



The University of Georgia

June 3, 2016

Dr. David Lee
Vice-President for Research
University of Georgia

Re: Final Investigation Committee Report of Dr. Azza El-Remessy

Dear Dr. Lee,

This letter contains the Final Investigation Committee Report regarding the alleged research misconduct of Dr. Azza El-Remessy. The form of the report follows to the best of our ability the guidelines of the UGA Policy on Responsible Conduct in Research and Scholarship. We have included a one-page executive summary to begin the document.

This Final Report takes into account the comments from the respondent (Attachment 32) and her legal counsel (Attachment 33) on the draft document of 2-27-16. We would also like to point out that it was the charge of this committee to investigate alleged research misconduct by the individual respondent and that it was outside our purview to investigate others.

Best Regards,

Lance Wells, Ph.D.
Chair of Investigation Committee
Georgia Research Alliance Lars G. Ljungdahl Distinguished Investigator,
Director of Graduate Affairs and Professor of Biochemistry and Molecular Biology
Adjunct Professor of Chemistry, Georgia Cancer Coalition Scholar
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Executive Summary:

Following review of allegations by the Research Integrity Officers at the University of Georgia (UGA), Augusta University (AU), and the Charlie Norwood Veterans Administration Medical Center (CNVAMC), an Inquiry Committee, and Institutional Officials, an Investigation Committee was charged in February of 2015 to examine allegations of research misconduct involving falsification and fabrication of data by Dr. Azza El-Remessy. Dr. El-Remessy is a tenured Associate Professor in the Department of Clinical and Administrative Pharmacy in the College of Pharmacy at UGA and a research pharmacologist at the CNVAMC. Prior to 2006, she was employed at AU. This committee consisted of 3 UGA faculty members, 1 AU faculty member, and a Career Scientist at CNVAMC. During the course of our investigation a total of thirteen allegations were investigated. Of the thirteen allegations reviewed, three had already resulted in manuscripts being retracted by the journal editors, one had editors reversing the decision to accept a manuscript, and four others had resulted in errata being issued. The committee reviewed the compiled information both individually and as a group and with the assistance of software analysis of figures supplied by third parties (editors/federal government). The committee also formulated written questions concerning the allegations as a whole and individually and considered the written answers supplied by multiple individuals. The committee considered several letters submitted by experts in related scientific fields that had been solicited by the respondent. Further, the committee met with the respondent and other appropriate persons and discussed each allegation as well as the matter as a whole prior to reaching a final conclusion.

Findings:

Of the thirteen allegations reviewed by the committee, it is the unanimous opinion of the committee that **ten of the allegations constitute research misconduct** and **three of the allegations are without sufficient evidence of research misconduct**. For nine of the ten allegations where we find research misconduct has occurred, we find by a preponderance of evidence that **the respondent** committed falsification and/or fabrication, that the actions were intentional to support the claims of the manuscripts/grant applications, and that the actions involved unsound practices that depart significantly from the standard practice in the field. The committee identified a recurring pattern of falsification of data to facilitate publication/funding over a long period of time with the only common author being the respondent that has led to multiple examples of misrepresentation of research findings to the scientific community.

Recommendations:

The committee considered several potential recommendations in response to our findings. Given the severity and frequency of falsification by the respondent over multiple years, the committee recommends the following actions in response to the 9 counts of research misconduct by the respondent:

1. Notification to the Office of Research Integrity of the National Institutes of Health and all relevant funding agencies of the findings of this committee.
2. Notification to editors of all the journals involved of the findings of this committee.
3. Notification to all co-authors of the manuscripts involved of the findings of this committee.
4. Communication of Research Investigation Findings to CNVAMC Medical Center Director so future actions can be pursued consistent with VHA Handbook 1058.02, Research Misconduct.
5. Termination of employment at UGA.*
6. Termination of Adjunct position at Augusta University.*

* Note that the CNVAMC member of the committee did not participate in these

recommendations in compliance with CNVAMC regulations.

1. Background & Process:

The investigation committee appointed to examine allegations of scientific research misconduct on behalf of the University of Georgia (UGA), Georgia Regents University (AU), and the Charlie Norwood Veterans Affairs Medical Center (CNVAMC) was charged on February 18th, 2015. The matter we were asked to consider involved allegations of falsification and/or fabrication of scientific data by Dr. Azza El-Remessy, Associate Professor, Department of Clinical and Administrative Pharmacy in the College of Pharmacy at the University of Georgia. Dr. El-Remessy is also a research pharmacologist at the CNVAMC and prior to 2006 was employed at AU. We were charged following reviews by research integrity officers, an inquiry committee, and institutional officials, who all concurred that a formal investigation should take place. Evidence related to the individual allegations was provided to the committee and establishment of procedure was established at the Charge meeting and subsequently via a secure dropbox account. The committee investigated each allegation separately with an individual member being assigned as the lead for each allegation. In the process of this due diligence by committee members, other allegations emerged that brought the total number of allegations considered by the committee to thirteen. Written questions from the committee were submitted to the respondent and other relevant individuals and replies returned to the committee. Next, the respondent, with legal representation present, met with the committee to discuss each of the allegations as well as the body of evidence as a whole. Following further discussions of the committee and further interviews with other relevant individuals as well as reviewing other relevant materials including expert data/image analysis by ORI and journals, as well as letters from scientist in related fields (that were supplied by the respondent and who did not see all the evidence seen by the committee), the committee then determined by vote for each allegation and for the body of allegations as a whole whether, by a preponderance of evidence standard, research misconduct had occurred, what type of misconduct had occurred, whether the respondent was responsible, whether it was a significant departure from standard practices in the field, and whether the misconduct was done knowingly, intentionally and/or recklessly as well as the seriousness of the impact of the misconduct on the validity of the research findings. Each lead committee member wrote the initial draft findings for their assigned individual allegations. The Chair edited and combined all individual allegations as well as drafted overarching sections of the report. The initial draft was read by the entire committee and edits relayed to the Chair. After several stages of revision, the final version submitted here was approved by the entire committee noting that the CNVAMC member did not participate in recommendations #5 and #6 in compliance with CNAV C regulations.

1A. Chronology of events

10-23-13: Consulting Editor of PLOS ONE contacts Respondent regarding concerns in **Diabetes and overexpression of proNGF cause retinal neurodegeneration via activation of Rho pathway** (pone.0054692). Figure 2A looked very similar to figure 5A in Molecular Vision 2012; 182993-3003; and figures 4B and 4C looked similar to figures 4A and 4C in Diabetologia 2013; 56:2329-2339.

04-29-14: Corrections published for above article.

08-18-14: Editors of Molecular Vision contact the respondent regarding "serious discrepancies" regarding several data figures where images "are duplicates or reverse duplicates of one another." Articles in question are Mol Vis 2000 6:243-51 (PMID: 11134581), Mol

Vis 2008 14:2190-203 (PMID: 19052649), and Mov Vis 2010 16:1487-95 (PMID: 20806080).

- 08-31-14: Editors of Molecular Vision retract the 3 above articles due to “substantive error in figure images such that the hypotheses were not tested and the conclusions were not supported.”
- 09-17-14: Executive Editor of Journal of Cell Science contacts the Respondent, the UGA RIO, and others regarding concerns in **Oxidative stress inactivates VEGF survival signaling in retinal endothelial cells via PI 3-kinase-tyrosine nitration** J Cell Sci 2005 118:243-252: doi10.1242. A reader had contacted the journal raising concerns about this paper and papers published in other journals from 2000 through 2013. The other publications of concern identified were the three Mol Vis articles noted above and **Diabetes-induced superoxide anion and breakdown of the blood-retinal barrier: role of the VEGF/uPAR pathway** PLOS ONE 2013 8:8: doi: 10.1371 /journal.pone.0071868.
- 10-01-14: HHS Division of Investigative Oversight in the Office for Research Integrity contact UGA regarding the three retracted Mol Vis papers and reaffirm the institutions obligations required under 42CFR93.
- 10-09-14: Editors of Mol Vis contact UGA RIO identifying discrepancies in figure 4D in **Thioredoxin-interacting protein: a novel target for neuroprotection in experimental thromboembolic stroke in mice** Mol Neuro 2014 PMID 24939693.
- 10-13-14: UGA RIO, Dr. Regina Smith, informs Respondent of the outcome of her pre-inquiry review and that a formal Inquiry would proceed; the Inquiry Committee is charged.
- 12-11-14: Molecular Neurobiology published erratum for **Thioredoxin-Interacting Protein: a Novel Target for Neuroprotection in Experimental Thromboembolic Stroke in Mice.**
- 12-20-14: Diabetologia publishes erratum for **Modulation of p75NTR prevents diabetes- and proNGF-induced retinal inflammation and blood-retina barrier breakdown in mice and rats.**
- 01-14-15: Inquiry Committee delivers their final report determining that the allegations of research misconduct were well-founded and recommended a formal Investigation.
- 02-09-15: Dr. Christopher King is appointed UGA RIO.
- 02-18-15: Investigation Committee is charged with three members from UGA, one from AU, and one from CNVAMC.

- 03-16-15: Via her legal representative, Mr. David Stewart of Crowder Stewart LLP, Respondent provides a letter to the Investigation Committee with additional information for their consideration
- 03-18-15: The Investigation Committee meets to review their charge and the evidence. At this meeting four additional articles with apparent falsification of figures were identified and added to the list of allegations. The additional articles were:
1. **Neurovascular Protective Effect of FeTPPs in N-Methyl-D-Aspartate Model**, Mohammed M.H. Al-Gayyar, Mohammed A. Abdelsaid, Suraporn Matragoon, Bindu A. Pillai, and Azza B. El-Remessy, The American Journal of Pathology, Vol. 177, No. 3, September 2010.
 2. **Peroxynitrite mediates VEGF's angiogenic signal and function via a nitration-independent mechanism in endothelial cells**, A. B. El-Remessy, M. Al-Shabrawey, D. H. Platt, † M. Bartoli, M. A. Behzadian, † N. Ghaly, N. Tsai, K. Motamed, and R. B. Caldwell, FASEB Vol. 21 August 2007.
 3. **Peroxynitrite Mediates Retinal Neurodegeneration by Inhibiting Nerve Growth Factor Survival Signaling in Experimental and Human Diabetes**, Tayyeba K. Ali, Suraporn Matragoon, Bindu A. Pillai, Gregory I. Liou, and Azza B. El-Remessy, DIABETES, VOL. 57, APRIL 2008.
 4. **Thioredoxin interacting protein is a novel mediator of retinal inflammation and neurotoxicity**. Al-Gayyar MM¹, Abdelsaid MA, Matragoon S, Pillai BA, El-Remessy AB. Br J Pharmacol. 2011 Sep; 164(1):170-80.
- 04-27-15: Via her legal representative, Mr. Stewart, Respondent provides written responses to questions posed by the Investigation Committee.
- 05-01-15: Investigation Committee interviews D. El-Remessy
- 05-12-15: Email follow up from Mr. Stewart regarding Respondent's interview with the Investigation Committee.
- 05-12-15: Respondent informs UGA RIO that the American Diabetes Association's Panel on Ethical Scientific Programs recommended to the editors of Diabetes to rescind the acceptance of **High fat diet-induced thioredoxin interacting protein drives retinal leukostasis and microvascular dysfunction** due to concerns regarding multiple figures in the manuscript.
- 06-02-15: A preliminary draft of the Investigation Report is provided to the Respondent for review and comment.
- 06-09-15: Extension is requested for submission of the Investigation Report to HHS ORI and UGA.
- 06-25-15: UGA RIO, Dr. Christopher King, meets with Respondent to review and discuss the investigation process.
- 07-03-15: Dr. El-Remessy provides a written response to the Investigation Committee regarding the preliminary draft of the Investigation Report.

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- 07-06-15: Mr. Stewart provides further written response to the Investigation Committee regarding the preliminary draft of the Investigation Report.
- 07-07-15: HHS ORI requests that the Investigation Committee evaluate additional scope, including her PHS grants.
- 07-31-15: Extension is requested for submission of the Investigation Report to UGA.
- 08-14-15: Extension is requested for submission of the Investigation Report to HHS ORI
- 09-02-15: Investigation Committee interviews Dr. Islam Mohamed.
- 09-04-15: Investigation Committee interviews Dr. Ruth Caldwell and Dr. Gregory Liou.
- 09-11-15: Dr. Caldwell provides clarification regarding FASEB article.
- 10-01-16: Extension is requested for submission of the Investigation Report to UGA.
- 11-20-15: Extension is requested for submission of the Investigation Report to HHS ORI.
- 11-30-15: HHS ORI provides image forensics to the Investigation Committee for the Respondent's PHS grants.
- 12-10-15: Extension is requested for submission of the Investigation Report to UGA.
- 12-17-15: UGA RIO, Dr. Christopher King, meets with Respondent to provide update, review, and discuss the investigation process.
- 12-21-15: Dr. El-Remessy provides response to ORI forensic analysis of figures from grant applications.
- 01-19-16: Investigation Committee sends written questions to Dr. Mohammed Al-Gayyar regarding figures generated for PHS grants.
- 01-20-16: Dr. Al-Gayyar provides a response to the Investigation Committee's written questions.
- 01-22-16: Extension is requested for submission of the Investigation Report to HHS ORI.
- 03-12-16: Draft final Investigation Report is submitted to Dr. El-Remessy for review and comment.
- 03-21-16: Respondent requests extension to 04-29-16 to return her responses on the draft report to the Committee; the extension is granted.

- 04-25-16: Respondent requests further extension to 05-13-16 to return her responses on the draft report to the Committee.
- 05-02-16: Extension to 08-01-16 for submission of UGA's final Investigation Report to ORI is requested and granted.
- 05-13-16: Responses to the draft Investigation Report from Dr. El-Remessy (Attachment 32) and her lawyer, Mr. Stewart, (Attachment 33) are received by the Committee.
- 05-17-16: Investigation Committee meets to deliberate and consider the responses of the Respondent and her lawyer.

1B. No Public Health Issues

2. Allegations:

See Appendix A

3. Sponsored Support of Application (by Allegation)

See Appendix A

4. University Inquiry

Summarized in report attached: see Attachment 6 and 7

5.A. Composition of Committee: These 5 members serve on more than fifteen editorial boards, ad-hoc review for other journals, and have served as reviewers for national/private funding organizations besides publishing 100's of manuscripts in the peer-reviewed literature and thus have considerable experience in accepted practices for publishing/presenting findings in the life sciences field.

Dr. Lance Wells (Chair)

GRA Investigator and Professor
Biochemistry & Molecular Biology
University of Georgia

Dr. Mary Ann Moran

Distinguished Research Professor
Marine Sciences
University of Georgia

Dr. Boris Striepen

Distinguished Research Professor
Cellular Biology
University of Georgia

Dr. Nevin Lambert

Regents' Professor and vice-chair
Pharmacology and Toxicology
Augusta University

Dr. Zheng Dong

Senior Research Career Scientist
Charlie Norwood VA Medical Center
Regents' Professor
Cellular Biology and Anatomy
Augusta University

5.B. Individuals Interviewed

- 5.B.1. Dr. Azza El-Remessy (video with David Stewart as legal counsel) 5-1-15
Attachment 12
- 5.B.2. Interview of Islam Mohamed (audio) 9-2-15
Attachment 18
- 5.B.3. Interview of Ruth Caldwell (video) 9-4-15
Attachment 21
- 5.B.4. Interview of Gregory Liou (video) 9-4-15
Attachment 22

5.C. Evidence Sequestered and Reviewed

See Appendix B

6. A-C. Analysis of Each Allegation (Background, analysis, and conclusions)

-Committee investigated allegations that exceeded the minimum requirement of ORI of 6 years.

TABLE 1. Summary of Allegations and Findings

#	Article	Findings in Question	Respondent's Role	Journal Action	Committee's Finding *
1	Mol Vis (2000) 6:243	Figs 4A, 6A, & 9A	First Author	Retracted	Research misconduct
2	J Cell Sci (2005) 118:243	Figs 3B, 4A, 4B, & 5B	First and Corresponding Author	Under Review	Research misconduct
3	Mol Vis (2008) 14:2190	Fig 8B	First Author	Retracted	Research misconduct
4	Mol Vis (2010) 16:1487	Figs 1C & 5A	First and Corresponding Author	Retracted	Research misconduct
5	PLoS ONE (2013) 8:e71868	Fig 4A	First Author	Erratum Submitted	Research misconduct
6	PLoS ONE (2013) 8:e54692	Figs 2A, 4B, & 4C	Corresponding Author	Erratum Issued	Research misconduct
7	Mol Neuro Biol (2015) 51:766	Fig 4D	Middle Author	Erratum Issued	Lacking in Evidence
8	FASEB J (2007) 21:2528	Figs 3A & 3C	First and Corresponding Author	No known action	Research misconduct
9	Diabetes (2008) 57:889	Fig 7A	Corresponding Author	No known action	Lacking in Evidence
10	Am J Pathol (2010) 177:1187	Fig 1, 2, & 4	Corresponding Author	Erratum Issued	Research misconduct
11	Br J Pharm (2011) 164:170	Figs 5A & 5B	Corresponding Author	No known action	Lacking in Evidence
12	Diabetes db15-0300 (2015)	Figs 4A, 6D, 1E, 2A (also 2B, 3A, 4A, 5A, 5D, 6A, 7B, S2A, S2B, S3B)	Corresponding author	Retracted initial acceptance before press	Research misconduct
13	R01EY 019275-01A2 and R01EY 022408-01	Fig 3E And Fig 2A (same figure)	PI	No known action	Research misconduct**

* Note: All decisions were unanimous (5-0)

**Note: While research misconduct was determined for allegation #13, it was the unanimous opinion of the committee that the preponderance of evidence did not support a finding of misconduct where the respondent was responsible.

Allegation #1:

Falsified research reported in Figures 4A, 6A, and 9A in El-Remessy et al. (2000) Regulation of interphotoreceptor retinoid-binding protein (IRBP) gene expression by cAMP in differentiated retinoblastoma cells. Molecular Vision 6: 243-51.

Dr. El-Remessy is the first author of this manuscript.

Manuscript retracted by journal editors.

Background

The editors of Molecular Vision received concerns regarding the integrity of figures presented as part of this publication from an unnamed reader of the article. The editors contacted Dr. Gregory Liou, the corresponding author, and Dr. El-Remessy (who served as first author) with their concern in August of 2014. The editors informed the corresponding author and Dr. El-Remessy of the decision of the journal to retract this publication (along with additional articles in the same journal by Dr. El-Remessy for which concern over data integrity had emerged).

Analysis

This article summarizes a study on the regulation of interphotoreceptor retinoid-binding protein (IRBP) gene expression by cAMP in differentiated retinoblastoma cells. Figures 4A and 6A show time course measurements of transcript abundance by hybridization analysis of RNA separated according to size by gel electrophoresis, so called Northern blots. Figure 5A shows an RNase protection assay over a time course. A critical part of these experiments is the detection of specific RNA molecules by hybridization of a radiolabelled probe that is documented by exposing the blot to film. The developed film shows the position and intensity of the molecules as bands or spots. As typical, the authors of this article normalize the change upon variation of conditions in their specific molecule of interest against a loading control.

While the presentation of the figure suggests that a picture or scan of the original film is shown, the images actually are a composite of individual bands. Importantly, the same individual bands were used multiple times within a single panel (Fig. 4A, 6A, and 9A), between IRBP and beta-actin control, and between figures (4A and 6A). There also appears to be duplication of a band in Figure 9A. As each band is supposed to represent a different experiment, this constitutes falsification.

In her written response to questions by the committee, Dr. El-Remessy stated that she and corresponding author Dr. Liou conducted the Northern blot experiments, that she as well as a laboratory technician scanned the films, and that Dr. El-Remessy assembled the figures, conducted the statistical analysis and described them in the article. It appears that Dr. El-Remessy no longer has access to the original films or the respective software files used in the assembly and annotation of the figures. In her written response, Dr. El-Remessy acknowledged that the images shown are composites. However, during the interview when asked whether certain bands represented identical images she stated that she no longer could make such a pronouncement given the time that had passed since the original publication.

Some of the bands shown are so called mirror or flip images of each other. This is of particular concern as this requires additional and deliberate manipulation of images and thus is not consistent with simple error in the naming or use of images files. As mirroring images changes the initial appearance of bands, this indicates a deliberate effort to disguise the use of identical images of bands. The committee asked specifically whether mirrored images were used in the preparation of the figure. Dr. El-Remessy did not provide a direct answer to this question in her written response and further chose not to address this question when asked again directly in the interview. Dr Liou during his interview implied that Dr. El-Remessy, though not the official corresponding author, acted as the corresponding author which is supported by email correspondence between the respondent and the journal. Dr. Liou later retracted this statement in writing.

The committee agrees with the analysis of the editors of Molecular Vision that the images shown in these three figures are highly manipulated in a way that is inconsistent with common scientific practice that was not disclosed to the reviewers or readers. The duplications are easy to spot upon visual inspection and there are numerous lines and breaks in contrast and background shadow between lanes that highlight insertion. The committee also notes the visible use of mirrored images of bands. The large number of duplications as well as the use of manipulated images is inconsistent with simple error in the assembly of figure panels and by a preponderance of evidence standard indicates intentional falsification.

The images in question are the basis of further quantitative and statistical analyses reported in the article. The lack of integrity of the initial data invalidates these subsequent analyses. The manipulated data form the substantive core of the experimental work presented in this article. The committee agrees with the assessment of the editors of Molecular Vision as published in the retraction of the article that due to the substantial problems with these three figures, hypotheses were not tested and conclusions were not supported. The committee further finds that manipulations occurred in segments of the preparation of the manuscript for which Dr. El-Remessy was responsible.

Conclusions

For the identified issue of alleged falsification, the committee finds that the respondent falsified data; that these actions represent a significant departure from the accepted practices of the relevant research community; that these actions were not honest errors or differences in interpretation of data; and that the allegation is proven by a preponderance of evidence.

The large number of duplicated bands along with the use of mirroring led the committee to the conclusion that the inappropriate presentation of data could not have been unintentional. The respondent was unable to produce original data or the files used to assemble the figure and avoided several direct questions on the topic of specific manipulations. The respondent was the author carrying the responsibility for the experiments and their documentation and analysis and it was the respondent who created the composite figures that represent a significant deviation from standard practice. The number and gravity of infractions are highly significant and invalidate the central conclusions of this article. While acknowledging the potential of errors, the respondent did not take the opportunity to acknowledge responsibility for her actions and did not proactively retract her article. Her assembly of figures differed significantly from the standard practice in the field, and appears to be made deliberately to support the conclusions of the manuscript. We agree with the editors that a full retraction of this paper was warranted. (Attachments 29.1)

Allegation #2:

2005 Journal of Cell Science: Falsified research reported in Figures 3B, 4A, 4B, and 5B in a Journal of Cell Science article, titled "Oxidative Stress Inactivates VEGF Survival Signaling in Retinal Endothelial Cells via PI 3-Kinase Tyrosine Nitration" (vol. 118. pt. 1, pp. 243-252), published in 2005.

Dr. El-Remessy is the first and the corresponding author.

Editorial action awaiting results of investigation.

Background

On August 13, 2014, Dr. Sharon Ahmad, Executive Editor of the Journal of Cell Science, contacted Dr. El-Remessy and several coauthors by e-mail to notify them of concerns regarding potential manipulation of Western blot data in a 2005 publication that had been raised by an anonymous source. The source pointed out bands that appeared to be duplicated within the same figure, specifically Figures 3B, 4A, 4B, and 5B. In response, Dr. El-Remessy sent copies of the original Western blot films to Dr. Ahmad on September 11, 2014. On September 17, 2014, Dr. Ahmad e-mailed AU officials (copied to Dr. El-Remessy and Dr. Regina Smith) to explain the allegations against Dr. El-Remessy and to indicate Dr. Ahmad's concern over both the seriousness of the matter and Dr. El-Remessy's explanation for why it occurred.

Analysis

The Journal of Cell Science 2005 article examines the mechanism by which VEGF, a factor that normally protects endothelial cells of the retina, is ineffective in diabetic retinopathy. In a general written response to Dr. Ahmad regarding the figures in question, Dr. El-Remessy stated on September 10, 2014 that there was "non-intentional oversight that resulted in data misrepresentation", that she "naively wanted to present clean and pretty representatives" and that there was "pressure from initial review that the Western blots that bands are "murky"". In an April 27, 2015, written response to questions posed by the Investigation Committee, Dr. El-Remessy indicated that she was responsible for generating the Western blots in question and assembling the figures for the paper. She also asserted that the findings of the paper were confirmed in subsequent published work from her group.

Figure 3B presents evidence that high levels of glucose and of a reactive oxygen species derived from high glucose concentrations (peroxynitrite) increase phosphorylation levels of p38 MAP kinase, thus converting p38 to P-p38. A band representing p38 loading for one of the treatments appeared to be a duplication of another band on the same gel. Dr. El-Remessy wrote on September 10, 2014 in response to the allegation that "the original band was a little bit higher than others and again naively and under the self-pressure to present exactly same band intensity". Thus, there is preponderance of evidence, in large part presented by the respondent herself, establishing a motivation to misrepresent data.

Figure 4A presents evidence that high levels of glucose and peroxynitrite act to increase nitration of p38. With regard to the allegations that a band representing nitration level was duplicated and that several bands in the p38 loading controls were direct or mirrored duplicates,

Dr. El-Remessy wrote on September 10, 2014, in her response to Dr. Ahmad that “naïve thinking that loading control should be ideal and same band intensity resulted in misrepresentation of the loading control” and “the original band is slightly higher in untreated control versus treated control” when the published gel was compared to a scan of the original gel. In her April 27, 2015, response to the Investigation Committee, Dr. El-Remessy quoted the reviewer’s comments that questioned whether the high background in the original submitted gel figure was due to non-specific staining. Dr. El-Remessy indicated that in order to respond to that reviewer comment, she had replaced the submitted figure “with a new blot showing significant increases in tyrosine nitration of p85 subunit under high glucose or peroxy nitrite treatments compared to normal glucose control”. This new figure is the one prompting allegations of direct and mirrored band duplications, as it includes one apparent case of direct duplication in the NY panel, and two apparent cases of direct duplication and two of mirrored duplication in the p85 panel.

The purpose of Figure 4B is to demonstrate that the regulatory p85 subunit of the PI 3-kinase was largely missing from the catalytic p110 subunit when glucose and peroxy nitrite concentrations were high. The anonymous reader who contacted the Journal of Cell Science raised concerns that two bands in this gel appear identical. The two weak bands that appear duplicated provide key support of the claim in the published paper that the p85 subunit was “hardly detected”. In her response of September 10, 2014, to Dr. Ahmad, Dr. El-Remessy provided a scan of the original gel showing that one of the two bands was considerably darker, and the figure had been substituted for publication with a lighter band. Dr. El-Remessy stated in her response to Dr. Ahmad that with regard to the band on the original film, “you can see that the band intensity was very low but had high background and looked murky...I admit using the lighter band was the wrong approach.” When questioned about this response during the Investigation Committee interview on May 6, 2015, Dr. El-Remessy indicated that she originally made the statement because she thought she had knowingly substituted the bands when assembling the figure (that she “used this one instead of that”), but later realized that the published image came from a larger panel of 9 blots, and that instead she had made a mistake when cutting the six blots from the original.

Figure 5B was used to demonstrate the importance of the PI 3-kinase in inhibiting cell death by analyzing endothelial cells with a constitutively expressed version of this protein. The concern raised with this figure was that the loading control for p38 appeared to have direct and mirrored duplicate bands. The original film scan provided by Dr. El-Remessy to Dr. Ahmad had different bands in the questioned positions compared to the published figure. Dr. El-Remessy wrote in her response to Dr. Ahmad on September 10, 2014 that “...the original bands were correct and show equal loading levels, however had strong background that made me think to use clean ones.” (Attachments 6, 7, 29.3, 31)

Conclusions

For the identified issue of alleged falsification, the committee finds that the respondent falsified data; that these actions represent a significant departure from the accepted practices of the relevant research community; that these actions were not honest errors or differences in interpretation of data; and that the allegation is proven by a preponderance of evidence.

There is visual evidence of direct and mirrored duplication or substitution of bands, and the substitution produced a figure that better supported the paper’s claims than the original data. The respondent indicated that she prepared the published figures. The respondent admitted that she had “misrepresented” data and that she had used the “wrong approach” in using different

bands for the images (Attachment 12). The intent of the respondent to falsify research findings in this instance is most clearly demonstrated by the respondent's written statements to the journal editor indicating that individual bands were chosen to improve the appearance of the figure. We recommend that a full retraction of this paper should be considered by the journal.

Allegation #3:

2008 Molecular Vision. Falsified research reported in Figure 8B in a Molecular Vision journal article, titled "Neuroprotective Effects of Cannabidiol in Endotoxin-Induced Uveitis: Critical Role of p38 MAPK Activation" (vol. 14, pp. 2190-2203), published in 2008.

Dr. El-Remessy is first author.

Manuscript retracted by journal editors.

Background

On August 18, 2014, the editors of Molecular Vision contacted Dr. El-Remessy and Dr. Gregory Liou by e-mail to indicate that several articles, including a 2008 article for which Dr. El-Remessy is first author, had serious discrepancies in data figures that involved duplicate or reverse duplicate images. The editors' e-mail stated that they were retracting the articles, and invited Drs. El-Remessy and Liou to request the retraction themselves, as well as to provide information on how the discrepancies arose, as these actions could affect the wording of the retraction statement and the editors' subsequent actions. In the 2008 paper in question, Figure 8B included two panels marked as a control and treated sample that appeared to show the same microscopic specimen. On August 25, 2014, Dr. El-Remessy responded to the Molecular Vision editors with an explanation of how the data misrepresentation occurred and provided them with original images. This paper was retracted by Molecular Vision, along with two others, on September 18, 2014. AU officials were notified by the journal of the retraction on that date, and UGA Research Integrity Officer, Dr. Regina Smith, received details from the journal on the retraction on October 9, 2014. (Attachments 6 and 7, specifically El-RemessySection5.pdf, and 29.2)

Analysis

The Molecular Vision 2008 article presents evidence that the anti-inflammatory compound cannabidiol acts by inhibiting reactive oxygen species formation and p38 MAPK activation. In her written response to the Molecular Vision editors regarding Figure 8B, Dr. El-Remessy stated on August 25, 2014 that "...misrepresentation of data was due to getting to deal with multiple images and data transfer from core facility..." and "...it appears that I picked the wrong image for the control...". She also took full responsibility for the assembly of the final figures in the paper. In an April 27, 2015, written response to questions posed by the Investigation Committee, Dr. El-Remessy reiterated that she was responsible for generating the figure in question and indicated that she had mistakenly selected the wrong image. In the May 1, 2015 interview with the Investigation Committee (Attachment 12), Dr. El-Remessy initially indicated that the microscope images were not duplicates by saying "They are not the same" but later agreed that they were when reminded of her previous statement in her August 25, 2014, written communication to the Molecular Vision editors.

Conclusions

For the identified issue of alleged falsification, the committee finds that the respondent falsified data; that these actions represent a significant departure from the accepted practices of the relevant research community; that these actions were not honest errors or differences in interpretation of data; and that the allegation is proven by a preponderance of evidence.

There is visual evidence of duplicated images; the duplication is acknowledged by the respondent. Dr. El-Remessy indicated that she selected the images and that she prepared the published figure. We find by a preponderance of evidence that this cannot be attributed to an honest mistake. The evidence indicates that the images used to construct the original figure were intentionally chosen for their visual appearance rather than being representative of the experimental conditions used to generate them. We agree with the editors that a full retraction of this paper was warranted.

Allegation #4:

Falsified research reported in Figures 1C and 5A in a Molecular Vision journal article, titled "Cannabidiol Protects Retinal Neurons by Preserving Glutamine Synthetase Activity in Diabetes" (vol. 16, pp. 1487-1495), published in 2010.

Dr. El-Remessy is both first and corresponding author.

Manuscript retracted by journal editors.

Background

On August 18, 2014, the editors of Molecular Vision contacted Dr. El-Remessy and Dr. Gregory Liou by e-mail raising concerns that this publication contained images that appeared to be duplicates. Specifically, the panels "C+CBD" and "D+CBD" in Figure 1C appeared to be duplicates, and the panels "Control" and "D+CBD" in Figures 5A appeared to be duplicates. On August 25, 2014, Dr. El-Remessy responded to the Molecular Vision editors with an explanation of how the data misrepresentation occurred and submitted original images. This paper was retracted by Molecular vision on September 18, 2014. AU officials were notified by the journal of the retraction on that date, and UGA Research Integrity Officer, Dr. Regina Smith, received details from the journal on the retraction on October 9, 2014.

Analysis

This Molecular Vision article presents evidence that "Cannabidiol Protects Retinal Neurons by Preserving Glutamine Synthetase Activity in Diabetes." Figure 1C presents representative images of DCF signaling to show that cannabidiol (CBD) reduced oxidative and nitroitive stress. Figure 5A includes representative TUNEL staining to show that CBD reduced cell death in

retinal cells in diabetic rats. The questioned images are important for the conclusions of this study. In her communications, including the May 6, 2015, interview with the Investigation Committee, Dr. El-Remessy acknowledged duplication of the images in these two figures. According to the information provided by Dr. El-Remessy, the images were collected by a technician/student in Dr. Liou's laboratory and transferred to her via email. Dr. El-Remessy assembled the figures including the questioned panels. She said these panels were included by mistake and she is responsible for the mistake. (Attachment 12 and 29.6)

Conclusions

For the identified issue of alleged falsification, the committee finds that the respondent falsified data; that these actions represent a significant departure from the accepted practices of the relevant research community; that these actions were not honest errors or differences in interpretation of data; and that the allegation is proven by a preponderance of evidence.

There is visual evidence of duplicated images; the duplication is acknowledged by the respondent; the respondent indicated that she selected the images and that she prepared the published figure. We find by a preponderance of evidence that this cannot be attributed to an honest mistake. The evidence suggests that the images used to construct the original figure were intentionally chosen for their visual appearance rather than being representative of the experimental conditions used to generate them. We agree with the editors that a full retraction of this paper was warranted.

Allegation #5:

Falsified research reported in Figure 4A in a PLoS ONE journal article, titled "Diabetes-Induced Superoxide Anion and Breakdown of the Blood Brain Barrier: Role of the VEGF /uPAR Pathway" (vol. 8, issue 8, e71868), published in 2013.

Dr. El-Remessy is first author.

Erratum has been submitted to the journal but has not been published.

Background

This allegation concerns immunoblots shown in Figure 4A. The blots were produced between 2002 and 2005 while Dr. El-Remessy was a postdoctoral fellow in the laboratory of Dr. Caldwell, the corresponding author for this paper. The manuscript was written in 2005, but it was put on hold due to a dispute between the senior authors (Dr. Behzadian and Dr. Caldwell). After Dr. Behzadian's retirement, Dr. Caldwell and Dr. El-Remessy added data to the manuscript for publication. Questions were raised over the apparent duplication of protein bands in the blots.

Analysis

This article provides evidence for the role of the VEGF/uPAR pathway in diabetes-induced superoxide anion and breakdown of the blood brain barrier. Figure 4A in this article was questioned. This figure was intended to show that high glucose induced phosphorylation of

GSK3beta which is mediated by VEGFR (VEGF receptor). The “NG” and “VEGF+VEGFRI” lanes appear to be identical to the mirror images, and the “HG-1d” and “HG-3d” lanes appear to be identical to the mirror images of the “VEGF” and “VEGF+VEGFRI” lanes. These lanes are important to support the conclusion that VEGFR accounts for the phosphorylation of GSK3beta and thus provide motive for potential manipulation. Dr. El-Remessy did not deny the fact that those lanes are identical bands. In her written response and the interview with the Investigation Committee, Dr. El-Remessy indicated that the duplicated bands were included in the blots by mistake. She pointed out that the duplication occurred, and stated that she asked the technician to provide similar or resembling bands and did not notice that the technician provided the same bands of the control (NG) condition. In her interview with the committee on 9/4/2015, the corresponding author, Dr. Caldwell, indicated that the editor had accepted that an erratum was appropriate, and had requested materials for an erratum on 4/21/2015. At the time of the interview Dr. Caldwell was surprised to learn that no erratum had yet been published. Dr. Caldwell forwarded to the committee an e-mail written to the editor on 4/24/2015 with an attached file to be used for an erratum. As of 2/10/2016 no erratum has been published by the journal, and no further correspondence between the journal and Dr. Caldwell has been forwarded to the committee. (Attachment 11, 12 and 29.9)

Conclusions

For the identified issue of alleged falsification, the committee finds that the respondent falsified data; that these actions represent a significant departure from the accepted practices of the relevant research community; that these actions were not honest errors or differences in interpretation of data; and that the allegation is proven by a preponderance of evidence.

The immunoblots in Figure 4A in this article contain identical protein bands that are duplications and mirror images. During the revision of the paper and thus providing motivation for manipulation, the respondent was primarily responsible for the submission of these falsified images. “Stitching” bands from different experiments or even from different blots from the same experiment is problematic and the presence of mirrored bands is most consistent with an intentional effort to manipulate data and both processes differ significantly from standard practice in the field. We find by a preponderance of evidence that this cannot be attributed to an honest mistake.

Allegation #6:

Falsified research reported in Figures 2A, 4B, and 4C in a PLoS One journal article, titled, “Diabetes and Overexpression of proNGF Cause Retinal Neurodegeneration via Activation of RhoA Pathway” (vol. 8, issue 1, e54692), published in 2013.

Dr. El-Remessy is the senior corresponding author.

Erratum issued by journal.

Background

On October 23, 2013, Iratxe Puebla, consulting editor for PLOS ONE, emailed Dr. El Remessy to notify her about concerns of potential duplication of images. The source pointed out that Fig

2A looked like image 5A in a previous publication, that Fig. 4B looked like the image in 4A in a different previous publication, and that one image in 4C looked like an image from 5F in the same previous publication. (Attachments 29.10 and 31)

Analysis

Dr. El-Remessy admitted that all 3 of these duplications had in fact taken place and suggested they were the unintentional result of breaking up a large manuscript into multiple publications.

Conclusions

For the identified issue of alleged falsification, the committee finds that the respondent falsified data; that these actions represent a significant departure from the accepted practices of the relevant research community; that these actions were not honest errors or differences in interpretation of data; and that the allegation is proven by a preponderance of evidence.

Dr. El-Remessy admitted that these were the same images and took responsibility for the actions that led to the duplication. The number of image duplications in this paper suggests that they were intentional and we find by a preponderance of evidence that this cannot be attributed to an honest mistake. While an erratum has been issued, we conclude that the journal editors should carefully consider a full retraction of the manuscript.

Allegation #7:

Falsified research reported in Figure 4D in a Molecular Neurobiology article, titled, “Thioredoxin-interacting Protein: a novel target for neuroprotection in experimental thromboembolic stroke in mice” e-published ahead of print on June 18, 2014.

Dr. El-Remessy is a middle author.

Erratum issued by journal.

Background

John Nickerson, an editor of Molecular Vision, reported the retraction of 3 articles on September 18, 2014, and called into questions certain figures in 3 additional manuscripts. This included Fig. 4D in this particular publication.

Analysis

Figure 4D contains duplication in that the images as sham and eMCAO/TKO group panels are the same for both DAPI staining and caspase-1 staining of the sham versus the eMCAO/TKO. As middle author, it is not clear what role if any Dr. El-Remessy played in this duplication. (Attachment 29.11)

Conclusions

For the identified issue of alleged falsification, the committee does not conclude, based on a preponderance of evidence standard, that the respondent engaged in research misconduct.

While, at the least, an error did take place, it is not clear what role the respondent played, as she is a middle author on this manuscript. The committee acknowledges that an erratum has been issued by the journal and in our opinion this is appropriate.

Allegation #8:

Falsified and Fabricated research reported in Figures 3A and 3C in a *FASEB Journal* article, titled “Peroxynitrite mediates VEGF's angiogenic signal and function via a nitration-independent mechanism in endothelial cells.” (Aug;21(10):2528-39), published in 2007.

Dr. El-Remessy is first and corresponding author.

No action taken by Journal editors.

Background

The investigation committee was charged with examining possible instances of misconduct in addition to the original allegations. In so doing, the committee discovered discrepancies in this publication that are consistent with those found as part of the original allegations.

Analysis

In Figure 3A a bar graph is shown depicting optical density ratios derived from three sets of two digitized Western blots (control and experimental). Four bars have identical values of 0.6, two have identical values of 0.7, two have identical values of 1.9, and two have identical values of 2.2. In all cases where bars are identical, error bars (representing the standard error of the mean) are also identical. All bars, including those that are unique, are integer multiples of 0.1. According to the methods section of the paper, optical density values were obtained from scanned images using ImageJ software, which typically reports a particular optical density to 8 bit (or greater) precision, i.e. 256 gray levels. In experiments of this type two identical ratios (out of 18) would be considered highly unlikely, but not impossible. On the other hand four identical ratios, and four occurrences of identical ratios (10 of 18 bars with at least one twin) with identical errors are implausible if the experiments were carried out as indicated. (Attachments 19 and 29.4)

The respondent's written response indicated that “The OD ratio bars values shown as bars in these figures are genuine”, and “the Excel files for compiled statistical analysis were not found due to Dr. El-Remessy's multiple moves”. During the interview the respondent reiterated the accuracy of this bar graph. When asked if she found the occurrence of identical values surprising she did not respond directly, but indicated that this was the first time she had looked at the figure in this way.

In Figure 3A, a representative Western blot is shown that contains at least three instances of bands that appear to be identical though they are supposed to represent different experimental conditions.

The respondent's written response indicated that "The attached original film shows that the bands are genuine and nearly identical". The written response also included a scan of the original film, at two different exposures, together with loading standards. During the interview, the respondent acknowledged that the supplied "original" only showed 17 bands, whereas the published figure showed 18 bands. The respondent indicated that a single band (7th from the left in the published figure) was digitally inserted into the final figure, and that this band was scanned from a different experiment which is not a standard practice in the field but would support the conclusions the respondent was trying to reach. The respondent agreed to identify the original source of this extra band for the committee, and supplied a schematic illustrating how this figure was constructed. However, the band indicated in this schematic as the source of the extra band in the published figure clearly does not match the published figure. The extra band in the published figure in fact appears to be a duplicate, and is identical to the band to its immediate left. Several additional bands also do not match the published figure in the supplied schematic, even taking contrast adjustment into account. It is not accepted practice to combine bands from different experiments in a single panel in this manner, as it is not possible to control for the many variables that contribute to the intensity of any individual band between experiments. The respondent suggested that this was done in a single experiment on two gels due to the limited number of lanes. Insertion of a single arbitrary band from a different gel in a large gel in this manner is not only contrary to accepted practice (both now and at the time of publication) it is also not logical or rational. Moreover, the gel shown as the sister parallel gel shows differences in band spacing and other features that suggest it was from an entirely separate experiment.

After the interview, analysis of the scans supplied by the respondent indicated that the loading standard did correspond to the loading standard shown in the published figure, although it was reversed (mirrored) left to right, and corresponded to only the leftmost 17 bands in the published figure. An 18th band was appended to the right side. No evidence of splicing at band #7 was apparent, as would have been the case if the figure had been manipulated as indicated by the respondent. The scan supplied by the respondent as the original experimental data displayed obvious discrepancies with the published figure, although some of the bands in the original did appear to correspond to those in the published figure. In addition to the extra band indicated by the respondent, the published figure included duplicate bands that did not correspond to the original data, and unique bands that did not appear to correspond to the original data.

During the interview the respondent was shown a magnified version of the bands in question with the duplicates indicated by colored boxes, and was asked if she thought that any action should be initiated with the journal (e.g. a correction). She replied that since the journal had taken no action, none was necessary on her part.

Figure 3C again shows a bar graph depicting optical density ratios derived from digitized Western blots. Three sets of bars and standard error bars have identical duplicates, as was the case for Figure 3A.

In her written response the respondent indicated that the bars in Figure 3C were genuine, and she provided scans of 3 original blots that she indicated were used for construction of Figure 3C (pp. 33-35 of Attachment 11). None of the supplied originals correspond to the published figure.

The loading controls supplied in the response document on pp. 34 and 35 are duplicates. She was not questioned about Figure 3C during the interview.

In her written response the respondent indicated that the work published in this paper was carried out by herself and a research technician in the laboratory (of Dr. Ruth Caldwell), and that she (the respondent) was responsible for constructing the figures, and that she was the corresponding author.

Conclusion

For the identified issue of alleged fabrication and falsification, the committee finds that the respondent fabricated and falsified data; that these actions represent a significant departure from the accepted practices of the relevant research community; that these actions were not honest errors or differences in interpretation of data; and that the allegation is proven by a preponderance of evidence.

We conclude that at least some of the data portrayed as bars in Figure 3A and Figure 3C are fabricated, as the number of identical values with identical errors is implausible. In addition, inappropriate manipulation of Figure 3A resulted in the appearance of duplicate bands, mismatched loading controls, and the false appearance that all data were derived from a single experiment and thus are falsification of data. The respondent's explanation for how this experiment was conducted and how the figure was prepared is not consistent with the available evidence. The effect of the misconduct is such that the data shown in Figure 3 cannot be considered reliable. As this figure is central to the overall thesis of the paper, the paper as a whole cannot be considered to be reliable.

Allegation #9:

Falsified research reported in Figure 7A in a Diabetes journal article, titled "Peroxynitrite mediates retinal neurodegeneration by inhibiting nerve growth factor survival signaling in experimental and human diabetes" (Apr;57(4):889-98), published in 2008.

Dr. El-Remessy is corresponding author.

No action yet taken by journal editors.

Background

The investigation committee was charged with examining possible instances of misconduct in addition to the original allegations. In so doing, the committee discovered discrepancies in this publication that are consistent with those found in the original allegations.

Analysis

Figure 7A of this paper shows a western blot wherein TrkA loading control bands appear to be duplicates. (Attachment 29.5)

In her written response the respondent stated that these were genuine, nearly-identical bands, and that she and Dr. Ali had performed the experiment and constructed the figure. She also supplied another (virtually identical) digital version of the figure in question as the original, although the original films were not located. Careful examination of the published figure suggested that the bands were duplicated. However, unlike the images supplied for other allegations, the quality of the digital images provided by the journal was insufficient to make a clear determination in this case.

Conclusion

For the identified issue of alleged falsification, the committee does not conclude, based on a preponderance of evidence standard, that the respondent engaged in research misconduct.

Allegation #10: Falsified research reported in Figures 1, 2, and 4 in an American Journal of Pathology article, titled “Neurovascular protective effect of FeTPPs in N-methyl-D-aspartate model: similarities to diabetes.” (Sep;177(3):1187-97), published in 2011.

Dr. El-Remessy is corresponding author.

Erratum issued by journal.

Background

This allegation was brought to the attention of the investigation committee by the Pubpeer website:

<https://pubpeer.com/publications/13195F168A40CCFC34DA228741954B>

Analysis

In this paper, two image panels in Figure 1 were from the same tissue section, but were labeled as originating from different samples. Similarly, one image in Figure 2 reappeared in Figure 4, again labeled as being from a different sample. (Attachment 29.7)

In her written response (Attachment 11) the respondent stated that Dr. Al-Gayyar performed this experiment. She noted that she had contacted the journal concerning these errors, and the journal was in the process of issuing an erratum (now issued).

During the interview (Attachment 12) the respondent explained how cutting and pasting images into multipanel figures could become confusing, and suggested that simple error led to the problems, likely by Dr. Al-Gayyar.

Conclusion

For the identified issue of alleged falsification, the committee finds that the respondent falsified data; that these actions represent a significant departure from the accepted practices of the relevant research community; that these actions were not honest errors or differences in

interpretation of data; and that the allegation is proven by a preponderance of evidence.

It is the conclusion of the committee that the recurrence of duplicate images in several figures in the paper in question in this allegation cannot reasonably be ascribed to honest error, and that data were intentionally manipulated by the respondent to support her conclusions.

The effect of the misconduct is such that the data shown in Figure 1, 2 and 4 cannot be considered reliable. These figures are central to the overall thesis of the paper. The committee is aware that the journal has already issued a correction, however it is our opinion that the journal editors should strongly consider retraction of the manuscript.

Allegation #11

Falsification of research data presented in Al-Gayyar et al. (2011) British Journal of Pharmacology 164:170-180, titled Thioredoxin interacting protein is a novel mediator of retinal inflammation and neurotoxicity, and showing Trx bands in Fig. 5 A and B that appear identical.

Dr. El-Remessy corresponding author.

No action taken by journal editors.

Background

A committee member noted a duplicated panel while examining the overall publication record of Dr. El-Remessy.

Analysis

The thioredoxin panels in Fig. 5 A and B are identical. Dr. El-Remessy acknowledged the duplication in her response but indicated that while no longer a common practice the data shown are correctly represented. After reviewing how the data is conveyed in the text of the manuscript, the committee agrees with this assessment. (Attachment 29.8)

Conclusions

For the identified issue of alleged falsification, the committee does not conclude, based on a preponderance of evidence standard, that the respondent engaged in research misconduct.

While duplications in figures are uncommon, this duplication does not appear to represent research misconduct and the respondent provided a satisfying explanation for the way the figure was assembled.

Allegation #12:

Falsified research reported in Figures 4A, 6D, 1E, 2A in a prepublication journal article, titled High fat diet-induced thioredoxin interacting protein drives retinal leukostasis and microvascular dysfunction (db15-0300), originally accepted by Diabetes.

Dr. El-Remessy is the senior corresponding author.

Upon further evaluation, the editors reversed their decision to accept the article.

Background

This manuscript was accepted for publication by the journal and was forwarded to the production unit for publication. As part of the production process the manuscript figures were subjected to routine analysis “to ensure that they conform to ADA’s digital editing policies”. This analysis uncovered anomalies that led to the publication being placed on hold until the source files could be analyzed further. Source files were analyzed by Dartmouth Journal Services, and an Image Forensics Report was supplied to ADA (the publisher of Diabetes). The respondent collated the data in question and corresponded with the journal editors. Based on the findings of the forensics report the Panel on Ethical Scientific Publication (ESP) of the ADA recommended that the editor rescind acceptance of the paper. This article was brought to the committee’s attention by the ESP during its ongoing evaluation of other allegations. (Attachment 17 and 29.12)

Analysis

Image contrast and background in Figures 4A, 6D, 1E, 2A have been adjusted beyond reasonable limits and quantification appears unreliable. Images have been manipulated and stitched together to appear to represent a single gel. The images referred to by the respondent as representative images are not, in fact, representative and the committee, after reviewing the data themselves, agree with the findings of the editors that they instead “have been deliberately selected to support the narrative and conclusions of the paper”.

Conclusions

For the identified issue of alleged falsification, the committee finds that the respondent falsified data; that these actions represent a significant departure from the accepted practices of the relevant research community; that these actions were not honest errors or differences in interpretation of data; and that the allegation is proven by a preponderance of evidence.

We agree with the decision of the editors to ultimately reject this manuscript.

Allegation #13:

Falsified research reported in 3E in grant application R01 EY019275-01A2 (Title: ProNGF is a novel mediator of diabetic retinopathy) and Figure 2A (same figure as 3E in previous grant) in grant application R01 EY022408-01(Title: Molecular mechanisms of diabetic retinopathy).

Dr. El-Remessy is the Principal Investigator

Background

The committee's scope of investigation included grant applications submitted to the PHS. UGA RIO requested forensic assistance from HHS ORI to analyze figures in these grants. This allegation resulted from the committee's evaluation of the forensic evidence. The respondent responded to this new allegation and indicated that her post-doc, Dr. Mohammed Al-Gayyar, had collected the original data, selected the representative images and prepared the figures in question (Attachment 27); Dr. Al-Gayyar confirmed this in his email communication of January 20, 2016 (Attachment 28).

Analysis

While there were many "abnormalities" found by forensic analysis of multiple figures in submitted grants (Attachment 24 and 25), the committee only pursued the 3E/2A figure that has been clearly enhanced to provide misleading information that supported the grant applications. As noted, Dr. Al-Gayyar, a post-doc in the El-Remessy lab at the time, collected the original data, selected the representative images, and prepared the figures in question. Dr. Al-Gayyar explained the abnormalities in the figures stating "as (I) had no previous experiences about working with blots or preparing the representative. I tried my best to remember how this difference in background could happen. So it might be the case that I tried to enhance the band, but it is not an intended to change the data. It is probably due to my low experience of how to prepare the figures. The data are consistent and did not different from the original blot or the additional blots."

Conclusions

For the identified issue of alleged falsification, the committee finds that scientific misconduct did occur. However, for the identified issue of alleged falsification, the committee does not conclude, based on a preponderance of evidence standard, that there is sufficient evidence to determine that the respondent was responsible for this research misconduct.

6. C-D. Overall Conclusions and Effect of Misconduct

Of the thirteen allegations reviewed by the committee, it is the unanimous opinion of the committee that ***nine of the allegations constitute research misconduct by the respondent and four of the allegations do not represent research misconduct by Dr. El-Remessy.*** Furthermore, for the nine allegations where we find research misconduct has occurred, we find by a preponderance of evidence standard that the respondent committed either falsification and/or fabrication, that the actions were intentional to support the claims of the

manuscripts/grants, and that the actions involved unsound practices that depart significantly from the standard practice in the field. There is a pattern of falsification of data to facilitate publication/funding over a long period of time with the only common author being the respondent. This research misconduct has led to multiple examples of misrepresentation of research findings to the scientific community.

7. Recommendation of Investigation Committee:

The committee considered multiple potential recommendations in response to our findings including those outlined by the respondent and her counsel. Given the severity and frequency of falsification by the respondent, the committee unanimously recommends the following actions in response to the 9 counts of research misconduct by the respondent:

- 7.1. Notification to the Office of Research Integrity of the National Institutes of Health and all relevant funding agencies of the findings of this committee.
- 7.2. Notification to editors of all the journals involved of the findings of this committee.
- 7.3. Notification to all co-authors of the manuscripts involved of the findings of this committee.
- 7.4. Communication of Research Investigation Findings to CNVAMC Medical Center Director so future actions can be pursued consistent with VHA Handbook 1058.02, Research Misconduct.
- 7.5. Termination of employment at UGA.*
- 7.6. Termination of Adjunct position at Augusta University.*

* Note that the CNVAMC member of the committee did not participate in these recommendations in compliance with CNVAMC regulations.

8. Attachments

Beyond appendixes and attachments cited above, a one-page executive summary was included at the beginning of this document.