Report of the Findings of the Investigation Committee in Regards to Research Misconduct by Dr. Nasser Chegini

Submitted to Dr. David Norton, Vice President of Research

October 18, 2013

DIO# 2012-13

1. Background

In June 2012, following a previous finding of research misconduct in 2011, National Institutes of Health, Office of Research Integrity, requested that the University of Florida re-open the investigation to determine if additional research misconduct had been committed by the Respondent and/or his laboratory staff, and the possible impact it has had on the practice of medicine and scientific research.

Consequently, in August, 2012, Dr. David Norton, Vice President for Research, University of Florida, directed M. Peter Pevonka, MS, RPh, FAPhA, Associate Vice President for Research, University of Florida, to establish a new faculty committee to conduct an expanded investigation. The Respondent was notified of the intent to do this in a letter from Dr. Barbara Wingo, Associate Vice President and Deputy General Counsel, University of Florida, dated August 16, 2012. The evidence reviewed by the Investigation Committee consisted of primary data, published manuscripts, and grant proposals submitted by the Respondent and members of his laboratory, and testimony from the people interviewed. The Investigation Committee examined research conducted in the Respondent's laboratory to determine if additional data was modified or manipulated. The overall conclusion of the Investigation Committee was that the Respondent had intentionally fabricated or falsified data in nine published manuscripts spanning the period of 2003-2008 that were examined by the committee. The previous committee identified falsified data in a manuscript published in 2010 that has since been retracted. Together, these instances of fabrications or falsifications of data represent repeated and significant research misconduct. This research misconduct has had an impact on scientific research as other laboratories have been funded to repeat or conduct follow-up research on the Respondent's work resulting in a substantial waste of time, effort and valuable grant funding. However, it appears that this research misconduct has not had a major or critical impact on the practice of medicine.

2. Allegations

A summary of all the allegations in tabular format showing the relationship among the published manuscripts and grant proposals is shown in Appendix 1.

1. The Respondent published fabricated values for data points or errors. The fabrications were done by creating values, multiplying a number represented as the mean by a constant or by using a constant numerical value. These fabrications occurred in the following:

   Figures 3, 4, 5, 6, 8 in Paper 1 (Appendix 2; p. 3-7)
   Figures 1, 2, 3A, 3B, 5, 6, 7 in Paper 2 (Appendix 2; p. 12-18)
   Figures 5, 8 in Paper 3 (Appendix 2; p. 37-38)
   Figures 1 in Paper 4 (Appendix 2; p. 42)
   Figures 1, 4A, 5, 6, 7, 10 in Paper 5 (Appendix 2; p. 56-59, 63)
   Figure 2A in Paper 6 (Appendix 2; p. 65-66)

Figures 2, 4, 5, 6, 7, 8-left, 8-right in Paper 7 (Appendix 2; p. 75, 77-82)
Figures 2, 3 in Paper 8 (Appendix 2; p. 87-88)

Fabrication of data points falsely represents the results of the experiments. The fabricated numbers are chosen to produce experimental results that are desired by the person who produced them. This was done to falsely manipulate the experimental results and to yield results that confirm the stated hypothesis.
Fabrication of errors gives the false representation of experimental error in each experiment. Reproducibility of the results and the probability that the results are not random is assessed using measures of variability in the data. Fabrication of these measures of variability (the error bars) falsely states that the experiments were repeated, that the results were consistent, and that experiments produced interpretable results.

2. The Respondent published falsified values for data points or errors. The falsifications were done by deleting, replacing or changing digits in a string of digits, multiplying or dividing values by a constant numerical factor or changing the location of the decimal point in the string of digits. These falsifications occurred in the following:

   Figures 5, 6, 8 in Paper 1 (Appendix 2; p. 5-7)
   Figures 2, 5, 7 in Paper 2 (Appendix 2; p. 13, 16, 18)
   Figures 4, 5, 8 in Paper 3 (Appendix 2; p. 36-38)
   Figures 1, 3A, 3B, 3C, 3D, 3E, 3F in Paper 4 (Appendix 2; p. 42-53)
   Figures 1, 6, 7, 8 in Paper 5 (Appendix 2; p. 56, 58-62)
   Figures 2A, 2B, 3, 4, 5 in Paper 6 (Appendix 2; p. 65-71)
   Figures 2, 3, 4, 5, 6, 7, 8-left, 8-right in Paper 7 (Appendix 2; p. 75-82)
   Figures 1, 2, 3 in Paper 8 (Appendix 2; p. 85-88)
   Figures 2, 3, 4 in Paper 9 (Appendix 2; p. 90-92)

   Falsifying the numbers that are used as the experimental results falsely represents results of experiments. The falsified numbers are chosen to produce experimental results that are desired by the person who produced them. This was done to falsely manipulate the experimental results and to yield results that confirm the stated hypothesis.

3. The Respondent falsified published Western blot data by substituting, reusing or changing images from different experiments. These falsifications occurred in the following:

   Western Blots in Paper 1 (Appendix 2; p. 8)
   Western Blots in Paper 2 (Appendix 2; p. 19)
   Western Blots in Paper 3 (Appendix 2; p. 39)

   Figures are falsified because either: 1) the stated experiment was not actually performed and the falsified results are introduced as results of the unperformed experiment; or 2) the results of the stated experiment as performed were not what the falsifier desired because they did not confirm the hypothesis or because the results were visually undesirable.

4. The Respondent falsified published data measured as a function of time or dose by changing the order of the time sequence or dose. These falsifications occurred in the following:

Figures 2, 3B in Paper 2 (Appendix 2; p. 13, 15)
Figures 6, 8, 10 in Paper 5 (Appendix 2; p. 58, 60-63)

These falsifications serve to show that there was a trend in the data, such that measured values varied in a predictable manner as a function of time or dose, when there was no such trend in the true data. Falsification of the data in this way shows that there was scientific significance to the observations when there was none.

5. The Respondent falsified published experimental groups by changing the identifiers of the groups. These falsifications occurred in the following:

   Figures 3A, 3B, 3C, 3D, 3E, 3F in Paper 4 (Appendix 2; p. 43-53)
   Figures 4A, 5, 8 in Paper 5 (Appendix 2; p. 57, 60-62)
   Figure 2A in Paper 6 (Appendix 2; p. 65-66)
   Figures 4, 8-left in Paper 7 (Appendix 2; p. 77, 81)
   Figures 1, 2, 3 in Paper 8 (Appendix 2; p. 85-88)
   Figure 4 in Paper 9 (Appendix 2; p. 92)

   These falsifications serve to misrepresent the effects of various treatments on protein and mRNA expression levels. This falsely gives significance to effects where there may be none or falsely reports the magnitude of the effect.

6. The Respondent falsified published number of experimental replicates. These falsifications occurred in the following:

   Figures 3, 4, 5, 6, 8 in Paper 1 (Appendix 2; p. 3-7)
   Figures 1, 2, 3A, 3B, 5, 6 and 7 in Paper 2 (Appendix 2; p. 12-18)
   Figures 5, 8 in Paper 3 (Appendix 2; p. 37-38)
   Figures 1, 3A, 3B, 3C, 3D, 3E, 3F in Paper 4 (Appendix 2; p. 42-53)
   Figures 1, 8 in Paper 5 (Appendix 2; p. 56, 60-62)
   Figure 2A in Paper 6 (Appendix 2; p. 65-66)
   Figures 2, 3, 6, 7 in Paper 7 (Appendix 2; p. 75-76, 79-80)
   Figures 2 and 3 in Paper 8 (Appendix 2; p. 87-88)

   These falsifications serve to falsely represent the experimental reproducibility of the data and to falsely represent the statistical significance of the experimentally determined values. These falsifications also serve to give the false impression that experiments were repeated more times than they were. Together, these falsifications serve to falsely increase the significance of the results.

It should also be noted that the fabricated or falsified Figures in the published manuscripts were also in the following 3 grants (Appendix 2; p. 20-33):

1. Grant # 2R01HD0374**32**-10
   Figures 4A and 4B in grant are same as Figures 5 and 6A in Paper 5 which have been falsified.

2. Grant # 1R01HD586**64**-01A1

Figures 6 (mir-181a and mir-142-5p) and 7 (mir-21) in grant are same as Figures 2 (mir-181a and mir142-5p) and 4 (mir-21) in Paper 9 which have been falsified.

3. Grant # 1**R03**HD058779-01A1
   Figures 4 (mir-181a) and 5 (mir-21) in grant are same as Figures 2 (mir-181a) and 4 (mir-21) in Paper 9 which have been falsified.

The fabricated or falsified data were included in published research manuscripts and in NIH grant proposals that were subsequently awarded to the Respondent.

3. PHS Support

A. Supporting Grant Proposals Listed in Investigation Report (Investigation Binder Tab A)
   1. 2 R01 HD037432, N. Chegini (PI); NIH/NICHD; Molecular mechanism of leiomyoma growth and regression
   2. 1 R01 HD58664, N. Chegini (PI); NIH/NICHD; Expression, hormonal regulation and function of microRNAs in leiomyoma
   3. 1 R03 HD058779, N. Chegini (Co-Invest); NIH/NIDCD; MicroRNA regulatory function in leiomyoma growth

B. Awards referenced in the "Acknowledgements" section of published manuscripts used in Investigation Report (Investigation Binder Tab B)
   1. R01 HD037432, N. Chegini (PI); NIH/NICHD; Molecular Mechanism of Leiomyoma Growth and Regression.
   2. UPN 07120257, O. Bukulmez; N. Chegini; FL Clinical Practice Assoc.; The Role of Micrornas in Regulation in Gene Expression in Endometriosis: Influence of Inflammation.
   3. R01 HD043175, David F. Archer; NIH/NICHD; Doxycycline of Bleeding in Progestin only Contraceptors.

4. Investigation Process

Policies and Procedures Followed

This re-investigation was reviewed according to the University Regulation 6C1-1.0101; Policy for Dealing with Conduct in Research (http://www.admin.ufl.edu/DDD/attach06-07/R10101-0704.pdf) and the Public Health Service Policies on Research Misconduct (42 CFR Part 93 http://ori.hhs.gov/documents/42_cfr_parts_50_and_93_2005.pdf).

Investigation Committee

The Investigation Committee consisted of Dr. Linda Bloom, Professor of Biochemistry; Dr. Charles Wood, Professor and Chair of the Department of Physiology and Functional Genomics; and Dr. Richard Snyder, Director of Biotherapeutic Programs from the University of Florida. The Investigation Committee also included an external member Dr. Kelle Moley, James P. Crane Professor, Department of Obstetrics and Gynecology, Vice Chair of Basic Science Research, Director, Basic Research Division, Washington University School of Medicine. Mr. Derrius Marlin, Information Security Engineer, Office of Information Security and Compliance, University of Florida, served as expert consultant to the Committee. M. Peter Pevonka, MS, RPh, FAPhA, Associate Vice President for Research and Dr. Irene Cooke, Director of Research Compliance, both from the Office of Research, University of Florida, supported the Investigation Committee throughout the process.

Meetings and Interviews; Interview Topics

The Investigation Committee met formally twenty-five times:

1. In person with Dr. David Norton, Vice President for Research, University of Florida, and Dr. Barbara Wingo, Associate Vice President and Deputy General Counsel, University of Florida on August 21, 2012 to charge the committee with expanding the investigation.
2. In person on August 28, 2012, to review the case and plan.
3. In person on September 7, 2012 to review published manuscripts.
4. In person on September 11, 2012 for a RECORDED interview with Dr. Steven Sugrue, Sr. Associate Dean for Research Affairs, College of Medicine, University of Florida.
    a. Topic: Historical account of initial inquiry and investigation was provided
5. In person on September 17, 2012 to visit the laboratory and discuss with Dr. Gregory Schultz, Professor of Obstetrics and Gynecology; Dr. Xiaoping Luo, Research Assistant Professor; and Dr. Tsai-Der Chuang, Postdoctoral Fellow.
    a. Topic: culture of the Chegini laboratory
6. In person on September 19, 2012 for a RECORDED interview with Nancy Schaefer, Associate University Librarian, University of Florida Health Science Center Libraries.
    a. Topics: methods for requested literature searches and citation searches, their analyses, and data presentations
7. In person on September 28, 2012 for a RECORDED interview with Dr. Padua, ex-Postdoctoral Fellow
    a. Topics: the culture in the Chegini laboratory during the time she was a post-doc, the circumstances leading up to the Primary allegation, and the inquiry and investigation
8. In person on October 5, 2012, for a RECORDED interview with Dr. Xiaoping Luo, Research Assistant Professor, in the Respondent's laboratory who has been associated with him for 10 years through the present time.
    a. Topics: clinical sample retrieval, labeling, and cell culturing practice, sample organization and logging, experimental design process
9. In person on October 12, 2012, to review progress and plan.
10. In person on October 19, 2012 for a RECORDED interview by phone with Dr. Bo Rueda, Associate Professor Department of Obstetrics, Gynecology and Reproductive Biology, Harvard Medical School Associate Director, Vincent Center for Reproductive Biology, Massachusetts General Hospital Massachusetts General Hospital.
    a. Topic: Dr. Rueda's research in the same field
11. In person on October 26, 2012 for a RECORDED interview by phone with Dr. Mindy Prucha, ex- Postdoctoral Fellow.
    a. Topics: the culture in the Chegini laboratory during the time she was a post-doc, the circumstances leading up to the Primary allegation, and the inquiry and investigation
12. In person on November 1, 2012 to review hard-copy notebooks from the Chegini Laboratory.
13. In person on November 2, 2012for a RECORDED interview with Dr. Xiaoping Luo.
    a. Topics: role on published manuscripts and grants, laboratory notebook policies, process for generating and analyzing data, and recording the information in notebooks and electronic files
14. In person on November 16, 2012 to meet with Dr. Gregg Schultz.
15. In person on November 16, 2012 for a RECORDED interview by phone with Dr. Kathleen Mayor-Lynn, ex-fellow now in private practice in Nashville/Murphreesboro, TN.
    a. Topics: role she had in the laboratory, culture in the laboratory, data generation and analysis, authorship

16. In person on November 30, 2012 for data analysis.
17. In person on December 7, 2012 for data analysis and planning.
18. In person on December 14, 2012 for a RECORDED interview with Dr. Xiaoping Luo.
    a. Topics: role in the laboratory, and contributions to data and papers, manuscripts, abstracts, and grants. Process that was followed in the laboratory from Primary data to publication.
19. In person on December 19, 2012 for a RECORDED interview with Dr. Xiaoping Luo.
    a. Topics: tour of her laboratory notebooks, tour of the Chegini laboratory shared computer drive, tour of Respondent's manuscript folder on the computer drive
20. In person on January 4, 2013 for data analysis and planning.
21. In person on January 11, 2013 for data analysis and planning.
22. In person on January 16, 2013 for data analysis and planning.
23. In person on January 23, 2013 for a RECORDED interview with the Respondent. Respondent's counsel was not present at this meeting. The University was represented by Dr. Barbara Wingo, Associate Vice President and Deputy General Counsel.
    a. Topics: Procedures for sample procurement and identification; data generation, analysis, review, and sharing; Procedures for writing and submitting manuscripts; Notebook and Computer file organization of Primary data, analyzed data, and data for publication; Analysis of individual published manuscripts and their associated Primary data; Tissue bank organization
24. In person on January 30, 2013 to plan the report
25. In person on February 8, 2013 to review a draft of the report

The interview recordings (Investigation Binder Tab D) were provided to each interviewee for their review and comment. The recorded interviews provided the Investigation Committee with leads and insight into the laboratory environment, tissue sample acquisition and cataloging, their process of data generation and analysis, manuscript preparation and publishing, notebooks, computer file organization and sharing, and impact of the work on science and medicine.

A draft report of the findings of the Investigation Committee was submitted to the Respondent through the University of Florida's Counsel on September 6, 2013 for comment. The Respondent replied on October 14, 2013. This final report considers the information provided by the Respondent in his comments to the draft report.

Published Manuscripts Analyzed by the Investigation Committee (Investigation Binder Tab C)

1. **Luo, X, Xu, J and Chegini, N**. (2003) The expression of smads in human endometrium and regulation and induction in endometrial epithelial and stromal cells by transforming growth factor-beta. *The Journal of clinical endocrinology and metabolism*, 88, 4967-4976. Included in the investigation due to "Subsequent Use Exception" as per 42 CFR 93.105
2. **Luo, X, Xu, J and Chegini, N**. (2003) Gonadotropin releasing hormone analogue (gnrha) alters the expression and activation of smad in human endometrial epithelial and stromal cells. *Reproductive biology and endocrinology : RB&E*, 1, 125. Included in the investigation due to "Subsequent Use Exception" as per 42 CFR 93.105
3. **Xu, J, Luo, X and Chegini, N**. (2003) Differential expression, regulation, and induction of smads, transforming growth factor-beta signal transduction pathway in leiomyoma, and myometrial smooth muscle cells and alteration by gonadotropin-releasing hormone analog. *The Journal of clinical endocrinology and metabolism*, 88, 1350-1361. Included in the investigation due to "Subsequent Use Exception" as per 42 CFR 93.105

4. **Li, R, Luo, X, Pan, Q, Zineh, I, Archer, DF, Williams, RS and Chegini, N**. (2006) Doxycycline alters the expression of inflammatory and immune-related cytokines and chemokines in human endometrial cells: Implication in irregular uterine bleeding. *Human reproduction*, 21, 2555-2563.
5. **Luo, X, Ding, L and Chegini, N**. (2006) Ccns, fibulin-1c and s100a4 expression in leiomyoma and myometrium: Inverse association with tgf-beta and regulation by tgf-beta in leiomyoma and myometrial smooth muscle cells. *Molecular human reproduction*, 12, 245-256.
6. **Pan, Q, Luo, X, Toloubeydokhti, T and Chegini, N**. (2007) The expression profile of micro-rna in endometrium and endometriosis and the influence of ovarian steroids on their expression. *Molecular human reproduction*, 13, 797-806.
7. **Li, R, Luo, X, Archer, DF and Chegini, N**. (2007) Doxycycline alters the expression of matrix metalloproteases in the endometrial cells exposed to ovarian steroids and pro-inflammatory cytokine. *Journal of reproductive immunology*, 73, 118-129.
8. **Toloubeydokhti, T, Pan, Q, Luo, X, Bukulmez, O and Chegini, N**. (2008) The expression and ovarian steroid regulation of endometrial micro-rnas. *Reproductive sciences*, 15, 993-1001.
9. **Pan, Q, Luo, X and Chegini, N**. (2008) Differential expression of micrornas in myometrium and leiomyomas and regulation by ovarian steroids. *Journal of cellular and molecular medicine*, 12, 227-240.

Supporting Grant Proposals Analyzed by the Investigation Committee (Investigation Binder Tab A)

1. **2 R01 HD037432**, N. Chegini (PI); NIH/NICHD; Molecular mechanism of leiomyoma growth and regression
2. **1 R01 HD58664**, N. Chegini (PI); NIH/NICHD; Expression, hormonal regulation and function of microRNAs in leiomyoma
3. **1 R03 HD058779**, N. Chegini (Co-Invest); NIH/NIDCD; MicroRNA regulatory function in leiomyoma growth

Data Files Analyzed by the Investigation Committee (Investigation Binder Tab E)

The Investigation Committee evaluated the primary data that was subsequently published in the manuscripts and found that the data were fabricated or falsified (Appendices 1 and 2). An IT search of the laboratory's shared drives by the committee assisted by Mr. Derrius Marlin identified files associated with primary data used in the published manuscripts. In the same search, several relevant files were found on what would map out on the Respondent's computer. This network location harbored the personal dedicated file space for the Respondent, and other than the IT support staff, only the Respondent's user account would have access to any files stored there. While there is no absolute way to know that was the case before 2010, that is and was meant to be the personal space dedicated to the Respondent and was not meant to be set up as shared space. The Committee was provided with copies of the data on the Respondent's laboratory's common network drive(s) and on Respondent's computer by Mr. Derrius Marlin. As the copies were not formally sequestered at the onset of the allegation in 2010, however, the Committee could not be certain that the information it contained was not corrupted.

Computers

Serial Numbers	Location	Make/Model	Primary Use	Hard Drive Make/Model	Capacity	HD Serial #
J2227D1	M323 - Lab Hallway	Dell Optiplex 745	lab	WD WD2500JS	250 GB	WCANKJ061319
33227D1	M323 - Lab Hallway	Dell Optiplex 745	lab	WD WD2500JS	250 GB	WCANKJ049962
C47SDP1	M323 - Lab	Dell Optiplex 780	lab	Samsung HD322GJ	320 GB	S2B0J90ZC15158
H7W8WK1	M323C	Dell Optiplex 960	Xiaoping Luo	Seagate ST9160412ASG	160 GB	5VG0Q9QL

DCV2SD1	M337G - Chegini Ofc	Dell Optiplex 745	Chegini	WD WD800ADFS	80 GB	WMANS1894556
4W6P721	N3-12 (IT Office)	Dell Optiplex GX260	retired PCR PC	IBM Deskstar	40 GB	VNC204A2J1JYPA

Network Shares

File Share	Path	Primary User	Location	Usage
LAB-CHEGIN	/chegini-lab	Chegini Lab	AHC Server Rm	34.4 GB
LAB-CHEGIN	/chegini-personal	Chegini Personal	AHC Server Rm	2.72 GB
LAB-CHEGIN	/hare5375	Harekrushna Panda	AHC Server Rm	23 MB
LAB-CHEGIN	/chuangtsaide	Tsai-Der Chuang	AHC Server Rm	3.05 GB
LAB-CHEGIN	/xiaoping	Xio Ping Lou	AHC Server Rm	5.00 GB
LAB-CHEGIN	/mpadua	Maria Padua	AHC Server Rm	5.94 GB
LAB-CHEGIN	/mprucha	Mindy Prucha	AHC Server Rm	19.5 GB

LAB-CHEGIN Source Path: \\hsc-fs-medclin\obg01\share\labs\lab-chegin

The names, folders and locations for the primary data and data published in the manuscripts are provided in the header of each of the panels in the Figures in Appendix 2.

5. Analysis

According to the Department of Health and Human Services Public Health Service Policy on Research Misconduct (42 CFR Part 93), research misconduct means fabrication (making up data or results and recording or reporting them), falsification (manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research in not accurately represented in the research record) and plagiarism (appropriation of another person's ideas, processes, results, or words without giving appropriate credit). A finding of research misconduct requires that there be a significant departure from accepted practices of the relevant research community and the misconduct be committed intentionally, knowingly or recklessly. The allegations must be proven by a preponderance of evidence.

In order to review the allegations, the Investigation Committee:

1. Reviewed published manuscripts (2003-2008) by the Respondent (Investigation Binder Tab C).
2. Reviewed the NIH grant proposals submitted by the Respondent (Investigation Binder Tab A).
3. Reviewed the primary data generated over a span of 2002-2010 that was used in the published manuscripts and NIH grant proposals (Investigator Binder Tab E).
4. Interviewed the Respondent, laboratory personnel and other University personnel involved with the initial investigation (Investigation Binder Tab D).

Further, the Investigation Committee also reviewed and analyzed the literature citations for impact on scientific research (Appendix 3; p. 1-72).

Specific Analysis of Each Allegation

In order to find the fabrications or falsifications, the Investigation Committee examined laboratory notebooks and computer assets from the respondent's laboratory and identified raw data associated with the figures in the published manuscript. The Investigation Committee then determined how the raw data were analyzed and ultimately used in the figures in the published manuscript. The fabrications or falsifications were identified during this process when the raw data or analyzed data values (e.g. means and standard errors of the means) did not match data or values that were used in the

figures in the published manuscript. This review process is shown schematically in the figures of Appendix 2 and reflected in the text of Appendix 2. The values and figures in the top panels show the raw data, and the figures in the bottom panels show the figures that were in the published manuscript. The locations for the "raw" data files and "manuscript" files are provided in the header of each of the panels of the figures in Appendix 2.

In general, the core of the allegations involved changing numerical values, changing the order of appearance of the numerical values, changing the identifiers of various groups, changing the number of experimental replicates and changing images. One or several of these patterns were repeated in multiple published manuscripts or grant proposals. Thus, the allegations can be grouped into 6 different patterns. The analysis of each of these allegations is provided below.

Allegation 1: The Respondent published fabricated values for data points or errors. The fabrications were done by creating values, multiplying a number represented as the mean by a constant or by using a constant numerical value. These fabrications occurred in the following:

Figures 3, 4, 5, 6, 8 in Paper 1 (Appendix 2; p. 3-7)
Figures 1, 2, 3A, 3B, 5, 6, 7 in Paper 2 (Appendix 2; p. 12-18)
Figures 5, 8 in Paper 3 (Appendix 2; p. 37-38)
Figures 1 in Paper 4 (Appendix 2; p. 42)
Figures 1, 4A, 5, 6, 7, 10 in Paper 5 (Appendix 2; p. 56-59, 63)
Figure 2A in Paper 6 (Appendix 2; p. 65-66)
Figures 2, 4, 5, 6, 7, 8-left, 8-right in Paper 7 (Appendix 2; p. 75, 77-82)
Figures 2, 3 in Paper 8 (Appendix 2; p. 87-88)

Analysis of Allegation 1: Fabrication of data points falsely represents the results of the experiments. The fabricated numbers are chosen to produce experimental results that are desired by the person who produced them. This was done to falsely manipulate the experimental results and to yield results that confirm the stated hypothesis. Fabrication of errors gives the false representation of experimental error in each experiment. Reproducibility of the results and the probability that the results are not random is assessed using measures of variability in the data. Fabrication of these measures of variability (the error bars) falsely states that the experiments were repeated, that the results were consistent, and that experiments produced interpretable results.

Allegation 2: The Respondent published falsified values for data points or errors. The falsifications were done by deleting, replacing or changing digits in a string of digits, multiplying or dividing values by a constant numerical factor or changing the location of the decimal point in the string of digits. These falsifications occurred in the following:

Figures 5, 6, 8 in Paper 1 (Appendix 2; p. 5-7)
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Figures 1, 2, 3 in Paper 8 (Appendix 2; p. 85-88)
Figures 2, 3, 4 in Paper 9 (Appendix 2; p. 90-92)

Analysis of Allegation 2: Falsifying the numbers that are used as the experimental results falsely represents results of experiments. The falsified numbers are chosen to produce experimental results

that are desired by the person who produced them. This was done to falsely manipulate the experimental results and to yield results that confirm the stated hypothesis.

Allegation 3: The Respondent falsified published Western blot data by substituting, reusing or changing images from different experiments. These falsifications occurred in the following:

Western Blots in Paper 1 (Appendix 2; p. 8)
Western Blots in Paper 2 (Appendix 2; p. 19)
Western Blots in Paper 3 (Appendix 2; p. 39)

Analysis of Allegation 3: Figures are falsified because either: 1) the stated experiment was not actually performed and the falsified results are introduced as results of the unperformed experiment; or 2) the results of the stated experiment as primarily performed were not what the falsifier desired because they did not confirm the hypothesis or because the results were visually undesirable.

Allegation 4: The Respondent falsified published data measured as a function of time or dose by changing the order of the time sequence or dose. These falsifications occurred in the following:

Figures 2, 3B in Paper 2 (Appendix 2; p. 13, 15)
Figures 6, 8, 10 in Paper 5 (Appendix 2; p. 58, 60-63)

Analysis of Allegation 4: These falsifications serve to show that there was a trend in the data, such that measured values varied in a predictable manner as a function of time or dose, when there was no such trend in the true data. Falsification of the data in this way shows that there was scientific significance to the observations when there was none.

Allegation 5: The Respondent falsified published experimental groups by changing the identifiers of the groups. These falsifications occurred in the following:

Figures 3A, 3B, 3C, 3D, 3E, 3F in Paper 4 (Appendix 2; p. 43-53)
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Analysis of Allegation 5: These falsifications serve to misrepresent the effects of various treatments on protein and mRNA expression levels. This falsely gives significance to effects where there may be none or falsely reports the magnitude of the effect.

Allegation 6: The Respondent falsified published number of experimental replicates. These falsifications occurred in the following:

Figures 3, 4, 5, 6, 8 in Paper 1 (Appendix 2; p. 3-7)
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Figure 2A in Paper 6 (Appendix 2; p. 65-66)
Figures 2, 3, 6, 7 in Paper 7 (Appendix 2; p. 75-76, 79-80)
Figures 2 and 3 in Paper 8 (Appendix 2; p. 87-88)

Analysis of Allegation 6: These falsifications serve to falsely represent the experimental reproducibility of the data and to falsely represent the statistical significance of the experimentally determined values. These falsifications also serve to give the false impression that experiments were repeated more times than they were. Together, these falsifications serve to falsely increase the significance of the results.

The fabricated or falsified data were included in published research manuscripts and in NIH grant proposals that were subsequently awarded to the Respondent. It should be noted that the NIH grant proposals contained figures from the published manuscripts which had been falsified (Appendix 2; p. 20-33).

Interview with the Respondent and Laboratory Members

At the interview of the Respondent on January 23, 2013, the Respondent first confirmed that the computer files shown to him were indeed his or his laboratory's (Investigation Binder Tab D). The Respondent was then presented with the Investigation Committee's investigation process and findings of fabrications or falsifications in two of the nine manuscripts analyzed (Paper 1 - Luo et al., J. Clin. Endocrinol. Metab., 88:4967-4976, 2003, and Paper 9 - Qun Pan, Xiaoping Luo and Nasser Chegini. J. Cell Mol. Med. 12:227-240, 2008). These served as representative samples of all the published manuscripts and grant proposals. The Respondent recognized and agreed with the Investigation Committee that the data in the two published manuscripts was fabricated or falsified, but was unable to provide an explanation of how the erroneous data was reported.

Further, at the Respondent's interview, he stated strongly that he had an open and highly interactive laboratory, including full involvement of laboratory members in manuscript preparation. (Investigation Binder Tab D). However, the Investigation Committee learned of the Respondent's practice, independently verified by three different members of his research group (Drs. Padua, Prucha and Luo), of assigning authorship to scientific manuscripts without the author's knowledge or approval, and independent of their relative contribution to the manuscript (Investigation Binder Tab D). During the Investigation Committee's interviews with Drs. Padua, Prucha and Luo, the Investigation Committee determined that, before 2010 (when the initial allegation was made), postdocs in the laboratory were not assigned specific projects. Instead they served more like technicians in as much as they were tasked to collect specific pieces of data but were never made aware of the complete data set for any particular project (Investigation Binder Tab D). This problem was compounded by a "feed forward" practice of manuscript preparation. Drs. Padua, Prucha and Luo stated that it was the practice in the laboratory that the person who actually generated the data gave the raw and/or pre-analyzed data to the Respondent, but subsequently had no involvement in the final analysis and presentation of those data (Investigation Binder Tab D). They further stated that when they did have the opportunity to edit the introduction, methods, results, or discussion sections of manuscripts containing data they generated, they were not provided the opportunity to write or even see the final manuscript (Investigation Binder Tab D).

Interview with Dr. Luo

During the investigation, the Investigation Committee also found that the same falsified data were included in a NIH R03 grant proposal that was submitted to the NIH by Dr Luo (Investigation Binder Tab A). Dr. Luo was asked to identify the source of the data used to generate the figures in the published manuscripts (these were also used in the grant proposals (Appendix 1)). The data in the grant proposals and associated published manuscripts did not reflect the raw data in the primary data files. Dr. Luo testified that she had never compared the published figures in the manuscripts to the primary data until the Investigation Committee showed them to her, where she recognized the falsification of the data (Investigation Binder Tab D). She did claim to participate in the preparation of the grant proposal and read the text before it was submitted (Investigation Binder Tab D).

Tissue Archives

The tissue procurement process was described during the interviews with Dr. Luo and members of the Respondent's research group (Investigation Binder Tab D). It was stated that the Respondent would personally go to the operating room, procure the tissue samples and report the identity of the tissue samples to the laboratory personnel. No independent verification of the identity of the tissue samples were made at this time of deposit of the tissue samples in the tissue archives. Furthermore, at the time of analysis, the Respondent would personally select the samples and provide them to the laboratory members for analysis.

Impact on Scientific Research

The Investigation Committee evaluated how often the published manuscripts from the Respondent's laboratory were cited during the period of 2006-2012 (Appendix 3) and found that the scientific community has steadily and significantly increased their citation of the Respondent's publications over this period. Thus, the published work has already had an impact on the scientific community, where the literature that cites the published work of the Respondent has increased substantially in the past few years (see Appendix 3, page 15).

Impact on the Practice of Medicine

Through interviews with scientists/medical practitioners and the Investigation Committee's own assessment that included a MD/PhD (with OB/Gyn specialty), the data generated over a span of 2002-2010 and published in 2003-2010 has and will have little impact on the practice of medicine, since all of it occurred at the basic mechanism level, and none of it was tested directly in vivo or in humans. The Respondent's research work proposed a novel pathway which could explain and treat human disease but a direct application of the research would require further testing.

Further, companies developing diagnostic tests based on Respondent's published work will likely have to validate the tests as required by the Food and Drug Administration prior to commercial sale. An inability to validate the tests would disqualify them from commercialization and medical use. As an indication of the lack of medical importance, to-date intellectual property filed by the Respondent has not been licensed out by University of Florida.

6. Findings

Research Misconduct

As stated in the Analysis of each allegation, the Investigation Committee reviewed the differences in the primary data with what was reported in the published manuscripts or grant proposals. By comparing the primary data to the data in the published journals and grants, the Investigation Committee found numerous instances of fabrications or falsifications. These fabrications or falsifications from two selected published manuscripts (as a representation of the fabrications or falsifications from all the published manuscripts and grant proposals) were shown to the Respondent during his interview. The Respondent recognized and agreed with the Investigation Committee that the data in the two published manuscripts was fabricated or falsified, but was unable to provide an explanation of how the erroneous data was reported.

According to the Public Health Service Policies on Research Misconduct (42 CFR 93.516(b)(i)), the inability of the Respondent to provide primary data can be considered evidence of research misconduct. The Investigation Committee concludes, therefore, that in light of the Respondent's inability to provide primary data that matches the results presented in the published manuscripts, and the fact that the results presented were different from those in the primary data analyzed by the

Investigation Committee, the published manuscripts and grant proposals were based on intentionally fabricated or falsified data.

Further, the Investigation Committee refuted the Respondent's claim that he had an open and highly interactive laboratory, including full involvement of all laboratory members in the manuscript preparation since it was inconsistent with the testimony from the laboratory members. This coupled with the "feed forward" practice of manuscript preparation not only deviated widely from standard scientific practice, but also helped create an ideal environment for data manipulation on the part of the Respondent. The Investigation Committee was also skeptical that laboratory members who were first authors on the published manuscripts did not compare their primary data to the published figures once the manuscripts were published. However, since ultimately, the Respondent was responsible for the conduct of the research in the laboratory as well as all the publications stemming from the laboratory, the Investigation Committee found the Respondent responsible for the research misconduct.

Thus, the Investigation Committee concludes that the data generated over a span from 2003-2010, in ten published manuscripts, including the manuscript identified in the first investigation, and 3 grant proposals has been falsified. The Respondent has committed research misconduct on multiple occasions during a period of 2003-2010.

Dr. Luo and RO3 Grant

The Investigation Committee concluded that the same falsified data were also included in a NIH R03 grant proposal that was submitted to the NIH by Dr. Luo. However, even though Dr. Luo was interviewed and questioned several times by the Investigation Committee, she insisted that she only participated as a laboratory technician in the generation of the data and the preparation of the manuscripts. Thus, even though Dr. Luo was the principal investigator responsible for writing and submitting the RO3 NIH grant, the Investigation Committee could not conclusively prove whether Dr. Luo was aware of the data fabrication or falsification or participated in it.

Tissue Archives

Since there was no independent verification of the identity of the tissue samples at the time of deposit of the tissue samples in the tissue archives and because the records were so poorly annotated, the Investigation Committee determined that tissue samples were of little scientific value.

Impact on Scientific Research

As stated in the Analysis, the literature that cites the published work of the Respondent has increased substantially in the past few years. Other laboratories have been funded to repeat or conduct follow-on research on the Respondent's work resulting in a substantial waste of time, effort and valuable grant funding.

Impact on the Practice of Medicine

It appears that the published work of the Respondent has not had a major or critical impact on the practice of medicine. Although many papers have been published, the work was still in the discovery phase and was not directly applicable to clinical practice. Potential targets for therapeutic interventions have been suggested but none of this research work has taken the field beyond the basic bench discovery change. Also, as stated in the Analysis, companies developing diagnostic tests based on the Respondent's published work will have to validate the tests prior to commercial sale. The inability to validate the tests would disqualify them from commercialization and medical use.

7. Recommended Institutional Actions

1. The Investigation Committee recommends the retraction of the nine published manuscripts that were analyzed.
2. The Investigation Committee also recommends that the collection of tissue samples not be utilized and be destroyed.

8. Attachments

a. Appendix 1 – Summary of grants and publications
b. Appendix 2 – Analysis of each allegation by publication
c. Appendix 3 – Journal citation reports and analysis of impact factor

Submitted October 18, 2013

Investigation Committee Members (alphabetical order)

Dr. Linda Bloom

Dr. Kelle Moley

Dr. Richard Snyder

Dr. Charles Wood