

**University of Utah
Consolidated Hearing Committee
Complaint – Research Misconduct**

Respondent: Dr. Ivana DeDomenico

Complainants: Dr. Thomas Parks & Dr. Vivian Lee

Panel Report and Recommendations

May 8, 2013

Overview

This is a proceeding to hear charges against Assistant Professor Ivana DeDomenico in the Department of Internal Medicine, Division of Hematology. The charges in this matter were brought by the Senior Vice-President for Health Sciences and the Vice-President for Research following a report by an Investigation Committee dated December 14, 2012. A hearing panel was convened by the President of the Academic Senate and a hearing was conducted on April 29, 2013.

The CHC Panel has concluded that Dr. DeDomenico has engaged in research misconduct by “reckless disregard of accepted practices” in her area of research.

The Panel also finds that her behavior was part of a larger pattern of complicity in misconduct within [REDACTED] laboratories. We emphasize that the institutional responsibility for these matters should not end with sanctions against Dr. DeDomenico.

Research Misconduct Policy and Procedure

UU Policy 7-001(IV)(H):

"Misconduct" or "Misconduct in Research" means fabrication, falsification, plagiarism, or other practices that seriously deviate from those practices that are commonly accepted within the research community for proposing, conducting, or reporting research. It does not include honest error or honest difference in interpretations or judgments of data.

UU Policy 7-001(V)(6):

A finding of misconduct requires that:

1. There is a significant departure from accepted practices of the research community for maintaining the integrity of the research record.
2. The misconduct be committed intentionally, or knowingly, or in reckless disregard of accepted practices and
3. The allegation is proven by a preponderance of evidence.

UU Policy 6-002(III)(10)(D)(3)(b):

viii. Complaints alleging misconduct in sponsored research.

The CHC must find, by a preponderance of the evidence, that the respondent(s) engaged in research misconduct as defined in Policy 7-001.

In summary, to find the Respondent guilty of research misconduct, the Complainants bear the burden of proof to show (1) by a preponderance of the evidence (2) that the Respondent committed fabrication, falsification, or serious deviations from accepted research practices, (3) with intent, knowledge, or reckless disregard of accepted practices.

Charges and Response

The chronology of this matter is a bit murky. Apparently, it began in the fall of 2011 with concerns expressed by editors of a journal in which one of Respondent's papers had been published. This concern was communicated to the University's Research Integrity Officer, Dr. Jeffrey Botkin, who contacted the Respondent and her mentor, Dr. Jerry Kaplan. In the meantime, additional concerns were communicated from the Federal Office of Research Integrity from an informant "who wished to remain anonymous," but who later was identified as a previous collaborator on published papers, a professor at UCLA, Dr. Tomas Ganz.

A total of 11 published papers have been examined in the course of these proceedings. Those papers are numbered 1-11 in the attached table. The numbering corresponds to the examination that was conducted by prior committees as explained here. The irregularities discussed in those examinations fall into three main categories, all dealing with figures published as if they reflected results of laboratory experiments: (1) misrepresentation of images from films of laboratory experiments (gels transferred to "western blot" images and then scanned into computer files), (2) misleading or erroneous creation of graph curves reflecting CD (circular dichroism) data, (3) and inaccurate error bars. The types of errors found in each paper are indicated in the attached table.

Dr. Botkin convened an Inquiry Committee on December 22, 2011, and charged the committee to look at alleged irregularities in three papers. The Inquiry Committee expanded its scope to six papers and submitted its report on February 16, 2012, with findings of errors with regard to several blot figures. A review by an independent statistician, however, found no significant difficulty with the error bars in those papers. The Inquiry Committee finished with these conclusions:

The Committee did not uncover evidence of intent to deceive or misrepresent the data from the experiments in question. Rather, there was extreme carelessness on the part of Dr DeDomenico in preparing the figures and little oversight from [REDACTED] in ensuring that the figures accurately reflected the primary data. . . . [W]e recommend that all papers jointly authored by Drs. DeDomenico [REDACTED] be independently reevaluated, and if additional errors are found, that these be fully disclosed to the editors of the journals involved.

Shortly thereafter, on March 4, 2012, Dr. Botkin received allegations again from Dr. Ganz of additional errors in two other published papers. Dr. Botkin met with Drs. DeDomenico [REDACTED] on March 5, 2012, and informed them of his decision to convene an Investigation Committee with regard to all questioned papers. That committee was formed in April 2012. It examined not just the six papers initially in question but went further to examine five additional papers on which Drs. DeDomenico [REDACTED] were co-authors. The committee produced a preliminary report on October 2, 2012, to which the Respondents were allowed to comment, and then produced its final report on December 14, 2012.

The Final Report of the Investigation Committee provided this summary conclusion:

From its investigation, the Committee has concluded that the irregularities . . . constitute misrepresentations of the primary data and reflect a serious breakdown in the processes required to ensure that the scientific literature is a faithful record of research results. The large number of instances, over a period of several years, indicates a reckless disregard for the integrity of the research record, as opposed to the occasional lapses that might occur in any laboratory, and the resulting record is now nearly impossible to reconstruct.

The Investigation Committee also declared that it found instances of intentional falsification or fabrication of data. The CHC Panel has concluded, as explained below, that there likely was intentional falsification of published data or images, but we could not determine by a preponderance of the evidence that these items were the work of Dr. DeDomenico.

Thus, the CHC finding of misconduct is based on reckless disregard of accepted practice, a finding heavily influenced by the number of departures from established norms over an extended period. We recognize that the “accepted practices” in this particular laboratory and some of its collaborating laboratories may have countenanced the carelessness and obfuscation described by both prior committees, but these irregularities exceeded both accepted practice in the broader research community in which Respondent was educated as well as basic norms of right and wrong.

Evidence

This proceeding has produced a rather voluminous record. The principal items of evidence consisted of the report of the Investigation Committee (a 97 page document thoroughly examining the graphs and images in all 11 papers), detailed responses of Respondent to that analysis, testimony at the hearing by Dr. Yost explaining some of the key points in the Investigation Committee report, testimony in support of Dr. DeDomenico by Drs. Kaplan and Coulombe, and statements by Respondent herself.

To simplify understanding of the record, the CHC Panel constructed a table listing each paper by number along with the types of alleged irregularities, the Investigating Committee conclusions regarding the allegations, and some indication of the evidence behind those conclusions.

At the hearing, Dr. Yost produced a PowerPoint and oral presentation focusing on three of the papers (## 1, 10, & 11) that seemed to be the key evidence of either intentional or reckless disregard of accepted practices. To clarify our own conclusions, the Panel will likewise concentrate here on those same three papers. What we have gleaned from these and Dr. Yost’s summary is that there was intentional misrepresentation of data in at least one instance but we cannot determine who did it, that Drs. DeDomenico [REDACTED] as either lead author or senior author bore responsibility for spotting what seemed in at least two instances to be attention-getting misrepresentations, that [REDACTED] was probably responsible for at least one irregularity that was beyond the knowledge base of Dr. DeDomenico, and that in sum total the number of instances of irregularities in these papers shows reckless disregard for accepted practices in the research community.

We have not taken instances of missing data to count against Dr. DeDomenico except in those instances in which she was constructing figures for publication and should have had the data to support those figures.

Respondent’s Procedural Concerns

Dr. DeDomenico objected to Dr. Botkin’s convening of an Investigation Committee. She asserted that the procedure violated University regulations, federal law, and due process. There were two separate sets of issues raised – one set of issues regarding the original six papers and the other regarding the additional five papers. The Chair treated these objections as a motion to dismiss and issued a ruling on April 17, 2013.

With regard to the first set of papers, the argument is that the Investigation was not warranted at all because the Inquiry Committee did not recommend further investigation after reviewing the papers that were subject of the original Inquiry. DeDomenico points out that no provision of law or University policy empowers the RIO to determine independently that an investigation is warranted or to act against the finding of the Inquiry Committee. The University position was that the Inquiry Committee found “some substance” to the allegations of misconduct on the initial papers and that in the midst of determining how to proceed at that point, more allegations came in, at which point Botkin decided, with the federal RIO’s blessing, to proceed with the investigation phase.

There are two important interests at stake in these proceedings, the importance of research integrity to the University and due process to the individual. The Chair agreed that the federal office could not speak for the University with regard to our procedures.

With regard to the first six papers, the Inquiry Committee did find “that each of these papers, and perhaps others from these combined authors, contain misrepresentations of the primary results and thus deviate significantly from accepted scientific practice.” The committee then recommended that “all papers jointly authored by Drs. DeDemonico [REDACTED] be independently reevaluated.” Although not a formal recommendation for the convening of an Investigation Committee, the conclusions did encourage the RIO to proceed further in light of departures from accepted scientific practice. Indeed, the University regulations do not explicitly preclude the RIO from convening an Investigation Committee in the absence of a formal recommendation from the Inquiry Committee. Although the regulations require the convening of an Investigation Committee when the Inquiry Committee recommends it, the integrity of the University could mandate an Investigation in any event. This prospect flows from the requirement that the “inquiry record must contain sufficiently detailed documentation of the inquiry to permit a later assessment of the reasons for determining that an investigation was not warranted,” and the requirement that the records be maintained in a secure manner for at least three years. All of these provisions look toward the prospect of a follow-up investigation at a later date.

Given that new allegations with respect to additional papers then surfaced, it was understandable that the RIO chose to manage procedures to ensure a thorough investigation, which resulted in charges brought before the CHC which must make its own findings on the evidence presented to it. Under these circumstances, the lack of an Inquiry Committee on the additional papers was not a sufficiently fundamental flaw as to require dismissal just to protect the integrity of University processes.

It is possible, however, with due process in mind, that Respondent was prejudiced in her ability to respond to the allegations by the timing of the two committee proceedings and the resulting methods of the Investigation. Under these circumstances, the Chair suggested that she explain any harm or prejudice that she experienced from the procedural posture of the proceedings.

In her written and oral statements, she did suggest that she would have been better prepared to respond to allegations if there had been an Inquiry Committee on the additional papers. She also pointed to a paucity of personal interaction with the Investigation Committee and to open hostility from one member of the Investigation Committee.

With regard to ability to respond, she did meet with the Committee three times and was given six weeks to respond to a preliminary report of the Committee, which she did in rather thorough fashion. With regard to personal hostility, when the Panel asked the Chair of the Investigation Committee about this, he responded that passions naturally run high in charges of misconduct and that he did not perceive any bias or prejudice on the part of the one rather outspoken member of the Committee. Respondent did not pursue this issue further during the hearing.

Findings

The hearing panel finds the following facts established by a preponderance of the evidence:

1. Paper 11 contained images that were intentionally manipulated to present false data. This was done by computer copying of information from one scanned image to another or in some instances by splicing of gel images to make one image. While the Panel agrees that this manipulation does appear to have been intentional, we cannot conclude that it was done by Dr. DeDomenico as opposed to an unknown third person. Nevertheless, the error appears so obvious that it should have been caught by a responsible lead or senior author.
2. Paper 1 contained several instances of flipped or mislabeled images. Although neither the Committee nor this Panel has found that these irregularities were intentional, the number and severity show reckless disregard to accepted practices. (Recklessness in this instance consists of proceeding with publication in the face of a very substantial risk of disseminating inaccurate information to the scientific community. The substantiality of risk stems from the number and severity of the errors.)

3. Paper 10 contained misleading graphs of CD data. The graphs were misleading by having been “smoothed out” in violation of usual practice in the field and fabricated by switching the sign of one data point so that the first half of the graph was inverted. Also significant and unlikely was that the CD data had exactly the same magnitude in different tables with a couple of exceptions; in addition, it was significant that the fabricated data were inconsistent with the conclusions of the paper. Dr. Kaplan testified that these graphs were produced by [REDACTED] and that he did not expect Dr. DeDomenico to have expertise with regard to these processes. Indeed, although Dr. DeDomenico was listed as lead author on this paper, it seems that she had little or nothing to do with the experiments leading to the contested portions of the paper. The Investigation Committee laid the blame for these errors squarely on the procedures in [REDACTED] laboratory.
4. The Investigation Committee listed 3 instances of what they described as “Alteration of Research Record.” These are highlighted at the end of the attached table. For the following reasons, the CHC Panel is not persuaded by a preponderance of the evidence that the alleged alterations of research records can be laid at the feet of Dr. DeDomenico:
 - a. As stated above, the CHC Panel cannot find that Dr. DeDomenico was responsible for the intentional manipulation in Paper 11.
 - b. Nor do we find the alleged falsification in Paper 6 to be supported by the record. The Committee stated: “At the least, the dates on the films and notes were most likely added several months after the work was done, and it is possible that the notes themselves were written then. This may have occurred after receipt of the allegations.” But MAY HAVE is not enough for our purposes; the evidence that she fabricated notebook pages is confusing and not sufficiently persuasive of intentional falsification.
 - c. With regard to Paper 10, the e-mail strings regarding handling of the CD data do not include [REDACTED] on whom Dr. Kaplan stated that he relied for the CD data presentation.
5. There are multiple instances of errors in 10 of the 11 papers examined. The only one in which no errors were found was the one in which Dr. DeDomenico was the “Senior Author,” meaning that other authors were responsible for the initial preparation of data, charts, and images. As first author on the other papers, she bore responsibility for checking all graphs and figures against the raw data and then maintaining an adequate record from which later researchers could replicate the experiment. Her explanations of these errors all relied on asserting that someone else did key parts of the work, but in almost all instances she was responsible for producing the actual images that were presented to the publisher. For two reasons, her explanations are inadequate:
 - a. if true, then her explanations show a lack of control over data for which she was responsible as first author or preparer of the figure for publication
 - b. it strains credulity that so many people could make similar errors without her catching at least some of them
6. In summary, our findings on the overall record are similar to what we found with regard to Paper 1. Although the Panel does not find that intentional irregularities can be attributed to Dr. DeDomenico, the number and severity of errors in the publications where she is first author show reckless disregard for accepted practices. Recklessness consists of proceeding with publication in the face of a very substantial risk of disseminating inaccurate information to the scientific community. The substantiality of risk stems from the number of publications affected and the severity of the errors.

Conclusions

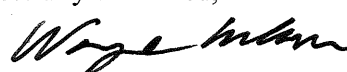
Based on the above findings, the panel concludes

1. Dr. DeDomenico violated the Faculty Code through Research Misconduct based on “reckless disregard of accepted practices.”
2. There was complicity in this misconduct within the laboratory that goes substantially beyond Dr. DeDomenico.

Recommendations

1. The Panel regretfully concurs with the Investigation Committee’s recommendation that Dr. DeDomenico be terminated or allowed to resign from the University.
2. The Panel is concerned that the University take full appropriate action with regard to the institutional difficulties uncovered in this proceeding. The problems outlined by the Investigation Committee are not likely to be resolved with one termination and one retirement. Thus, we recommend further investigation of the laboratory procedures uncovered in this investigation.

Respectfully submitted,

 5/8/13

Wayne McCormack, Chair, College of Law

Richard Dorsky, Neurobiology & Anatomy

Scott Wright, Nursing

Jon Rainier, Chemistry

Darrell Davis, Medicinal Chemistry

Mikhail Skliar (Alternate), Chemical Engineering

Table of Investigation Committee Report Items Regarding Dr. DeDomenico

Paper & Date	Problem	Evidence & Invest. Comm Conclusions	Lead Author	Senior Author
1 (2011)	blot manipulation	no indication of where original film is located ██████ files not examined for originals or notebooks - her computer had no files deleted - she says "three people participated in experiments" - not clear who had control of blots and films but she was primary author	DeDomenico	Kaplan
	error bars	Stoddard found no problem with calculations but doubted veracity of original data		
2 (2008)	blots flipped & duplicated	"We were unable to establish a cogent explanation for these irregularities aside from the possibilities of carelessness, negligence, capriciousness with flagrant or reckless disregard for fidelity of the published report of the original data, and/or intent." ██████ did not rule out possibility of carelessness in lab processes.	DeDomenico	Kaplan
3 (2009)	duplication of data in two publications	"The findings are most consistent with carelessness, but the Committee could not exclude negligence, capriciousness with flagrant or reckless disregard for fidelity of the original data, or intent."	DeDomenico	Kaplan
4 (2009)	duplication of data in two publications	"The data in Figure 4A in Paper 4 appear to be correct as labeled, based on the statements of Drs. Kaplan and De Domenico. Therefore, the duplication and misrepresentation were in Paper 3, the PNAS article."	Koenig	DeDomenico
5 (2007)	same photo shown twice	"In summary regarding this allegation, the Investigation Committee concludes that there was duplication of data in this publication. The findings are suggestive of carelessness, but the Committee cannot exclude negligence, extreme capriciousness, or intent." Code in notebooks "illicitly discarded by dismissed technician"	DeDomenico	Kaplan
6 (2011)	error bars	"The issue of error bars was not discussed further with her or ██████ in the interviews." ██████ stated that the processes for calculating these were consistent with his scientific expertise.	DeDomenico	Kaplan
	fig. 4B blot disparities	"Our major conclusion is that the path from the primary data to the publication has been so poorly documented and corrupted by relabeling that no confidence can be placed on the published figure."		
	fig. 5B film date disparities	"The available records are inadequate to determine whether the published figure was correctly labeled. The inconsistencies between the dates shown on the film, the notes and the submission date raise additional doubts about the reliability of the notes."		

6 (cont'd)	general concerns	"The failure of Dr. De Domenico to provide the computer files documenting the data analysis in the published paper (and the failure of the Committee to find such files through a systematic search) is evidence of recklessness in maintaining the research record." Her response is that Committee was asked to look at Kaplan's records and no request was made to Kaplan for original data.		
7 & 8 (2007)	gel lane inaccuracies	Kaplan stated that cell expansion easily accounts for apparent lane violations	DeDomenico	Kaplan
	inaccurate splicing of gel images	"It appears that Drs. De Domenico [REDACTED] had full control over presentation of the experimental data and both of them must be held responsible for the misrepresentations that have come to light. The Investigation Committee considers it unlikely that these errors were due to simple carelessness during the preparation of the figures for publication. The Committee is also struck by the conspicuous failure of all coauthors, particularly [REDACTED], to catch and correct these mistakes before publication."		
9 (2007)	splicing of gels	"Based on the inconsistencies in the execution of the experiments and in the preparation of the figures, little confidence can be placed on the accuracy of the published data." No finding of intent or reckless disregard [REDACTED] stated she was responsible for making figures.	DeDomenico	Kaplan
10 (2008)	error bars	Kaplan stated that statistical analysis was consistent with his scientific practices.	DeDomenico	Kaplan
	CD graphs	Kaplan stated that he saw no problem with "smoothing" of data and that he knew DeDomenico had no expertise in CD. No finding of intent from the Invest. Committee.		
	NMR data	Kaplan stated that he did not trust the data so omitted it.		
	general concerns	DeDomenico was not involved in these experiments. Committee stated: "Particularly in light of his own lack of expertise in these techniques, [REDACTED] should have ensured that all of the data were shared among the participants. In summary, the Committee concludes that this paper contains instances of data falsification and data fabrication and that this paper should be retracted. The circumstances leading to the publication of falsified and fabricated data indicate flaws in the management of the laboratory and collaboration."		
11	blot manipulation	"substantial concerns" that published images were misrepresentations of scans	Kieffer	Kaplan -- DeDomenico is contributor

"Alteration of Research Record"				
Allegation 1 (paper 1)	12 cell / 10 cell issue	Kaplan stated that he had seen "swelling" account for the apparent disparity		
Allegation 2 (paper 6)	incorrect dates on film and notebook pages	"At the least, the dates on the films and notes were most likely added several months after the work was done, and it is possible that the notes themselves were written then. This may have occurred after receipt of the allegations." No direct evidence that she altered dates and particularly not after allegations		
Allegation 3 [IC labelled 4] (paper 11)	CD data	"The preponderance of evidence leads the Committee to conclude that the notebook pages provided by Dr. De Domenico on 9-11-12 were most likely created after she became aware of concerns regarding the CD spectra and were intended to mislead the Committee and shift responsibility to Dr. Ganz." Kaplan made it clear that he did not expect CD expertise from DeDomenico. He stated that "I think [REDACTED] sent Ganz the manuscript."		

Paper 1: De Domenico I, Lo E, Yang B, Korolnek T, Hamza I, Ward DM, Kaplan J. (2011). The Role of Ubiquitination in Hepcidin-Independent and Hepcidin-Dependent Degradation of Ferroportin. *Cell Metabolism* Nov 2;14(5):635-46

Paper 2: De Domenico I, Lo E, Ward DM, Kaplan J. Hepcidin-induced internalization of ferroportin requires binding and cooperative interaction with JAK2. *Proceedings of the National Academy of Sciences USA* 2009; 106: 3800-3805

Paper 3: De Domenico I, Zhang TI, Koenig CL, Branch RW, London N, Lo E, Daynes RA, Kushner JP, Li D, Ward DM, Kaplan J. Hepcidin mediates transcriptional changes that modulate acute cytokine-induced inflammatory responses in mice. *Journal of Clinical Investigation* 2010; 120: 2395-2405.

Paper 4: Koenig CL, Miller JC, Nelson JM, Ward DM, Kushner JP, Bockenstedt LK, Weis JJ, Kaplan J, De Domenico I. Toll-like receptors mediate induction of hepcidin in mice infected with *Borrelia burgdorferi*. *Blood* 2009; 114: 1913-1918.

Paper 5: De Domenico, Vaughn MB, Yoon D, Kushner JP, Ward DM, Kaplan J. Zebrafish as a model for defining the functional impact of mammalian ferroportin mutations. *Blood* 2007; 110: 3780-3783.

Paper 6: De Domenico I., Vaughn, M.B, Paradkar, P.N., Lo, E., Ward, D.M. and Kaplan, J. (2011) Decoupling ferritin synthesis from free cytosolic iron results in ferritin secretion. *Cell Metabolism*. 13, 57-67.

Paper 7: De Domenico, I., D. M. Ward, M. C. di Patti, S. Y. Jeong, S. David, G. Musci & J. Kaplan (2007). "Ferroxidase activity is required for the stability of cell surface ferroportin in cells expressing GPI-ceruloplasmin" *EMBO J* 26(12): 2823-2831.

Paper 8: De Domenico, I., D. M. Ward, C. Langelier, M. B. Vaughn, E. Nemeth, W. I. Sundquist, T. Ganz, G. Musci and J. Kaplan (2007). "The molecular mechanism of hepcidin-mediated ferroportin down-regulation." *Mol Biol Cell* 18(7): 2569-2578.

Paper 9: De Domenico, I, McVey Ward, D, Musci, G and Jerry Kaplan. "Evidence for the multimeric structure of ferroportin." *Blood* 2007 Mar 1;109(5):2205-9

PAPER 10: De Domenico I., Nemeth, E., Nelson, J.M., Philips, J.D., Ajioka, R.S., Kay, M.S., Kushner, J.P., Ganz, T, Ward, D.M. and Kaplan, J. (2008) The hepcidin-binding site on ferroportin is evolutionarily conserved. *Cell Metabolism*. 8, 146-156.

PAPER 11: Kieffer, C., Skalicky, J. J., Morita, E., De Domenico, I., Ward, D. M., Kaplan, J. and Sundquist, W. I. (2008). Two distinct modes of ESCRT-III recognition are required for VPS4 functions in lysosomal protein targeting and HIV-1 budding. *Dev Cell* 15: 62-73.