an extension of time will be needed to respond to your November 21, 2018 letter. We will determine how much additional time is needed once we receive the requested materials.

Thank you,

Karen Karas

Karen S. Karas ▫ Attorney At Law
Cohen Seglias Pallas Greenhall & Furman PC
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P: 202.466.4110 ▫ F: 202.380.0514

[website](#) | [vCard](#) | [offices](#) | [email](#)



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VERIFICATION

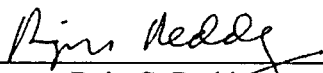
I, Aravind R. Tarugu, have read the foregoing Complaint and verify that the factual statements therein are true and correct to the best of my knowledge, or information and belief. This verification is made subject to the penalties of 18 Pa.C.S.A. § 4904 relating to unsworn falsifications to authorities.

Aravind T. Reddy
Aravind R. Tarugu

Dated: 08-09-2019

VERIFICATION

I, Raju C. Reddy, have read the foregoing Complaint and verify that the factual statements therein are true and correct to the best of my knowledge, or information and belief. This verification is made subject to the penalties of 18 Pa.C.S.A. § 4904 relating to unsworn falsifications to authorities.



Raju C. Reddy

Dated: 08-09-2019