



Final Report of the College of Medicine Investigation Committee Concerning Allegations of Research Misconduct (DIO 6816)

April 17, 2020

Executive Summary

According to The Ohio State University (OSU) Policy and Procedures Concerning Research Misconduct¹ (the "Policy"), a College of Medicine Investigation Committee (the "COMIC") conducted a formal Investigation under University Rule 3335-5-04 with respect to the allegations of potential Research Misconduct against Dr. Flavia Pichiorri, Ph.D., former Post-Doctoral Researcher (10/01/2004-06/30/2010), Research Scientist (07/01/2010-11/30/2011) and OSU Assistant Professor (12/01/2011-08/16/2016), Division of Hematology, College of Medicine (the "Respondent"). Three (3) Complainants provided allegations of data falsification and/or fabrication against Dr. Pichiorri between March 27, 2017 and November 18, 2018. In total, ten (10) allegations in four (4) manuscripts² were investigated by the COMIC. The Manuscript and Allegation numbers used in this report correspond to the numbers used in the Inquiry.

The COMIC determined at a preponderance of the evidence and/or at the clear and convincing evidence standard that nine (9) allegations (Allegations #2-8, #12 and #15) do constitute Research Misconduct as defined in the Policy III. A and 42 C.F.R. § 93.103 (b). The COMIC determined, at a preponderance of the evidence, that one (1) allegation (Allegation #14) does not constitute Research Misconduct as defined in the Policy III. A and 42 C.F.R. § 93.103 (b) and should be dismissed. A review of each specific allegation is provided in the "Investigation Committee Analysis" section of this report.

The COMIC recommends retraction of two (2) manuscripts (Manuscripts #1 and #2) and correction of one (1) manuscript (Manuscript #5). For Manuscript #6, the paper was retracted formerly (08/03/2017) so no further action is recommended by the COMIC. As Dr. Pichiorri is a former OSU employee, the COMIC recommends that she be made permanently ineligible for rehire at OSU.

Allegation Summary³

Manuscript #14: Pichiorri F*, Suh SS*, Rocci A, De Luca L, Taccioli C, Santhanam R, Zhou W, Benson DM Jr, Hofmeister C, Alder H, Garofalo M, Di Leva G, Volinia S, Lin HJ, Perrotti D, Kuehl M, Aqeilan RI, Palumbo A, and Croce CM. "Downregulation of p53-inducible microRNAs 192, 194, and 215 impairs the p53/MDM2 autoregulatory loop in multiple myeloma development." *Cancer Cell*. 2010 Oct 19;18(4):367-81. *Co-first authors

CORRECTED- 08/08/2016^{5, 6}

¹ Ex. 1 - University Policy and Procedures Concerning Research Misconduct

² This report refers to submitted manuscripts and publications as "Manuscripts" to maintain consistency with the Inquiry.

³ Due to nature of when allegations arose and/or when Dr. Pichiorri was notified, the numbering of allegations is not consecutive.

⁴ Ex. 4 - Pichiorri et al., *Cancer Cell* 2010

⁵ Ex. 5 - Correction-*Cancer Cell* 2010

⁶ Correction of Figures 4A and 7A only



- Allegation #2 – Falsification of Figure 4A by reuse of same data in the MDM2 lanes in the MM1s panel and in the MDM2 lanes in the NCI-929 panel
- Allegation #3 – Falsification of Figure 5A by reuse of same data in the Scr/5-10 μ M lanes and in the miR-194/2.5-5 μ M lanes of the p53 blots
- Allegation #4 – Falsification of Figure 5A by reuse of same data in the blot for p53 of miR-192 and in the alpha-puma blot for miR-192 (horizontal mirror image)
- Allegation #5 – Falsification of Figure 7A by reuse of same data in the GAPDH blot in the left panel (MM1s WT TP53) and in the Akt blot in right panel (RPMI-8226 Mut TP53)
- Allegation #15 - Falsification of Figure 4D or 7A by the reuse of the same data in the MDM2 blot (flipped) in the MM1s panel of Figure 4D and in the right three lanes in the IGF-1 blot in the MM1s WT TP53 panel of Figure 7A

Manuscript #2⁷: Pichiorri F*, Palmieri D*, De Luca L, Consiglio J, You J, Rocci A, Talabere T, Piovan C, Lagana A, Cascione L, Guan J, Gasparini P, Balatti V, Nuovo G, Coppola V, Hofmeister CC, Marcucci G, Byrd JC, Volinia S, Shapiro CL, Freitas MA, and Croce CM. "In vivo NCL targeting affects breast cancer aggressiveness through miRNA regulation." *J Exp Med*. 2013 May 6; 210(5):951-68. Epub 2013 Apr 22.

*Co-first authors

- Allegation #6 – Falsification of Figure 1E by reuse of the same data in the RNU6 lanes (Northern blot analysis of total RNA from HeLa cells co-transfected with pri-miR-21 expression vector (pMIRNA1-pri-miR-21) and in the three right-hand RNU6 lanes in the pri-miR-155 lanes in Figure 1F

Manuscript #2 Correction⁸: Pichiorri F*, Palmieri D*, De Luca L, Consiglio J, You J, Rocci A, Talabere T, Piovan C, Lagana A, Cascione L, Guan J, Gasparini P, Balatti V, Nuovo G, Coppola V, Hofmeister CC, Marcucci G, Byrd JC, Volinia S, Shapiro CL, Freitas MA, and Croce CM. Correction: In vivo NCL targeting affects breast cancer aggressiveness through miRNA regulation." *J Exp Med*. 2017 May 1;214(5):1557. Epub 2017 Jan 19. (Correction of Figures 1E and 1F). *Co-first authors

- Allegation #7 – Falsification of the corrected Figure 1E by reuse of the same RNU6 lanes data (flipped horizontally) from the published Figure 1E (rotated) as the corrected Figure 1E
- Allegation #8 – Falsification of the corrected Figure 1F by reuse of the same RNU6 blot data in the pri-miR-155 panel (flipped horizontally) taken from Pichiorri et al., (2010) "Downregulation of p53-inducible microRNAs 192, 194, and 215 impairs the p53/MDM2 autoregulatory loop in multiple myeloma development" *Cancer Cell*, 18, Figure 1E, the left four lanes of the RNU6 blot in the Nutlin panel ("Manuscript #1)

Manuscript #5⁹: Canella A, Nieves HC, Sborov DW, Cascione L, Radomska HS, Smith E, Stiff A, Consiglio J, Caserta E, Rizzotto L, Zanesi N, Stefano V, Kaur B, Mo X, Byrd JC, Efebera YA, Hofmeister CC*, and Pichiorri F*. "HDAC inhibitor AR-42 decreases CD44 expression and sensitizes myeloma cells to lenalidomide." *Oncotarget*. 2015 Oct 13; 6(31): 31134–31150. *Co-corresponding authors

- Allegation #12 – Falsification of Western blot data by falsely labeling of cell line MM.1S in Figure 3B, when the original research records indicates the data are from the MM.1R cell line

⁷ Ex. 6 - Pichiorri et al., *J Exp Med* 2013

⁸ Ex. 7 - Correction- *J Exp Med* 2013

⁹ Ex. 10 - Canella et al., *Oncotarget* 2015



Manuscript #6¹⁰: Trapasso F*, Pichiorri F*, Gaspari M, Palumbo T, Aqeilan RI, Gaudio E, Okumura H, Iuliano R, Di Leva G, Fabbri M, Birk DE, Raso C, Green-Church K, Spagnoli LG, Venuta S, Huebner K, Croce CM. Fhit interaction with ferredoxin reductase triggers generation of reactive oxygen species and apoptosis of cancer cells. *J Biol Chem*. 2008 May 16;283(20):13736-44. Epub 2008 Mar 3. *Co-first authors.

RETRACTED 08/03/2017¹¹

- Allegation #14 – Falsification of Western blot data in Figure 5H by reuse of same data for 24 and 48 hr AdFhit lanes and for the 48 and 72 hr AdGFP lanes in the CoxIV blot

Subsequent Use Summary¹²

Title 42 C.F.R. §93.105(a) and the Policy, Section V.I. set a six-year time limitation for reviewing claims of research misconduct, unless, among other things, the Respondent “subsequently uses” the questioned manuscript. The Office of Research Compliance (ORC) conducted an initial review and determined that Manuscripts #1 and #6 questioned in this Investigation were published more than six years before the date the University received the initial allegations. Each manuscript was then reviewed to determine if the subsequent use exception applied.

ORC determined that while Manuscripts #1 and #6 were outside the six-year time limitation, Dr. Pichiorri continued to cite the questioned publications in the following instances:

Manuscript #1: *Cancer Cell* 2010

- Cited in the "Selected peer-reviewed publications" section in the 1 R21 CA186001-01 (2014) grant application. Dr. Pichiorri is listed as a PI on the grant application.
- Cited in Sung-Suk Suh, Ji Young Yoo, Gerard J. Nuovo, Young-Jun Jeon, Seokho Kim, Tae Jin Lee, Taewan Kim, Arianna Bakacs, Hansjuerg Alder, Balveen Kaur, Rami I. Aqeilan, Flavia Pichiorri, Carlo M. Croce. "miR-25/32 restore p53 activity" *PNAS* April 3, 2012 109 (14) 5316-5321; DOI: 10.1073/pnas.1202465109
- Cited in Manuscript #2 (*J Exp Med*. 2013)

Manuscript #6: *JBC* 2008

- Cited in the "Contribution to Science" section in the 1 R01 CA194742-01A1 (2015) grant application. Dr. Pichiorri is listed as a multi-PI.

Therefore, the subsequent use exception to the time limitation applied for both manuscripts #1 and #6, and the Committee included both in their review.

Preliminary Assessment Summary¹³

On June 7, 2017, Dr. David Wright,¹⁴ Ph.D., External, Independent Research Integrity Officer, Dr. Julia Behnfeldt, Associate Director and Research Integrity Officer, and Dr. Robert Bornstein, Vice Dean for Academic

¹⁰ Ex. 11 - Trapasso et al., *JBC* 2008

¹¹ Ex. 12 - Retraction-*J. Biol. Chem.*-2017-Trapasso-14279(1)

¹² Ex. 2 - Subsequent Use Exception Process-V1

¹³ Ex. 20 - 20171128 - Pichiorri Preliminary Assessment Letter

¹⁴ Dr. Wright served as an External, Independent Research Integrity Officer (RIO) for the PA and Inquiry.



Affairs, College of Medicine, met to review fourteen (14) allegations and conduct a Preliminary Assessment (PA) under the Policy. The Preliminary Assessment determined that a portion of the allegations were credible and specific, and recommended that they be moved forward to a Committee of Initial Inquiry (CII) for further review under the Policy. On November 28, 2017, the Preliminary Assessment letter regarding the allegations of possible Research Misconduct was submitted to the Deciding Official in this matter, Karla Zadnik, O.D., Ph.D., Dean and Glenn A. Fry Professor in Optometry and Physiological Optics, OSU, with the recommendation that this case be moved forward to a CII.¹⁵ On November 30, 2017, Dr. Zadnik concurred with the Preliminary Assessment and indicated that a CII should be initiated.¹⁶

On November 16, 2017, Dr. Pichiorri was notified via teleconference of the allegations against her.¹⁷ Dr. Wright and Dr. Behnfeldt participated in that notification meeting by teleconference, discussed the allegations with Dr. Pichiorri, and provided information regarding OSU's Policy and process. To facilitate the notification, officials from Dr. Pichiorri's current institution, the Beckman Research Institute of the City of Hope (COH) Comprehensive Cancer Center, were present with Dr. Pichiorri (Dr. Beverly Alger, COH Research Compliance Officer, Ms. Jennifer Ing, COH Deputy General Counsel, and Ms. Lydia Chan, COH Deputy General Counsel).

Sequestration of Data Summary

Directly following the notification on November 16, 2017, data were sequestered from Dr. Pichiorri's laboratory. As Dr. Pichiorri is no longer employed by OSU, nor present on campus, officials at Dr. Pichiorri's current institution, COH Comprehensive Cancer Center, assisted OSU in sequestration. Dr. Alger, Ms. Ing and Ms. Chan accompanied Dr. Pichiorri to her COH laboratory to sequester all relevant research records related to the allegations. COH provided the original notebooks containing data generated at OSU that Dr. Pichiorri had taken with her when she moved to COH on March 15, 2018.¹⁸ In addition, data related to Manuscripts #1 and #2 were sequestered from Dr. Carlo Croce's laboratory on July 20, 2017.¹⁹ Dr. Croce was Dr. Pichiorri's former post-doctoral advisor and corresponding author on Manuscripts #1, #2 and #6. An external hard drive sequestered from Dr. Croce's laboratory ("CMC-8") contained a folder titled "Flavia Cancer Cell Data," which contained images of scanned data used in Manuscript #1.^{20,21} The external hard drive was stored in the office of Dr. Dorothee Wernicke, Dr. Croce's lab manager. Dr. Wernicke explained that when students and researchers left Dr. Croce's lab, they were supposed to leave their data with her. The external hard drive "CMC-8" also contained data from other researchers not implicated in this Investigation. The files found in the "Flavia Cancer Cell Data" folder were identical to those provided directly by Dr. Pichiorri, with the exception of two files as described in the COMIC Analysis for Allegation #2 below.

Complainant Summary²²

1. David Sanders, Ph.D., Associate Professor of Biological Sciences at Purdue University. On March 27,

¹⁵ Ex. 21 - 20171128 - Email RIO to DO PA Letter

¹⁶ Ex. 22 - 20171130 - DO to RIO PA Letter Recommendation

¹⁷ Ex. 62 - 20171116 OSU Notification Memo for FP- signed

¹⁸ Ex. 24 - 20180315 Data Sequestration Sheet- COH

¹⁹ Ex. 25 - 20170720 Data Sequestration Sheet Catalogued_redacted FP

²⁰ Ex. 179 -Flavia Cancer Cell Data Folder

²¹ D:\Exports\A0038_WD_USB_Drive\Data\Flavia Cancer Cell Data

²² Complainants provided allegations beyond those specifically referenced here. However, those allegations were dismissed during the Inquiry and therefore not included in this Investigation.



2017, Dr. Sanders emailed concerns on Manuscript #1²³ and Manuscript #2.²⁴ On November 21, 2018, Dr. Sanders provided an additional allegation (Allegation #15) in Manuscript #1.²⁵

2. Hanna Radomska, Ph.D., Research Scientist, OSU Comprehensive Cancer Center, former post-doctoral researcher in Dr. Pichiorri's laboratory at OSU. On March 31, 2017, Dr. Radomska provided the allegation in Manuscript #5 in person to Dr. Behnfeldt and Dr. Jennifer Yucel, Associate Vice President, Office of Research Compliance.
3. Anonymous complainant, referred to OSU by Beckman Research Institute of the City of Hope (COH) Comprehensive Cancer Center Director, Dr. John Zaia. On June 5, 2017, Dr. Zaia forwarded an allegation²⁶ on Manuscript #6, which was published by Dr. Pichiorri during her time at OSU.

Committee of Initial Inquiry Summary

A Committee of Initial Inquiry (the "CII") was formed on January 19, 2018, to review allegations of possible Research Misconduct made against Dr. Pichiorri. On November 6, 2018, the CII issued their Preliminary Report.^{27,28} On November 21, 2018, Dr. Pichiorri provided her response to the Preliminary Report.²⁹ On December 7, 2018, the CII issued their Final Report,^{30,31,32} which determined that nine (9) allegations (Allegations #2-8, #12, #14) **did** have sufficient substance to warrant further Investigation under the Policy, three (3) allegations (Allegations #1, #9, #13) **did not** have sufficient substance to warrant further Investigation, and two (2) allegations (Allegations #10-11) were not under OSU jurisdiction and therefore the CII ceded Investigation of those allegations to the COH (the Respondent's current employer and site of the alleged Falsification). Dr. Pichiorri did not file an appeal, as allowed by the Policy.³³ On December 20, 2018, the Deciding Official, Dr. Karla Zadnik, concurred with the CII determinations.³⁴ On December 20, 2018, Dr. Pichiorri was notified of the DO decision.³⁵ On December 20, 2018, Complainants, Dr. Hanna Radomska³⁶ and Dr. David Sanders³⁷ were also notified of the DO decision.

As the allegations against Dr. Pichiorri span her time as both a Post-Doctoral researcher (a staff position) and subsequently as a faculty member in the College of Medicine, on January 8, 2019, the decision³⁸ to initiate an Investigation was referred to both the Office of Human Resources and the College of Medicine. The Investigation would be conducted pursuant to the Policy, under the Office of Human Resources policies (for allegations occurring during Dr. Pichiorri's tenure as staff) and under the University Rule 3335-5-04(E) (for

²³ Ex. 17 - Cancer Cell, Volume 18 2010, Pages 367-381

²⁴ Ex. 18 - Journal of Experimental Medicine 2013, 210 951-968

²⁵ Ex. 71 - David Sanders letter to Dr. Wright (OSU) (2)

²⁶ Ex. 23 - Journal Biological Chemistry 283, 13736-13744

²⁷ Ex. 95 - 20181106-Letter RIO to FP-PR

²⁸ Ex. 94 - 20181106-CII Preliminary Report-Pichiorri

²⁹ Ex. 72 - Pichiorri Point by point response to CII Nov.21-2018

³⁰ Ex. 97 - 20181207-CII Final Report-Pichiorri

³¹ Ex. 98 - 20181207-CII Final Report-Pichiorri v2

³² At the request of the DO, the final report was revised on 12/18/2018 to clarify the roles of interview participants on page 8. The revised report is Ex. 98 - 20181207-CII Final Report-Pichiorri v2.

³³ Ex. 99 - 20181217-Email FP to RIO-No appeal

³⁴ Ex. 100 - 20181220-DO to RIO-DO CII Decision

³⁵ Ex. 104 - 20181220- DO to Pichiorri-DO Decision

³⁶ Ex. 106 - 20181220- DO to Radomska-DO Decision

³⁷ Ex. 108 - 20181220- DO to Sanders-DO Decision

³⁸ Ex. 110- 20190108 - Letter Chair to COM and HR-Pichiorri



allegations occurring during Dr. Pichiorri's tenure as faculty). On January 11, 2019, the Office of Research Integrity for the U.S. Department of Health and Human Services was notified of the CII Final Report and the determination that an investigation was warranted.³⁹

College of Medicine Investigation Committee

After screening each potential College of Medicine Investigation Committee (the "COMIC") member to ensure that each was free from any possible conflict of interest that could prevent a fair and impartial review of the allegations, the COMIC members were charged⁴⁰ on February 18, 2019, to: (1) examine all evidence and collect any additional evidence it deemed appropriate; (2) determine if each allegation constitutes Research Misconduct (i.e., meets all of the criteria required for a finding of Research Misconduct as outlined in the Policy Section III.A – see below subsection), and if so, whether Dr. Pichiorri is responsible for the Research Misconduct; and (3) recommend sanctions if the COMIC determines that Dr. Pichiorri committed Research Misconduct.

In order to ensure that the investigation was conducted with the appropriate scientific domain experience and expertise, the College of Medicine Investigation Committee served as the primary body charged with conducting the investigation to determine if Research Misconduct had occurred. A member of the College of Medicine's Human Resources (COM HR) staff was appointed to the College of Medicine Investigation Committee to consider the interests of Dr. Pichiorri during her time as a staff member (as a post-doctoral researcher). The COM HR member, Ms. Colleen Rupp, had voting rights on only those allegations occurring during Dr. Pichiorri's time as a staff member (Allegations #2, 3, 4, 5, 14, 15).

The composition of the COMIC was as follows:

- Arthur Burghes, Ph.D. (**Chair**) Professor, Department of Biological Chemistry and Pharmacology, College of Medicine
- Brandon Biesiadecki, Ph.D., Associate Professor, Department of Physiology & Cell Biology, College of Medicine
- Jonathan Davis, Ph.D., Professor, Department of Physiology and Cell Biology, College of Medicine
- Jill A. Rafael-Fortney, Ph.D., Professor, Department of Physiology & Cell Biology, Biological Chemistry & Pharmacology, College of Medicine
- Yutong Zhao, M.D., Ph.D., Professor, Department of Physiology and Cell Biology, College of Medicine
- Thomas Hund, Ph.D. (**non-COM representative**), Professor, Department of Biomedical Engineering, College of Engineering
- Loren Wold, Ph.D. (**non-COM representative**), Professor, Colleges of Nursing and Medicine (Physiology and Cell Biology)
- Colleen Rupp (**COM HR representative**), Senior Employee and Labor Relations Consultant, Wexner Medical Center Human Resources

College of Medicine Investigation Committee Meetings

The COMIC met on the following dates to review the allegations and case materials and/or to interview participants:

³⁹ Ex. 114 - 20190111 ORI Notice CII Final Report_Pichiorri

⁴⁰ Ex. 120 - 20190218 - COMIC Charge - Pichiorri



- 02/18/19: COMIC charge meeting. Dr. Behnfeldt and Ms. Emily Schriver, OSU Senior Associate General Counsel, Office of Legal Affairs, discussed the University Policy and Procedures Concerning Research Misconduct and process and the specific charge of the CII. Dr. Burghes was chosen as the committee chair
- 03/11/19: CII working meeting
- 03/25/19: CII working meeting
- 04/01/19: CII working meeting
- 04/08/19: CII working meeting
- 04/15/19: CII working meeting
- 04/22/19: CII working meeting to prepare for interviews
- 04/29/19: COMIC interview of Complainant, Dr. Hanna Radomska
- 04/29/19: COMIC interview of Complainant, Dr. David Sanders
- 05/13/19: COMIC interview of Respondent, Dr. Flavia Pichiorri
- 06/10/19: COMIC working meeting
- 06/17/19: COMIC working meeting
- 06/24/19: COMIC working meeting
- 07/01/19: COMIC working meeting
- 08/05/19: COMIC working meeting
- 08/16/19: COMIC voting meeting
- 09/09/19: COMIC working meeting
- 11/04/19: COMIC working meeting
- 02/17/20: COMIC working meeting

Written Responses Provided by the Respondent

Over the course of the Preliminary Assessment, Inquiry, and Investigation, Dr. Pichiorri and/or her counsel provided numerous written responses to the ORC. For completeness, all responses have been listed below, even those related to allegations dismissed at the Inquiry stage. Additionally, in the various responses, Dr. Pichiorri often refers to specific "document #s." However, the "document #s" provided in the different responses from Dr. Pichiorri are not always consistent across the responses, (e.g., "Document 1" from the November 21, 2018 written response does not include the same content as "Document 1" from the April 10, 2019 written response). Therefore, the specific responses and documents used as evidence by the COMIC are described and footnoted in the "Investigation Committee Analysis" section below for the relevant allegation (please note that some of these responses were sent to ORC in the same month but different year, and the date is cited completely in the "Investigation Committee Analysis" section).

1. April 26, 2017: "Flavia Pichiorri Documents,"⁴¹ - A 65-page document containing email correspondence between Dr. Pichiorri and Dr. Radomska, submitted on behalf of Dr. Pichiorri by Julie Davis, counsel to Dr. Pichiorri.⁴²
2. January 22, 2018: "Dear OSU Research Compliance Officer Pichiorri F,"⁴³ - A 23-page document regarding Allegations #10-#13 that contained data scans and email correspondence between Dr. Pichiorri and Dr. Radomska, submitted directly by Dr. Pichiorri.⁴⁴

⁴¹ Ex. 43 - Flavia Pichiorri Documents

⁴² Ex. 44 - 20170426 Email Pichiorri Counsel to GG Rokous

⁴³ Ex. 27 - 20180122 - "Dear OSU Research Compliance Officer Pichiorri F."

⁴⁴ Ex. 45 - 20180122 Email Pichiorri to RIO



3. April 12, 2018: "Point by point Response to OSU April 13th Research misconduct Allegations,"⁴⁵ - A 6-page response with 19 separate documents (exhibits)⁴⁶ submitted directly by Dr. Pichiorri.^{47, 48}
4. May 16, 2018: "2018-05-16 – OSU- Response to New Allegation Final (with Exhibits),"⁴⁹ - A 178-page document submitted on behalf of Dr. Pichiorri by Paul Thaler, counsel to Dr. Pichiorri.⁵⁰
5. November 21, 2018: "Pichiorri Point by point response to CII Nov.21-2018"⁵¹ - A 9-page document submitted by Dr. Pichiorri in response to the Preliminary Report with 13 separate documents (Exhibits #74-86), some with multiple sub-files.
6. April 10, 2019: "Pichiorri point-by -point April 10th-2019"⁵² - A 19-page document submitted by Dr. Pichiorri with 20 separate documents (Exhibits 131-150), some with multiple sub-files. Dr. Pichiorri also forwarded⁵³ her email communication⁵⁴ with J Exp Med. in 2017.
7. May 16, 2019: "Post-Interview Submission re Figure 3B further data to the IC"⁵⁵ - A 2-page document submitted by Dr. Pichiorri to clarify statements made in her May 13, 2019 interview with 4 separate documents (Exhibits 167-170), some with multiple sub-files.
8. July 29, 2019: "To Dr. Burghes OSU 7-29-2019"⁵⁶ - A 1-page response submitted by Dr. Pichiorri to answer questions regarding her mention of previous allegations in the April 10, 2019 response.

As described in the Sequestration of Data Summary section above, limited information was sequestered from COH on November 16, 2017, and sequestered from Dr. Carlo Croce's laboratory on July 20, 2017. The eight additional responses from Dr. Pichiorri listed above were provided to ORC after Dr. Pichiorri was aware of the allegations. Thus, there is no way to verify or independently confirm the notations on the scans of films for original raw data that was provided as documents/exhibits with Dr. Pichiorri's written responses.

Notification of Additional Allegations

In his November 15, 2018 written response to the Preliminary Report of the CII, Dr. Sanders, Complainant, provided an additional allegation regarding Cancer Cell 2010, Manuscript #1 (Exhibits 70-71).^{57, 58} In the Final CII Report,⁵⁹ provided to the Respondent on December 7, 2018, and in the associated letter from the CII chair to the Deciding Official,⁶⁰ the CII recommended by a 3-0 vote that the allegation (subsequently numbered Allegation #15)⁶¹ be moved forward for review by the Investigation Committee.

⁴⁵ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations

⁴⁶ Ex. 38 - Documents 1-19 Combined

⁴⁷ Ex. 46 - 20180412 Email Pichiorri to RIO 1

⁴⁸ Ex. 47 - 20180412 Email Pichiorri to RIO 2

⁴⁹ Ex. 42 - 2018-05-16 - OSU- Response to New Allegation Final (with Exhibits)

⁵⁰ Ex. 48 - 20180516 - Email R to RIO re. new allegation response

⁵¹ Ex. 72 - Pichiorri Point by point response to CII Nov.21-2018

⁵² Ex. 128 - Pichiorri point-by -point April 10th-2019

⁵³ Ex. 129 - 20190411-Email Pichiorri to RIO_JEM emails

⁵⁴ Ex. 130 - 20190411-Email Pichiorri to RIO_JEM emails_Pdf Original Figure 1E and 1 F

⁵⁵ Ex. 166 - Post-Interview Submission re Figure 3B further data to the IC

⁵⁶ Ex. 178 - To Dr. Burghes OSU 7-29-2019

⁵⁷ Ex. 70 - 20181115 Email Sanders to RIO-Response to PR

⁵⁸ Ex. 71 - David Sanders letter to Dr. Wright (OSU) (2)

⁵⁹ Ex. 98 - 20181207-CII Final Report-Pichiorri v2

⁶⁰ Ex. 89 - 20181207- Letter CII Chair to DO- Pichiorri Final Report

⁶¹ Ex. 71 - David Sanders letter to Dr. Wright (OSU) (2)



Interview Summaries

Dr. Sanders, Complainant, was interviewed by the COMIC on April 29, 2019 via teleconference.⁶² In general, Dr. Sanders was asked about how he came to know about and submit the specific allegations against Dr. Pichiorri.

Dr. Radomska, Complainant, was interviewed by the COMIC on April 29, 2019.⁶³ During the interview, Dr. Radomska was shown a PowerPoint presentation regarding Allegation #12 ("20190429-Source data_Oncotarget #12"⁶⁴). Dr. Radomska's specific statements are provided in the "Investigation Committee Analysis" section below.

Dr. Pichiorri was interviewed by the COMIC on May 13, 2019.⁶⁵ During the interview, Dr. Pichiorri was shown a PowerPoint presentation summarizing the allegations under investigation ("Summary Figure Forensics_Pichiorri"⁶⁶). Dr. Pichiorri's specific statements are provided in the "Investigation Committee Analysis" section below.

The COMIC requested to interview as a witness Dr. Carlo Croce, Dr. Pichiorri's former graduate and post-doctoral advisor and laboratory PI, however Dr. Croce declined that invitation.^{67,68}

External Notifications

In its review of the case materials and responses from the Respondent regarding Manuscript #2 (JEM 2013), the COMIC determined that it required additional information from JEM Executive Editor, Dr. Teodoro Pulvirenti. In accordance with the Policy Section I.D., on April 9, 2019, Dr. Behnfeldt requested approval from Dr. Morley Stone, OSU Senior Vice President for Research, to contact Dr. Pulvirenti and submit a list of written questions to Dr. Pulvirenti regarding this matter.⁶⁹ On April 12, 2019, Dr. Stone approved the request to contact Dr. Pulvirenti.⁷⁰ Per the Policy, on April 17, 2019, Dr. Pichiorri was notified of the external contact to Dr. Pulvirenti.⁷¹ On April 17, 2019, Dr. Behnfeldt submitted a list of questions to Dr. Pulvirenti.⁷² On May 21, 2019, Dr. Pulvirenti provided his response to the questions.^{73,74} Dr. Pulvirenti's specific responses on Manuscript #2 are provided in the "Investigation Committee Analysis" section below.

⁶² Ex. 161 - 20190429 -COMIC Interview +Errata - Sanders

⁶³ Ex. 160 -20190429- COMIC Interview + Errata - Radomska

⁶⁴ Ex. 187 – 20190429-Source data_Oncotarget #12

⁶⁵ Ex. 165 - 20190513 - COMIC Interview + Errata - Pichiorri

⁶⁶ Ex. 124- Summary Figure Forensics_Pichiorri

⁶⁷ Ex. 163 - 2019.05.03 J. Arnold ltr re_Dr. Croce req. for interview

⁶⁸ Ex. 162 - 20190509-Email Croce to RIO_Decline Interview

⁶⁹ Ex. 151 - 20190409-Email RIO to DO_contact external party

⁷⁰ Ex. 152 - 20190412-Email DO to RIO_request approval

⁷¹ Ex. 153 -20190417 - Letter RIO to Pichiorri - Notify external contact

⁷² Ex. 154 -20190417 - Letter RIO to JEM

⁷³ Ex. 159 - 20190521-Email JEM to RIO_Response to Questions

⁷⁴ Ex. 158 - JEM answers to OSU



COMIC Analysis of Criteria Required for a Finding of Research Misconduct

Per the Policy, Section III.A., Research Misconduct means Fabrication, Falsification or Plagiarism in proposing, performing, or reviewing research, or in reporting research results. The allegations reviewed in this Investigation Report are the Falsification of data. Falsification is defined as:

Section III.F: Falsification. "Falsification" is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.

In the "Investigation Committee Analysis" section below, the COMIC used forensic analysis to determine which of the questioned figures have been falsified by the reuse of the same blot to represent different experimental conditions and proteins. In most instances, the Respondent does not dispute the duplication of data. Additionally, in some instances, the Falsification was supported by the fact that corrections were published regarding a portion of the questioned figures, but the corrections stated that data were "inadvertently duplicated" or "mistakenly replaced".⁷⁸

Per the Policy, Section III.A.1, a finding of Research Misconduct requires:

- A. That there be a significant departure from the accepted practices of the relevant research community; and
- B. The misconduct be committed intentionally, knowingly, or recklessly; and
- C. The allegation be proved by a Preponderance of the Evidence.

Analysis of criteria A: "That there be a significant departure from the accepted practices of the relevant research community." The COMIC determined that the relevant research community for this Investigation would be experienced biomedical researchers using molecular biology, biochemical and molecular genetic techniques in an academic setting with experience in publishing and grant writing. The COMIC members, with the exception of the HR staff representative, all represent this community with their experience and status as either associate or full professors with experience in molecular biology research with numerous grants and publications. Specifically, the COMIC faculty members have each been in various positions required in the academic pathway to become a faculty member who oversees trainees, including being a graduate student followed by post-doctoral researcher training. At each stage of their careers, the COMIC members have participated in Responsible Conduct of Research (RCR) training and have a firsthand understanding of the knowledge, independence and responsibilities of a trainee at each level. As a collective, the COMIC has trained 30+ post-doctoral researchers and 29+ graduate students. Three COMIC members have been directly involved in the formal teaching of RCR in Universities courses required for trainees including, but not limited to, topics on professional ethics, proper figure generation,

75 [REDACTED]
76 [REDACTED]
77 [REDACTED]

78 Ex. 5 - Correction-Cancer Cell 2010



data analysis and plagiarism. Further, all of the COMIC members train their own mentees and lab members on accepted practices and RCR. Therefore, their assessment of what is an accepted practice is based on their collective knowledge of and active participation in the relevant academic biomedical research community.

Analysis of criteria B: "The misconduct be committed intentionally, knowingly, or recklessly." The definitions of "intentionally, knowingly, or recklessly" are not listed in the Policy, nor in the federal regulations (42 C.F.R § 93) applicable in this Investigation. Based on federal, state, and university guidance, the COMIC used the following definitions for this investigation:

Intentionally: Respondent directly engages in Fabrication, Falsification or Plagiarism with the intent, or purpose, of misleading the readers of the research record.

Knowingly: Respondent has actual knowledge of the Fabrication, Falsification or Plagiarism or acts in deliberate ignorance or plain indifference of the Fabrication, Falsification or Plagiarism.

Recklessly: Respondent is on notice of a significant increased risk of falsified, fabricated, or plagiarized data and/or text being used or generated, or the risk is so obvious that a typical researcher in the relevant research community should have known, and through action or inaction, the respondent uses, or allows the use of, the falsified, fabricated, or plagiarized data and/or text.

Analysis of criteria C: "The allegation be proved by a Preponderance of the Evidence". The preponderance of the evidence standard comes from the federal regulations under CFR 93.104 (c) and the University Policy Section III.H., which states:

"Preponderance of the Evidence" means proof by information that, compared with that opposing it, leads to the conclusion that the fact at issue is more probably true than not.

The COMIC generally will interpret preponderance of the evidence to mean at a certainty of greater than 50%. In addition, as required by the Policy and University Rule 3335-5-04, to determine appropriate sanction recommendations for a faculty Respondent, the COMIC must also consider the allegations at the 'Clear and Convincing' standard as set forward in the University Rule.

Per the Policy Section III.A.2, Research Misconduct specifically does not include honest error or differences of opinion. As stated in 42 CFR 93.106(b)(2), the Respondent has the burden of proving, by a preponderance of the evidence, any affirmative defense or honest error. The COMIC must determine whether any claim of honest error or an affirmative defense is proven by the preponderance of the evidence.

Investigation Committee Analysis

The COMIC reviewed and made determinations on all the allegations detailed below. As Dr. Pichiorri left OSU in 2016, and there was little raw data for the questioned figures included in the sequestered materials, the COMIC was limited in its review of raw data to those documents provided by Dr. Pichiorri at various times during the Inquiry and Investigation.

During the Investigation, the COMIC identified additional evidence in the raw data files provided by Dr. Pichiorri that influenced the final findings. A summary of the COMIC's final findings of Research Misconduct is provided at the end of the analysis section.



Manuscript under review - Pichiorri et al., Cancer Cell 2010 (5 allegations)⁷⁹

Pichiorri F*, Suh SS*, Rocci A, De Luca L, Taccioli C, Santhanam R, Zhou W, Benson DM Jr, Hofmeister C, Alder H, Garofalo M, Di Leva G, Volinia S, Lin HJ, Perrotti D, Kuehl M, Aqeilan RI, Palumbo A, Croce CM. "Downregulation of p53-inducible microRNAs 192, 194, and 215 impairs the p53/MDM2 autoregulatory loop in multiple myeloma development." *Cancer Cell*. 2010 Oct 19;18(4):367-81. [The publication lists support by: OSU Targeted Investment in Excellence Award and the Kimmel Foundation award (FP). PubMed citation lists support by NIH P01 CA129242 (to C.M. Croce) and K12 CA133250 (to J. Byrd and W. Carson).] *Co-first authors.

Corrected: 08/08/2016⁸⁰

Manuscript #1, Allegation #2 - F. Pichiorri falsified Figure 4A by the reuse of the same data in the MDM2 lanes 1-4 in the MM1s panel Western blot and in the MDM2 lanes 2-5 in the NCI-929 panel Western blot in Pichiorri et al., Cancer Cell 2010.

Finding of Fact:

- 1) Figure 4A shows the expression level of p53, MDM2, p21 and GAPDH loading control following transfection of miR-192, miR-194, miR-215 or Scrambled (Scr) control and 12 hr of nongenotoxic activation of p53 by Nutlin-3a in both the MM1s cell line and the NCI-929 cell line. Quantification of the blots is provided in Figures 4B and C (see slide #4⁸¹).
- 2) Adobe Photoshop forensic overlay analysis shows that the 4 lanes of the MDM2 panel in MM1s cells are identical to 4 of the 5 lanes (lanes 2-5) of the MDM2 panel in the NCI-929 cells in Figure 4A. Since the panels are reported to represent MDM2 expression in 2 different cell types and transfected with different miRs, this duplication shows that at least one of these duplicated panels must be false and not scientifically valid (see slide #5⁸²).
- 3) Dr. Pichiorri responded to the allegation during the Inquiry on April 12, 2018.⁸³ Dr. Pichiorri provided an attachment named "Document 2," (and subsequently renamed as "Document 4"⁸⁴ in her April 10, 2019 response to the COMIC), which is a file of 2-pages containing multiple scanned films attached to each page.⁸⁵ Dr. Pichiorri did not state which of the films were used to construct Figure 4A, but she did write that the editor of the *Cancer Cell* journal has the original films.
- 4) Document 2, page 2⁸⁶ is labeled with hand-written notes for "Figure 4A" and "H929 Nutlin treated 09/10/2008." One film attached to page 2, labeled "TOT MDM-2," matches the MDM2 blot for NCI-929 cells in Figure 4A, but the blot in the figure has been flipped upside down compared to the scanned film (see slide #6⁸⁷). The vertical flip does not impact the reported experimental outcome.
- 5) The hand-written notes on Document 2, page 2 indicate that the experiments were done on 9/10/2008, and represent treatment of H-929 cells with "Nutlin," and the published Figure 4A shows treatment with "Nutlin-3A". In her written response, provided to the COMIC on April 10, 2019⁸⁸, Dr.

⁷⁹ Dr. Pichiorri was a staff member at the time this manuscript was published, therefore voting will be at the preponderance of evidence standard only and will include a vote from the HR representative.

⁸⁰ Ex. 5 - Correction-Cancer Cell 2010

⁸¹ Ex. 123 - COMIC Figure Forensics_Pichiorri

⁸² Ex. 123 - COMIC Figure Forensics_Pichiorri

⁸³ Ex. 37 Point by point Response to OSU April 13th Research misconduct Allegations

⁸⁴ Ex. 134 - 20190410-Documents-Folder 4, Fig.4A

⁸⁵ Ex. 90 - 20180412_Document 2, page 2

⁸⁶ Ex. 90 - 20180412_Document 2, page 2

⁸⁷ Ex. 123 - COMIC Figure Forensics_Pichiorri

⁸⁸ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 6



Pichiorri stated that "... we specifically used Nutlin-3A in which we wrote the specific name of the compound "Nutlin-3A." Thus, Dr. Pichiorri claimed that if experiments were designed using Nutlin-3A, the films would be labeled with "Nutlin-3A," which is not the case in this instance.

- 6) Document 2, page 1 shows scans of films provided by Dr. Pichiorri on April 12, 2018, and includes hand-written notes for "fig 4a," "exp. 2," "MDM-2" and "MM-1S".⁸⁹ The COMIC found that the top two films on page 1 show different exposures of data for MDM2 protein expression in MM1s cells. The labels on the films are consistent with the experimental design in Figure 4A. These films show the same experimental trend seen in the published Figure 4A for MDM2 MM1s, with lower expression of MDM2 in miR192 and miR215 treatments compared to the higher expression of MDM2 in miR194 and scrambled (Scr) control treatments (see slide #7⁹⁰), but this film was not the one used for MDM2 in MM1s in the original published Figure 4A. Thus, the data provided appears to be a similar experiment that was performed but these results were not used in the published figure.
- 7) A correction for the MDM2 MM1s blot in Figure 4A was published on August 8, 2016⁹¹. The data on Document 2, page 1, were used for the MDM2 blot in MM1s cells in the correction of Figure 4A (see slide #7⁹²).
- 8) The correction indicates that the authors did not dispute the duplication of the panels in the published figure, but Dr. Pichiorri claimed that the duplication was an honest error. It is not clear when the data used for the correction of Figure 4A were generated, since these films are undated, and another film on Document 2, page 1 is dated 09/26/2009, while the films on Document 2, page 2 are dated 09/10/2008. Both dates precede the submission of the Cancer Cell paper, which was April 19, 2010.
- 9) Additionally, on the external hard drive sequestered from Dr. Croce's laboratory on 07/20/19, a file labeled "Data Fig.4A MM-1S P53-MDM2-P21" was discovered.⁹³ This document contains a scan of the films that completely matches page 1 of 20180412_Document 2, except there is an additional p21 blot on the page and handwritten text, slightly illegible, that appears to state "look at figure in the 2016 correction." The 'last date modified' of the file located in the sequestered data is 05/12/17, while the date of creation of the "Document 4"⁹⁴ is 06/30/2016.
- 10) Also on the external hard drive sequestered from Dr. Croce's laboratory on 07/20/19, a file labeled "Data Fig.4A H929 P53-MDM2-P21" was discovered.⁹⁵ This document contains a scan of the films that completely matches page 2 of 20180412_Document 2, except the p21 blot has only five lanes compared to 7 lanes in Document 2 and the handwriting, while describing the same experimental conditions, is also different. Lastly, in Document 2, page 2, there is a GAPDH blot that is not present in the sequestered electronic scanned file document. The 'last date modified' of the file is 05/12/17, while the date of creation of the "Document 4"⁹⁶ is 06/30/2016.
- 11) The duplicated data published in Figure 4A for the MDM2 MM1s panel did not drastically change the reported results, since the corrected figure for the MDM2 MM1s showed the same relative expression pattern.
- 12) Thus, the forensic analysis and review of Document 2 show that for Figure 4A, it seems that contemporaneous data existed for the data reported for MDM2 in NCI-929 cells. However, this data was incorporated into Figure 4A MDM2 NCI-929 panel with a vertical flip which did not affect the

⁸⁹ Ex. 90 - 20180412_Document 2

⁹⁰ Ex. 123 - COMIC Figure Forensics_Pichiorri

⁹¹ Ex. 5 - Correction-Cancer Cell 2010

⁹² Ex. 123 - COMIC Figure Forensics_Pichiorri

⁹³ Ex. 180 -Data Fig.4A MM-1S P53-MDM2-P21

⁹⁴ Ex. 134 - 20190410-Documents-Folder 4, Fig.4A

⁹⁵ Ex. 181- Data Fig.4A H929 P53-MDM2-P21

⁹⁶ Ex. 134 - 20190410-Documents-Folder 4, Fig.4A



overall reported results. The same data were also used for the 4 lanes for MDM2 in MM1s cells, and also flipped in relation to the scanned film. When the duplication was identified, it appears that original data for MDM2 in MM1s was identified, and these data were then used for the correction of Figure 4A in Cancer Cell in August 2016. The corrected Figure 4A for MDM2 in MM1s showed the same trends of MDM2 expression as the original published Figure 4A, so overall the duplication did not change the reported experimental results.

- 13) From the data provided by Dr. Pichiorri in Document 2 (and subsequently renamed as Document 4⁹⁷ in her April 10, 2019 response to the COMIC), it appears that Dr. Pichiorri's standard practice for record keeping of Western blots was to cut out small pieces of autoradiography film (i.e., the bands of interest) and tape them to a blank piece of paper. In the case of Figure 4A, the films were sometimes undated, the experimental treatments and cell types were not always noted on the films, and sometimes the treatments and protein of interest were scribbled on the paper and not the film. The slightly different versions of the scanned data discovered in the two files on Dr. Croce's external hard drive⁹⁸ further lead the COMIC to question the dates and accuracy of the scanned documents. The COMIC finds this method of data storage to be very confusing and disorganized. In addition, Dr. Pichiorri did not correlate these data with a laboratory notebook or other research record to describe how the experiments were actually performed. Based on the COMIC's expertise and experience, the method of data storage and lack of descriptive record keeping could lead to choosing incorrect data when generating figures for publication.
- 14) As the COMIC reviewed Figure 4A, the COMIC also noted that the graphical representation of the densitometric quantification analysis in Figure 4B and 4C relies on accurate Western blots being analyzed and therefore the data in Figure 4B/C could be impacted by the false images in Figure 4A. The quantifications in Figure 4B and 4C would require multiple biological replicates to be scientifically valid. When asked about the densitometric analysis⁹⁹, Dr. Pichiorri stated that the experiments were run numerous times, but she was unable to recall the specifics of the experiments performed to quantitate the data, nor did she provide any data related to the quantification. Dr. Pichiorri also could not answer the questions related to the COMIC being unable to replicate the quantitative data when Dr. Burghes examined the films shown in Figure 4A¹⁰⁰.
- 15) The COMIC performed their own Image J analysis on the published and corrected MDM2 blots for Figure 4A.¹⁰¹ Overall, from its own analysis, the COMIC found that the corrected blot for MDM2 for the MM.1S cell line is similar but not identical to the graphical representation shown in Figure 4B. However, for NCI-929 cells in Figure 4C, the COMIC analysis produced results that were different from the published Figure 4C. In particular the two scrambled controls were different and both could not be set at 1 and the miR data was slightly different in relative intensity. Importantly, the COMIC determined that it was not possible to generate error bars for the graphical representation in either Figure 4B or 4C, since there were no replicate data provided. Thus, it is unclear to the COMIC how error bars are present on the published Figure 4B and 4C. The COMIC is therefore cannot verify the accuracy of the data represented in Figures 4B and 4C.

⁹⁷ Ex. 134 - 20190410-Document-Folder 4, Fig.4A

⁹⁸ Ex. 179 -Flavia Cancer Cell Data Folder

⁹⁹ Ex. 165 - 20190513 - COMIC Interview + Errata – Pichiorri, pages 42-45

¹⁰⁰ Ex. 182 - COMIC Quantification Analysis_Cancer Cell

¹⁰¹ Ex. 182- COMIC Quantification Analysis_Cancer Cell



Respondent's Response:

- 1) In her interview with the CII on April 13, 2018, when questioned about Cancer Cell Figure 4A, Dr. Pichiorri stated that she put together Figure 4A and admitted that she was responsible if there is a mistake in the figure.¹⁰²
Dr. Pichiorri: *"But if there is a mistake, I made a mistake, because I did -- I put together this thing."*
CII member: *"Okay, So you prepared the figure?"*
Dr. Pichiorri: *"It's not – yes. It is my fault."*
- 2) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that the reason for the mistake was being overwhelmed with work, difficulties using Photoshop, and a lack of scanners in Dr. Croce's laboratory.¹⁰³
- 3) In her written response, provided to the CII on April 12, 2018¹⁰⁴, Dr. Pichiorri stated that original data films were with the editor of Cancer Cell but Dr. Pichiorri was able to provide scans of those films as "Document 2".¹⁰⁵ Dr. Pichiorri stated that the mistake was because she did not have *"large high resolution screens nor the experience to assemble complicated manuscripts."*
- 4) In her written response, provided to the CII on April 12, 2018¹⁰⁶, Dr. Pichiorri further explained that her *"computer skills to work on imaging software were extremely limited"* and that she *"asked for help but unfortunately we did not have more experienced laboratory personnel to help us."*
- 5) In her written response, provided to the COMIC on April 10, 2019¹⁰⁷, Dr. Pichiorri stated that the mistake in Figure 4A has been corrected. Dr. Pichiorri further stated that as there is original data supporting the conclusion, there was no reason to falsify the blot, and the duplication occurred as a result of an honest error.
- 6) In her interview with the COMIC on May 13, 2019, Dr. Pichiorri was asked how a single Western blot was used to make a panel that contained four lanes (in the MM1s) and also used to make a panel that contained five lanes (in NCI-929). Dr. Pichiorri stated that sometimes the same Western blot film was scanned multiple times and that she was determining which lanes to capture directly in the scanner machine by selecting specific lanes to scan, and not scanning the entire film.¹⁰⁸ Dr. Pichiorri explained that this method of scanning partial Western blot films was done because the whole image was too large to fit on her memory key (i.e., flash drive).

Respondent's Responsibility:

- 1) Dr. Pichiorri is listed as a co-first author on Cancer Cell 2010 [REDACTED]. In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that she did put together Figure 4A and that if a mistake occurred it was her fault.
- 2) [REDACTED]
- 3) Thus, since Dr. Pichiorri admitted that she was the person who generated Figure 4A, the COMIC finds that as co-first author, she had the responsibility to ensure that all figures included in the publication were correct.

¹⁰² Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 37 lines 3-8

¹⁰³ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 37-38

¹⁰⁴ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations

¹⁰⁵ Ex. 90 - 20180412_ Document 2

¹⁰⁶ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations

¹⁰⁷ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 5

¹⁰⁸ Ex. 165 - 20190513-COMIC Interview + Errata, page 19 (lines 18-20), page 22 (lines 24-25), page 23 (lines 17-25), page 24 (lines 1-

6).
¹⁰⁹ [REDACTED]



Respondent's Intent:

- 1) Dr. Pichiorri admitted to putting the figure together. The COMIC found Dr. Pichiorri's claims that the duplication in the published figure was a mistake not credible since other inaccuracies in the construction of the published figure were identified. The published figure used the raw data for the MDM2 NCI-929 panel for both the NCI-929 and MM1s cell types, and both panels were in an upside down orientation compared to the raw data. According to Dr. Pichiorri's responses, the correct raw data for MDM2 in MM1S cells existed, but it was not used and then it was found and used for the correction. While the inaccuracies in the figures did not alter the overall reported results, the COMIC found Dr. Pichiorri's poor data management practices very concerning.
- 2) It appears that original data for the MDM2 in MM1s was identified and used for the correction of Figure 4A in Cancer Cell, in August 2016. The COMIC cannot determine whether Dr. Pichiorri had these data when the original Figure 4A was constructed. At best, the data were not readily available and were then found at a later time when the correction was made. At worst, these data were not available when Figure 4A was constructed, and the experiments were performed at a later time.
- 3) Since the COMIC cannot determine what occurred for the duplication of the MDM2 data in the original figure, the COMIC concludes that Dr. Pichiorri's poor data management practices created a risk for false data to be included in Figure 4A. The COMIC determined that Dr. Pichiorri was aware, or should have been aware, that there was an increased risk of false data being used or generated since the risk would be obvious for a typical researcher at Dr. Pichiorri's level of experience, but nevertheless Dr. Pichiorri selected and used the incorrect data for the published figure. The following facts support this conclusion:
 - a. In her written response, provided to the CII on April 12, 2018¹¹⁰, Dr. Pichiorri stated that she had limited skills in imaging software and that she asked for help, but did not receive any. The COMIC believes that Dr. Pichiorri's act of asking for help on the imaging software indicates that she was aware of her limited abilities. The COMIC believes that a typical researcher at Dr. Pichiorri's level would know that continuing to make figures and publish data with her limited skills could result in the use of false data in constructing the figures.
 - b. In her written response, provided to the COMIC on April 10, 2019¹¹¹, Dr. Pichiorri stated that she had never prepared a manuscript completely by herself before, which is a fact she would have known at the time when she was generating the figures for publication. For any researcher publishing their first manuscript, the COMIC believes, based on their experience, that a typical researcher at Dr. Pichiorri's level (a post-doctoral researcher) would have taken extra time to review and double check the research data for accuracy.
 - c. In her April 10, 2019 written response to the COMIC,¹¹² Dr. Pichiorri wrote that her practice was to save small cropped images on memory keys and create the subpanels for the figures in Cancer Cell by looking at raw data she had or PowerPoint slides that she or others generated, to "match by eye sight alone" the cropped panels with the correct raw data. Dr. Pichiorri claimed she did not have access to a printer or a big screen to compare images, and this caused her unintentional mistakes. The COMIC believes these practices are inconsistent with practices of a typical researcher at Dr. Pichiorri's level..
 - d. The COMIC determined that Dr. Pichiorri's method of taping small pieces of autoradiography film to white paper with inconsistent and often incomplete labeling, as shown in the data Dr. Pichiorri provided as "Document 2" for Figure 4A, are practices that are inconsistent with appropriate practices of a typical researcher at Dr. Pichiorri's level.

¹¹⁰ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations, page 1

¹¹¹ Ex. 128- Pichiorri point-by -point April 10th-2019, page 4

¹¹² Ex. 128 - Pichiorri point-by -point April 10th-2019, page 4



- e. Based on the limited data provided, it appears that Dr. Pichiorri had the data for MDM2 in MM1s, which was ultimately used in the correction for Figure 4A. The COMIC has determined that as the co-first author on Cancer Cell, Dr. Pichiorri had the opportunity to prevent the falsification if she had reviewed the available raw data for MDM2 in MM1s cells that appears to have existed at the time and if she had reviewed the raw data and figures included in Cancer Cell prior to publication, but she did not.
 - f. Dr. Pichiorri constructed the MDM2 panels in Figure 4A using the data from the film that was in Document 2, page 2, labeled as "TOT MDM2." The film had 7 lanes of data, with labels over each lane on the film for the different microRNA treatments. The published Figure 4A included the MDM2 panel for NCI-929 cells (with 5 lanes, vertically flipped) that was reused for MM1s cells (with 4 lanes, vertically flipped). The COMIC found that even if Dr. Pichiorri used the small cropped image as she claimed, the labeling on the film would have made it clear to her which of the 7 lanes should be used, which panels represented which miRNA treatments and cell types, and whether the image was vertically flipped. The COMIC believes that Dr. Pichiorri disregarded the risk that a false image could be included in Figure 4A by ignoring the labels on the films and that a reasonable researcher in this community would ensure that the correct data, in the correct orientation, were included in the original published figure.
 - g. At the time the questioned manuscript was published, Dr. Pichiorri was in her third year of postdoctoral training. The COMIC believes that someone at this level of training should have had the knowledge of how to generate figures properly and use practices for storing data that would not lead to such confusion.
- 4) The COMIC found that the increased risk of false data being used or generated due to the poor practices and methods employed by Dr. Pichiorri is clearly demonstrated by the indisputable fact that the same issue of the reuse of data for different experiments occurred five separate times in the Cancer Cell 2010 publication alone (this allegation and below). The scope of numerous falsifications leads the COMIC to believe that the cause of this instance of falsification goes beyond a mistake, as claimed by Dr. Pichiorri, or "sloppy science", or even negligence, and instead demonstrates a pattern of reckless Research Misconduct by Dr. Pichiorri.

Significance:

The Committee determined that Dr. Pichiorri's reckless actions caused the falsification of Figure 4A in Allegation #2, as described above. The falsified data did not drastically change the reported results, as the falsified data showed roughly the same expression pattern and supported similar conclusions as the original raw data provided by Dr. Pichiorri. Thus, the significance of this duplication of data to the reported results is relatively minor. However, Dr. Pichiorri's improper laboratory practices led to the falsification of Figure 4A, where the original MDM2 NCI-929 was vertically flipped compared to the raw data, the correct MDM2 MM1s panel appears to have existed but was not used in constructing Figure 4A, and instead the MDM2 NCI-929 panel was cropped to 4 lanes and reused for the MM1s cells. Further, the COMIC notes that as the graphical representation of the densitometric quantitative analysis shown in Figures 4B/C relies on the correct representation of Western blots in Figure 4A, there is a potential impact on the graphical data reported in Figures 4B/C, which increases the significance of the falsification of Figure 4A. The consequence of the incorrect blot being used for the MM1s MDM2 lanes in Figure 4A is that a scrambled (Scr) sample (shown in MDM2 NCI-929, lane 2) was used as miR194 in MDM2 MM1s. Furthermore, the correction for the MDM2 blot for the MM1S cells now shows miR194 expression as lower than Scr expression with nearly zero expression of miR192 and miR215, whereas the original falsified blot showed a more equal expression of miR194 and Scr with a near equal decrease of expression of miR192 and miR215. The falsification deviated from accepted practices of the relevant research community as it is not acceptable, nor is it standard practice, to reuse and relabel data to represent two different experimental conditions and proteins.



Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 8 in favor to 0 against, that the Respondent recklessly falsified Figure 4A and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #1, Allegation #3 - F. Pichiorri falsified Figure 5A by the reuse of the same data in the p53 blot for Scr/5-10 μ M lanes (lanes 3 and 4) and in the p53 blot for miR-194/2.5-5 μ M lanes (lanes 2 and 3) in Pichiorri et al., Cancer Cell 2010.

Finding of Fact:

- 1) Figure 5A shows the effects of the miRNA inhibitor MI-219 at different doses (0-10 μ M) on MM1s cells transfected with different miRNAs and a scrambled control (Scr), for the expression of p53, MDM2, α -Puma, p21, and GAPDH levels (see slide #9¹¹³).
- 2) Adobe Photoshop forensic overlay analysis shows that the Scr/5-10 μ M MI-219 (lanes 3 and 4) are identical to the miR-194/2.5-5 μ M MI-219 (lanes 2 and 3) for the p53 panels in Figure 5A (see slide #10¹¹⁴), which is not scientifically valid as the cell types and treatments are completely different.
- 3) Dr. Pichiorri provided scans of films on April 12, 2018, purportedly representing the original data for Figure 5A, labeled as Document 3.¹¹⁵ Document 3 contains 5 pages, with various sections of film taped to each of the pages.
- 4) Document 3, page 1, has hand-written labels on the page for "Fig 5A," " α p53," " α GAPDH," "MI-219 (MM1s) cells" and "0-2.5-5-10 μ M (24 hrs)" and four sections of films are taped to page 1. Two films are labeled for p53 with one dated 05/16/2009, and 2 films are labeled for GAPDH with one dated 05/18/2009. The 4 films are also labeled with the specific miRNA and the dose response for treatment with "Nutlin." The published Figure 5A indicates treatment with "MI-219" (see slide #11¹¹⁶).
- 5) The COMIC does not know whether these hand-written labels on the films or on the page of Document 3, were added when the experiments were performed or at a later time. Regardless, the COMIC finds the labeling for both "MI-219" on the paper, and "Nutlin" handwritten on the films is confusing and contradictory.
- 6) Based on the films provided by Dr. Pichiorri in Document 3, page 1, the p53 blot for the miR-194 panel was the data used in the published Figure 5A, however the labeling of the drug treatment on the top of the film indicates "Nutlin", and the published Figure 5A is reported as MI-219 treatment (see slides #11 and #12¹¹⁷).
- 7) Based on the films provided in Document 3, page 1 (2nd film from top), the p53 blot for the Scr panel also existed, albeit also labeled as treatment with "Nutlin" instead of MI-219. However, the Scr data was not used and instead the published Scr panel was constructed using the miR-194 treatment panel's (Document 3, page 1, top film) three contiguous lanes (lanes for 0, 2.5 and 5 μ M treatment) plus a blank section of the autoradiography film taken from between 0 μ M and the ladder markers) (see slide #11¹¹⁸).
- 8) The original raw data for the Scr control (Document 3, page 1) showed a very slight increase in p53

¹¹³ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹¹⁴ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹¹⁵ Ex. 91 -20180412_ Document 3

¹¹⁶ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹¹⁷ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹¹⁸ Ex. 123 - COMIC Figure Forensics_Pichiorri



expression in the 2.5 μ M lane.¹¹⁹ The duplicated 194 treatment data used for the published Scr panel showed no p53 expression in the 2.5 μ M treated lane. The falsified published Scr panel more convincingly supported the hypothesis of the figure that is an increase of p53 expression in miRNA-transfected cells treated with MI-219 when compared to control (Scr treated) cells, whereas the original Scr data showed a similar, but not as convincing, pattern of expression.

- 9) Nutlin and MI-219 are two different MDM2 inhibitors, so while they perform similar functions, the published Figure 5A does not match the experimental treatment indicated by the original labeling and thus misrepresents the experimental conditions used.
- 10) The COMIC also noted that the films themselves for Figure 5A for MDM2¹²⁰ were labeled for "Nutlin", the films for α -puma¹²¹ were labeled for "Nutlin" and "Nutlin 3a", and the films for p21¹²² were unlabeled for treatment type.
- 11) As the COMIC reviewed Figure 5A, the COMIC noted that the graphical representation of the densitometric quantification analysis in Figure 5B relies on accurate Western blots being analyzed and therefore the data in Figure 5B could be impacted by the false images published in Figure 5B. Since there was no raw data provided to show the generation of the densitometry quantification, the COMIC is unsure of the accuracy of the data represented in Figure 5B.

Respondent's Response:

- 1) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that she put together Figure 5A and there was a mistake¹²³ and that the reason for this mistake was being overwhelmed with work and a lack of supervision.¹²⁴
- 2) Conversely, in her written response provided to the COMIC on April 10, 2019¹²⁵, Dr. Pichiorri stated that she did not remember who performed the Western blots for Figure 5A or who scanned and acquired the subpanels for Figure 5A. Dr. Pichiorri wrote that she only remembered that she included the entire Figure 5A with the sub-panels in Photoshop. The COMIC finds that Dr. Pichiorri's interview and written statements are inconsistent and therefore not reliable.
- 3) In her written response to the CII on April 12, 2018¹²⁶, Dr. Pichiorri stated that she provided the original data (as "Document 3"¹²⁷) and the data supported the scientific conclusions.
- 4) In her written response provided to the COMIC on April 10, 2019,¹²⁸ Dr. Pichiorri disagreed with the CII conclusion that the entire Figure 5A is a misrepresentation because the original films she provided are labeled with "Nutlin" treatment versus MI-219 labeling in the published Figure 5A. Dr. Pichiorri explained that the experiments were reported correctly and the labeling on the films was a "superficial mistake" and should have been labeled with MI-219, not Nutlin.
- 5) In her written response, provided to the COMIC on April 10, 2019¹²⁹, Dr. Pichiorri stated that she now knows that Nutlins (a cis-imidazoline analog) and MI-219 (a spiro-oxindole analog) are different compounds, but at the time the paper was published, the structural information about MI-219 was

¹¹⁹ Ex. 91 - 20180412_ Document 3, page 1

¹²⁰ Ex. 91 - 20180412_ Document 3, page 2

¹²¹ Ex. 91 - 20180412_ Document 3, pages 4-5

¹²² Ex. 91 - 20180412_ Document 3, page 3

¹²³ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 40

¹²⁴ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 41 lines 1-5

¹²⁵ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹²⁶ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations, page 1

¹²⁷ Ex. 92 - 20180412_ Document 3

¹²⁸ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹²⁹ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6



unknown and MI-219 was only referred to as “a small molecule inhibitor of the MDM-p53 interaction.” Thus, she called all the small molecule inhibitors able to block MDM2 and induce p53, collectively “nutlins”.

- 6) The COMIC notes that after Dr. Pichiorri provided the original films for Figure 5A in 2018, which were labeled with “Nutlin,” she justified why these films were not labeled with MI-219 by stating that there was not enough known about MI-219 when the Cancer Cell paper was published in 2010. However, the COMIC reviewed a 2008 PNAS paper (Shangary, S., *et al.* PNAS 105:3933-3938, 2008)¹³⁰ that was referenced in the Cancer Cell paper, and found that the 2008 PNAS paper clearly describes MI-219 as a new class of MDM2-p53 inhibitors that is promising for cancer therapy. The 2008 PNAS paper also provides the chemical structures for MI-219 and Nutlin-3a in Figure 1A. Thus, the COMIC finds that Dr. Pichiorri’s statements regarding her understanding of the difference between the two compounds not credible.
- 7) Further, in her written response provided to the COMIC on April 10, 2019,¹³¹ Dr. Pichiorri wrote that “*she asked for and received*” MI-219 from Dr. Shaomeng Wang’s laboratory to perform oral gavage experiments on mice, and received a specific laboratory protocol from Dr. Wang that she provided as Document 6 with the response.¹³² The COMIC finds that since Dr. Pichiorri requested the compound and referenced the PNAS paper in Cancer Cell and in her response to the COMIC, she had to have known that MI-219 was a separate and distinct compound from Nutlin and which was well-described by Dr. Wang’s group in 2008.
- 8) In her written response, provided to the COMIC on April 10, 2019¹³³, Dr. Pichiorri justified that the films labeled with Nutlin were actually experiments performed with MI-219 and stated that “*We did not write MI-219 for other experiments when we specifically used Nutlin-3A in which we wrote the specific name of the compound “Nutlin-3A”*”. Thus, Dr. Pichiorri claimed the hand-written notation on Document 3, page 1 for “MI-219” is the correct treatment, because if Nutlin had been used for the experiment, the films would be specifically labeled as “Nutlin-3A” not simply “Nutlin.”
- 9) The COMIC found this statement to be inconsistent with a review of films provided by Dr. Pichiorri for other experiments that did represent treatment with Nutlin-3A. Specifically, in the April 10, 2019 response, Dr. Pichiorri included a folder (Document 4) for data for Figure 4A in Cancer Cell 2010¹³⁴ in which 2 files were included; “Data Fig4AH929p53-MDM2” and “Data Fig.4A MM-1s p53-MDM2.” The published Figure 4A is an experiment using “Nutlin 3a” treatment and the films supporting this experiment are simply labeled with “Nutlin”, similar to the films supporting Figure 5A.
- 10) Further, Dr. Pichiorri stated in the April 10, 2019 response, that even the mouse experiments that were done with MI-219, were labeled in the record as “Nutlin”, because MI-219 was “*the only compound that could have been used in the animal, as Nutlin, which is only soluble in pure DMSO, would have killed them immediately or made them extremely sick.*”¹³⁵ In its review, the COMIC found a review paper published in 2004 (Vassilev, L.T. *et al.*, *Science*, 303:844-848, 2004¹³⁶) describing the use of Nutlin *in vivo* with an oral dose of Nutlin-3 for 20 days tolerated well by nude mice. In addition, the COMIC found that studies in other fields have also used DMSO to solubilize drug compounds for *in vivo* use (Naryshkin *et al* *Science* (2014) 8;345(6197):688-93¹³⁷). The COMIC believes that a typical researcher at Dr. Pichiorri’s level of experience would perform a literature search if the use of

¹³⁰ Ex. 171 – Shangary *et al.* PNAS (2008) 105:3933-3938

¹³¹ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹³² Ex. 136 - 20190410-Document 6 MI-219 for Oral Dosing

¹³³ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹³⁴ Ex. 134 - 20190410-Document-Folder 4 Fig.4A

¹³⁵ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹³⁶ Ex. 172 – Vassilev *et al.*, *Science* (2004) 303:844-848

¹³⁷ Ex. 190 - Naryshkin *et al* *Science* (2014) 8;345(6197):688-93



a new compound was being proposed for *in vivo* experiments and Dr. Pichiorri would have known that DMSO could be used *in vivo*. Thus, Dr. Pichiorri's justification that MI-219 had to have been used for an *in vivo* experiment, lacks credibility and there is no reason to believe that a film labeled "Nutlin" represented results of experiments performed with MI-219.

- 11) Thus, the COMIC finds Dr. Pichiorri's statements regarding why the research record includes a "Nutlin" label when the experiments were done with MI-219 not credible. The COMIC also finds that none of the evidence provided by Dr. Pichiorri verify that experiments with MI-219 were ever performed and thus, the lack of research records is evidence that the entire Figure 5A is false and is a significant departure from accepted practices of this research community.

Respondent's Responsibility:

- 1) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that she put together Figure 5A.¹³⁸
- 2) Conversely, in her interview with the COMIC on May 13, 2019, Dr. Pichiorri claimed that she "didn't do Figure 5A" and that other unnamed students and visiting scholars made the figures and did the experiments because she had been put on different projects by her PI, Dr. Croce.¹³⁹
- 3) Dr. Pichiorri was listed as a co-first author on Cancer Cell [REDACTED]
- 4) The COMIC noted that the labeling on the source data films provided by Dr. Pichiorri appears to be the same, and it is more likely than not labeling by Dr. Pichiorri, since similar notations are on documents for all of the allegations under review for Cancer Cell and for documents of other manuscripts under review (JEM 2013-see exhibit Document-Folder 11 Nucleolin RNA¹⁴¹, pages 1-6, which Dr. Pichiorri states come from her own lab notebook The COMIC believes that this shows that Dr. Pichiorri was involved in performing the experiments for Figure 5A and she would have known what the raw data looked like that should have been used to construct the figure.

Respondent's Intent:

- 1) Although Dr. Pichiorri provided raw data for similar experiments as those included in Figure 5A, there are concerns with these data. The raw data films are labeled for "Nutlin", not "MI-219" as reported in the published figure, and the COMIC is unable to determine when the single handwritten notation on Document 3, page 1 for "MI-219" was added to the page. In addition, Dr. Pichiorri did not provide any evidence that experiments using "MI-219" had been performed except to provide a single laboratory protocol for the preparation of the "MI-219" compound.¹⁴²
- 2) The COMIC determined that a careful review of the responses from Dr. Pichiorri (see above) to explain why the films were labeled with "Nutlin" show numerous inconsistencies, lack scientific validity and are not credible.
- 3) In addition, the COMIC determined that even if Dr. Pichiorri's explanation regarding the "Nutlin" labeling were credible, and it is not, the duplication of the p53 miR194 panel and the p53 Scr panel could not have occurred as a result of an honest mistake for the following reasons:
 - a. The COMIC believes that Dr. Pichiorri was involved with all the data for Figure 5A, by putting the subpanels into Photoshop, as she admits, and likely labeling the sections of films for Figure 5A that she provided, which all appear to have the same hand writing.
 - b. The COMIC finds that the data for the p53 Scr panel (albeit labelled as Nutlin treatment) were

¹³⁸ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 40

¹³⁹ Ex. 165 - 20190513-COMIC Interview + Errata - Pichiorri, page 26 (lines 21-25), pages 27-28

¹⁴⁰ [REDACTED]

¹⁴¹ Ex. 141- 20190410-Document-Folder 11 Nucleolin RNA

¹⁴² Ex. 136 - 20190410-Document 6 MI-219 for Oral Dosing



taken from different lanes from labeled raw data of the miR194 film, (including a blank lane)). The films were labeled to show the cell type and dosage.

- c. The duplication provides a figure that better supports the hypothesis.
- 4) Based on these facts, the COMIC finds that Dr. Pichiorri committed intentional and/or knowing falsification of data by using data for an experiment performed with another treatment than the treatment reported in Figure 5A and by reusing the same incorrect raw data for both the miR194 and Scr p53 Western blot panels.

Significance:

The Committee has determined that Dr. Pichiorri's intentional and/or knowing actions caused the falsification of Figure 5A in Allegation #3, as described above. The data as presented do alter the interpretation and conclusions since the re-use of the miR194 p53 lanes for the scrambled p53 lanes presents the wrong concentration of drug in the Scr panel and exaggerates the differences between the miR treatment and the control (Scr). In particular, the authors intended to show that expression of the miRs 192,194, and 215 in the presence of MI-219 resulted in an increase in p53 expression and a decrease in MDM2 expression. However, the falsification of the controls (Scr) alters the reported result and there is no valid control to compare with the miR treatment. As such, one does not know whether p53 is increased with miR treatment and whether low concentrations of drug treatment change the sensitivity of the MM1s cells through altering p53, a major hypothesis of the paper. As the graphical representation of the densitometric quantification analysis shown in Figure 5B relied on the integrity of Western blots presented in Figure 5A, there is potential that the data in Figure 5B has also been impacted. The falsification of the figure deviated from accepted practices of the relevant research community as it is not acceptable, nor is it standard practice, to reuse and relabel data to represent two different experimental conditions and proteins.

Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 8 in favor to 0 against, that the Respondent intentionally and/or knowingly falsified Figure 5A and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #1, Allegation #4 - F. Pichiorri falsified Figure 5A by the reuse of the same data in the Western blot for p53/miR-192 and in the Western blot for alpha-puma/miR-192 in Pichiorri et al., Cancer Cell 2010.

Finding of Fact:

- 1) Adobe Photoshop gradient mapping and forensic overlay analyses show that the blot published for p53 for miR-192 is identical to the alpha-puma blot for miR-192 in Figure 5A, which would not be scientifically valid as p53 and alpha puma are different proteins (see slide #13¹⁴³).
- 2) The two blots are flipped vertically relative to each other.
- 3) The scan of the p53 films provided by Dr. Pichiorri on April 12, 2018 as "Document 3"¹⁴⁴ page 1, (2nd film strip on the page) appears to contain the data used to generate the p53 miR-192 published image (see slide #14). However, the scan clearly demonstrates that the experiment is labeled at the top of the film strips as treatment with "Nutlin", while the published Figure 5A reports treatment with "MI-219" (see slide #14¹⁴⁵). "Document 3", page 1, has "MI-219" hand-written on the page, but "Document 3", page 4 has "Nutlin 3A" written on it, while all films labeled for treatment are labeled for "Nutlin".

¹⁴³ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹⁴⁴ Ex. 91 - 20180412_Document 3

¹⁴⁵ Ex. 123 - COMIC Figure Forensics_Pichiorri



- 4) The COMIC does not know whether the hand-written labels on the films, or on the paper, were added when the experiments were performed or at a later time.
- 5) The scans of the alpha puma blots provided by Dr. Pichiorri on April 12, 2018 as "Document 3", page 4 do not appear to contain the data used to generate the alpha-puma miR-192 published image or any of the published alpha-puma blots as the experimental set up is different than the published figure (i.e., the samples are grouped by drug concentration rather than grouped by miR treatment type). Additionally, the alpha-puma blots on page 4 do not contain any 2.5 μ M treatment samples, while the published Figure 5A does.
- 6) Upon review, the alpha-puma blots on "Document 3", page 5 do not appear to be the data that was published, nor do they support the hypothesis of the paper. The scans show "dirty" blots and the arrow presumably pointing to the alpha-puma band shows protein expression only at the highest treatment dose of 10 μ M "Nutlin," compared to the published Figure 5A, which shows alpha-puma expression observable at the lower treatment dose of 2.5 μ M.
- 7) The original data for the alpha-puma expression blots were not located by the Respondent.
- 8) In her written response provided to the COMIC on April 10, 2019,¹⁴⁶ Dr. Pichiorri provided the first generation of Figure 5A, where the alpha-puma expression experiment was not included in the composite figure, and which shows a creation date of April 15, 2010.¹⁴⁷
- 9) In her written response, provided to the COMIC on April 10, 2019,¹⁴⁸ Dr. Pichiorri provided the second generation of the figure, where the alpha-puma expression blots were included in a composite figure, and which shows a creation date of June 3, 2010.¹⁴⁹

Respondent's Response:

- 1) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that she put together Figure 5A and admitted that she mistakenly flipped and reused the image.¹⁵⁰
Dr. Pichiorri: *"That's just -- I made -- I told Dr. Croce I made this mistake when I put together the figure. It's not that I lied. I know that."*¹⁵¹
- 2) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that the reason for this mistake was being overwhelmed with work and being pressured by Dr. Croce to get it done.¹⁵²
Dr. Pichiorri: *"Did I make these mistakes when I flipped? Yes, I did. Why I did it? Too much by myself. It was too much. Too much. That's it."*¹⁵³
- 3) In her interview with the CII on April 13, 2018, Dr. Pichiorri also stated she was not getting help from her co-authors and that she could not stay late every night anymore because she had a child at home.¹⁵⁴
- 4) In her written response provided to the CII on April 12, 2018,¹⁵⁵ Dr. Pichiorri stated that original data scans were provided (as "Document 3"¹⁵⁶) but that she believes the lysates were run again since the alpha-puma signal was not clean. Dr. Pichiorri indicated that the experiments were repeated

¹⁴⁶ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹⁴⁷ Ex 131- 20190410-Document-Folder 1 Manuscript 1 Tiff small panels and Sup. Fig., "Fig 5a"

¹⁴⁸ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹⁴⁹ Ex. 131- 20190410-Document-Folder 1 Manuscript 1 Tiff small panels and Sup. Fig. , "Fig 5a-after first review"

¹⁵⁰ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 40 lines 12; page 42 line 23-24

¹⁵¹ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 43 lines 3-5;

¹⁵² Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 43 lines 1-5;lines 13-24, page 44 lines 10-12

¹⁵³ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 42 lines 23-24, page 34 lines 1-2

¹⁵⁴ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 43 lines 16-24; see errata from Dr. Pichiorri on page 109

¹⁵⁵ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations, page 2

¹⁵⁶ Ex. 91 - 20180412_ Document 3



numerous times and supported the scientific conclusions. The data provided by Dr. Pichiorri shows only 2 runs of the alpha-puma experiment.

- 5) Conversely, in her written response provided to the COMIC on April 10, 2019,¹⁵⁷ Dr. Pichiorri stated that she included the entire subpanel of Figure 5A into Figure 5 in Photoshop but that she did not remember who did the experiment or scanned in the individual panels. The COMIC finds that Dr. Pichiorri's interview with the CII and the COMIC are inconsistent and therefore her statements are not reliable.
- 6) As described in Allegation #3 above, Dr. Pichiorri does not think the entire Figure 5A is a misrepresentation due to the labeling on the raw data as "Nutlin" versus the published Figure 5A representing MI-219 treatment.¹⁵⁸
- 7) In her written response provided to the COMIC on April 10, 2019,¹⁵⁹ Dr. Pichiorri stated that they were not able to find "*the original films or original scans of the puma ultimately used for the published figure.*" Dr. Pichiorri further stated that her concern is that "*a copy of these blots were in my personal laptop that broke in 2011 and Dr. Croce was not able to find the original films left in his laboratory from the person that performed the experiment.*" Dr. Pichiorri also stated that the fact that there are two generations of Figure 5A, one with and one without alpha-puma expression panels supports her belief that the blot "*was not kept with the rest of the original films since the Western blot was run later and the films scanned at separate times.*"¹⁶⁰ The COMIC believes that if the blots were kept in completely separate places, then there would have been little chance to mistakenly rescan the p53/miR192 blot and flip and reuse it as the published alpha-puma/miR192 blot.

Respondent's Responsibility:

- 1) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that she put together Figure 5A.
- 2) Conversely, in her written response provided to the COMIC on April 10, 2019,¹⁶¹ Dr. Pichiorri stated that she only included the entire subpanel of Figure 5A into Figure 5. The COMIC finds that Dr. Pichiorri's interview and responses with the CII and the COMIC are inconsistent and therefore her statements are not reliable.
- 3) Dr. Pichiorri was listed as a co-first author on Cancer Cell [REDACTED]
- 4) As stated in Allegation #3, which also involves Figure 5A, the COMIC notes that the labeling on the source data films provided by Dr. Pichiorri is the similar and it is more likely than not labeling from Dr. Pichiorri, since it is the same handwriting on documents for all of the allegations under review for Cancer Cell and for documents of other manuscripts in review (JEM 2013-see Ex. 141- Document-Folder 11 Nucleolin RNA¹⁶³, pages 1- 6, which Dr. Pichiorri states come from her own lab notebook). The COMIC believes that this documentation shows that Dr. Pichiorri was involved in the experiments performed for Figure 5A and would have known what the raw data looked like that should have been used to construct the figure.

Respondent's Intent:

- 1) The COMIC determined that since there was no evidence provided by Dr. Pichiorri to verify that any

¹⁵⁷ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹⁵⁸ Ex. 128 - Pichiorri point-by -point April 10th-2019,

¹⁵⁹ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹⁶⁰ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 7

¹⁶¹ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹⁶² [REDACTED]

¹⁶³ Ex. 141- 20190410-Document-Folder 11 Nucleolin RNA



experiments had been done with "MI-219", the lack of research records is evidence that the entire Figure 5A is false and is also a significant departure from accepted practices of this research community.

- 2) The COMIC believes that Dr. Pichiorri was involved with all the data for Figure 5A, by putting the subpanels into Photoshop, as she admits, and likely labeling the sections of films for Figure 5A that she provided, which all appear to have similar labeling. The COMIC finds that the alpha-puma mi192 blots (albeit labelled as Nutlin treatment) provided by Dr. Pichiorri did not support the hypothesis of Figure 5, where alpha-puma expression increases at a lower level. Further, the films and/or the paper to which they are taped, were labeled to show the cell type and dosage, suggesting that, if these data are accurate as claimed, Dr. Pichiorri would have known which film to include in the Photoshop subpanels.
- 3) The COMIC believes that based on Dr. Pichiorri's statement in her April 10, 2019 written response and the submission/revisions dates listed for Cancer Cell 2010, the difference between the first generation of Figure 5A (no alpha puma expression blots, April 15, 2010) and the second generation of Figure 5A (with alpha puma expression blots and containing the falsified data, June 2, 2010) suggests that including the false alpha puma blots might have been due to the author's urgency to get the paper published and/or respond to reviewer comments. The COMIC believes that this suggests motivation to falsify the alpha-puma data since the original raw data for the alpha-puma experiments provided by Dr. Pichiorri do not show as strong of a response as in the published figure (i.e., upregulation of alpha puma upon treatment and a negative response for the Scr (scrambled control) cells). The Cancer Cell paper also shows that there was a short turnaround time between submission (April 19, 2010) and revision (June 16, 2010).
- 4) Regarding the conclusions of Figure 5A, the text of Cancer Cell 2010 reads "*p53 re-expression and subsequent p21 and Puma upregulation was observed in these cells [miR-192 and 215] and in miR-194-transfected cells and is clearly visible following 24 hr of 2.5 mM MI-219 treatment (Figure 5A). In control cells (Scr), the treatment was ineffective (Figure 5A).*" As the conclusions as written in the paper do not align with the experimental results shown in the scanned films from Dr. Pichiorri (i.e., control treated cells (Scr) showed similar upregulation of alpha-puma as did experimental treated cells), the COMIC believes that the falsification was performed with the intent to mislead the readers to believe there was a stronger effect of the treatment with the miRs versus control than the original research records showed.
- 5) Based on these facts, the COMIC finds that Dr. Pichiorri committed intentional and/or knowing falsification of data by using data for an experiment performed with another treatment than the treatment represented in Figure 5A and by reusing the same incorrect raw data to represent p53 and alpha-puma in miR192 panels since the research record did not support the alpha-puma results.

Significance:

The Committee determined that Dr. Pichiorri's intentional and/or knowing actions caused the falsification in Figure 5A of Allegation #4, as described above. The falsified data for the alpha-puma blot changed the reported results by potentially altering interpretation of differences between p53 and alpha-puma expression in the miR192 panels treated with or without MI-219. Figure 5A has two data falsification allegations (Allegation #3 and Allegation #4). As the graphical representation of the densitometric quantification analysis shown in Figure 5B relies on the correct Western blots being shown in Figure 5A, there is a potential that the data in Figure 5B have also been impacted. The falsification deviated from accepted practices of the relevant research community as it is not acceptable, nor is it standard practice, to reuse and relabel data to represent two different experimental conditions and proteins. It was concerning to the COMIC that Dr. Pichiorri used film panels taped to a blank lab notebook page that indicated treatment strategies and the labels could have been added at any time. As first author, it was Dr. Pichiorri's responsibility to maintain the integrity of the data and to ensure that all notebooks were maintained using acceptable scientific practices.



Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 8 in favor to 0 against, that the Respondent intentionally and/or knowingly falsified Figure 5A and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #1, Allegation #5 - F. Pichiorri falsified Figure 7A by the reuse of the same data in the GAPDH Western blot in the left panel (MM1s WT TP53) and in the Akt Western blot in the right panel (RPMI-8226 Mut TP53) in Pichiorri et al., Cancer Cell 2010.

Finding of Fact:

- 1) Figure 7A shows the effect of miR-192, miR-194, miR-215, and a scrambled control (Scr) in WT TP53 (MM1s) and mutant (RPMI-8226) cell lines on the expression of IGF-1, IGF-1R, pS6, S6, pAkt, and Akt proteins with a GAPDH loading control (see slide #16¹⁶⁴).
- 2) Adobe Photoshop forensic overlay analysis shows that the blot for the GAPDH lanes in the left panel (MM1s WT TP53) is identical to the blot for the Akt lanes in the right panel (RPMI-8226 Mut TP53) (see slide #17¹⁶⁵). This would not be scientifically valid as the panels represent two different cell lines and different proteins.
- 3) Dr. Pichiorri provided scans of films on April 12, 2018 as "Document 4"¹⁶⁶ that included 3 pages with strips of film attached to each page. Page 1 of "Document 4" is dated 02/26/2009. The film scans on page 2 are labeled "α-Akt" and "GAPDH," (see slide #19¹⁶⁷); however, the Akt and GAPDH films in "Document 4" do not match the Akt and GAPDH panels published in the original published Figure 7A, although they show relatively the same equal expression pattern.
- 4) A correction for Figure 7A was published August 8, 2016.¹⁶⁸ In the correction the authors state, "*In addition, because multiple normalizations of the same set of samples were performed due to the use of phospho-antibodies, the authors inadvertently duplicated the *Gadph*¹⁶⁹ image of MM1s in the total Akt image of NCI-H929 in the same panel. The results were not affected by this duplication. The corresponding total Akt and *Gapdh* images used for pAkt normalization for both RPMI-8226 and MM1s are now included in the corrected Figure 7A.*"¹⁷⁰
- 5) The scans of films provided by Dr. Pichiorri on April 12, 2018 as "Document 4", page 1¹⁷¹ appear to contain the Akt and GAPDH films used for the corrected Figure 7A (see slide #20¹⁷²). "Document 4", page 1 contains hand-written labels for "new 7A (correction)", to indicate which strips of film were used in the correction. As the correction was published in 2016, the COMIC is unsure of when these data were created or when the labeling was added to the white piece of paper.
- 6) The correction of Figure 7A published by the authors indicates that a duplication had occurred in Figure 7A, but that it was an inadvertent error.

¹⁶⁴ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹⁶⁵ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹⁶⁶ Ex. 92 - 20180412_ Document 4

¹⁶⁷ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹⁶⁸ Ex. 5 - Correction-Cancer Cell 201

¹⁶⁹ Spelling error present in the published correction.

¹⁷⁰ Ex. 5- Correction-Cancer Cell 2010

¹⁷¹ Ex. 92- 20180412_ Document 4

¹⁷² Ex. 123 - COMIC Figure Forensics_Pichiorri



Respondent's Response:

- 1) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that she put together Figure 7A.¹⁷³ Dr. Pichiorri: *"I think I -- I -- I put together this figure. It was me. I put together the figure yes. But I did not do some of this western blot... I know that if there are mistakes in the generation of the figure, I must have done that, I think."*
- 2) In her written response provided to the CII on April 12, 2018¹⁷⁴, Dr. Pichiorri stated that she was providing copies of the original data ("Document 4"¹⁷⁵) to support the scientific conclusions. Dr. Pichiorri further stated that this was a copy of the original films that she had provided to the editor of Cancer Cell, which resulted in the journal publishing a correction.
- 3) In her written response provided to the COMIC on April 10, 2019, Dr. Pichiorri wrote, *"I do not recall who assembled and scanned the subpanels that I included from the photo-shop composite figures. To the best of my knowledge, I do not believe I was the individual who created the subpanel composite figure"* and Dr. Pichiorri also wrote, *"if mistakes occurred, they were only associated with our inexperience using graphic software, not due to an intent to falsify data to support incorrect scientific conclusions."*¹⁷⁶]

Respondent's Responsibility:

- 1) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that she believed she put together Figure 7A.¹⁷⁷
- 2) In her written response provided to the COMIC on April 10, 2019¹⁷⁸, Dr. Pichiorri stated that she does not believe she is the one who assembled and scanned the subpanels. The COMIC finds that Dr. Pichiorri modified her statements in the interviews with the CII and the COMIC and therefore questions Dr. Pichiorri's credibility.
- 3) Dr. Pichiorri was listed as a co-first author on Cancer Cell [REDACTED]

Respondent's Intent:

- 1) The COMIC was unable to confirm which data were used in the original Figure 7A for Akt and GAPDH. However, purportedly contemporaneous data provided by Dr. Pichiorri were used in the corrected Figure 7A and showed similar conclusions.
- 2) Since the COMIC cannot determine what occurred for the duplication of the Akt and GADPH panels in the original figure, the COMIC concludes that Dr. Pichiorri's poor data management practices created a risk for false data to be included in Figure 7A. The COMIC determined that Dr. Pichiorri was aware, or should have been aware, that there was an increased risk of false data being used or generated, since the risk would be obvious for a typical researcher at Dr. Pichiorri's level of experience, but nevertheless Dr. Pichiorri used the incorrect data. The following facts support this conclusion:
 - a. In her written response, provided to the CII on April 12, 2018,¹⁸⁰ Dr. Pichiorri stated that she

¹⁷³ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 45 lines 1-2

¹⁷⁴ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations

¹⁷⁵ Ex. 92 -20180412_ Document 4

¹⁷⁶ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 8

¹⁷⁷ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 45 lines 1-2

¹⁷⁸ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 6

¹⁷⁹ [REDACTED]

¹⁸⁰ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations, page 1



- had limited skills in imaging software and that she asked for help, but did not receive it. The COMIC believes that Dr. Pichiorri's act of asking for help on the imaging software indicates that she was aware of her limited abilities, which could cause her to publish incorrect figures..
- b. In her written response, provided to the COMIC on April 10, 2019¹⁸¹, Dr. Pichiorri stated that she had never prepared a manuscript completely by herself before, which is a fact she would have known at the time she was generating the figures for publication. The COMIC believes that Dr. Pichiorri, as a post-doctoral researcher publishing her first manuscript, should have taken extra time to review and double check the research data for accuracy, knowing that failure to do so could cause the publication of incorrect figures, and a reasonable researcher at Dr. Pichiorri's level would have done so.
 - c. In her April 10, 2019 written response to the COMIC,¹⁸² Dr. Pichiorri wrote that her practice was to save small cropped images on memory keys and create the subpanels for the figures in Cancer Cell by looking at raw data she had or PowerPoint slides that she or others generated, to "match by eye sight alone" the cropped panels with the correct raw data. Dr. Pichiorri claimed she did not have access to a printer or a big screen to compare images, and this caused her unintentional mistakes. The COMIC believes these practices are inconsistent with practices of a typical researcher at Dr. Pichiorri's level.
 - d. Dr. Pichiorri's methods of taping small pieces of autoradiography film to white paper with inconsistent labeling practices as shown in the data Dr. Pichiorri provided as "Document 4" are practices that are inconsistent with practices of a typical researcher at Dr. Pichiorri's level.
 - e. Based on the limited raw data provided, it appears that Dr. Pichiorri had the data for the Akt blot (RPMI-8226 Mut TP53), which was ultimately used in the correction for Figure 7A, but she failed to review the data for Akt, that purportedly was available at the time, to ensure the correct data was included in the original published figure.. The COMIC has determined that as the first co-author on Cancer Cell, Dr. Pichiorri had the opportunity and responsibility to prevent the falsification by reviewing the raw data used to make the figures and reviewing the figures included in Cancer Cell prior to publication, and failed to do so
 - f. At the time the questioned manuscript was published, Dr. Pichiorri was in her third year of postdoctoral training. The COMIC believes that someone at this level of training should have had the knowledge of how to generate figures properly and use practices for storing data that would not lead to such confusion.
- 3) The COMIC found that the increased risk of false data being used or generated due to the practices and methods employed by Dr. Pichiorri is clearly demonstrated by the fact that the same issue (i.e., the reuse of data for different experiments) occurred five separate times in the Cancer Cell 2010 publication alone. The number of falsifications leads the COMIC to believe that the cause of this instance of falsification goes beyond honest mistake, as claimed by Dr. Pichiorri¹⁸³, or "sloppy science", or even negligence, and instead demonstrates a pattern of reckless Research Misconduct by Dr. Pichiorri.

Significance:

The Committee determined that Dr. Pichiorri's reckless actions caused the falsification in Figure 7A of Allegation #5, as described above. This falsification changed the reported results by mixing panels for two different controls, along with mixing the wild-type (WT TP53) and mutant (RPMI Mut p53) cell groups. This data was used in the publication to support the hypothesis that WT TP53 and the mutant cell line RPMI-8226 have different levels of IGF-1, IGF-1R, pS6, S6, pAkt and Akt levels. Since the control bands

¹⁸¹ Ex. 128 - Pichiorri point-by -point April 10th-2019, page 4

¹⁸² Ex. 128 - Pichiorri point-by -point April 10th-2019, page 4

¹⁸³ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 45 lines 1-2



were falsified, this would significantly change the interpretation of protein levels when normalized to control, potentially causing a wrong interpretation of the data. This falsification deviated from acceptable practices of the relevant research community by not only reusing data, but within two different treatment strategies. As the first author, it was Dr. Pichiorri's responsibility to ensure the integrity of the data and to maintain a lab notebook that was not able to be altered.

Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 8 in favor to 0 against, that the Respondent recklessly falsified Figure 7A and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #1, Allegation #15 - Falsification of Figure 4D or 7A by the reuse of the same data in the MDM2 blot (flipped) in the MM1s panel of Figure 4D and in the right three lanes in the IGF-1 blot in the MM1s WT TP53 panel of Figure 7A.

Finding of Fact:

- 1) Figure 7A shows the effect of miR-192, miR-194, miR-215 and a scrambled control (Scr) on WT TP53 (MM1s) and mutant (RPMI-8226) cell lines for the expression of IGF-1, IGF-1R, pS6, S6, pAkt, and Akt proteins with a GAPDH loading control (see slide #21¹⁸⁴).
- 2) Figure 4D shows the protein expression of p53, MDM2, p21 and GAPDH control after 48 hr miR-192, miR-194, miR-215 (pool), and Scr ASOs transfection in MM1s or NCI-H929 cells after 12 hr of treatment with 10 mM Nutlin-3a.
- 3) Adobe Photoshop forensic overlay analysis shows that the MDM2 blot of the MM1s panel in Figure 4D is identical to lanes 2-4 of the IGF-1 blot in the MM1s WT TP53 panel of Figure 7A, when flipped horizontally and vertically (see slide #22¹⁸⁵). This would not be scientifically valid as the two figures are showing the data from two completely different experiments, including different treatment types and different cell lines tested.
- 4) The COMIC identified that this same Western blot was also used to represent a p53 blot in MM1s cells in the first generation of Figure 4A, Cancer Cell, which was provided by Dr. Pichiorri as a Photoshop tiff file (see slide #23¹⁸⁶).¹⁸⁷ In the second generation of Figure 4A, also provided by Dr. Pichiorri, the p53/MM1s panel was replaced with the blot that was ultimately used in the final published Figure 4A.¹⁸⁸ It is unclear to the COMIC why the duplicated p53 panel was included in the first generation Figure 4A and then replaced, but this is an additional instance indicative of the overall pattern of data duplication occurring in this manuscript.
- 5) Therefore, a single Western blot was used in three different figures (Figure 4D for MDM2/MM1s; Figure 7A for IGF/MM1s; and Figure 4A for p53/MM1s) to represent three different protein expressions with different treatments.
- 6) The provenance of this reused Western blot for the MDM2 experiment cannot be determined and it was not located in any of the sequestered data or the original raw data provided by Dr. Pichiorri. Thus, it is unknown whether the MDM2 blot in MM1s cells in the published Figure 4D, is an accurate representation of the experimental results.

¹⁸⁴ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹⁸⁵ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹⁸⁶ Ex. 123 - COMIC Figure Forensics_Pichiorri

¹⁸⁷ Ex. 131- 20190410-Document-Folder 1 Manuscript 1 Tiff small panels and Sup. Fig, "Fig 4A"

¹⁸⁸ Ex. 131 - 20190410-Document-Folder 1 Manuscript 1 Tiff small panels and Sup. Fig "Fig 4A Review 1"



- 7) In her written response, provided to the COMIC on April 10, 2019¹⁸⁹, Dr. Pichiorri stated that she agrees that the published Figure 7A blot for IGF-1/MM1s does not match the original source data. Dr. Pichiorri stated that the correct IGF-1 blot for the MM1s panel should have been the data shown in "IGF-1, IGF1R."¹⁹⁰ The "IGF-1, IGF1R" file is a one page document containing three pieces of Western blots cut out and taped to a white piece of paper, labeled for IGFR, GAPDH, and IGF in RPMI and MM1s cells.

Respondent's Response:

- 1) As this allegation was submitted after the conclusion of the Inquiry, there are no statements about this allegation by Dr. Pichiorri during the CII interview.
- 2) In her written response, provided to the COMIC on April 10, 2019¹⁹¹, Dr. Pichiorri stated that she agrees that the published and questioned Figure 7A IGF-1/MM1s blot does not match the original source data and that in 2016 she noted a problem. She wrote, "*When Dr. Croce asked me to look at the copy of the original data in 2016 I immediately realized that the IGF-1 panel of MM.1S in Figure 7A, were not matching with the original films.*"
- 3) During her interview with the COMIC on May 13, 2019, Dr. Pichiorri first stated that Dr. Croce told her not to worry about reviewing all the other data when they were issuing the 2016 correction because Dr. Sanders (the Complainant) would notice any other issues: "*And Dr. Croce said don't spend your precious time, because if something is wrong, Saunders¹⁹² will be after us no matter what*"¹⁹³
- 4) However, during her interview with the COMIC on May 13, 2019, Dr. Pichiorri reiterated that she actually had reviewed this issue and had informed Dr. Croce of this mistake.¹⁹⁴ According to Dr. Pichiorri, she believed that Dr. Croce communicated the issue to the Cancer Cell editors.¹⁹⁵
- 5) During her interview with the COMIC on May 13, 2019, Dr. Pichiorri was asked if she believed she had a responsibility as a first author to contact the journal herself when she first noticed the inaccuracy of the IGF-1 blots in Figure 7A. Dr. Pichiorri stated that she wanted to contact the journal but believed an attorney for Dr. Croce was going to take care of all of it.¹⁹⁶
- 6) In her written response, provided to the COMIC on April 10, 2019,¹⁹⁷ Dr. Pichiorri also stated "*In fact, both IGF-1 in MM.1S were run at the same time in the same gel side-by-side with the IGF-1 in RPMI-8226, which was reported correctly in Figure 7A.*" The COMIC reviewed this statement and found that the published blot for IGF-1 in RPMI-8226 cells is identical to the source data provided by Dr. Pichiorri for the IGF-1 blot in MM1s cells (see slide #24¹⁹⁸). Thus, not only is the IGF-1 for MM1S in Figure 7A incorrect, but the blot for IGF-1 for RPMI-8226 cells is also incorrect and inconsistent with Dr. Pichiorri's statement above. Thus, Dr. Pichiorri's statement to the COMIC is incorrect and false. The COMIC finds the false statement made by Dr. Pichiorri particularly troubling, since the expectation is that any researcher responding to allegations of research misconduct would spend extra time and care to ensure their review of the data is correct.

¹⁸⁹ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 4

¹⁹⁰ Ex. 132 - 20190410-Document-Folder 2 Fig.7A, "IFG-1, IFG-1R"

¹⁹¹ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 4

¹⁹² Spelling error of "Sanders" present in interview; corrected in errata.

¹⁹³ Ex. 165 -20190513-COMIC Interview + Errata - Pichiorri, page 36, lines 3-5

¹⁹⁴ Ex. 165 -20190513-COMIC Interview + Errata - Pichiorri, page 36, lines 21-25, page 37, page 38, lines 1-16

¹⁹⁵ Ex. 165 -20190513-COMIC Interview + Errata - Pichiorri, page 38, lines 17-24

¹⁹⁶ Ex. 165 -20190513-COMIC Interview + Errata - Pichiorri, page 39 lines 9-18

¹⁹⁷ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 4

¹⁹⁸ Ex. 123 - COMIC Figure Forensics_Pichiorri



Respondent's Responsibility:

- 1) In her written response, provided to the COMIC on April 10, 2019,¹⁹⁹ Dr. Pichiorri stated that she did not think she made this figure. Dr. Pichiorri claims that her inability to locate the Figure 7A tiff in the folder of "small tiff panels"²⁰⁰ she provided proves that she did not make this figure. Although it is not clear to the COMIC if Dr. Pichiorri generated Figure 7A, the COMIC believes that Dr. Pichiorri was aware of the correct data that should have been inserted into Figure 7A since the labeling on the source data films is similar (and is more likely than not by Dr. Pichiorri) throughout all of the allegations under review for Cancer Cell. Further, the films themselves are labeled with the cell type, protein and treatment conditions for the experiment.
- 2) In both her written response and her interview with the COMIC, Dr. Pichiorri stated she was aware that the published IGF-1 data in Figure 7A did not match the original source data. Dr. Pichiorri stated that she became aware of this issue after the 2016 correction occurred.²⁰¹ Despite stating she knew there was an issue with the IGF-1 blot in 2016, Dr. Pichiorri did not contact the journal to correct this problem (see statement below) and instead believed it was Dr. Croce's responsibility.
- 3) The COMIC believes that a typical researcher of Dr. Pichiorri's status (Associate Professor at this time) would have contacted the journal directly and immediately after determining there was an issue with the IGF-1 blot. While not a research misconduct issue, this failure to disclose the error or try to correct the error is very troubling to the COMIC and is inconsistent with the standard practices in the research community.

Respondent's Intent:

- 1) Although purportedly contemporaneous data for IGF-1 in MM1s and RPMI-8826 cells appears to exist (see "IFG-1, IGF-1R"), the COMIC confirmed that these data were not used correctly in the published Figure 7A. The published IGF-1/MM1S data in Figure 7A used the same data that were used in Figure 4D, and also in the first generation, unpublished Figure 4A for different experiments, as explained above, and for different protein expression. The published IGF-1/RPMI data used in Figure 7A were actually IGF-1 data in MM1s cells. Thus, none of the IFG-1 data in Figure 7A are correct. The COMIC believes that once again Dr. Pichiorri's poor data management practices allowed false data to be included in Figure 7A.
- 2) Further, the COMIC could not locate the original data for the MDM2 experiment represented in Figure 4D. The use of 3 lanes of the MDM2 blot in Figure 4D, and 4 lanes of the same data in Figure 7A, suggests cropping, stretching and flipping of the data. The COMIC believes this is not a simple pasting error, but rather there was a deliberate action to obscure the similarity of the reused blots in Figures 4D and 7A.
- 3) In addition, based on Dr. Pichiorri's statements regarding her knowledge in 2016 that the source data for IGF-1 did not match what was published in Figure 7A, the COMIC finds that Dr. Pichiorri knowingly allowed the false data to remain in the published literature.
- 4) Therefore, the COMIC believes that Dr. Pichiorri exhibited similar reckless data management practices regarding this allegation as with the other allegations, and the additional falsifications identified by the COMIC leads the COMIC to find that this allegation represents intentional and/or knowing falsification of the data in Figures 4D and Figure 7A.

Significance:

The Committee determined that Dr. Pichiorri's intentional and/or knowing actions caused the falsification in Figure 4A of Allegation #15 to occur. This allegation is related to Allegation #5 and was discovered

¹⁹⁹ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 4

²⁰⁰ Ex. 131- 20190410-Document-Folder 1 Manuscript 1 Tiff small panels and Sup. Fig

²⁰¹ Ex. 165 - 20190513-COMIC Interview + Errata -Pichiorri, page 39 line 5-8



following the Initial Inquiry phase completed. The COMIC felt that this falsification drastically affected the reported results as the same blot was used to represent different proteins under different treatment strategies. This would nullify any conclusions that could be drawn from these data and alter the conclusions of the manuscript. The COMIC finds these obvious falsifications and reuse of the same data for multiple different experimental treatments and proteins very alarming and it suggests that Dr. Pichiorri intentionally and/or knowingly choose to use results to fit a defined hypothesis. As first author Dr. Pichiorri's was responsible for ensuring the integrity of the data and maintaining all data records accordingly. In addition, the COMIC was troubled by the actions of Dr. Pichiorri in allowing what she knew to be false data to remain in the published literature as described above. This behavior is not consistent with standard practices of a typical researcher at Dr. Pichiorri's level in the research community.

Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 8 in favor to 0 against, that the Respondent intentionally and/or knowingly falsified Figure 4D and/or Figure 7A and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript under review - Pichiorri et al., JEM 2013 (3 allegations)

Pichiorri F*, Palmieri D*, De Luca L, Consiglio J, You J, Rocci A, Talabere T, Piovan C, Lagana A, Cascione L, Guan J, Gasparini P, Balatti V, Nuovo G, Coppola V, Hofmeister CC, Marcucci G, Byrd JC, Volinia S, Shapiro CL, Freitas MA, Croce CM. "In vivo NCL targeting affects breast cancer aggressiveness through miRNA regulation." J Exp Med. 2013 May 6;210(5):951-68. Epub 2013 Apr 22. *Co-first authors.

Manuscript #2 **Correction:** Pichiorri F*, Palmieri D*, De Luca L, Consiglio J, You J, Rocci A, Talabere T, Piovan C, Lagana A, Cascione L, Guan J, Gasparini P, Balatti V, Nuovo G, Coppola V, Hofmeister CC, Marcucci G, Byrd JC, Volinia S, Shapiro CL, Freitas MA, and Croce CM. Correction: In vivo NCL targeting affects breast cancer aggressiveness through miRNA regulation." J Exp Med. 2017 May 1;214(5):1557. Epub 2017 Jan 19. *Co-first authors. **Correction of Figures 1E and 1F**

NOTE REGARDING MANUSCRIPT #2. ALLEGATIONS #6-8: For the allegations under review for JEM 2013 and the JEM 2017 correction, two pieces of "raw data" were provided by Dr. Pichiorri and were used in a variety of formats as explained below. Dr. Pichiorri claimed the "raw data" are for a four (4) lane blot for pri-miR21 RNU6 data used in Figure 1E and an eleven (11) lane blot for pri-miR155 RNU6 data used in Figure 1F. In the analysis of this allegation, three different versions of the Figures 1E and 1F were identified, including an "original submission" figure that was provided to the journal, a "published" figure, and a "corrected" figure (6 figures total).

Manuscript #2, Allegation #6 - F. Pichiorri falsified Figure 1 by the reuse of the same RNU6 data in the RNU6 Northern blot panel Figure 1E (pri-miR21) and in the RNU6 Northern blot panel Figure 1F lanes 2-4 (pri-miR-155) of Pichiorri et al., JEM 2013.

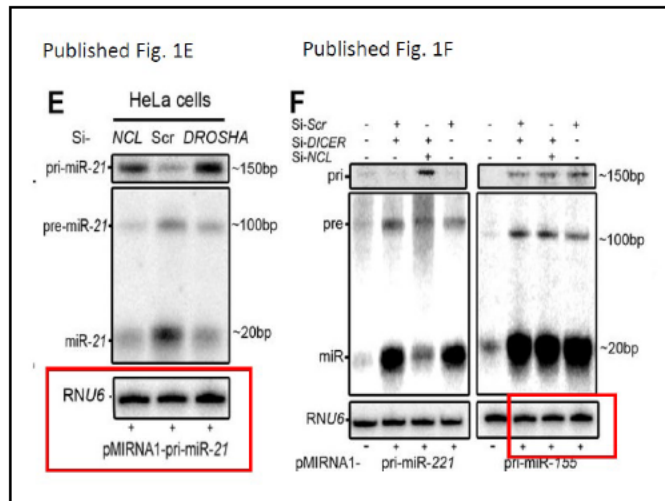
Finding of Fact:

- 1) Figure 1 in JEM shows the extent to which microRNA (miRNA) expression is regulated by nucleolin (NCL), and shows that a subset of miRNAs are regulated by NCL. Figure 1E and 1F are Northern blot analyses using RNA from HeLa cells transfected with primary miR-21 (Figure 1E) or primary miR122 and miR155 (Figure 1F) with NCL, DROSHA (a nuclease that is involved in the processing of miRNA), or Scrambled RNA (Scr). RNU6 is used as a loading control.
- 2) Adobe Photoshop forensic overlay analysis shows clearly that the published RNU6 blots have been



duplicated in Figures 1E and 1F (see slide #28²⁰²). Specifically, the three lanes in the RNU6 blot in Figure 1E are identical to lanes 2-4 in the RNU6 blot in Figure 1F.

- 3) Figure 1E and Figure 1F are purported to represent different experimental conditions, so the reuse of the RNU6 blot as a control would not be scientifically valid.



- 4) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that the mistake in the figure was made by the JEM staff. Dr. Pichiorri claimed that the figures that she submitted originally were not of the format and resolution that JEM required; and, subsequently she submitted the originals and JEM compiled the final figures for publication.²⁰³
- 5) In a written response provided to the CII on April 4, 2018,²⁰⁴ Dr. Carlo Croce, the corresponding author of the manuscript, provided email correspondence between the JEM editor and Dr. Pichiorri, on which he was copied.²⁰⁵ In Dr. Croce's written response,²⁰⁶ Dr. Croce indicated that there likely was a duplication between figures 1E and 1F but that the duplication was introduced in the final production process, most likely by the journal, and not the result of possible misconduct by anyone in his laboratory.
- 6) Based on the email correspondence provided by Dr. Croce on April 4, 2018, it appears that the JEM Executive Editor, Teodoro Pulvirenti, first contacted Dr. Croce on January 9, 2017 regarding the duplication and asked Dr. Croce for an explanation.²⁰⁷
- 7) Dr. Pichiorri, using her City of Hope email, responded to Dr. Pulvirenti on January 10, 2017, stating that she and Dr. Croce had provided the raw images to JEM after the journal had asked them to provide higher resolution images in 2013 and Dr. Pichiorri attached the figures that they had originally submitted to the journal.²⁰⁸
- 8) An internal search of Dr. Croce's email verified the email exchanges between Dr. Croce and JEM.²⁰⁹

²⁰² Ex. 123 - COMIC Figure Forensics_Pichiorri

²⁰³ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 48, line 8; page 51, line 4

²⁰⁴ Ex. 50 - 20180404 Email Croce to RIO

²⁰⁵ Ex. 51 - Attachment 1

²⁰⁶ Ex. 50 - 20180404 Email Croce to RIO

²⁰⁷ Ex. 51 - Attachment 1, page 12

²⁰⁸ Ex. 51 - Attachment 1, page 13-16

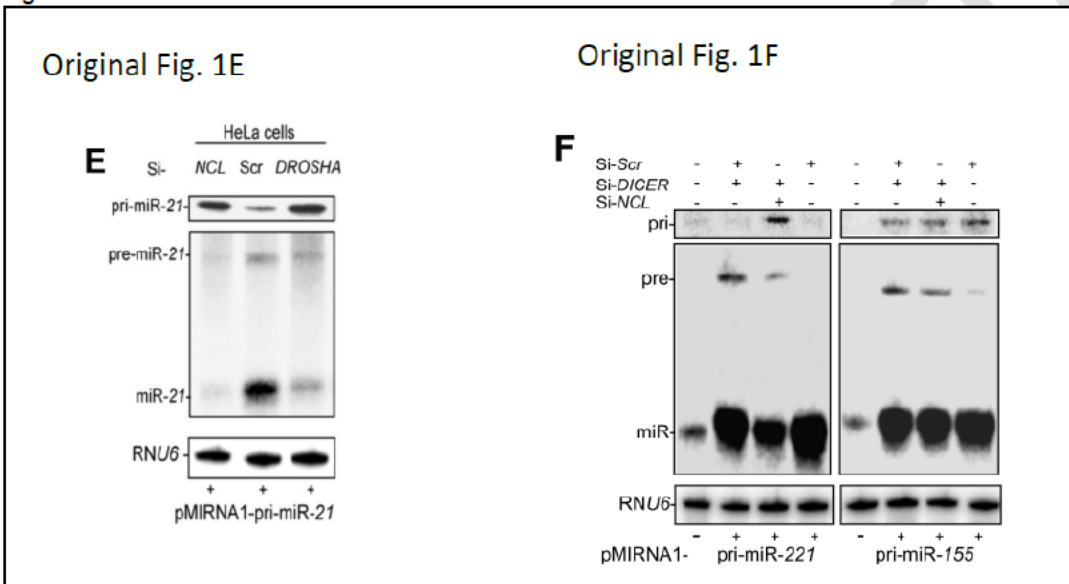
²⁰⁹ Ex. 173 - JEM Emails; This is a PDF portfolio document with each separate email listed by date (range is from 01/10/17-02/07/2017).



ORC was not able to find any 2013 emails between Dr. Pichiorri and JEM from Dr. Pichiorri's email account to confirm what was originally submitted to the journal. In a series of emails from January 10 - 17, 2017, with subject lines "JEM manuscript 20120950" and "JEM20120950 Figure Correction," Dr. Pichiorri corresponded with JEM staff, with Dr. Croce copied, to correct Figures 1E and 1F.

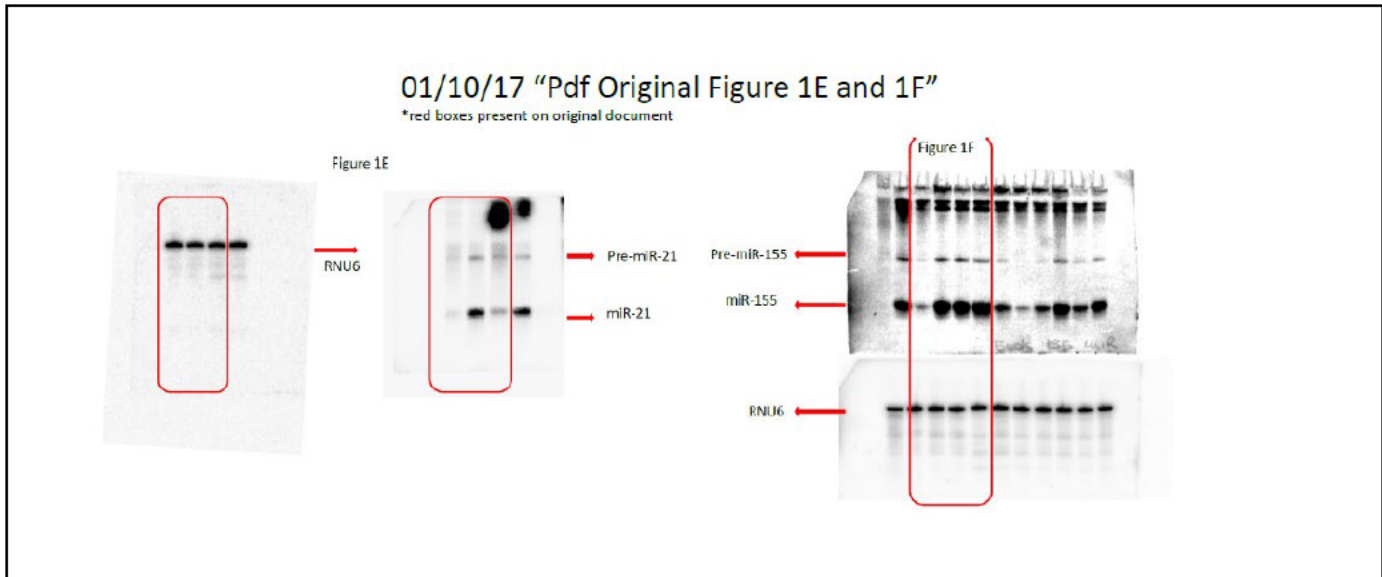
- 9) In her January 10, 2017 email response to JEM, Dr. Pichiorri provided the original Figure 1 that was sent to JEM ("Figure 1 Sent to reviewers"²¹⁰) and two pieces of "raw data" that she had sent to JEM following their request for higher resolution images ("Pdf Original Figure 1E and 1F,"²¹¹) purportedly representing the RNU6 blots in Figure 1E and 1F (images extracted from the email below).
- 10) Based on the January 10, 2017 email attachment "Pdf Original Figure 1E and 1F," the COMIC determined that the RNU6 raw data blot for Figure 1E sent to JEM when compared to the originally submitted Figure 1E RNU6 blot, were different RNU6 blots. The COMIC also determined that the lanes outlined in red by Dr. Pichiorri as the raw data used for miR-155 RNU6 in Figure 1F (raw data lanes #2-5) were not used in the originally submitted Figure 1F for miR-155 RNU6 blot.

Figure 1 Sent to reviewers



²¹⁰ Ex. 173 - JEM Emails, email sent Tuesday, January 10, 2017 6:28:06 PM see attachment labeled "Figure 1 Sent to reviewers"

²¹¹ Ex. 173 - JEM Emails, email sent Tuesday, January 10, 2017 6:28:06 PM see attachment labeled "Pdf Original Figure 1E and 1F"



- 11) At the request of the COMIC, ORC contacted JEM on April 17, 2019, to determine if, as stated by Dr. Pichiorri, the published Figures 1E and 1F were compiled by JEM and the journal was responsible for the duplicated RNU6 blots in the figure.²¹²
- 12) On May 21, 2019, JEM Editor, Dr. Teodoro Pulvirenti, responded to the April 17, 2019 questions from ORC and confirmed that the data originally submitted for the RNU6 blots were different than those published because the authors did not have higher resolution original data so instead provided new data. Dr. Pulvirenti stated, "*Preflight editors requested higher resolution images for Figure 1E and 1F from the authors. The authors did not have them, so instead they provided new images.*"²¹³ This is consistent with the COMIC's determination that the raw data in "Pdf Original Figure 1E and 1F" were not the same as the RNU6 data in the original Figure 1E and 1F submitted to JEM ("Figure 1 Sent to reviewers").
- 13) In the written response provided to the COMIC on April 10, 2019, Dr. Pichiorri provided a scan of a page of a lab notebook²¹⁴ purporting to show a Northern blot for miR-21 (Figure 1E) that had been run previously and then saved at a higher resolution for the journal.²¹⁵ Dr. Pichiorri stated that this was the image that had been sent to the graphical office of JEM when the journal requested high resolution images and "*The graphical office included the high-resolution panels in the specific figures, resized and changed the disposition of several figures and published the manuscript.*"
- 14) In the email communication between JEM and ORC on May 21, 2019, JEM Editor, Dr. Teodoro Pulvirenti, responded that JEM editors would not ever insert raw data provided by authors into a panel but that JEM "*preflight editors on the other hand, who are part of the production staff and do not have a scientific background could take raw data provided by the authors and insert it into a panel for a manuscript figure. Any figure is then reviewed by the authors in the galley proofs prior to publication.*" Thus, the COMIC finds that even if Dr. Pichiorri's explanation that JEM duplicated the RNU6 panels is viewed as credible, Dr. Pichiorri would have been provided galley proofs of the updated figures

²¹² Ex. 154 - 20190417 - Letter RIO to JEM

²¹³ Ex. 158 - JEM answers to OSU

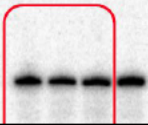
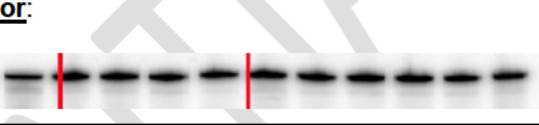
²¹⁴ Ex. 141- Document-Folder 11 Nucleolin RNA, page 6

²¹⁵ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 10



prior to publication.

- 15) Beyond the published RNU6 blots under review in this allegation, the COMIC noted that there were three (3) different versions of the figures generated for Figures 1E and 1F, (i.e., the originally submitted figure, the published figure, and a corrected figure for each). The COMIC examined the similarities and differences between these versions of the figures and whether the RNU6 panels correlated to the raw data that was provided for Figure 1E and 1F by Dr. Pichiorri in "Pdf Original Figure 1E and 1F".²¹⁶
- 16) Based on the original data provided by Dr. Pichiorri, the COMIC determined that certain lanes from the following had been reused multiple times: (a) the four (4) lane blot purportedly representing the RNU6 control for miR-21 in Figure 1E and; (b) the eleven (11) lane blot, purportedly representing the RNU6 control for miR-155 in Figure 1F. These data were reused to represent different experimental conditions and treatments as indicated below. (Note: the table below is also relevant to Allegations #7 and #8 since these allegations also involve the reuse of this same original data.)

4 lanes raw data ²¹⁷ for miR-21 Figure 1E was used for:	11 lanes raw data ²¹⁸ for miR-155 Figure 1F was used for:
	
Published Fig 1E = lanes 3, 2, 1 and Published Fig 1F = lanes 4, 3, 2, 1 (the allegation)	Original Fig 1E = used lanes 5, 4, 3 (from raw data 1F)
	Original Fig 1F miR-221 = lanes 11, 10, 9, 8 Original Fig 1F miR-155 = lanes 7, 6, 5, 4
Corrected Fig 1E = lanes 1, 2, 3 (lanes of the published figure flipped - Allegation #7)	Corrected Fig 1F miR-155 = lanes 2, 3, 4, 5 (Allegation 7)
	Also used for RNU6 in Figure 1E in Cancer Cell, Allegation 8 below Cancer Cell Fig 1E DMSO = lanes 10, 9, 8, 7, 6 Cancer Cell Fig 1E Nutlin = lanes 5, 4, 3, 2, 1

Thus, for Figure 1E:

- i. The original submission of Figure 1E (miR-21) RNU6 used lanes from data that Dr. Pichiorri provided to the COMIC as the original data for Figure 1F for miR-155 (see slide #32²¹⁹).
- ii. The published figure changed the RNU6 data and used 3 lanes of data that Dr. Pichiorri said was the high resolution data for Figure 1E (miR-21) and that she claimed was given to JEM and mistakenly flipped by the journal, and then subsequently flipped back for the corrected figure.

For Figure 1F:

- i. The original submission of Figure 1F for miR-221 and miR-155 RNU6 used various lanes from the raw data that Dr. Pichiorri provided as the raw data for RNU6 miR-155 (miR-221 panel used lanes 11, 10, 9, 8 and miR-155 panel used lanes 7, 6, 5, 4, which was the raw data in a flipped orientation).

²¹⁶ Ex. 173 - JEM Emails, email sent Tuesday, January 10, 2017 6:28:06 PM see attachment labeled "Pdf Original Figure 1E and 1F"

²¹⁷ Ex. 123 - COMIC Figure Forensics_Pichiorri

²¹⁸ Ex. 123 - COMIC Figure Forensics_Pichiorri

²¹⁹ Ex. 123 - COMIC Figure Forensics_Pichiorri



- ii. The published Figure 1F for miR-155 used the RNU6 data that Dr. Pichiorri said was the high resolution data for Figure 1E (miR-21) given to JEM, but used four (4) lanes of the data
 - iii. The corrected Figure 1F for miR-155 changed the RNU6 panel to a different set of lanes from the data Dr. Pichiorri provided as raw data for RNU6 miR-155 (using lanes 2, 3, 4, 5), which was different from the lanes chosen for the miR-155 panel in the original submission or the published figure.
 - iv. The RNU6 panel used for the miR-221 cells in both the originally submitted and the published figures were different, with the original miR-221 figure using RNU6 data from the miR-155 cells. No RNU6 original data for the miR-221 transfected cells were provided by Dr. Pichiorri.
- 17) The forensic analysis for the overlay of lanes of raw data with the various figures is provided on slides 29-32.²²⁰
- 18) The COMIC finds that based on the JEM response, it might be possible that an error in the published figure could have been introduced by "preflight editors". However, this explanation seems highly unlikely since the JEM editorial office would have had to mistakenly use 3 lanes in the wrong orientation from the RNU6 panel for Figure 1E (lanes 3, 2, 1) and 4 lanes of the same raw data for miR-155 (lanes 4, 3, 2, 1) on its own without input from Dr. Pichiorri. This is further viewed unlikely since the JEM editor, Dr. Pulvirenti, confirmed that authors are provided with the galley proofs for review prior to publication.
- 19) The COMIC finds that the seemingly arbitrary reuse of lanes from the same original data for miR-155 RNU6 in 6 different figures, with different experimental conditions, decreases the likelihood that the duplications under review in this allegation were introduced by the JEM editors, and more likely than not were a result of the poor data management practices of Dr. Pichiorri.

Respondent's Response:

- 1) In her interview with the COMIC on May 13, 2019, Dr. Pichiorri stated that she did not make the figures for 1E or 1F.²²¹
- 2) In the written response provided to the CII on April 12, 2018, Dr. Pichiorri stated that the original blots were given to JEM, and it was the JEM staff that made the mistake.²²² Dr. Pichiorri agrees with the duplication in the figures, but places all responsibility on the JEM staff.
- 3) In the written response provided to the COMIC on April 10, 2019,²²³ Dr. Pichiorri stated that when the manuscript was pre-accepted in March 2013, JEM contacted her asking for higher resolution images for the RNU6 blots in Figures 1E and 1F.
- 4) In the written response provided to the COMIC on April 10, 2019, Dr. Pichiorri provided a scan of a page of a lab notebook²²⁴ purporting to show a Northern blot for miR-21 (Figure 1E) that had been run previously and then saved at a higher resolution for the journal.²²⁵ Dr. Pichiorri states it was this image that was sent to the graphical office of JEM in 2013.

Respondent's Responsibility:

- 1) Based on HR records and Dr. Pichiorri's statement in her April 10, 2019²²⁶ response to the COMIC, Dr. Pichiorri had her own independent laboratory at the time the JEM manuscript was published. The

²²⁰ Ex. 123 - COMIC Figure Forensics_Pichiorri

²²¹ Ex. 165 - 20190513-COMIC Interview + Errata – Pichiorri , page 51 lines 4-9

²²² Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations

²²³ Ex. 128 -Pichiorri point-by-point April 10th-2019, page 9-11

²²⁴ Ex. 141 - Document-Folder 11 Nucleolin RNA, page 6

²²⁵ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 10

²²⁶ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 1 and page 9



COMIC believes that a similar researcher at that level should know how to prepare a figure and include accurate control data.

- 2) Dr. Pichiorri stated in her April 10, 2019,²²⁷ response to the COMIC that Dr. Palmieri (co-first author of the manuscript) was the one responsible for finalizing the figures before the JEM submission. However, Dr. Pichiorri is listed as both the co-first and co-corresponding author on this manuscript.
- 3) Although Dr. Pichiorri does not admit to generating the final figure, the COMIC finds that at a minimum Dr. Pichiorri's status as a co-first and co-corresponding author while being an independent faculty member indicates that she would have had oversight over the generation and accuracy of the published figures.
- 4) Dr. Pichiorri provided "Document 11"²²⁸ in her April 10, 2019 written response to the COMIC, and stated that it was a copy of *her* laboratory notes showing that the experiments were "performed correctly."²²⁹ The COMIC views this documentation as further evidence that Dr. Pichiorri was the person responsible for performing the experiments and responsible for knowing which RNU6 control data should have been incorporated into a figure.²³⁰
- 5) Dr. Pichiorri, not Dr. Palmieri, was the author in contact with JEM in 2017 regarding the corrections and responded to Dr. Croce, the other co-corresponding author, to describe the details for the generation of Figure 1E and 1F.²³¹
- 6) Dr. Pichiorri is the common author between the JEM manuscript and the Cancer Cell 2010 manuscript, in which the purported raw data for JEM Figure 1F was also published as Cancer Cell 2010 Figure 1E (see Table above and Allegation 8 below). As Dr. Palmieri was not a listed author on the Cancer Cell 2010 manuscript, the COMIC finds it unlikely that he would have had access to the raw data and/or generated the original figures for JEM.

Respondent's Intent:

- 1) Based on the forensic analysis and statements from Dr. Pichiorri, she does not dispute the reuse of the data in the published Figure 1E and Figure 1F.
- 2) The COMIC determined that the originally submitted Figures 1E and 1F already had internal duplications of RNU6 data with the reuse of the miR155 RNU6 raw data, lanes 5, 4, 3 used in Figure 1E and lanes 7, 6, 5, 4 used in Figure 1F (lanes that are **bolded** were reused; see table above). The COMIC believes that the existing lane duplications could explain why, when asked for higher resolution images for Figures 1E and 1F, the authors submitted new images for publication. Then, apparently Dr. Pichiorri chose to submit the raw data for miR21 RNU6 (the only high resolution images identified), lanes 3, 2, 1 for Figure 1E and also for lanes 4, 3, 2, 1 for Figure 1F, which was subsequently published.
- 3) The COMIC found that the presence of data duplications in the originally submitted figures prior to the duplications seen in the published figures supports the conclusion that Dr. Pichiorri—and not the journal—was responsible for the duplications in the published figures. Further, the published figures were provided to Dr. Pichiorri in a galley proof, as stated by the journal²³² and the first author,²³³ and it was Dr. Pichiorri's responsibility to carefully review them.
- 4) The continued reuse of the eleven (11) lanes of the same raw data by Dr. Pichiorri in the originally

²²⁷ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 9

²²⁸ Ex. 128 - Pichiorri point-by-point April 10th-2019, Document 11

²²⁹ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 11, first full paragraph

²³⁰ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 9 page 11

²³¹ Ex. 173 - JEM emails , Dr. Palmieri is not copied on any of the 21 emails sent regarding the JEM correction between the dates 1/10/2017 - 2/7/2017

²³² Ex. 158 - JEM answers to OSU, page 1

²³³ Ex. 165 - 20190513-COMIC Interview + Errata – Pichiorri , page 53, lines 11-21



submitted Figures 1E and 1F, the corrected Figure 1F, and Figure 1E in Cancer Cell 2010 leads the COMIC to believe that Dr. Pichiorri simply added RNU6 control lanes/blots to the figures with complete indifference and plain disregard for whether the data were accurate, and without any verification that these were the correct data.

- 5) Therefore, the COMIC finds that Dr. Pichiorri's mishandling of the data created a significant risk for the falsification of the RNU6 data in the published Figure 1E and other falsifications found in the originally submitted and corrected Figure 1F. The COMIC finds this behavior is inconsistent with the standards for proper data handling by a researcher at Dr. Pichiorri's level and further, Dr. Pichiorri was given every opportunity to ensure the correct data were used. The COMIC finds that Dr. Pichiorri's disregard for ensuring correct data were used in the figures despite the significant risk was reckless and led to the falsification of Figure 1E and 1F, as described above.

Significance:

The Committee has determined that the reckless actions of Dr. Pichiorri caused the falsification of Figures 1E and 1F in Allegation #6 as described above. The falsified data (Fig.1E and 1F) are internal loading controls for Northern blotting. Without the correct internal loading control information, a conclusion about the changes indicated in the figures is not possible. The use of internal loading control data that is not from the same samples as the Northern blotting data is not an acceptable practice in the scientific community. The falsified data were used to demonstrate the mechanisms of *siNCL* regulation of miR-21 and miR-221 and this data does not impact the major conclusion of the manuscript. The publication of this false data is, however, a record for an unproven mechanism by which *siNCL* regulation of miR-21 and miR-221 occurs and the publication of this false data by itself may mislead future scientific investigations by other investigators. Dr. Pichiorri as the first and corresponding author had the responsibility to ensure that correct information is published.

Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor to 0 against, that the Respondent recklessly falsified Figures 1E and/or 1F and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor to 0 against, that the Respondent recklessly falsified Figures 1E and/or 1F and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #2, Allegation #7- F. Pichiorri falsified the corrected Figure 1E by reuse of the same data (flipped horizontally) in the RNU6 lanes from the published RNU6 lanes of Figure 1E of Pichiorri et al., JEM 2013.

Finding of Fact:

- 1) Adobe Photoshop forensic overlay analysis demonstrates that in the corrected Figure 1E, the RNU6 blot is identical to the published Figure 1E data, but is flipped horizontally (see slide #33²³⁴).
- 2) Specifically, in the originally published Figure 1E, the lanes were in 3, 2, 1 order compared to the raw data provided by Dr. Pichiorri in "Pdf Original Figure 1E and 1F," but in the corrected Figure 1E the lanes are now ordered 1, 2, 3, which would not be scientifically valid as the data are reported to

²³⁴ Ex. 123 - COMIC Figure Forensics_Pichiorri



- represent different experimental conditions (see slide #29²³⁵).
- 3) Documents reviewed indicated that JEM knew that the proposed corrected Figure 1E included a rotation of the published Figure 1E data, as highlighted by the visual aid they provided to Dr. Pichiorri (see slide #35²³⁶).
 - 4) Dr. Pichiorri also provided "Document 11"²³⁷ (in her April 10, 2019 written response to the COMIC), and stated that it was a copy of her laboratory notes showing the miR-21 expression blot and U6 control blot (see slide #34).²³⁸ The data in Document 11, page 6, appears to be the same as the data provided by Dr. Pichiorri in the "Pdf Original Figure 1E and 1F" for the U6 blot, but not the same data for the experimental miR-21 blot.²³⁹ The notebook pages show lanes labeled as "siNCL, diScr, SiDrosha" and a fourth unreadable lane label, but since there is no labeling to indicate miR-21 on the page, it is not clear if the scanned film actually represents results for the miR-21 RNU6 blot. At the lower right corner of the scan, "U6" is hand-written into the corner. However, it is not known when this label was written onto the page.
 - 5) Based on that labeling of the U6 raw data in Document 11, page 6, the corrected Figure 1E is in the same orientation. However, the experimental miR 21 raw data in Document 11, page 6, is different than the published miR21 data and the miR21 data found in the "PDF Original Figure 1E and 1F".
 - 6) The differences in the miR21 experimental data, the differences in the original submission data, the incomplete labeling on Document 11, page 6, and the Respondent's pattern of reuse of the RNU6 control raw data in several figures as described above creates concern for the COMIC as to whether the RNU6 blot in the published and corrected Figure 1E, actually represents the correct RNU6 blot for the miR21 experiment.

Respondent's Response:

- 1) In her interview with the CII on April 13, 2018, Dr. Pichiorri stated that the original mistake (i.e., the duplication between Figure 1E and 1F) in the published figure was made by the JEM staff. Dr. Pichiorri maintains that the RNU6 blot published in 2013 was for the miR21 experiment and the JEM editors mistakenly flipped the data to the wrong order (lanes 3, 2, 1), and when the correction was published, the figure was corrected and used the same RNU6 blot, but the order was flipped (lanes 1, 2, 3).²⁴⁰
- 2) However in her email to JEM editor Shauna O'Garro on January 17, 2017, Dr. Pichiorri stated, "*We realized we made a mistake in the line order of the corresponding gel but if there was a duplication of the image this was coming from the editorial office no from us.*"²⁴¹
- 3) In her email to Dr. Carlo Croce on January 20, 2017,²⁴² Dr. Pichiorri explained, "*For Figure 1E when they assembled the original figure with the original tiff. they rotated the RNU6 of 180@ instead that 123-321summary it is their fault that the RNU6 of Figure 1E got rotated....it was our fault that in the original Figure 1E (RNU6 for miR-155) we indicated the wrong lanes.*"
- 4) Conversely, in her April 10, 2019 written response to the COMIC, Dr. Pichiorri stated that "*the post-doc erroneously flipped the Northern for miR-21 180 degrees, but did not also flip the RNAU6*"²⁴³.²⁴⁴

²³⁵ Ex. 123 - COMIC Figure Forensics_Pichiorri

²³⁶ Ex. 123 - COMIC Figure Forensics_Pichiorri

²³⁷ Ex. 128 - Pichiorri point-by-point April 10th-2019, Document 11

²³⁸ Ex. 141- Document-Folder 11 Nucleolin RNA, page 6

²³⁹ Ex. 173 - JEM Emails, email sent Tuesday, January 10, 2017 6:28:06 PM see attachment labeled "Pdf Original Figure 1E and 1F"

²⁴⁰ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 53, lines 20-24

²⁴¹ Ex. 51 - Attachment 1, page 26

²⁴² Ex. 51 - Attachment 1, page 30

²⁴³ The typo "RNAU6" is present in Dr. Pichiorri's written response. The COMIC understood it to be "RNU6."

²⁴⁴ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 10



Respondent's Responsibility:

- 1) In her email to JEM editor Shauna O'Garro on January 17, 2017, Dr. Pichiorri wrote that the incorrect lane order in Figure 1E was introduced by the authors stating, "*We realized we made a mistake in the line order of the corresponding gel*"²⁴⁵
- 2) JEM staff responded to Dr. Pichiorri with the proposed corrections based on the raw data that Dr. Pichiorri provided. Dr. Pichiorri did not object to those corrections at the time and neither did JEM.
- 3) Based on HR records and Dr. Pichiorri's statement in her April 10, 2019, response to the COMIC, Dr. Pichiorri had her own independent laboratory at the time the JEM manuscript was published.
- 4) Only Dr. Pichiorri provided data to JEM and responded to questions about the data for RNU6 in Figures 1E and 1F. Dr. Pichiorri was the only author who provided the corrected data and was tasked with reviewing the corrected images that were sent to her for review.²⁴⁶ Thus, Dr. Pichiorri appeared to accept the responsibility for ensuring the correction to Figure 1 was valid.

Respondent's Intent:

- 1) Based on the explanation provided by Dr. Pichiorri and the email exchange between Dr. Pichiorri and JEM, the COMIC finds that both Dr. Pichiorri and JEM were aware of the reuse and flipping of the original Figure 1E RNU6 data for the corrected Figure 1E. Therefore, the COMIC believes that if Dr. Pichiorri's claim that the blot represents accurate RNU6 for miR21 is valid, the reuse and flipping of the data would be acceptable
- 2) However, the COMIC does not believe that Dr. Pichiorri's claim is valid, nor does it believe that the RNU6 data in the corrected Figure 1E are accurate for the following reasons:
 - a. The corrected Figure 1E used bands from a scan of raw data presented in Document 11, page 6, which may, or may not, represent the miR21 experiment.
 - b. The published Figure 1E RNU6 bands for (lanes 3, 2, 1) had been duplicated in the published Figure 1F (lanes 4, 3, 2, 1) in the JEM paper.
 - c. The originally submitted Figure 1E to JEM included an RNU6 miR21 panel that used the data provided by Dr. Pichiorri for RNU6 for miR155²⁴⁷ (using lanes 5, 4, 3 from raw data for miR155 in Figure 1F).
- 3) Thus, the COMIC finds that a repeating pattern of the Respondent using one set of data to represent numerous experimental conditions and concludes that Dr. Pichiorri appears to insert RNU6 data based on what she needs to show in the figure (e.g., equal loading) regardless of whether the data represent the correct experimental controls. The COMIC cannot verify the accuracy of the RNU6 data in the corrected Figure 1E based on the data provided by Dr. Pichiorri and the COMIC did not find any of Dr. Pichiorri's responses credible as to whether the RNU6 control data for the miR21, miR221, or miR155 experiments in Figures 1E and 1F are accurately represented in the correction.
- 4) The COMIC believes that the inability of Dr. Pichiorri to maintain accurate records for experiments that were performed and published is inappropriate and inconsistent with accepted practices of a typical researcher at Dr. Pichiorri's level.
- 5) The COMIC finds that the increased risk of false data being used or generated due to the practices and methods employed by Dr. Pichiorri is clearly demonstrated by the reuse of the same raw data for multiple different experiments. The risk of using false data was increased by Dr. Pichiorri's lack of appropriate labeling of the scanned data. In addition, Dr. Pichiorri was already on notice about the risk of falsification occurring when she was contacted by JEM about the duplication in the published

²⁴⁵ Ex. 51 - Attachment 1, page 26

²⁴⁶ Ex. 173 - JEM Emails, RE: JEM manuscript 20120950" sent on Thursday, January 12, 2017 4:50:50 PM with four attachments "Figure 1E pre and Mature miR-21.tiff", "Fig 1E U6.tif", "Fig 1F pre and Mature miR-155.tif", and "U6 Fig1F.tif"

²⁴⁷ Ex. 173 - JEM Emails, email sent Tuesday, January 10, 2017 6:28:06 PM see attachment labeled "Pdf Original Figure 1E and 1F"



figure. Dr. Pichiorri ignored the significant risk and continued to submit data that cannot clearly be identified as accurate. The COMIC believes that any researcher at Dr. Pichiorri's level, as an Assistant Professor with significant prior training and oversight of the research, should have the ability to maintain accurate records to ensure the proper data is selected for any published figure, and certainly for a corrected figure. Thus, while the COMIC cannot determine if Dr. Pichiorri intentionally or knowingly falsified the correction for Figure 1E, the COMIC believes Dr. Pichiorri's poor handling of the purported raw data for the correction of Figure 1E and her acceptance of the responsibility for correcting Figure 1 in JEM is at a minimum reckless.

Significance:

The Committee determined that the falsification as described in Allegation #7 was an attempt to correct the lane order, which was initially incorrect in the published Figure 1E, as described by Dr. Pichiorri. JEM was aware that the correction used the same data that was published in Figure 1E with the order flipped. Therefore, the COMIC finds there is no merit to this allegation as it is currently stated because the journal was aware that the correction was a flip of the original data.

However, the COMIC has significant concerns about whether the data actually represents the experimental conditions since the originally submitted data was different from the published data, and the raw data provided by Dr. Pichiorri from her lab notebook did not properly indicate if the blot was a RNU6 blot for miR21. As the questioned data are loading controls, their accuracy is vital to show that the changes in experimental data are due to the treatments and not due to unequal loading. The falsified data (in Fig. 1E) is an internal loading control for Northern blotting. Without the correct internal loading control information, any conclusions drawn about the changes indicated in the figure, are not possible. The use of internal loading control data that is not from the same samples as the Northern blotting data is not an acceptable practice of a typical researcher in the relevant scientific community. The falsified data was used to demonstrate the mechanisms of *siNCL* regulation of miR-21 and miR-221 and this data does not impact the major conclusion of the manuscript. The publication of this false data is, however, record for an unproven mechanism by which *siNCL* regulation of miR-21 and miR-221 occurs and the publication of this false data by itself may mislead future scientific investigations by other investigators. Dr. Pichiorri as the first and corresponding author has the responsibility to ensure that correct information is published.

Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor to 0 against, that the Respondent recklessly falsified Figure 1E and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor to 0 against, that the Respondent recklessly falsified Figure 1E and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript #2, Allegation #8 - F. Pichiorri falsified the corrected Figure 1F in JEM by reuse of the same data in the RNU6 panel in the pri-miR-155 panel (flipped horizontally) taken from Pichiorri et al., (2010), "Downregulation of p53-inducible microRNAs 192, 194, and 215 impairs the p53/MDM2 autoregulatory loop in multiple myeloma development." Cancer Cell, 18. ("Manuscript #1") in Figure 1E, the left four lanes of the RNU6 blot in the Nutlin panel.

Finding of Fact:

- 1) The seven panels comprising Figure 1 in Cancer Cell 2010 show different experiments to identify the



specific miRNAs that are regulated by p53 in multiple myeloma cells. Figure 1E in Cancer Cell 2010 shows the kinetics of miR34a, miR-194, miR-192, and miR-215 RNA expression by Northern blot analysis in MM 1s cells treated with DMSO or Nutlin 3a. Nutlin is a small molecule inhibitor of the protein murine double minute 2 (MDM2), which is an inhibitor of the p53 protein. Thus, when MDM2 expression is inhibited by Nutlin, p53 is active as a tumor suppressor.

- 2) Although the experiments in Figure 1E, Cancer Cell 2010 use miRNAs, the cell type and experimental design (MM1s cells, time course for expression of 3 specific miRNAs with DMSO or Nutlin treatment) are completely different than Figure 1 in JEM (HeLa cells, miRNA expression with treatment by different agents).
- 3) Adobe Photoshop forensic overlay analysis shows that in the corrected miR-155 Figure 1F, the RNU6 blot, when flipped horizontally, is identical to the RNU6 blot (left four lanes) in Figure 1E for Nutlin in the Cancer Cell paper (see slide # 37²⁴⁸). The reuse would not be scientifically valid as the RNU6 blots would be controls for completely different experimental conditions.
- 4) Further, the COMIC determined that the same raw data were used within and between these figures representing different experiments, prior to the duplications occurring in the corrected JEM figure under review in this allegation. The originally submitted Figure 1F to JEM, for the RNU6 blots for both miR-221 (lanes 11, 10, 9, 8) and miR-155 (lane 7, 6, 5, 4), contained different lanes of the same raw data as those shown in Cancer Cell 2010, Figure 1E, Nutlin RNU6 panel (lanes 5, 4, 3, 2, 1) and also the DMSO panel (lanes 10, 9, 8, 7, 6) (see Table on page 36).
- 5) The COMIC tallied up how many times the same raw data were reused and determined that a single piece of "raw data" purportedly representing RNU6 data for Figure 1F, JEM, was reused in six separate panels for RNU6, to represent completely different experiments. (see Table on page 36).
- 6) The use of different lanes of RNU6 raw data by Dr. Pichiorri for the corrected Figure 1F for miR-155 was supported by the email from the JEM staff member, Rochelle Ritacco asking Dr. Pichiorri on January 12, 2017, to confirm that the corrected Figure 1F includes bands from the same RNU6 raw data (lanes 2, 3, 4, 5) as the bands used in the 2013 original submission (lanes 7, 6, 5, 4).²⁴⁹
- 7) In addition, for miR221 in Figure 1F, Dr. Pichiorri gives no explanation about why different lanes were used in the originally submitted Figure 1F miR221 RNU6 blot versus both the published and corrected versions of Figure 1F miR221 RNU6 blot.
- 5) The COMIC identified additional issues with Figure 1F beyond the issues stated in Allegation #8. "Document 13 FIG 1 WITH ORIGINAL PICTURES,"²⁵⁰ provided to the COMIC in Dr. Pichiorri's point-by-point response on April 10, 2019, includes a PowerPoint slide of the original Figure 1 submitted to JEM, including Figure 1 panels A-G. A Northern blot panels are included as Figure 1B, but these Northern blot panels are not included in the published JEM figure (see slides #38 and 39²⁵¹).
- 6) Dr. Pichiorri wrote in the April 10, 2019 response²⁵² that by uncropping the images, the original raw data is revealed. The COMIC reset/uncropped the two (2) lanes for the RNU6 blot that was part of Figure 1B, Document 13 and it reveals a six (6) lane blot of raw data. The COMIC noted that four lanes (lanes 3-6) are identical to the published and corrected miR-221 RNU6 blot in Figure 1F. The use of lanes 3, 4 in Figure 1B in Document 13 and Figure 1F for miR-221 (lanes 3, 4, 5, 6) in the published and corrected JEM figure would not be scientifically valid as they represent different experimental conditions. Although it is unknown how Figure 1B was used, its discovery in the

²⁴⁸ Ex. 123 - COMIC Figure Forensics_Pichiorri

²⁴⁹ Ex. 51 - Attachment 1, page 19 -20

²⁵⁰ Ex. 143 - "Document 13 FIG 1 WITH ORIGINAL PICTURES

²⁵¹ Ex. 123 - COMIC Figure Forensics_Pichiorri

²⁵² Ex. 128 - Pichiorri point-by-point April 10, 2019, page 12



research record is yet another example of using the same “raw data” in another figure for a different experimental condition (see slides #38 and 39²⁵³).

Respondent’s Response:

- 1) In her interview with the CII on April 13, 2018, Dr. Pichiorri mentioned that Dr. Dario Palmieri was also involved in putting the data together²⁵⁴ but that she personally sent the correction to JEM.²⁵⁵
- 2) In the written response provided to the CII on April 12, 2018,²⁵⁶ Dr. Pichiorri stated there was a mistake in this figure but that it was inadvertent and due to the fact that the RNU6 blots often look the same.²⁵⁷ Dr. Pichiorri asserted that there was no motive for the duplications.
- 3) Based on the email correspondence provided to the CII by Dr. Croce on April 4, 2018, JEM staff member Rochelle Ritacco asked Dr. Pichiorri on January 12, 2017 to confirm the proposed corrections based on the raw data that Dr. Pichiorri had provided (using her COH email). Ms. Ritacco attached a visual aid to show Dr. Pichiorri that the corrections were based on the data that had been provided to JEM by Dr. Pichiorri (see slide #35²⁵⁸). In that email, Ms. Ritacco asked Dr. Pichiorri to confirm that the corrected JEM Figure 1F is the same bands used in the 2013 original submission (not the 2013 published 1F) but flipped horizontally and using different lanes.²⁵⁹
- 4) In her written response provided to the COMIC on April 10, 2019,²⁶⁰ Dr. Pichiorri wrote that when she provided the data for the correction for Figure 1F in 2017, she believed that it was correct data since she had provided that same RNU6 data for the originally submitted RNU6 miR-155 data in 2013. The COMIC notes that while the same “raw data” were given to JEM in 2013 and 2017, the lanes for the RNU6 panels were different lanes and the lanes were flipped in 2013 (see Table on page 36).
- 5) In her written response provided to the COMIC on April 10, 2019, Dr. Pichiorri also wrote that the duplication between RNU6 in Figure 1E Cancer Cell 2010 and the corrected Figure 1F JEM was a mistake.²⁶¹ Dr. Pichiorri provided a complicated explanation regarding Cancer Cell Figure 1E and Cancer Cell Supplementary Figure 1D, and how the same RNAs were used for these figures. The figures were separated following review and she claims that the wrong RNU6 blot was mistakenly used for Cancer Cell Figure 1E because “*somebody erroneously saved the scan of the film under Nucleolin instead that Nutlin and we got confused, since we were working on both manuscripts at the same time.*” The COMIC finds this explanation cannot be valid since not only was treatment different, but different cell types were used for JEM Figure 1F (HeLa cells) and Cancer Cell Figure 1E (MM1s cells).
- 6) In her written response provided to the COMIC on April 10, 2019,²⁶² Dr. Pichiorri wrote that “*We were consistent and honest with the data that we provided to JEM for the corrected figure, and we did not change them.*” The COMIC finds this statement is not credible as different lanes of raw data were provided for Figure 1F in the original submission versus what was submitted for the corrected Figure 1F. The COMIC believes that based on the careless recordkeeping of the experimental results, it appears to be unlikely that Dr. Pichiorri could possibly know which data, in what order, are correct.

²⁵³ Ex. 123 - COMIC Figure Forensics_Pichiorri

²⁵⁴ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 57, lines 3-6

²⁵⁵ Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 57, lines 19-20

²⁵⁶ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations

²⁵⁷ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations, page 2

²⁵⁸ Ex. 123 - COMIC Figure Forensics_Pichiorri

²⁵⁹ Ex. 51 - Attachment 1, page 19 -20

²⁶⁰ Ex. 128 - Pichiorri point-by-point April 10, 2019, pages 12-14

²⁶¹ Ex. 128 - Pichiorri point-by-point April 10, 2019, page 13

²⁶² Ex. 128 - Pichiorri point-by-point April 10th-2019, page 14



- 7) In her written response provided to the COMIC on April 10, 2019,²⁶³ Dr. Pichiorri wrote, *"I want to also specify that I either did not perform these experiments nor did I personally save the original scans. I only checked the quality of the data and kept the copy of the original scans for record. I think all the experiments were correctly performed and the confusion once again came from the unorganized manner in which data were kept in Dr. Croce's laboratory."*
- 8) In her interview with the COMIC on May 13, 2019,²⁶⁴ Dr. Pichiorri was asked if it was more important to show the correct data for an experiment or if it was okay to show another piece of data that roughly shows the same outcome. Dr. Pichiorri's response was that after 2015 she knew that a *"representative picture is a representative picture of a set of experiments that have been done at the same identical time with the action has to be associated with the same treatment and everything has to be aligned."*²⁶⁵ Dr. Pichiorri went on to explain that prior to 2015 she didn't know that it was so important that the representative data were identical to the data represented in the figure.

Respondent's Responsibility:

- 1) The forensic analysis clearly demonstrates that the RNU6 blot for miR-155 treatment in the 2017 corrected JEM Figure 1F is identical (flipped horizontally) to 4 lanes of the RNU6 blot for Nutlin treatment published in Figure 1E of Cancer Cell 2010.
- 2) Dr. Pichiorri submitted to JEM the same raw data for RNU6 blot for the originally submitted JEM Figure 1F in 2013 and again for the 2017 correction of Figure 1F, although different lanes and orientations of the raw data were provided (see slide #35²⁶⁶).
- 3) Dr. Pichiorri does not dispute the duplication between the JEM paper and the Cancer Cell paper, but says it was an honest error. However, the COMIC finds that the duplications were in the original submission of the figures in 2013 between miR-221 Figure 1F and DMSO Cancer Cell Figure 1E, and between miR-155 Figure 1F and Nutlin Figure 1E, Cancer Cell (see Table on page 36). The COMIC believes that the multiple acts of reusing apparently arbitrary lanes and flipping the orientation for the RNU6 data cannot be the result of an honest error or mistake.
- 4) Based on HR records and Dr. Pichiorri's statement in her April 10, 2019 response to the COMIC, Dr. Pichiorri had her own independent laboratory at the time the JEM manuscript was published.
- 5) Dr. Pichiorri was responsible for the correction of JEM Figure 1F as she was the author who corresponded with the editors and provided the corrected data; and she was also responsible for reviewing and checking the correction of Figure 1F for accuracy.

Respondent's Intent:

- 1) From the forensic analysis and the responses from Dr. Pichiorri, the inappropriate reuse of the same data in the corrected JEM Figure 1F and Cancer Cell Figure 1E is not disputed.
- 2) Based on the evidence above and Dr. Pichiorri's own admissions, the data were placed in wrong folders and were unorganized.
- 3) Dr. Pichiorri personally confirmed to the journal that the lanes for the correction of Figure 1F were different than the original submission and were correct. The COMIC believes that this act of providing the falsified data and subsequently confirming that it was correct, suggests that Dr. Pichiorri acted with the possible goal of getting the correction published quickly.
- 4) The continued reuse of the eleven (11) lanes of RNU6 "raw data" for the original JEM Figures 1E and 1F, the corrected Figure 1F, and Figure 1E in Cancer Cell 2010, led the COMIC to believe that these actions were performed intentionally by Dr. Pichiorri.

²⁶³ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 14

²⁶⁴ Ex. 165- 20190513-COMIC Interview + Errata, page 34 lines 3-25, page 35 1-12

²⁶⁵ Ex. 165- 20190513-COMIC Interview + Errata, page 12-17

²⁶⁶ Ex. 123 - COMIC Figure Forensics_Pichiorri



Significance:

The Committee determined that the intentional actions of Dr. Pichiorri led to the falsification of Figure 1F in Allegation #8 as described above. The falsified RNU6 data (Fig. 1F) is an internal loading control for Northern blotting. Without the correct internal control information, a conclusion about the changes indicated in the figures is not possible. The use of internal loading control data that is not from the same samples as the Northern blotting data is not an acceptable practice of a typical researcher in the relevant scientific community. The falsified data were used to demonstrate the mechanisms of *siNCL* regulation of miR-21 and miR-221 and this data does not impact the major conclusion of the manuscript. The publication of this false data is, however, a record for an unproven mechanism by which *siNCL* regulation of miR-21 and miR-221 occurs and the publication of this false data by itself may mislead future scientific investigations by other investigators. Dr. Pichiorri as the first and corresponding author has the responsibility to ensure that correct information is published.

Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor to 0 against, that the Respondent intentionally and/or knowingly falsified the corrected Figure 1F in JEM and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor to 0 against, that the Respondent intentionally and/or knowingly falsified the corrected Figure 1F in JEM and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript under review – Canella et al., Oncotarget 2015 (1 allegation)

Manuscript #5: Canella A, Nieves HC, Sborov DW, Cascione L, Radomska HS, Smith E, Stiff A, Consiglio J, Caserta E, Rizzotto L, Zanesi N, Stefano V, Kaur B, Mo X, Byrd JC, Efebera YA, Hofmeister CC*, and Pichiorri F*. "HDAC inhibitor AR-42 decreases CD44 expression and sensitizes myeloma cells to lenalidomide." *Oncotarget*. 2015 Oct 13; 6(31): 31134–31150. *Co-corresponding authors.

Manuscript #5, Allegation #12 - F. Pichiorri falsified Western blot data in Figure 3B by falsely labeling the cell line MM.1S in Canella et al., Oncotarget 2015, when the original research record indicates the data are from the MM.1R cell line.

Finding of Fact:

- 1) Figure 3B in *Oncotarget 2015* shows the effect on CD44 expression upon Drosha knockdown using RNA silencing, both by Western blot expression and a bar graph (with error bars), in the MM.1S cell line. The figure shows that upon Drosha knockdown in MM.1S cells, CD44 protein expression increases by approximately 2X (see slide #41²⁶⁷).
- 2) Dr. Hanna Radomska, Complainant #2, provided "Exhibit B"²⁶⁸ on April 11, 2017, which shows a single Western blot experiment performed using both MM.1S and MM.1R cell lines and probing for Drosha, Ikaros, CD44 and GAPDH expression (see slide #42²⁶⁹).
- 3) Adobe Photoshop forensic overlay analysis demonstrates that the published data for DROSHA,

²⁶⁷ Ex. 123 - COMIC Figure Forensics_Pichiorri

²⁶⁸ Ex. 55 - Exhibit B

²⁶⁹ Ex. 123 - COMIC Figure Forensics_Pichiorri



CD44, and GAPDH in Figure 3B, are from the MM.1R cell line panel in Exhibit B (see slides #43-44²⁷⁰). However, the published Figure 3B indicates that the experiments were performed in MM.1S cells. As MM.1S and MM.1R are different cell lines, with different expression profiles, it would not be scientifically valid to label the figure as MM.1S.

- 4) Exhibit B, provided by the Complainant, shows a graphical representation of CD44 expression levels and indicates that the knockdown of Drosha does not increase expression of CD44 in MM.1S cells, but does increase expression of CD44 in MM.1R cells (see green bars in graph on slide #42²⁷¹). As the Complainant claimed there was only a single Western blot replicate of this experiment performed by the Complainant, she did not include error bars on the bar graph showing the relative expression of the Western blot data. Conversely, the published bar graph does have error bars, which should not be present if only a single Western blot experiment was performed.
- 5) In her interview with the CII on April 6, 2018, Dr. Radomska stated that she did the experiment a single time with both MM.1S and MM.1R cells and gave the data to Dr. Pichiorri. Dr. Radomska stated that Dr. Pichiorri then stretched the MM.1R blot and labeled it as MM.1S in the figure. Dr. Radomska also stated that this is a significant mistake because the CD44 response in the two different cell lines is opposite: CD44 is increased upon siDrosha transfection in MM.1R cells, but the same was not true in the MM.1S cells.²⁷²
- 6) In her interview with the COMIC in April 29, 2019, Dr. Radomska stated that this experiment was only performed a single time.²⁷³ Dr. Radomska indicated that she knew it was only performed once because she ran out of reagents, which were too expensive to reorder, and Dr. Pichiorri did not tell her to repeat the experiment.²⁷⁴
- 7) In her interview with the COMIC on April 29, 2019, Dr. Radomska denied making the figure as it is shown in the published paper, but indicated she possibly could have written the legend but would not have mislabeled the cell line as she would have known those data were MM.1R.²⁷⁵
- 8) The COMIC reviewed three grant applications (R01 CA172965-01A1²⁷⁶, R01 CA201382-01²⁷⁷ R01 CA201382-01A1²⁷⁸) and a rejected manuscript²⁷⁹ with figures (Blood²⁸⁰ - provided by Dr. Pichiorri to the CII on April 20, 2018²⁸¹) and found that the figure was labeled with the correct cell line, MM.1R in these four instances (see slides #45 and 46²⁸²).
- 9) The Blood manuscript (submitted February 13, 2015), the R01 CA172965-01A1 (November 11, 2014), and the R01 CA201382-01 (February 2015) submissions occurred before the Oncotarget paper was accepted, while the R01 CA201382-01A1 (November 2015) submission was received after the Oncotarget paper was accepted. The figure is labeled correctly in all four of these instances.
- 10) In her interview with the COMIC on May 13, 2019, Dr. Pichiorri maintained that Dr. Radomska was

²⁷⁰ Ex. 123 - COMIC Figure Forensics_Pichiorri

²⁷¹ Ex. 123 - COMIC Figure Forensics_Pichiorri

²⁷² Ex. 34 - 20180406-CII Interview +errata - Radomska, page 57 lines 18-24 through page 59 lines 1-19

²⁷³ Ex. 160 - 20190429-COMIC Interview Radomska + Errata, page 18, lines 19-25, page 19, lines 1-7

²⁷⁴ Ex. 160 - 20190429-COMIC Interview Radomska + Errata, page 26 , lines 1-13

²⁷⁵ Ex. 160 - 20190429-COMIC Interview Radomska + Errata, page 31, lines 1-5 and lines 14-22

²⁷⁶ Ex. 174- R01 CA172965-01A1

²⁷⁷ Ex. 175- R01 CA201382-01

²⁷⁸ Ex. 176- R01 CA201382-01A1

²⁷⁹ Ex. 57 - MS

²⁸⁰ Ex. 58 - 2Blood Final Figures 1-7, Figure 3B on page 3

²⁸¹ Ex. 56 - 20180420- Email Pichiorri to RIO Oncotarget Submission

²⁸² Ex. 123 - COMIC Figure Forensics_Pichiorri



- responsible for making the figure and labeling the legend.²⁸³
- 11) In her interview with the COMIC on May 13, 2019, Dr. Pichiorri was asked about the error bars and replicates of the experiment, to which she stated she had the Western blots and would send them to the committee.²⁸⁴
 - 12) On May 16, 2019, Dr. Pichiorri emailed a response letter²⁸⁵ to the COMIC with additional data regarding the replicates and error bars for Figure 3B. In the letter, Dr. Pichiorri wrote that she found the original blots from Dr. Radomska²⁸⁶ that were saved in the laboratory folder.²⁸⁷ Dr. Pichiorri stated that she found another run of the GAPDH blot.²⁸⁸ Dr. Pichiorri further explained that she believed the experiment was performed in triplicate but *"even if the experiment was not run in the triplicate, the manuscript did not publish false information because it did not make any representations to this effect."*²⁸⁹
 - 13) The COMIC reviewed the data provided by Dr. Pichiorri on May 16, 2019, and found no evidence that the experiment was performed in triplicate, as the only blot for CD44 was a single one that Dr. Radomska had previously provided.
 - 14) The COMIC reviewed the figure legend and noted that the figure legend does not indicate what the error bars represent nor does it state that Figure 3B was performed in triplicate. However, the Material and Methods section under "Statistics" (p. 31146) states, "All preclinical data were obtained from at least three independent experiments and are expressed as mean \pm standard deviation (SD)."
 - 15) Furthermore, Dr. Pichiorri responded to questions from the COMIC regarding a statement she had made about previous allegations in 2012.²⁹⁰ In a response letter to the COMIC,²⁹¹ Dr. Pichiorri explained that she *"was asked in 2013 to follow an orientation training as to how to correctly save my own laboratory data following NIH standards"*.
 - 16) ORC located the 2013 action plan summary, generated by Dr. Pichiorri, for the planned practices that she would institute in her own laboratory to prevent future data handling and publication errors. With Dr. Pichiorri's consent^{292,293} ORC provided that document²⁹⁴, and the associated 2013 email,²⁹⁵ to the COMIC for their review.

Respondent's Response:

- 1) In both the Inquiry and Investigation, Dr. Pichiorri has maintained that Dr. Radomska was responsible for the experiment and figure preparation of Figure 3B and that the mislabeling was an honest error done by Dr. Radomska.
 - a. In her response letter to the CII dated January 22, 2018,²⁹⁶ Dr. Pichiorri writes that Dr. Radomska performed the experiment, made the figure, wrote the figure legend, and submitted the manuscript

²⁸³ Ex. 165- 20190513-COMIC Interview Pichiorri + Errata, page 77, lines 1-5

²⁸⁴ Ex. 165- 20190513-COMIC Interview Pichiorri + Errata, page 77, lines 10-24

²⁸⁵ Ex. 166 - Post-Interview Submission re Figure 3B further data to the IC

²⁸⁶ Ex. 167 - 20190516-Document 1 Folder

²⁸⁷ Ex. 168 - 20190516-Document 2 Folder

²⁸⁸ Ex. 169- 20190516-Document 3 Folder

²⁸⁹ Ex. 166- Post-Interview Submission re Figure 3B further data to the IC, page 2

²⁹⁰ Ex. 128- Pichiorri point-by-point April 10th-2019, page 3, footnote #4

²⁹¹ Ex. 179- To Dr. Burghes OSU 7-29-2019

²⁹² Ex. 183- 20190822-Email RIO to Pichiorri_Lab Practices 2013 documents

²⁹³ Ex. 184- 20190822- Email Pichiorri to RIO_Approval to provide documents

²⁹⁴ Ex. 186 - 20130925 - Pichiorri Lab Practice

²⁹⁵ Ex. 185 - 20130925 - Email Pichiorri to RIO - Lab Practices

²⁹⁶ Ex. 27 - 20180122 - "Dear OSU Research Compliance Officer Pichiorri F.", page 5



along with Dr. Canella, as at that time, Dr. Pichiorri was at the American Society of Hematology Meeting. Dr. Radomska had saved the images as MM1S Western blot siDrosha. Dr. Pichiorri stated that she is willing to fix Dr. Radomska's mistake and publish data from both cell lines (MM.1S and MM.1R).

- b. In the point-by-point response provided to the CII on April 12, 2018, Dr. Pichiorri reiterates that Dr. Radomska performed the experiment, wrote the legends, and submitted the paper to Oncotarget along with Dr. Canella. Dr. Pichiorri also stated that Drs. Radomska and Canella wrote the response to the reviewers' comments. Dr. Pichiorri goes on to say that the mistake in the figure does not change the conclusion.²⁹⁷
- c. In an email written to the CII on April 20, 2018,²⁹⁸ Dr. Pichiorri once again reiterated that the figure was made, legend written, and the final version sent to her for approval by Dr. Radomska. Dr. Pichiorri did not notice the mistake. She states that it was an honest error. Dr. Pichiorri stated that in a previous submission to the journal "Blood," the very same figure was presented but it was correctly labeled as MM.1R cells.^{299, 300}
- d. In her May 16, 2019, response letter to the COMIC,³⁰¹ Dr. Pichiorri again maintains that the error in labeling was made by Dr. Radomska and that Dr. Pichiorri would be happy to correct the paper.

Respondent's Responsibility:

- 1) Dr. Pichiorri was the final and co-corresponding author on Oncotarget 2015. The Oncotarget paper lists author contribution on p. 31147, and states that "FP and CCH [Craig C. Hofmeister] approved the final manuscript."
- 2) In the interview with the CII on April 13, 2018, Dr. Pichiorri stated that Dr. Radomska "did the figure".³⁰²
- 3) In her interview with the COMIC on May 13, 2019, Dr. Pichiorri maintained that Dr. Radomska was responsible for making the figure and doing the experiment.³⁰³
- 4) The COMIC is not able to definitively determine who labeled the figure in question.
- 5) However, it is the COMIC's understanding that the standards in the field are that Dr. Pichiorri, as the co-corresponding author, should review all figures and all text in the manuscript. The experiments in this manuscript were conducted when Dr. Pichiorri was a PI with staff under her guidance.
- 6) Furthermore, Dr. Pichiorri's responsibility as a PI is to provide oversight of the experiments performed and review primary data before making conclusions in the manuscript and submitting for publication as a corresponding author. Dr. Radomska stated that there were not enough reagents to perform the experiment more than once.³⁰⁴ It is the PI's responsibility to provide the necessary resources to perform experiments to the minimum accepted level in the field (i.e., at least 3 biological replicates performed, at least in duplicate) to account for natural variation (biological replicates) and technical errors (technical replicates). If the resources cannot be provided, then the experiments should be designed with the limited resources in mind - different experiments, different questions, or collaborations as needed.

²⁹⁷ Ex. 37 - Point by point Response to OSU April 13th Research misconduct Allegations, page 5

²⁹⁸ Ex. 56 - 20180420- Email Pichiorri to RIO Oncotarget Submission

²⁹⁹ Ex. 57 - MS, page 16

³⁰⁰ Ex. 58 - 2Blood Final Figures 1-7, Figure 3B on page 3

³⁰¹ Ex. 166 - Post-Interview Submission re Figure 3B further data to the IC, page 1

³⁰² Ex. 36 - 20180413-CII Interview + Errata – Pichiorri, page 91, line 7- pg 92, line 15

³⁰³ Ex. 165- 20190513-COMIC Interview Pichiorri + Errata, page 72 lines 22-25, page 73, lines 1-25, page 80 lines 12-22

³⁰⁴ Ex. 160 - 20190429-COMIC Interview Radomska + Errata, page 26 , lines 1-13



Respondent's Intent:

- 1) While the COMIC cannot definitively determine who made the figure, the COMIC believes that Dr. Pichiorri was aware, or should have been aware, that there was an increased risk of false data being used or incorrectly labeled due to previous experiences. In 2013, Dr. Pichiorri was provided with additional training regarding proper laboratory data storage and record keeping following identification of deficiencies in these areas. In 2013, Dr. Pichiorri was required to submit a lab practices document³⁰⁵ for proper data handling and retention in her own laboratory to prevent publication errors. As this publication in question was published in 2015, Dr. Pichiorri was already on notice of how errors occur, had received additional training in proper data handling and storage, and had submitted a lab practices document to the University to prevent publication errors. Despite that Dr. Pichiorri was unable to locate any additional replicates, nor did she check the labeling of the experimental data she claimed was performed by her staff.
- 2) Therefore, the COMIC has determined that since Dr. Pichiorri was already on notice that poor laboratory data management practices could lead to incorrect data being included in a figure, Dr. Pichiorri's inability to retrieve the data in triplicate experiments, her inability to provide physical evidence to show who created the figure, besides her own claims that she did not make the figure, and her apparent poor oversight to ensure that her laboratory did have proper data management practices, after she was already on notice were reckless and led to the mislabeling and falsification of Figure 3B. These practices are not consistent with the standards in the relevant research community.

Significance:

The Committee determined that Dr. Pichiorri's reckless actions led to the mislabeling and falsification of Figure 3B in Manuscript #5 for Allegation #12, as described above. The falsified data drastically impact the reported results since the falsified data show an opposite result (i.e., an increase in CD44 expression) to the single and only data set that the COMIC could verify was actually collected for this figure. The single experiment showed a decrease in CD44 expression for the MM1s cells. Dr. Pichiorri's improper laboratory practices also led to the graphical misrepresentation (both in direction and quantification) of the densitometric analysis shown in Figure 3B, as well as the falsified error bars. These falsifications deviated from accepted practices of the relevant research community as it is not acceptable, nor is it standard practice to mislabel, misrepresent, or falsify statistical representations (e.g., error bars) of data.

Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 7 in favor to 0 against, that the Respondent recklessly falsified Figure 3B and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

By clear and convincing evidence, the Committee finds by a vote of 7 in favor to 0 against, that the Respondent recklessly falsified Figure 3B and this act constitutes Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Manuscript under review - Trapasso et al., JBC 2008 (1 allegation)

Trapasso F*, Pichiorri F*, Gaspari M, Palumbo T, Aqeilan RI, Gaudio E, Okumura H, Iuliano R, Di Leva G, Fabbri M, Birk DE, Raso C, Green-Church K, Spagnoli LG, Venuta S, Huebner K, Croce CM. Fhit interaction with ferredoxin reductase triggers generation of reactive oxygen species and apoptosis of cancer cells. J Biol Chem. 2008 May 16;283(20):13736-44. Epub 2008 Mar 3. *Trapasso and Pichiorri are co-first authors.

³⁰⁵ Ex. 185- 20130925 - Pichiorri Lab Practice



Retracted - 07/03/2017

Manuscript #6, Allegation #14 - F. Pichiorri falsified Western blot data in Figure 5H by reuse of the same data in the AdFHIT 24- hour and 48-hour lanes and in the AdGFP 48-hour and 72-hour lanes in the CoxIV blot.

Finding of Fact:

- 1) Adobe Photoshop gradient mapping (see slide #48³⁰⁶) and forensic overlay (see slide #49³⁰⁷) demonstrate that the AdFHIT 24- and 48-hour lanes are identical to the AdGFP 48- and 72-hour lanes in the CoxIV blot in Figure 5H. This would not be scientifically valid as they represent different experimental conditions.
- 2) This manuscript was retracted on August 3, 2017. The retraction notice stated there were errors in the construction of Figs. 1D, 3C, 5C, 5H and Supplemental 1A.
- 3) On May 16, 2018, Dr. Pichiorri responded through her legal counsel, Mr. Paul Thaler, and stated the following:
 - a. Dr. Pichiorri did not perform the experiments associated with Figure 5H and was not in charge of preparing the manuscript,³⁰⁸
 - b. Dr. Pichiorri was informed by co-first author Dr. Trapasso that it was not Dr. Pichiorri's responsibility to review a co-author's data for accuracy,³⁰⁹ and
 - c. In June 2017, an editor from JBC contacted Dr. Croce regarding concerns. Dr. Croce contacted Dr. Trapasso, who had moved back to Italy in 2004, and asked for all the data related to the concerns, to which Dr. Trapasso indicated that he had lost the data.
- 4) In her written response to the COMIC on April 10, 2019, Dr. Pichiorri stated that she was not involved in performing the experiment shown in Figure 5H and has no knowledge of who generated the figure.³¹⁰
- 5) In the April 10, 2019 response, Dr. Pichiorri further stated that she was responsible for the flow analysis in Figures 4A, 4B, 4E and 6D; the Western blot in Figure 2C; the fluorescence reported in Figure 4C; and the colony assays reported in Figure 4F. Dr. Pichiorri stated that this was all correct and that she had previously sent the flow data to OSU (see Ex. 42 - 2018-05-16 – OSU – Response to New Allegations Final (with Exhibits)).
- 6) The COMIC confirmed that the flow analysis data provided by Dr. Pichiorri matched the published results in Figure 4E (D1 raw data provided on page 122, 124 and 125, while E1 raw data provided on page 132, 134 and 135)³¹¹, Figure 4B (E1 raw data provided on page 163, 164 and 165, while D1 data provided on page 166, 167 and 168) and Figure 4A (pages 170-176)³¹².
- 7) The COMIC confirmed the Western blot data provided by Dr. Pichiorri matched the published results for Figure 2C (raw data provided on page 169³¹³).
- 8) Based on the data Dr. Pichiorri provided to the COMIC and the fact that the corresponding author, Dr. Croce, contacted the other co-first author for the questioned data, the COMIC finds Dr. Pichiorri's explanation credible and despite being co-first author on this publication, she was not involved in the

³⁰⁶ Ex. 123 - COMIC Figure Forensics_Pichiorri

³⁰⁷ Ex. 123 - COMIC Figure Forensics_Pichiorri

³⁰⁸ Ex. 42 - 2018-05-16 – OSU – Response to New Allegations Final (with Exhibits)

³⁰⁹ Ex. 42 - 2018-05-16 – OSU – Response to New Allegations Final (with Exhibits)

³¹⁰ Ex. 128 - Pichiorri point-by-point April 10th-2019, page 18

³¹¹ Ex. 42 - 2018-05-16 – OSU – Response to New Allegations Final (with Exhibits)

³¹² Ex. 42 - 2018-05-16 – OSU – Response to New Allegations Final (with Exhibits)

³¹³ Ex. 42 - 2018-05-16 – OSU – Response to New Allegations Final (with Exhibits)



apparent falsification of Figure 5H. The COMIC believes that since there are two co-first authors and this was a collaborative effort with individuals outside of OSU, it is possible that another author generated Figure 5H and that the duplication went unnoticed by Dr. Pichiorri.

Respondent's Response:

- 1) Dr. Pichiorri stated that she was not involved in the generation of the figure in question, nor the experiments represented in the figure.

Respondent's Responsibility:

- 1) As this paper has a co-first author and was a collaborative effort between individuals outside of OSU, it is very possible that another author generated Figure 5H and that the duplication went unnoticed by Dr. Pichiorri.

Respondent's Intent:

- 1) The COMIC finds no evidence to suggest intentional, knowing, or reckless falsification of Figure 5H by Dr. Pichiorri.

Significance:

The Committee has determined that the falsification in Allegation #14 was not performed by Dr. Pichiorri. As the paper has been retracted, no other action is required for this publication.

Committee Conclusion:

By a preponderance of the evidence, the Committee finds by a vote of 8 in favor to 0 against, that the Respondent **did not** intentionally, knowingly and/or recklessly falsify Figure 5H and this act **does not** constitute Research Misconduct as described in the Policy III. A and 42 C.F.R. § 93.103 (b).

Summary of Investigation Committee Conclusions

As defined under the University's Policy and Procedures Concerning Research Misconduct, "Falsification" is "manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in research record." Further, a finding of Research Misconduct requires that there is a significant departure from accepted practices of the relevant research community, and the misconduct be committed intentionally, knowingly, or recklessly, and the allegation be proved by a "Preponderance of the Evidence" under the federal regulations and by "Clear and Convincing Evidence" under the University Rule 3335-5-04 regarding complaints made against faculty members.

Based on the Preponderance of the Evidence standard, the COMIC determined for five (5) of the six (6) allegations occurring during Dr. Pichiorri's tenure as a postdoctoral researcher (Allegations #2, 3, 4, 5 and 15), that Dr. Pichiorri committed Research Misconduct by deviating from the accepted practices of image handling and figure generation and intentionally, knowingly, and/or recklessly falsifying research data.

The COMIC determined at both the Preponderance of the Evidence and Clear and Convincing Evidence standards that for all four (4) allegations (Allegations #6, 7, 8 and 12) occurring during Dr. Pichiorri's tenure as an assistant professor at Ohio State, that Dr. Pichiorri committed Research Misconduct by deviating from the accepted practices of image handling and figure generation and intentionally, knowingly, and/or recklessly falsifying research data.

During the course of the Investigation, the COMIC identified other issues that became part of the findings of Research Misconduct involving Figures 1E, 4A, 5A, 4D and 7A in Cancer Cell 2010, Oct 19;18(4):367-81, and



Figures 1E and 1F in *J Exp Med.* 2013 May 6; 210(5):951-68. A summary of the COMIC's final findings of Research Misconduct are listed below:

- I. Dr. Pichiorri intentionally, knowingly, and/or recklessly falsified Figure 4A, Figure 4D, Figure 5A, and Figure 7A in *Cancer Cell* 2010, Oct 19;18(4):367-81, by:
 - a) recklessly causing the falsification of Figure 4A by the reuse of the same Western blot data for the MDM2/ MM1s panel, lanes 1-4 and for the MDM2/NCI-929 panel, lanes 2-5
 - b) intentionally and/or knowingly falsifying Figure 5A by claiming the experiment represented treatment with MI-219, when the raw data shows treatment with Nutlin, and by:
 - i. reusing the same Western blot data for p53 for Scr/5-10 μM (lanes 3 and 4) and for p53 for miR-194/2.5-5 μM (lanes 2 and 3)
 - ii. reusing the same Western blot data for p53/miR-192 and for alpha-puma/miR-192, where the original raw data did not support the results represented in the alpha-puma/miR192 panel
 - c) recklessly causing the falsification of Figure 7A by the reuse of the same Western blot data for the GAPDH in MM1s WT TP53 cells and for the Akt in RPMI-8226 Mut TP53 cells
 - d) intentionally and/or knowingly falsifying Figure 4D and/or Figure 7A, by the reuse of the same data in the MDM2/MM1s panel (flipped) in Figure 4D and in the right three lanes in the IGF-1/MM1s WT TP53 panel in Figure 7A, and further falsifying Figure 7A by using the raw data for IGF-1 in MM1s cells for the IGF-1 in RPMI-8226 Mut TP53 cells.
- II. Dr. Pichiorri intentionally, knowingly and/or recklessly falsified Figure 1E and 1F in *J Exp Med.* 2013 May 6; 210(5):951-68, in the corrected Figure 1E in *JEM*, and the corrected Figure 1F in *JEM* and/or Figure 1E in *Cancer Cell*, 2010, Oct 19;18(4):367-81 by:
 - a) recklessly causing the falsification of Figure 1E and/or 1F, by the reuse of the same Northern blot data in the RNU6 panel in Figure 1E (for pri-miR21) and in 3 of 4 lanes (lanes 2-4) in the RNU6 Northern blot panel in Figure 1F (for pri-miR-155)
 - b) recklessly causing the falsification of the corrected Figure 1E by continuing to use the same Northern blot RNU6 data that was included in the published Figure 1E, but flipped horizontally, when the accuracy of the RNU6 data could not be verified from the raw data
 - c) intentionally and/or knowingly falsifying the corrected Figure 1F in *JEM* and/or Figure 1E in *Cancer Cell*, 2010, by using the same raw data to represent the RNU6 Northern blot panel in the corrected Figure 1F for the miR-155 panel (raw data lanes 4, 3, 2, 1) as in the published Figure 1E, *Cancer Cell* for the RNU6 Northern blot in the Nutlin3a panel (raw data lanes 5, 4, 3, 2, 1). Different lanes of this same raw data, purportedly representing a Northern blot for RNU6 miR155, were also used in other figures all with different experimental designs for:
 - i. the originally submitted Fig 1E miR-21 (lanes 5, 4, 3)
 - ii. the originally submitted Fig 1F miR-221 (lanes 11, 10, 9, 8)
 - iii. the originally submitted Fig 1F miR-155 (lanes 7, 6, 5, 4)
 - iv. *Cancer Cell* Fig 1E DMSO (lanes 10, 9, 8, 7, 6)
- III. Dr. Pichiorri recklessly caused the falsification of Western blot data and the associated densitometry quantification in Figure 3B in *Oncotarget* 2015, Oct 13; 6(31): 31134–31150, by falsely labeling the cell line as MM.1S, when the original research record indicates the data are from the MM.1R cell line, and by including error bars in the graphical representation of densitometry when there was no raw data to support any replication of the experiment.

In summary, the COMIC finds that the overwhelming evidence demonstrates that Dr. Pichiorri committed serious and significant Research Misconduct. The COMIC is troubled by Dr. Pichiorri's apparent lack of research



ethics and lack of data for published work when she was both a postdoctoral researcher as well as a faculty member. The COMIC was also concerned with Dr. Pichiorri's dismissive response to the COMIC's questions and concerns regarding the lack of replicates required to show error bars present on Figure 3 in Allegation #12, when she wrote:

*"Regardless, however, neither the legend nor the method section stated that this experiment was performed in triplicate or that it was a pool of three, nor did it report the statistical significance of such conditions. Consequently, even if the experiment was not run in the triplicate, the manuscript did not publish false information because it did not make any representations to this effect."*³¹⁴

The COMIC is concerned that a practicing scientist would respond in such a manner considering the widely accepted standard of performing at least three replicates. The COMIC finds that Dr. Pichiorri undermines the scientific endeavor by trying to argue a "technicality" regarding the error bars. Finally, based on the small cropped pieces of data provided to the COMIC by Dr. Pichiorri, and statements made by Dr. Radomska during her interview with the COMIC, the COMIC believes that Dr. Pichiorri does not have the skills to keep her laboratory data in an organized and logical manner.

*Dr. Radomska: "All I can say is Flavia was a little bit messy. She wasn't well organized. She couldn't find samples. She couldn't. Even the samples that she brought with her from her postdoctoral position, she didn't label them properly. Then she didn't know what it was in the tube."*³¹⁵

RESPONSE TO THE PRELIMINARY REPORT

Dr. Pichiorri was provided a copy of the Preliminary Investigation Report³¹⁶ on November 6, 2019. As per the Policy, Dr. Pichiorri was given thirty (30) days to file a written response. On November 11, 2019, Dr. Pichiorri requested, through her attorney, an extension of the deadline until February 3, 2020.^{317, 318} Dr. Pichiorri provided a response to the Preliminary Investigation Report on February 2, 2020,³¹⁹ with thirty-nine (39) attachments.³²⁰ Additionally, Dr. David Sanders (Complainant) was provided a redacted version of the Preliminary Investigation Report, specific to the allegations he had made against Dr. Pichiorri,³²¹ and he has not provided any response. Dr. Radomska (Complainant) was also provided with a redacted version of the Preliminary Investigation Report, specific to the allegations she had made against Dr. Pichiorri,³²² and she has not provided any response. The COMIC carefully reviewed Dr. Pichiorri's response and the supporting documentation. The COMIC has not changed its determination regarding findings of Research Misconduct against Dr. Pichiorri under the Policy for Allegations #2-8, #12, and 15. Below are the primary issues included in Dr. Pichiorri's February 2, 2020 response.

³¹⁴ Ex. 166- Post-Interview Submission re Figure 3B further data to the IC, page 2

³¹⁵ Ex. 160 – 20190429-COMIC Interview + Errata – Radomska, page 41 lines 19-25

³¹⁶ Ex. 201 - 20191106 COMIC Preliminary Report -Pichiorri

³¹⁷ Ex. 191 - 2019-11-11 Ltr. to C. Culley with Ohio State University re Dr. Flavia Pichiorri

³¹⁸ Ex. 194 - 20191118 - RIO to FP - PR Response Deadline Extended

³¹⁹ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments

³²⁰ Ex. 199 - Dr. Flavia Pichiorri - Attachments to Investigation Report Comments

³²¹ Ex. 202 - 20191106 COMIC Preliminary Report -Pichiorri_Redacted Sanders

³²² Ex. 203 - 20191106 COMIC Preliminary Report -Pichiorri_Redacted Radomska



Dr. Pichiorri claims that she had not received training from Dr. Croce on how to generate figures and that she worked under Dr. Croce's direction. Dr. Pichiorri claims that the few mistakes that were made were unintentional and that the primary reason for these mistakes was inexperience and the lack of knowledge on how to store and maintain data.³²³ Dr. Pichiorri claims that as a postdoctoral fellow she still needed supervision herself.³²⁴ The COMIC agrees that postdoctoral training is important, but also believes that at this stage of her postdoctoral training, Dr. Pichiorri should already have known how to collect and maintain data and how to create figures. Dr. Pichiorri presumably included figures in her doctoral thesis, in four (4) published papers as a co-author and one (1) published paper as a first author between March 2006 – May 2010, and in three (3) additional papers published between 2011 and 2012, indicating that Dr. Pichiorri had significant experience. The COMIC believes that if Dr. Pichiorri did not know how to collect and maintain data and how to create figures, it was her responsibility to seek out information or guidance to ensure her research would be represented accurately.

Dr. Pichiorri admitted that she had extreme difficulty in keeping everything organized and that this disorganization resulted in incorrect experimental records being used.³²⁵ Dr. Pichiorri also claimed that "*my ability to work with these programs were zero.*"³²⁶ The COMIC believes that these admissions by Dr. Pichiorri are consistent with statements in the Preliminary Investigation Report and that they are incompatible with how a typical postdoctoral researcher would behave; i.e., to continue to do protocols and make figures despite a realization that you do not have the ability or knowledge to use the programs.

Dr. Pichiorri claims that mistakes occurred because lab members, herself included, did not have computers connected to OSU servers and used personal computers.³²⁷ The COMIC believes that a connection to a server is not pertinent to the specific image manipulations in question.

For each manuscript in question, Dr. Pichiorri claims that she was not responsible for any of the figures in the allegations.

For Cancer Cell 2010 (Manuscript #1, Allegations #2-5, and #15), Dr. Pichiorri claims that [REDACTED] and Dr. Pichiorri was only provided with the data to make high resolution tiff figures.³²⁸

[REDACTED] Dr. Pichiorri claims she moved PowerPoint images provided by others to high resolution tiffs and assembled the high resolution figures, and she later realized that the high resolution figures were imported as entire panels and not as single subpanels, as she had previously claimed.³³⁰ Dr. Pichiorri claims that she performed experiments only for the figures that were not involved in the allegations.³³¹

³²³ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, pp. 5-6

³²⁴ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, p. 6

³²⁵ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, p. 6

³²⁶ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, p. 16

³²⁷ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, pp. 5-6

³²⁸ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, pp. 10-11

³²⁹ [REDACTED]

³³⁰ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, pp. 7, 12, 17, 19

³³¹ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, p. 10



For JEM 2013 (Manuscript 2, Allegations #6-8), Dr. Pichiorri claims that Drs. Palmieri, De Luca and Rocci made the figures and that Dr. Pichiorri did not “generate, save, or edit any of the figures in Manuscript #2 containing the mistakes.”³³²

For Oncotarget 2015, (Manuscript #3, Allegation #12), Dr. Pichiorri claims that Drs. Radomska and Canella assembled and corrected all the figures and that Dr. Radomska wrote and corrected the figure legends. Dr. Pichiorri maintains that she was responsible only for the correct figures that were presented in the grant applications.³³³

The COMIC notes that Dr. Pichiorri has shifted responsibility for the falsifications in these three manuscripts to co-authors who might have performed the experiments. The COMIC believes that the responsibility should lie with the individual assembling the figures, which by her own admissions, is Dr. Pichiorri. The COMIC notes that of the co-authors named by Dr. Pichiorri, only Dr. Pichiorri is a common author on all three manuscripts. In addition, the COMIC believes that it is standard lab practice for co-authors to review all raw data included in a paper, especially for the first or last authors, regardless of whether the individual actually performed the experiments.

Dr. Pichiorri claims that she provided corrections to the journal for Cancer Cell 2010, Figures 4A and 7A (Allegations #2 and #5) before the allegations were raised, as evidence that she sought to ensure the paper did not contain any errors.³³⁴ The COMIC finds it particularly disturbing that the additional errors in Figures 5A and 4D/7A (Allegations #3, #4 and #15) were not identified by Dr. Pichiorri at that time. The COMIC believes that a typical researcher alerted to a problem with any of the figures in the manuscript would have been very careful to ensure that *all* of the data in the full manuscript was reviewed for accuracy.

The COMIC also believes that falsification/research misconduct is not diminished because the conclusions of the research remain unchanged or if other laboratories obtained the same conclusions, as claimed by Dr. Pichiorri throughout the response. For example, the COMIC strongly disagrees with Dr. Pichiorri’s claim that the p53 Scr data in Figure 5A (Allegation #3) was irrelevant and does not impact the manuscript’s conclusions.³³⁵ Without valid control data there is no way to judge the accuracy of any experimental result. The COMIC believes that it is alarming that any researcher at Dr. Pichiorri’s level would believe that control data are irrelevant.

The COMIC notes that Dr. Pichiorri’s explanations have changed in subtle ways throughout the proceedings, weakening the trustworthiness of her current explanations. The COMIC believes that none of Dr. Pichiorri’s current arguments justify how an image would be altered by stretching, flipping or inverting. The COMIC also believes that Dr. Pichiorri did not provide sufficient evidence to prove that high resolution figures were imported as entire panels and not as single subpanels, as she initially had claimed. The COMIC believes that Dr. Pichiorri’s claims regarding her knowledge that she was inexperienced, disorganized, did not check all the data when alerted to a problem, and in 2013 knew about poor data collection and maintenance issues, all provide evidence of reckless behavior, at the very least. In summary, based on all of the evidence reviewed throughout the duration of the case, including Dr. Pichiorri’s comments to the Preliminary Investigation Report, the COMIC affirms its earlier conclusion that nine (9) allegations (Allegations #2-8, #12 and #15) do constitute Research Misconduct as defined in the Policy III. A and 42 C.F.R. § 93.103 (b) and that one (1) allegation

³³² Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, p. 21-22

³³³ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, pp. 27-28

³³⁴ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, pp. 20-21

³³⁵ Ex. 198 - 2020-02-03 Pichiorri Investigation Report Comments, p. 14



(Allegation #14) does not constitute Research Misconduct as defined in the Policy III. A and 42 C.F.R. § 93.103 (b) and should be dismissed.

Recommended Actions

Under the University Policy and Procedures Concerning Research Misconduct, section IV.F.5, the Committee shall include recommended sanctions in cases where allegations of Research Misconduct are substantiated. Given the pattern and scope of the Research Misconduct findings against Dr. Pichiorri, the COMIC would strongly recommend that the following sanctions be imposed:

1. Given the gravity of the offenses, the COMIC believes that the revocation of tenure and termination of employment (which would necessarily include ending her ability to conduct research, oversee graduate student research, and participate in service) are appropriate sanctions. However, since Dr. Pichiorri is no longer employed by Ohio State following her resignation on August 16, 2016, the COMIC cannot impose these sanctions. Therefore, it recommends that, as to her employment, Dr. Pichiorri should be deemed permanently ineligible for rehire at Ohio State."
2. RETRACTIONS - The COMIC recommends that Dr. Pichiorri be required to work with the Institution and the other co-authors in contacting the following journals to request the immediate retraction of the following manuscripts:
 - a. Manuscript #1 – Pichiorri et al., *Cancer Cell* 2010; 18(4):367-368.
 - b. Manuscript #2 – Pichiorri et al., *JEM* 2013; 210(5): 951-968.

In the event that Dr. Pichiorri does not immediately retract these publications, the COMIC recommends that the Institution take whatever actions are needed to effect retraction of these publications.

3. CORRECTIONS - The COMIC recommends that Dr. Pichiorri be required to work with the Institution and the other co-authors in contacting the following journals to process corrections for the following manuscripts. In the event that figures cannot be corrected with verified original research records, then retraction will be required:
 - a. Manuscript #5 – Canella et al., *Oncotarget* 2015; 6(31): 31134–31150. Correction of Figure 3B

In the event that Dr. Pichiorri does not immediately take steps to correct this publication, the COMIC recommends that the Institution take whatever actions are needed to effect retraction of the publication.

Review of ORI requested publications and grants

On January 11, 2019, Ohio State notified ORI that an investigation was warranted in this case. In response to OSU's notification, ORI sent a letter, dated January 22, 2018, stating:

"The committee should focus on the scope of the misconduct (per 42 C.F.R. Part 93.3 10(h)), including Dr. Pichiorri's papers, manuscripts submitted but not accepted for publication, and any grant applications (submitted or not) and progress reports, subject to the time limitations stated in 42 C.F.R. Part 93.105. See the enclosed lists of PHS-supported published papers and NIH grant applications."

Ohio State reviewed the thirty-four (34) publications listed in the attachment to ORI's letter of publications that were not included in the allegations under review but had Dr. Pichiorri as an author and reviewed nineteen



(19) grant applications and progress reports also listed in the attachment to ORI's letter. ORC found no additional credible or specific allegations to include in the Investigation.³³⁶

Length of Proceedings

The proceedings have taken longer than the regulatory allotted one hundred and twenty (120) days to complete due to the extensive nature and scope of the allegations, the large number of manuscripts involved each containing many questioned figures, and the Respondent no longer being at Ohio State. The Ohio State University Office of Research Compliance did obtain all necessary and appropriate extensions to the deadline from the Office of Research Integrity during this process.^{337,338,339,340,341,342,343}

Previous Corrections/Retractions

Manuscript #1³⁴⁴: Pichiorri F*, Suh SS*, Rocci A, De Luca L, Taccioli C, Santhanam R, Zhou W, Benson DM Jr, Hofmeister C, Alder H, Garofalo M, Di Leva G, Volinia S, Lin HJ, Perrotti D, Kuehl M, Aqeilan RI, Palumbo A, and Croce CM. "Downregulation of p53-inducible microRNAs 192, 194, and 215 impairs the p53/MDM2 autoregulatory loop in multiple myeloma development." *Cancer Cell*. 2010 Oct 19;18(4):367-81. **CORRECTED-08/08/2016**^{345, 346} *Co-first authors

Manuscript #2³⁴⁷: Pichiorri F*, Palmieri D*, De Luca L, Consiglio J, You J, Rocci A, Talabere T, Piovan C, Lagana A, Cascione L, Guan J, Gasparini P, Balatti V, Nuovo G, Coppola V, Hofmeister CC, Marcucci G, Byrd JC, Volinia S, Shapiro CL, Freitas MA, and Croce CM. "In vivo NCL targeting affects breast cancer aggressiveness through miRNA regulation." *J Exp Med*. 2013 May 6; 210(5):951-68. Epub 2013 Apr 22. **CORRECTED-05/01/2017**³⁴⁸ *Co-first authors

Manuscript #6³⁴⁹: Trapasso F*, Pichiorri F*, Gaspari M, Palumbo T, Aqeilan RI, Gaudio E, Okumura H, Iuliano R, Di Leva G, Fabbri M, Birk DE, Raso C, Green-Church K, Spagnoli LG, Venuta S, Huebner K, Croce CM. Fhit interaction with ferredoxin reductase triggers generation of reactive oxygen species and apoptosis of cancer cells. *J Biol Chem*. 2008 May 16;283(20):13736-44. Epub 2008 Mar 3. *Trapasso and Pichiorri are co-first authors. **RETRACTED 08/03/2017**³⁵⁰ *Co-first authors

³³⁶ Ex 189 - Response to ORI Request for Additional Review

³³⁷ Ex. 125 - 20190522 - ORI Extension Request -DIO 6816

³³⁸ Ex. 188 – 20190923- ORI Extension Request-DIO 6816

³³⁹ Ex. 204 - 20191118 - RIO to ORI - DIO 6816 Update and Extension Request

³⁴⁰ Ex. 205 - 20191118 - ORI to RIO - Extension Granted

³⁴¹ Ex. 206 - 20200312 - ORI Extension Request

³⁴² Ex. 207 - 20200312 - Email RIO to ORI - Extension Request

³⁴³ Ex. 208 - 20200312 - Email ORI to RIO - Extension granted

³⁴⁴ Ex. 4 - Pichiorri et al., *Cancer Cell* 2010

³⁴⁵ Ex. 5 - Correction-Cancer Cell 2010

³⁴⁶ Correction of Figures 4A and 7A only

³⁴⁷ Ex. 6 - Pichiorri et al., *J Exp Med* 2013

³⁴⁸ Ex. 7 - Correction- *J Exp Med* 2013

³⁴⁹ Ex. 11 - Trapasso et al., *JBC* 2008

³⁵⁰ Ex. 12 - Retraction-*J. Biol. Chem.*-2017-Trapasso-14279(1)



Appendix

Complainants:

1. David Sanders, Ph.D., Associate Professor of Biological Sciences at Purdue University;
Counsel to David Sanders: William Nolan, Esq. Barnes and Thornburg LLP
2. Hanna Radomska, Ph.D., Research Scientist, OSU Comprehensive Cancer Center;
3. Anonymous - referred by Beckman Research Institute of the City of Hope (COH) Comprehensive Cancer Center.

Respondent:

Flavia Pichiorri, Ph.D., former OSU Assistant Professor, Division of Hematology, College of Medicine. Current Position/Institution: Associate Professor, Judy and Bernard Briskin Center for Multiple Myeloma Research, Beckman Research Institute of the City of Hope (COH) Comprehensive Cancer Center.

Counsel to Flavia Pichiorri: Paul Thaler, Esq. Cohen Seglias PC

Committee Members:

- Arthur Burghes, Ph.D. **(Chair)** Professor, Department of Biological Chemistry and Pharmacology, College of Medicine
- Brandon Biesiadecki, Ph.D., Associate Professor, Department of Physiology & Cell Biology, College of Medicine
- Jonathan Davis, Ph.D., Professor, Department of Physiology and Cell Biology, College of Medicine
- Jill A. Rafael-Fortney, Ph.D., Professor, Department of Physiology & Cell Biology, Biological Chemistry & Pharmacology, College of Medicine
- Yutong Zhao, M.D., Ph.D., Professor, Department of Physiology and Cell Biology, College of Medicine
- Thomas Hund, Ph.D. **(non-COM representative)**, Professor, Department of Biomedical Engineering, College of Engineering
- Loren Wold, Ph.D. **(non-COM representative)**, Professor, Colleges of Nursing and Medicine (Physiology and Cell Biology)
- Colleen Rupp **(COM HR representative)**, Senior Employee and Labor Relations Consultant, Wexner Medical Center Human Resources, voting member only on allegations occurring during Respondent's HR designation of "staff"

Ex Officio Members/OSU Office of Research Compliance Staff:

- Dr. Julia Behnfeldt, Associate Director and Lead Research Integrity Officer (RIO)
- Ms. Courtney Mankowski, Associate Director/RIO
- Ms. Linda Neidhardt, Program Director

OSU Office of Legal Affairs Staff:

- Ms. Emily Schriver, Senior Associate General Counsel
- Mr. Brandon Lester, Associate General Counsel
- Ms. Nilu Ekanayake, Associate General Counsel

Known Research Support:

Manuscript #1: Pichiorri et al., Cancer Cell 2010 [In publication citation of support by: OSU Targeted Investment in Excellence Award and the Kimmel Foundation award (FP).PubMed citation of support by: NIH PO1 CA129242 (to C.M. Croce) and K12 CA133250 (to J. Byrd and W. Carson)]

Manuscript #2: Pichiorri et al., JEM 2013 [Supported by: NCI grants to C.M. Croce, the Kimmel Foundation award (to F. Pichiorri), OSU Start-up Funds (to F. Pichiorri), and CA107106 (to M.A. Freitas). This study was



partially supported by NCI grant U01 CA154200 and by the Spielman Fund for breast cancer research (to C.L. Shapiro).]

Manuscript #5: Canella et al., Oncotarget 2015 [Supported by: Award U01CA076576, Award T32CA165998 (DWS), Pelotonia award for medical students (AS), Award R21CA156222 (CCH, FP, JC, JW, ZL, and HSR) American Cancer Society seed grant (FP; partial support), Multiple Myeloma Opportunities for Research & Education (MMORE), ARNO Therapeutics.]

Manuscript #6: Trapasso F et al., J Biol Chem 2008 [Supported by: National Institutes of Health Grants CA77738 and CA78890.]

Correspondence and Documentary Evidence:

- Ex. 93 - 20180411 - Letter ORI to OSU - DIO 6657
- Ex. 96 - 20181121 Email Pichiorri to RIO-Response to PR
- Ex. 97 - 20181207-CII Final Report-Pichiorri
- Ex. 101 - 20181218 CII Chair to RIO-Extension
- Ex. 102 - 20181207-CII Final Report-Pichiorri_revised 20181218
- Ex. 103 - 20181219 Email RIO to CII Chair - Extension Granted
- Ex. 105 - 20181220- Email RIO to Pichiorri-DO Decision
- Ex. 107- 20181220- Email RIO to Radomska-DO Decision
- Ex. 109 - 20181220- Email RIO to Sanders-DO Decision
- Ex. 111 - 20190108- Email RIO to COM HR-Referral
- Ex. 112 - 20190111 - Email Notice to ORI and NIH of Investigation - Pichiorri
- Ex. 113 - 20190111 - Memo to ORI re electronic documents
- Ex. 115 - 20190122 -Letter ORI to RIO-Response to Inv. Notice_FP
- Ex. 116 - 20190220-RIO to Pichiorri-COMIC Comp
- Ex. 117 - 20190227 - Email Pichiorri to RIO-COMIC Comp
- Ex. 118 - 20190304-Email RIO to Pichiorri - COMIC Request
- Ex. 119 - 20190304- Letter RIO to Pichiorri - COMIC Request
- Ex. 121 - Exhibit 1-Summary of Pichiorri Allegations for Investigation
- Ex. 122 - Exhibit 1-Summary of Pichiorri Allegations for Investigation revised 20190312
- Ex. 124 - Summary Figure Forensics_Pichiorri
- Ex. 126 - 20190412- Email RIO to Pichiorri
- Ex. 127 - 20190411-Email Pichiorri to RIO_Point by point
- Ex. 164 - 20190516-Email Pichiorri to RIO_Fig 3B
- Ex. 167 - 20190516-Document 1 5-16
- Ex. 168 - 20190516-Document 2 5-16
- Ex. 169 - 20190516-Document 3 5-16
- Ex. 170 - 20190516-Document 4 5-16
- Ex. 192 - 20191115 - Email RIO to SVPR - Request extension
- Ex. 193 - 20191115 - Email SVPR to RIO - Extension approved
- Ex. 195 - 2020-01-07 Letter to Ms. Ekanayake re Dr. Pichiorri
- Ex. 196 - 20200107 - Email Counsel to LA - request extension
- Ex. 197 - 20200110 - RIO to FP - Deadline Extension Denied
- Ex. 200 - 20200103 - Email Counsel to LA - Response to PR