

February 23, 2017

Dr. Tei-Wei Kuo
Executive Vice President for Academic & Research
National Taiwan University

Dear Executive Vice President Kuo,

This is part II of our report from the Ad Hoc Committee that was assembled to investigate the possible scientific misconduct by Min-Liang Kuo, PhD (郭明良), professor in the Colleges of Medicine and Life Science, and former Dean of the College of Life Science, NTU, his team, and his collaborators including President Pan-Chyr Yang (楊泮池). In part I of our report, we analyzed two of Prof. Kuo's papers, already retracted, containing perhaps the most serious offenses (Nature Cell Biology 2016 and Journal of Biol Chem 2008; see Appendix 01.Ad Hoc Comm Report I.pdf), and our results were consistent with the interim College Investigation Committee reports. In the next phase of investigation, our Committee focused on the investigation of President Yang – and that is the main theme of this report.

A. Summary:

National Taiwan University appointed this special Ad Hoc Committee to investigate the possible scientific misconduct of Professor Min-Liang Kuo, his team, and his collaborators including President Pan-Chyr Yang. Although when we were investigating Prof. Kuo and his team's involvement (Phase I) our committee included two senior NTU vice presidents, they and a member resigned when we started to investigate President Yang's case (Phase II) in order to ensure there was no potential conflict of interest. Thus for Phase II investigation our committee had six members, none of them from NTU. Although these members were recruited under the condition of anonymity, they are highly qualified to investigate this matter, as shown by their composition and expertise. Thus the members include Academicians of Academia Sinica (3); current or former senior executives (President, Dean, Director) of major organizations (5); a chair of US university investigation committees who interacted closely with ORI; and former Deputy Director of the US Office of Research Integrity (ORI), the top government agency in charge of investigating scientific misconduct in that country. In addition to investigating President Yang, our Committee was also asked to review the interim and final reports from the two Investigation Committees from the Colleges of Medicine and Life Science, in order to ensure the quality and cross-college consistency of their investigations. The results of our Phase I investigation are consistent with those of the college committees, and established that Prof. ML Kuo and some of his team members indeed committed scientific misconduct (Phase I report). The case before us, in this Phase II investigation, concerns the following scenario: Dr. Yang, an expert in the basic and clinical biology of lung cancer, began in early 2000's to collaborate with Dr. Kuo, a basic scientist, to study lung cancer, by providing clinical and translational insights, suggestions on

research direction, review of manuscript, and a panel of human lung cancer cell lines with various potential to undergo metastasis. This resulted in several collaborative publications since early 2000's in which Dr. Kuo was the Corresponding Author with Dr. Yang as a Co-author. In November 2016 seven of these collaborative papers were alleged by PubPeer to contain problematic figures. Of these, the Medical College Investigation Committee concluded that four indeed involved scientific misconduct and assigned primary responsibilities to their First Authors who produced these problematic data and Corresponding Author, Dr. Kuo (detailed in the Medical College report). The questions our Committee sought to address are: (i) Did Dr. Yang make sufficient contributions to qualify him as a co-author in the 7 papers mentioned above? (ii) If the answer is yes, should Dr. Yang bear any responsibility, as a co-author, in the four papers that contain problematic data/figures? and, (iii) depending on the answers to these two questions, should Dr. Yang resign from the Presidency? An unexpected obstacle of our investigation was that, although the qualification and responsibility of the First Author (who produced most of the data/figures) and the Corresponding Author (the leader of the project responsible for the overall integrity of the data/figures) were well-defined in the literature, those of the Co-author were not. Many opinions exist, but they are divergent and often contradictory to each other. After an in-depth analysis of these opinions, our Committee decided that we should follow the regulation from our own Ministry of Science and Technology (MOST; 科技部), not only because many of the studies were supported by MOST, but also because its definition of co-authorship is fair, practical, and consistent with opinions we received from the former Executive Editor of Nature Journals. Thus Article 9 in the MOST "Academic Ethics Guidelines for Researchers" states: "Co-authors shall provide significant and substantial academic contribution (such as the conception and design of the research, data collection and processing, data analysis and interpretation, and writing of the research paper) before they may be listed for the paper. According to the principle of joint responsibility, co-authors shall be responsible for the corresponding contents in the paper within a reasonable scope. In other words, any co-author listed in the paper shall be responsible *for the part that they have contributed.*" (科技部對研究人員學術倫理規範 9. 共同作者的責任: 共同作者應為對論文有相當程度的實質學術貢獻 (如構思設計, 數據收集及處理, 數據分析及解釋, 論文撰寫) 始得列名. 基於榮辱與共的原則, 共同作者在合理範圍內應對論文內容負責, 共同作者一旦在論文中列名, 即須對其所貢獻之部分負責). According to these regulations, President Yang qualified as a co-author in these papers. Moreover, since the problematic figures were produced by members of Dr. Kuo's lab and had nothing to do with *the part that Dr. Yang has contributed*, Dr. Yang is not responsible for the misconduct and is, in fact, an innocent victim who suffered from mistakes made by unscrupulous collaborators. Based on these findings, our Committee does not see any reason why President Yang should resign, and it hopes that he can use this experience as an opportunity to initiate educational and training programs to ensure that scientists at all levels in NTU are aware of, and adhere to, best research practices so that misconduct will be less likely to occur in the future.

B. Revised Charges and Change in Membership

During the earlier phase I of the investigation (when we investigated the involvement of Prof Min-Liang Kuo and his team members other than President Yang), our committee consisted of 7

members from outside of NTU, plus two NTU vice presidents. In the second phase of the investigation when we moved on to investigate President Pan-Chyr Yang, to avoid a potential conflict of interest, the two NTU officials and one outside member resigned. So our committee now consisted of six members, none of them from NTU. Although these reviewers were recruited under the condition of anonymity, they are highly qualified to investigate this matter, as shown by their composition and expertise: Academicians of Academia Sinica (3); current or former senior executives (President, Dean, Director) of major research organizations (5); chair of US university investigation committees who interacted closely with ORI (1); and former Deputy Director of the US Office of Research Integrity (ORI), the top government agency in charge of investigating scientific misconduct in the US. Our Committee met four times by semi-teleconference, and prepared the following report.

C. The Respondent:

Pan-Chyr Yang, MD, is Professor in Internal Medicine in the NTU College of Medicine, and, since 2013, President of NTU. He served as Chair of the Department of Internal Medicine and Dean of the NTU Medical College. His work on lung cancer biology, genomics and precision medicine is internationally recognized. He lists 622 papers many of which published in top-notch journals and are highly cited. These papers include one describing the classification of lung cancer (J Thoracic Oncology 2011, cited 2520 times); identification of the gene and microRNA signatures of lung cancer (New England J Medicine, 746 times; and Cancer Cell 2008, 690 times), lung cancer cell line models of lung cancer metastasis (Am J Respiratory Cell and Mol Biol 1997, 398 times); sonography in determining the nature of pleural effusion (Am J Roentgenology 2005, 389 times). His papers have garnered a total of 35,000 citations, with an h-index of 94 <https://scholar.google.com/citations?user=uhM7QZ8AAAAJ&hl=en>, which is highly respectable as, among 36 new inductees in the US National Academy of Sciences in biological and biomedical sciences in 2005, the median h-index was 57 https://en.wikipedia.org/wiki/H-index#cite_note-Hirsch2005-3. Consistent with this, Dr. Yang has received numerous national and international awards, including member of Academia Sinica, Fellow of National Academy of Inventors, Academician of the Academy of Sciences for the Developing World, National Chair Professor of the Ministry of Education, Taiwan ROC. He has served as Editor-in-Chief for two international journals, i.e., Lung Cancer: Targets and Therapy (2012~Present), and MicroRNA (2011~2014), and been on the editorial board of many journals including PLoS One, J Clinical Oncology, Carcinogenesis, Am J Respir Cell Mol Biol. and J Thoracic Oncology.

D. Papers in Question:

In this report, we focused on a subset of seven papers, in which Dr. Yang is a co-author, that are under investigation by the College Committees. These papers are listed below chronologically and assigned #1 to #7. Each reference is followed by the investigative conclusions drawn by the Medical College Investigation Committee (in Chinese). Of these, papers #2 and #3 were thought to involve serious misconduct possibly requiring retraction, papers #4 and #7 involve relatively

minor misconduct possibly resolvable by correction, while allegations against papers #1, 5 and 6 were deemed to be without merit (gray font).

1. Connective tissue growth factor and its role in lung adenocarcinoma invasion and metastasis, J. Natl. Cancer Inst., 2004, Cheng-Chi Chang, Jin-Yuan Shih, Yung-Ming Jeng, Jen-Liang Su, Been-Zen Lin, Szu-Ta Chen, Yat-Pang Chau, **Pan-Chyr Yang**, Min-Liang Kuo, [ID 04-] <https://pubpeer.com/publications/14996858> JNCI 2004 圖被用於 JNCI 2006 論文中，故 JNCI 2004 本身並無問題
2. The VEGF-C/Flt-4 axis promotes invasion and metastasis of cancer cells Cancer Cell, 2006, Jen-Liang Su, **Pan-Chyr Yang**, Jin-Yuan Shih, Ching-Yao Yang, Lin-Hung Wei, Chang-Yao Hsieh, Chia-Hung Chou, Yung-Ming Jeng, Ming-Yang Wang, King-Jen Chang, Mien-Chie Hung, Min-Liang Kuo* [ID 06-02]
<<https://pubpeer.com/publications/FA2209426FC5F07DAFA90A5B726FC7>
大量圖片重複使用，且交錯使用，嚴重違反學術倫理。
3. Knockdown of Contactin-1 Expression Suppresses Invasion and Metastasis of Lung Adenocarcinoma, Cancer Research 2006, Jen-Liang Su, Ching-Yao Yang, Jin-Yuan Shih, Lin-Hung Wei, Chang-Yao Hsieh, Yung-Ming Jeng, Ming-Yang Wang, **Pan-Chyr Yang** and Min-Liang Kuo*, [ID 06-01]
<<https://pubpeer.com/publications/022D597A8C72CE8661D19B2FE17468>
大量圖片重複使用，且交錯使用，嚴重違反學術倫理。
4. Effect of connective tissue growth factor on hypoxia-inducible factor 1alpha degradation and tumor angiogenesis, J. Natl. Cancer Inst., 2006, Cheng-Chi Chang, Ming-Tsai Lin, Been-Ren Lin, Yung-Ming Jeng, Szu-Ta Chen, Chia-Yu Chu, Robert J Chen, King-Jen Chang, **Pan-Chyr Yang**, Min-Liang Kuo*, [ID 06-03]
<https://pubpeer.com/publications/16849681> JNCI 2006 已提出更正，但並無正確之圖片，且第一作者將責任推給他人，該作者則不承認會是由他所造成，加上第一作者另有其他類似錯誤貼圖之情形，小組雖未能完全確定此篇違反學術倫理，但第一作者仍應負相當之責任。
5. Tumor-Associated Macrophage-Induced Invasion and Angiogenesis of Human Basal Cell Carcinoma Cells by Cyclooxygenase-2 Induction. Tjiu JW, Chen JS, Shun CT, Lin SJ, Liao YH, Chu CY, Tsai TF, Chiu HC, Dai YS, Inoue H, **Yang PC**, Kuo ML, Jee SH. J Invest Dermatol. 2009 Apr 129(4):1016-25. <https://pubpeer.com/publications/21841313> 可接受為無心之過
6. miR-107 promotes tumor progression by targeting the let-7 microRNA in mice and humans, J. Clin. Invest., 2011, Pai-Sheng Chen, Jen-Liang Su, Shih-Ting Cha, Woan-Yuh Tarn, Ming-Yang Wang, Hsing-Chih Hsu, Ming-Tsan Lin, Chia-Yu Chu, Kuo-Tai Hua, Chiung-Nien Chen, Tsang-Chih Kuo, King-Jen Chang, Michael Hsiao, Yi-Wen Chang, Jin-Shing Chen, **Pan-Chyr Yang**, Min-Liang Kuo*, [ID 11-01] <https://pubpeer.com/publications/21841313> 可接受為無心之過
7. CCN2 inhibits lung cancer metastasis through promoting DAPK-dependent anoikis and inducing EGFR degradation, Cell Death and Differentiation (2013) 20, 443–455, C-C Chang1, M-H Yang, B-R Lin, S-T Chen, S-H Pan, M Hsiao, T-C Lai, S-K Lin, Y-M Jeng, C-Y

Chu, R-H Chen, **P-C Yang**, Y Eugene Chin and M-L Kuo [ID 13-01] 仍然出現錯誤貼圖，第一作者屢次出現類似之不當的錯誤貼圖，(再加上其他幾篇已被認定違反學術倫理之論文中，第一作者需負責)，小組認定第一作者違反學術倫理。

E. Goals of Our Investigation:

To investigate President Yang's involvement, we asked the following three questions:

- **Question one:** Did Dr. Yang make sufficient contributions to warrant co-authorship?
- **Question two:** If the answer is yes, whether Dr. Yang bears any responsibilities for the problematic data/figure in these papers? and,
- **Question three:** Should Dr. Yang resign from the Presidency?

While questions 1-2 need to be addressed for papers #2, #3, #4 and #7, which contain problematic data, only questions one is relevant for papers #1, 5 and 6, which do not appear to contain significant misconduct.

In examining questions #1 and #2, we wanted to develop criteria that can be applied fairly and uniformly to all the co-authors in this case, while examination of question #3 involves special considerations uniquely applicable to President Yang.

Before we can address questions #1 and #2, however, we must define (i) what contributions one has to make in order to warrant co-authorship, and (ii) a co-author's responsibility in case the paper turns out to contain problematic data. Since there are widely divergent and often contradicting opinions about these two issues, we found it necessary to first conduct an in-depth analysis of these topics, i.e., the qualification and responsibilities of co-authorship (see next section).

F. A Discussion of Authorship: Qualification, Responsibility and Investigation:

We will discuss below mainly how we came to a decision about the qualification and responsibility of co-authors. However, for the purpose of comparison and completeness we will also review those of the Corresponding and First author.

F-1. Corresponding authorship: qualifications and responsibilities

Qualifications:

- Usually the director of the team.
- Approve data presentation as representative of the original data. Be responsible for the integrity of the work as a whole, and ensure that reasonable care and effort have been taken to determine that all the data are complete, accurate, and reasonably interpreted.

- Ensure that original data upon which the submission is based is preserved and retrievable for reanalysis.
- Fulfill editorial duties including ensuring that all authors approve of the final version of the manuscript, communicating with the journal, verifying that research on animals or human subjects has met necessary regulatory protocols.

Responsibility if the paper turns out to contain problematic data:

Since misconduct can occur occasionally in any laboratory, rules of the US Office of Research Integrity (ORI) do not automatically assume that the PI of the lab is responsible. This is because “A committed cheater can elude detection for years by playing on the trust — and the self-interest — of his or her colleagues.” (New York Time October 22, 2006). See Francis Collins case (Dahlberg workshop II slides 14-16, and 39; also see later). However, the Corresponding author is responsible **IF**:

- S/he is involved in, or responsible for, generating the problematic data and/or figures, or is aware of the occurrence but does not take appropriate actions.
- Multiple staff commit misconduct over a period of years suggesting a lab culture in which the staff assume that such practices are acceptable or even expected.

Investigation of Corresponding author’s responsibility in research misconduct cases:

- Determine whether the PI is actually responsible for the generation of the problematic data.
- Determine whether the PI knew about the research misconduct, or created a lab culture due to insufficient supervision and lack of mentorship where research misconduct was widespread in his/her lab (Dahlberg workshop II slide 40).

F-2. First authorship: qualifications and responsibilities:

Qualifications:

Usually the person who has performed the bulk of the work and generated most of the data/figures.

Responsibilities:

- Can understand the conceptual background and explain/defend the entire work.
- Is involved in the writing and editing of the paper.
- To organize and submit all the original data to the PI so that they are available for later re-evaluation.

Investigation:

Identify the person (first author or otherwise) who is responsible for generating and/or producing all the figures.

F-3. Qualification for Co-authorship:

Divergent opinions:

There are divergent and often contradicting opinions about *who qualifies to be a co-author*. On one extreme are the criteria suggested by the International Committee of Medical Journal Editors (ICMJE), which states that "authorship" (presumably including co-authorship) be based on the simultaneous satisfaction of ALL of the following 4 criteria: (i) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; and (ii) Drafting the work or revising it critically for important intellectual content; and (iii) Final approval of the version to be published; and (iv) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

A more practical and generally accepted view is that someone can make a broad spectrum of contributions to deserve co-authorship. For example, former Deputy Director of US Office of Research Integrity (ORI) stated that such contributions include at least the following: "(a) Development of model cell or animal systems crucial to the ongoing direction of the research project; (b) Expertise in a technique or reagent not otherwise available to a laboratory that is vital to answering key questions related to the project; this could involve cutting edge techniques new to the institution or equipment that is so expensive to purchase or operate that they require a core facility to be available to multiple laboratories; (c) Extensive experience/expertise essential to ensure that the experimental results obtained by more junior members of the laboratory are correctly interpreted and that the relevant scientific literature is carefully reviewed and accurately cited; (d) Often scientists with expertise not available from within a laboratory need to be included as co-authors due to their unique knowledge."

In support of this latter idea, i.e., co-authorship may be earned by a wide range of contributions: (i) Nature Journals stated, under their Authorship Policy, that "The Nature journals do not prescribe the kinds of contributions that warrant authorship but encourage transparency by publishing author contributions statements." (ii) A recent Nature article suggests to develop "digital taxonomies" to help researchers to self-identify their contributions to collaborative projects ["Publishing: Credit where credit is due", by Liz Allen, et al, *Nature* 508, 312–313; 17 April 2014; <http://www.nature.com/news/publishing-credit-where-credit-is-due-1.15033>]. Along the same line, Kakoli Majumder described many categories of author contributions including study conception, methodology, performing the experiments, data collection, resources, manuscript preparation, review or revision ["Defining authorship: A taxonomy to assign contributor roles in multi-author papers", Editage Insights, a Resources for authors and Journals,

May 5, 2014; <http://www.editage.com/insights/defining-authorship-a-taxonomy-to-assign-contributor-roles-in-multi-author-papers>].

Perhaps most relevant to the investigation of the current case, the Ministry of Science and Technology (MOST) defines the qualification of co-authors as: "Co-authors shall provide significant and substantial academic contribution (such as the conception and design of the research, data collection and processing, data analysis and interpretation, and writing of the research paper) before they may be listed for the paper" (Article no. 9 in the "Academic Ethics Guidelines for Researchers" of MOST, under the title of "Responsibility of co-authors"). [科技部對研究人員學術倫理規範. Article 9. 共同作者的責任：共同作者應為對論文有相當程度的實質學術貢獻（如構思設計、數據收集及處理、數據分析及解釋、論文撰寫）始得列名].

<http://www.cla.nchu.edu.tw/download/1050325/0001-6.pdf>

Conclusion: we adopt the MOST regulations to define what qualifies someone to be a co-author

Our Committee decided that, for this investigation, it makes sense for us to follow the MOST guideline, not only because many of the questioned studies were funded by MOST, but also because: (i) It has become increasingly necessary for a lab to collaborate with many other labs in order to take multidisciplinary or basic/clinical collaborative approaches. Often, these collaborative labs are located in other institutions or even be in other countries or continents. This makes it impractical for all authors to be able to fully conversant with, and "accountable for all aspects of the work." In this regard, the ICMJE requirement is excessively stringent and it can greatly discourage such collaborations. This view is supported by Dr. Linda Miller, former Executive Editor of Nature Journals, who stated that such stringent criteria seem to be "more idealistic than practical" (see her Appendix 02.Miller L letter). (ii) A prevailing view is that a wide range of contributions are accepted as worthy of co-authorship, as exemplified by the policy of the Nature Journals, which "do not prescribe the kinds of contributions that warrant authorship". Finally, (iii) article no. 9 of the MOST ethics statement: "Co-authors shall provide significant and substantial academic contribution (such as the conception and design of the research, data collection and processing, data analysis and interpretation, and writing of the research paper) before they may be listed for the paper." This MOST regulation seems to be practical, fair, and quite consistent with the prevailing view as discussed above.

F-4. Responsibilities for co-authorship:

Given the divergent opinions about what contributions warrant co-authorship, it is not surprising that there are correspondingly divergent opinions about the co-author's responsibilities in case a collaborative paper turns out to contain problematic data. For example, a 2009 Nature Editorial quoted the investigation report on the (in)famous Schon case, in stating that "the issue of the responsibilities of co-authors (is an) extremely difficult" one because "no clear, widely accepted standards of behavior exist".

<http://www.nature.com/nnano/journal/v4/n6/full/nnano.2009.125.html>.

On one extreme, the ICMJE holds the view that every (co-)author should be “accountable for all aspects of the work”. As mentioned, this view is not practical given the trend that biomedical research, to be competitive, increasingly requires interdisciplinary collaborations involving multiple labs.

Finally, the Ministry of Science and Technology (MOST) defines the responsibility of co-authors as: “According to the principle of joint responsibility, co-authors shall be responsible for the corresponding contents in the paper within a reasonable scope. In other words, any co-author listed in the paper shall be responsible for the part that they have contributed.” [科技部對研究人員學術倫理規範. Article 9. 共同作者的責任：基於榮譽與共的原則，共同作者在合理範圍內應對論文內容負責，共同作者一旦在論文中列名，即須對其所貢獻之部分負責]. (Article no. 9 in the MOST’s “Academic Ethics Guidelines for Researchers” re “Responsibility of co-authors”).

Conclusion: we adopt the MOST regulations to define the co-authors’ responsibilities

Again, our Committee felt that, for this investigation, it makes sense for us to follow the MOST guideline, not only because many of the questioned studies were funded by MOST, but also because: (i) the ICMJE’s suggestion that every (co-)author should be “accountable for all aspects of the work” is simply unreasonable and discourages collaboration; and (ii) the MOST regulation is balanced, fair, and is consistent with the prevailing view that is held by, for example, the University of Washington’s Policies for Authorship, which states that “Each co-author is responsible for the content of all appropriate portions of the manuscript”
<http://research.wustl.edu/PoliciesGuidelines/Pages/AuthorshipPolicy.aspx>.

G. Overall Strategies:

In carrying out our investigation, we adopted the following strategies:

- We dissect a large, more complicated question into smaller sub-questions that are more easily answerable.
- “We want to assign responsibility for misconduct solely on the basis of well-defined regulations and a rigorous set of criteria in order to prove that an individual was responsible.” (per Former ORI Deputy Director).
- For each question, we set up two opposing views and try to strengthen both views as much as possible, so that our members can debate the issues more thoroughly before voting.
- In writing this report, we want to make sure that each section is self-sufficient, even if that means some degree of redundancies.

H. Question One: Did Dr. Yang Make Sufficient Contributions to Qualify as a Co-author?

H-1. Investigation/considerations: Prof. Yang’s contributions to the papers:

Below is a list of the seven papers, followed by Prof. Yang's contributions based on statement from Prof. Yang (in English; 03a.Appendix Yang contribution – Yang PC) and Prof. Kuo (Chinese; Appendix 03b.Yang contribution - Kuo ML).

1. Connective tissue growth factor and its role in lung adenocarcinoma invasion and metastasis. Chang CC, Shih JY, Jeng YM, Su JL, Lin BZ, Chen ST, Chau YP, **Yang PC**, Kuo ML. J Natl Cancer Inst. 2004 Mar 3;96(5):364-75.

<https://pubpeer.com/publications/14996858>

Yang's contribution to this paper: Prof. Yang provided lung cancer invasion/ metastasis cell line models and the concept of CRMP-1 involved in lung cancer metastasis for the study of CTGF gene in lung cancer metastasis. Prof. Yang made contributions in the study design and the research direction of lung cancer metastasis from clinical point of view and clinical significance of CTGF and CRMP-1 genes in lung cancer progression. He also reviewed and approved the parts of this paper where he made contributions. 提供肺癌細胞株，並幫忙檢視本論文及提出修改意見。

2. The VEGF-C/Flt-4 axis promotes invasion and metastasis of cancer cells. Su JL, **Yang PC**, Shih JY, Yang CY, Wei LH, Hsieh CY, Chou CH, Jeng YM, Wang MY, Chang KJ, Hung MC, Kuo ML. Cancer Cell. 2006 Mar 9(3):209-23.

<https://pubpeer.com/publications/FA2209426FC5F07DAFA90A5B726FC7>

Yang's contribution to this paper: Prof. Yang provided the fundamental clinical research concept of VEGF-C involved in lung cancer invasion and metastasis and an *in vitro* model of lung cancer invasion and metastasis, which was established in 1997 and 2001. The series of cell lines with different invasion ability and microarray expression profiles of invasion related genes constituted a very powerful model to study the molecular mechanisms of cancer metastasis. This paper followed this concept, and used the series of invasion/metastasis cell lines (CL1-0, CL1-3, CL1-5) and the *in vitro* model to study VEGF-C/Flt-4 signal pathway involved in lung cancer metastasis. Prof. Yang made major contributions from the clinical point of view in study design, research direction, and interpretations of clinical significance. He also reviewed and approved his contributing part of this manuscript. 提供由楊校長實驗室自行建立取自台灣肺癌病人一系列不同轉移能力的細胞株，這些細胞株對這篇論文的機制探討有很大幫忙，同時楊校長議提供肺癌病人癌症轉移之臨床意見。

3. Knockdown of contactin-1 expression suppresses invasion and metastasis of lung adenocarcinoma. Su JL, Yang CY, Shih JY, Wei LH, Hsieh CY, Jeng YM, Wang MY, **Yang PC**, Kuo ML. Cancer Res. 2006 Mar 66(5):2553-61.

<https://pubpeer.com/publications/022D597A8C72CE8661D19B2FE17468> Yang's contribution

to this paper: Prof. Yang provided high invasive and low invasive lung cancer cell lines and lung cancer invasion/metastasis models for the study of contactin-1 involved in lung cancer metastasis. Prof. Yang provided information of clinical significance, and made suggestions for the study design and research direction. He also reviewed and

approved his contributing part of the manuscript. 幫忙檢視本篇論文內容並提供修正意見。

4. Effect of connective tissue growth factor on hypoxia-inducible factor 1alpha degradation and tumor angiogenesis. Chang CC, Lin MT, Lin BR, Jeng YM, Chen ST, Chu CY, Chen RJ, Chang KJ, **Yang PC**, Kuo ML. J Natl Cancer Inst. 2006 Jul 98(14):984-95.

<https://pubpeer.com/publications/16849681> Yang's contribution to this paper: Prof. Yang provided high invasive and low invasive lung cancers cell lines and cancer invasion/metastasis models for the study of CTGF and tumor angiogenesis in lung cancer metastasis. Prof. Yang provided clinical concept, and made suggestions for research design and direction. He also reviewed and approved his contributing part of the manuscript. 提供細胞株及肺癌病人的臨床經驗的諮詢並幫忙閱讀及檢視論文。

5. Tumor-Associated Macrophage-Induced Invasion and Angiogenesis of Human Basal Cell Carcinoma Cells by Cyclooxygenase-2 Induction. Tjiu JW, Chen JS, Shun CT, Lin SJ, Liao YH, Chu CY, Tsai TF, Chiu HC, Dai YS, Inoue H, **Yang PC**, Kuo ML, Jee SH. J Invest Dermatol. 2009 Apr 129(4):1016-25. <https://pubpeer.com/publications/21841313>

Yang's contribution to this paper: Prof. Yang provided clinical concept of tumor associated macrophage involvement in cancer invasion and metastasis, and made suggestions for study design and research direction. He also reviewed and approved his contributing part of the manuscript. 提供 tumor-associated macrophage 相關知識諮詢

6. miR-107 promotes tumor progression by targeting the let-7 microRNA in mice and humans. Chen PS, Su JL, Cha ST, Tarn WY, Wang MY, Hsu HC, Lin MT, Chu CY, Hua KT, Chen CN, Kuo TC, Chang KJ, Hsiao M, Chang YW, Chen JS, **Yang PC**, Kuo ML. J Clin Invest. 2011 Sep 121(9):3442-55. <https://pubpeer.com/publications/21841313>

Yang's contribution to this paper: Prof. Yang provided clinical hypotheses of cancer invasion and metastasis, and made suggestions for study design and research direction. He also reviewed and approved his contributing part of the manuscript. 提供臨床經驗的諮詢

7. CCN2 inhibits lung cancer metastasis through promoting DAPK-dependent anoikis and inducing EGFR degradation. Chang CC, Yang MH, Lin BR, Chen ST, Pan SH, Hsiao M, Lai TC, Lin SK, Jeng YM, Chu CY, Chen RH, **Yang PC**, Chin YE, Kuo ML. Cell Death Differ. 2013 Mar 20(3): 443-455. Yang's contribution to this paper: Prof. Yang provided lung cancer invasive/metastasis cell line models and the research concept of EGFR pathway in lung cancer progression for this study to prove that DAPK and EGFR degradation played significant roles in regulating lung cancer metastasis. In addition, Prof. Yang made suggestions for study design and research direction. He also reviewed and approved his contributing part of the manuscript. 提供細胞及論文修改意見。

H-2. Conclusion One: Dr. Yang Qualifies as a Co-author in These Papers

By a vote of 6 to 0, our Committee concluded that, based on MOST regulation, Dr. Yang warrants co-authorship in the above seven papers, because the statements from Profs. Yang and Kuo regarding Prof. Yang's contributions, although differ in lengths, are reasonably consistent. Specifically, they indicate that Dr. Yang contributed cell lines (for the importance of these cell lines, see Appendix 3a. Yang contribution - Yang), clinical insights, as well as manuscript-related work. Thus this Committee concluded that Dr. Yang's contributions satisfy MOST's definition of co-authorship, i.e., "Co-authors shall provide significant and substantial academic contribution (such as the conception and design of the research, data collection and processing, data analysis and interpretation, and writing of the research paper) before they may be listed for the paper" (Article no. 9 in the "Statement on Academic Ethics" of MOST, under the title of "Responsibility of co-authors"). This conclusion is supported by an independent evaluation letter provided by Dr. Linda Miller, Executive Editor of *Cancer Immunology Research* of the American Association for Cancer Research; she was Senior Editor of *Science*, Executive Editor of *Nature*, Founding and Chief Editor of *Nature Immunology*, and Editor-in-Chief of the Rockefeller University Press (see Appendix 02. Miller L).

I. Question Two: Does Dr. Yang Bear Any Responsibilities for the Problematic Data/figure in These Papers?

I-1. Investigation/considerations:

a. Is Dr. Yang responsible for the potentially problematic data? Since the MOST regulation specifies that "any co-author listed in the paper shall be *responsible for the part that they have contributed*", we next considered whether Dr. Yang's contributions had anything to do with the problematic data/figures in these papers. As discussed above, Dr. Yang's contributions are limited to the provision of several lung cancer cell lines that have different invasion/metastasis potential, clinical insights, suggestions on research direction and design, and review and approval of his contributed parts of the manuscripts.

b. Should Dr. Yang, as a co-author, have detected the flawed data/figures before the papers were submitted for publication? In Dr. Yang's statement (Appendix 03a. Yang contribution - Yang PC.pdf), he said: *"My collaboration with Professor Min-Liang Kuo's research team mainly took place more than ten years ago. For our co-authored papers, I provided research concepts and suggestions, especially on the clinical part of lung cancer research, and also provided a series of "lung cancer invasion and metastasis cell line models" and the concept and technology of "microarray gene expression profiling of lung cancer invasion/metastasis." Professor Kuo's team conducted laboratory research and analyzed data. Based on the trust principle between team members, co-authors reviewed and checked what they contributed to the paper, and the corresponding author was responsible for the integration of the whole paper. During the submission process of the manuscript, as one of the co-authors, I did carefully review the paper and approve the part related to my contribution, but it was difficult to tell whether the images and graphic figures from other co-authors were presented correctly. Some of the papers in question later required errata after publication. Although these errors are not related to my contributions, I*

feel deeply regretful about that." **The committee** agreed that it can indeed be extremely difficult for a collaborator/co-author to detect image manipulations, because the only sure way to detect such is by comparing, side by side, the original data with the finished figures. This step, i.e., the examination of the original data, can usually be done ONLY by the corresponding author (in this case Prof. ML Kuo); hence this is Prof. Kuo's primary responsibility. Collaborators/co-authors rarely, if ever, are given the opportunity to examine the original data generated by another lab.

I-2. Conclusion two: Dr. Yang does not bear any responsibility for the problematic data in these paper

By a vote of 6 to 0, our Committee concluded that, based on MOST regulation, Dr. Yang bears no responsibility for the manipulated figures that involve mainly immunoblots, which Prof. Kuo's lab is responsible for, and that it is not reasonable to blame Dr. Yang, as a co-author, for not having detected the problematic data that were generated by Prof. Kuo's laboratory members.

J. Question Three: Should Dr. Yang Resign?

J-1 In this section, we address the following three questions: First, should Dr. Yang, as the President of NTU, bear extra responsibility for his collaborator Prof. Kuo's misconduct? Second, did he make a bad decision in appointing Prof. Kuo as Dean of the College of Life Science? Finally, since Minister Wei-ling Chiang (蔣偉寧部長) of the Ministry of Education was implicated in a 2014 case of scientific misconduct by Drs. CW Chen and CY Chen and he resigned, shouldn't President Yang do the same?

J-2 Investigation/considerations:

a. Should Dr. Yang, as the President of NTU, bear extra responsibility for his collaborator Prof. Kuo's misconduct?

It happened at the top, "what could have been done to catch this sooner?" The Francis Collins case: Amitav Hajra, a former star MD/PhD student in Francis Collins's lab in the University of Michigan, moved to NIH in 1993 with Dr. Collins who was appointed Director of the National Human Genome Research Institute (NHGRI). Hajra was then found to have fabricated 75-90 percent of the data in his doctoral thesis, leading to the retraction of five papers in which he and Dr. Collins were the first and corresponding author, respectively. This case was so serious, that the University of Michigan officials said that "On a scale of 1 to 10, with 10 being the most severe, the committee concludes that the academic misconduct here rates 10." (*Nature* 388, 313; 24 July 1997). Dr. Collins commented about his former student: "He was very motivated, determined and clever. I still don't know how he produced some of the primary data he brought to lab meetings" (*Nature* 388, 313; 24 July 1997); and "the problem with the student in my lab was not a consequence of a busy mentor. It was the clever and intentional deception of numerous individuals by a student determined to fabricate data" (*The Scientist* May 12, 1997). Dr. Collins said that he was "grateful for the care that reviewer took looking at a figure that I must have

looked at 50 times and that other people in the laboratory had looked at least as often, in seeing what had eluded all of us" (New York Times, Oct 30th, 1996). These illustrate how difficult it is for even a top scientist of the world to detect frauds committed by a determined cheater. Dr. Collins further commented: "I find myself now being more vigilant, viewing data with more skepticism, which I'm not sure is a good thing" (*Nature* 388, 313; 24 July 1997). Careful investigation by the University of Michigan and ORI concluded that Hajra was solely responsible for the misconduct, and the University rescinded his MD as well as PhD degrees. The investigation further concluded that neither Dr. Collins nor other co-authors had any involvement. Dr. Collins continued to serve as the director of NHGRI, and was later promoted in 2009 to become, and still is, the director of the entire US National Institutes of Health. Dr. Collins said: "(I had been) haunted since (then) about what could have been done to catch this sooner, and I do not have a good answer" (New York Times, Oct 30th, 1996).

How much (extra) responsibility should a department Chair, Dean or President bear when a collaborator in his organization, unbeknown to him, committed scientific misconduct? It is notable that even Francis Collins, current NIH Director, failed to detect problematic figures in his retracted papers in which he was the corresponding author ("I must have looked at (the figure) 50 times and that other people in the laboratory had looked at at least as often", but the problematic data "eluded" him; see above). Therefore, it is unreasonable to expect a co-author, in this case Dr. Yang, to be able to spot effectively the problematic data that are not in his areas of contribution. This is particularly difficult because, as mentioned earlier, co-authors are rarely, if ever, offered the opportunity to compare the figures with the original data from a collaborator. That's why the Taiwanese Ministry of Science and Technology (MOST) regulation stipulates that *"co-authors shall be responsible for the corresponding contents in the paper within a reasonable scope. In other words, any co-author listed in the paper shall be responsible for the part that they have contributed."* This regulation acknowledges the difficulties for a co-author to spot a problem that is NOT related to his/her contributions. This regulation should be applied fairly to all investigators, and should have nothing to do with whether a co-author is a Chair, Dean or President of the organization. It is not reasonable to assign extra blame to these leadership people simply because they are the 'boss'. In addition, this will strongly discourage them from collaborating with his/her colleagues in their organization – which will be an extremely unfortunate outcome. Finally, former Deputy Director of ORI commented: "The ad hoc committee has concluded that Dr. Yang's contributions to the papers he co-authored with Dr. Kuo's laboratory that have been questioned by PubPeer warrant his inclusion as a co-author. The committee has also concluded that the falsified data present in those publications occurred exclusively under Dr. Kuo's supervision and represented results and experimental approaches over which Dr. Yang could not have readily detected intentional or inadvertent errors. Thus he cannot be held responsible in any way for whatever research misconduct occurred. Similarly, he should not be liable for some sort of administrative responsibility. Most of the disputed data was obtained and published many years ago, and it is inappropriate to consider that because Dr. Yang currently has a prominent position as President of NTU that he somehow now has some sort of post hoc and poorly defined responsibility, which presumably he would not be expected to bear if he were not in his current position."

b. Did President Yang make a bad decision in appointing Prof. Kuo as Dean of the College of Life Science? Available information indicates that Dr. Min-Liang Kuo was actually first appointed in August 2012 as Dean of the College of Life Science by former President Si-Chen Lee (李嗣涇), and reappointed in August 1, 2015 by President Yang. The fact that around the same time Dr. Kuo was offered Vice Presidency by Kaohsiung Medical University attested Dr. Kuo's qualification for Deanship at NTU. In this regards, Dr. Yang's decision in reappointing Dr. Kuo in 2015 as Dean seems totally reasonable. Consistent with this, Dr. Yang stated: "I never in my position as an administrative supervisor gave special treatments to Prof. Kuo in terms of his appointment, promotion and resource distribution including lab space and salary. All decisions related to him were made according to appropriate institutional procedures, rules or considered judgments" (see Appendix 03c.Yang response-interview).

c. Since Minister Wei-ling Chiang (蔣偉寧部長) of the Ministry of Education was implicated in a 2014 case of scientific misconduct by Drs. CW Chen and CY Chen and he resigned, shouldn't President Yang do the same?

The Chen brothers case: Peter Chen (Chen-Yuan Chen; 陳震遠), formerly of National Pingtung University of Education, Taiwan (NPUE), and his twin brother C.-W. Chen (Cheng-Wu Chen; 陳震武), formerly 高雄海洋科大海事資訊科技研究所副教授, published a large number of papers in several journals including the Journal of Vibration and Control (JVC). Investigations by JVC revealed, however, that these authors established a fake reviewer ring using fabricated reviewer identities and 130 fake email accounts so that they could recommend these faked reviewers, and be asked by the Journal to serve as the 'reviewers' to evaluate their own papers. On July 8, 2014, JVC published online a highly unusual Notice listing the unprecedented mass retraction of 60 papers by the Chen brothers, and apologized: "We regret that individual authors have compromised the academic record by perverting the peer review process and apologize to readers." (<http://journals.sagepub.com/doi/abs/10.1177/1077546314541924>). In "The Retraction Watch Leaderboard" that lists "Who has the most retractions" in the world, Peter Chen ranks no. 5 (43 retractions) and CW Chen no. 13 (28 retractions). <http://retractionwatch.com/the-retraction-watch-leaderboard/>. This case is exceptionally serious and made international headlines, because it was done knowingly and intentionally, and it fundamentally compromised the peer review system, which is the bedrock of scientific publication. The seriousness of this case led to the resignation of the then Editor-in-Chief of JVC, Professor Ali H. Nayfeh. Moreover, since CW Chen, a former graduate student of Professor Wei-ling Chiang (蔣偉寧), listed Chiang (without informing him) as a co-author in 5 of the retracted papers, this also led Professor Chiang to resign as the Minister of Education. Our Committee concluded, however, that President Yang's case fundamentally differs from this earlier case in nature and the magnitude of the offense, and in that our detailed investigation showed that Dr. Yang made sufficient contributions to warrant co-authorship in the questioned papers, and bears no responsibilities in the problematic data that were generated by Prof. Kuo's lab. Therefore, we feel that it is inappropriate to suggest that, based on this earlier case, President Yang should resign.

The Francis Collins case: Dr. Francis Collins's case, as discussed above, is much more serious than Dr. Yang's, in that the former was the corresponding author in five retracted papers (rated 10 in degree of seriousness in a scale of 1-10 with ten being the most serious; see above and *Nature* 388, 313; 24 July 1997), while the latter was only a co-author in four problematic papers (2 may require retraction; for details see Medical College Investigation Report). In both cases, detailed investigation cleared the respondents' responsibilities (see *Nature* 388, 313; 24 July 1997; and discussion of Questions 1 and 2 above). Thus in both cases, Drs. Collins and Yang fell victim to unscrupulous collaborators (see Burden comments below; and Appendix 04a.Burden S letter), and both were emotionally devastated. Dr. Yang said in his statement that "*Although these errors are not related to my contributions, I feel deeply regretful about that*" (Appendix 03b.Yang contribution – Yang PC), and was quoted by the press as saying "楊泮池坦承面臨學術生涯最大危機. 但會坦誠面對, 嚴肅對待". He also stated that "對於郭明良研究團隊有 11 篇論文遭質疑, 楊泮池毫不猶疑地說, '論文造假就是不對的, 對於台大發生這種事他很難過, 校方已在進行調查, 若查證確有違反學術倫理的事, 一定會嚴懲.'" (<https://udn.com/news/story/1/2116173>). Similarly, Dr. Collins said: "It was my darkest professional hour" (Cell 124:873, 2006; New York Times, Oct 30th, 1996). It should be noted that Dr. Francis Collins did not resign from the Directorship of the Human Genome Research Institute of NIH, and was actually promoted later to become Director of the entire NIH.

d. Statement from David G. Beer: Dr. Beer, Professor of Surgery, University of Michigan, commented: "As a lung cancer researcher I am very familiar with Dr. Yang and his tremendous contribution to the field. The investigative committee has determined that he was qualified to be co-author on the six papers in question that appear to have problematic data and figures but it is Dr. Kuo's laboratory that has key responsibility for this work." He also stated: "I do not feel that it is the responsibility of Dr. Yang to resign for what has happened. It may be more appropriate for him to acknowledge that it did happen, to help determine why it happened, and then initiate potential safe-guarding steps so that it will not happen again. By clearly leading and defining expectations to his collaborators, Dr. Yang can provide a teachable moment to prevent any future missteps. This in the end will have more impact than his resignation could" (see Appendix 04b.Beer DG letter).

e. Statement from Steven Burden: Dr. Burden, Professor of Cell Biology at NYU, commented: "From my understanding of the documents and information you provided, President Yang collaborated with Professor Kuo by providing several important lung cancer cell lines with different metastatic potential, as well as clinical expertise, in the six questioned papers. As such, it is reasonable to expect that President Yang would be a co--author on these papers. The data fabrication in these publications were unrelated to President Yang's contributions. I understand that despite the fact that President Yang read and reviewed the manuscripts prior to submission, he was unable to detect that some data in these manuscripts had been manipulated by Professor Kuo's group. Further, it is my understanding that questions about Professor Kuo's misconduct surfaced only a few months ago, almost a decade after President Yang initiated his collaboration with Professor Kuo. As such, there is no reason to believe that President Yang used poor judgment to continue his collaboration with Professor Kuo. I believe

that Dr. Yang, as the President of NTU, has the responsibility to ensure that those who committed misconduct will be treated appropriately. However, it would seem very inappropriate to penalize President Yang, who in this case is an innocent victim, for Professor Kuo's misconduct, as this will send an alarming message to other scientists, dissuading them from collaborative studies" (see Appendix 04a.Burden S letter)

f. Statement from John Dahlberg: Dr. Dahlberg, former Deputy Director of ORI, commented: "I believe that it would be inappropriate to hold President Yang responsible in any way for the behavior of members of Dr. M.L. Kuo's laboratory. It is notable that serious issues with the papers from Dr. Kuo's group were not detected by Dr. Kuo, reviewers, copy editors, or readers until in most cases many years later. Thus, it is difficult to understand how Dr. Yang, as a collaborator whose expertise did not directly overlap with the particular analyses carried out by Dr. Kuo's laboratory could have been aware of the issues prior to the PubPeer postings in 2016. I also believe that rather than resigning, it would be far better for Taiwanese science for President Yang to use this experience as an opportunity to initiate educational and training programs to ensure that scientists at all levels are aware of, and adhere to, best practices so that misconduct is less likely to occur."

K-3 Conclusion Three: Since Dr. Yang Warrants Co-authorship and Bears No Responsibility for the falsified/fabricated Data Generated by Dr. Kuo's Lab, There Is No Reason Why Dr. Yang Should Resign.

Based on the above investigations/considerations, the Committee agreed, **by a vote of 6 to 0**, with the above statement, i.e., since Dr. Yang warrants the co-authorship, bears no responsibility for the problematic data generated by Dr. Kuo's lab, there is no reason why Dr. Yang should resign.

L. Review of the College Investigation Reports:

Since our committee has been charged to "review the reports by the college Investigation Committees on the involvement of other authors (other than Dr. Yang)", we interacted with the Chairs of Investigation Committee from the Colleges of Medicine and of Life Science, and reviewed their reports. We found that both committees functioned very well. Since the Medical College report covers all of the questioned papers and authors, we will further comment on this report. The Medical College Committee (MCC), consisting of 4 NTU faculty (including non-Medical College faculty) and 4 outside experts, initially examined 17 PubPeer-questioned papers, which they then narrowed down to 12 for detailed analyses. This represents a huge workload that, if investigated by US universities, takes at least 12-18 months to complete. Working under tremendous time pressure, this committee met 7 times in the last three months (November 16, 2016 to February 15, 2017). Based on their investigative results, the MCC assigned responsibilities for eight individuals (Prof. ML Kuo, Dr. ST Cha, Dr. CL Su, Prof. CC Chang, Ms. YH Kuo, Dr. PS Chen, Prof. MT Lin and Dr. CT Tan). Moreover, the Medical College Committee made specific academic penalty recommendations, when appropriate, for all these individuals except

Prof ML Kuo, whose penalty has been recommended by the College of Life Science. Overall, members of both college Investigation Committees should be commended for their efforts and sacrifices. For example, a member of our committee commented: "I have read the report, with great appreciation for the time and efforts dedicated by the committee members." The former Deputy Director of ORI commented: "I found (the Medical College Investigation report) very helpful, and considering the time pressures (as well as the reality that committee members have day jobs as well), I consider it to be quite thorough, particularly with respect to identifying the responsibilities of the authors for the questioned data and for questionable authorship practices. *All things considered, I was impressed.*"

M. Conclusions and Recommendations:

M-1. Main conclusions

Based on an in-depth analysis of the literature, our committee decided to adopt the requirement and responsibility of co-authorship according to an MOST regulation, which is fair, practical, and consistent with the prevailing view. These considerations facilitated our investigation, and led us to draw the following conclusions.

- Dr. Yang warrants co-authorship in the questioned papers (6 to 0 votes);
- Dr. Yang bears no responsibility for the problematic data in these papers, which were generated by Prof. Kuo's lab (6 to 0); and
- Since Dr. Yang warrants co-authorship and bears no scientific responsibility for the problematic data generated by Dr. Kuo's lab, there is no reason why he should resign from the Presidency (6 to 0).

M-2. The investigation: room for improvement

The Case: This case surfaced in early November, 2016 when allegations appeared in PubPeer, a website for anonymous whistle-blowers, reporting many problematic figures in a Nature Cell Biology paper by Prof ML Kuo's group (published online on August 15, 2016). This triggered the scrutiny of other papers from the same group, and, within a month, more than a dozen of Dr. ML Kuo's papers were alleged to be problematic on PubPeer. Dr. Kuo soon retracted this NCB paper, as well as a 2008 paper published in the Journal of Biological Chemistry.

Responsible investigation takes time: This case attracted broad attention because: (i) it involved the retraction of a paper from a prominent journal, (ii) Dr. ML Kuo is a well-known professor, former Dean of the NTU College of Life Science and VP of Kaohsiung Medical University, and (iii) Dr. PC Yang, current President of NTU, co-authored several of the questioned papers with Dr. Kuo. Since Dr. Kuo was affiliated earlier with the NTU College of Medicine, before becoming the Dean of the NTU College of Life Science in 2013, NTU organized two Investigation Committees in the two colleges to investigate papers published while he was with these organizations. While the Investigation Committees were still in the process of collecting data (which did not complete

until late December 2016/early January 2017), many demanded immediate actions from NTU, MOE and MOST. Such an unrealistic expectation limits how much the committees can do, and is harmful for the investigation process. It should be noted that if a case with a comparable magnitude is investigated in the US by university committees, it typically requires at least 12-18 months to complete.

Need for well-defined regulations and legal tools: A major obstacle we encountered early into our investigation is the lack of consensus about what qualifies for “co-authorship” and what responsibility it entails. There are plentiful of opinions, but they are divergent, confusing and often contradictory to each other. The former Deputy Director of ORI commented: “It was vital to assign responsibility for misconduct solely on the basis of well-defined regulations and a rigorous set of criteria in order to prove that an individual was responsible.” That is why our Committee did an in-depth analysis of the literature on “co-authorship”. We hope Taiwan can establish an ORI-like system with clearly defined rules and regulations, which can greatly facilitate future investigations (and possibly prevention) of scientific misconduct. Another major obstacle, evidenced from the Medical School Committee report, has to do with their uncertainty whether the institutional officials have the legal right to enter into the respondents’ lab unannounced in order to seize evidence. A legal basis for doing so, if not yet in place, should be developed (see below).

M-3. Responsible authorship

Under the current system, authorship is largely decided by the Corresponding Author/Principal Investigator, with or without consulting with other authors. This process is therefore quite opaque and can cause problems. For a detailed discussion on the qualification, responsibility and investigation of the Corresponding Author, First Author, and Co-author see Sections F-1, F-2 and F-3, respectively. Here is a list of possible steps that can increase the transparency and quality of this decision-making process.

- Corresponding author: One of his primary responsibilities is to check the primary data on a routine basis (at least weekly), and to compare, side-by-side, the assembled figures with the original data, to ensure that the figures are faithful representation of the data. He must make sure that the original data are well-organized and stored in a safe place for 6 or 7 years, depending on the requirement of the funding agency, journal or institute – so that such data are readily retrievable if requested by a journal or investigative body. It is questionable whether someone who provides resources or makes other contributions but does not routinely interact with the First Author and see the original data should be a Corresponding/last author.
- First author: This position is usually reserved for a junior staff member who has generated most of the data /figures. He is responsible for depositing all the original data, organized under each figure, in the designated lab/institute server, and make sure that the PI will carefully compare the final figures with the original data. When he leaves the lab, he should

submit all of his lab notebooks and experimental material to the PI, as these materials may provide in future investigations the crucial evidence that can clear his name. Moreover, lab notebooks, experimental data and materials are the properties of the lab/institute.

- Co-author: Here one may adopt the Nature journals policy that encourages transparent listing of each co-author's contributions. The PI should discuss this list (showing the names in the order they will appear in the paper) with all the team members periodically as the project moves forward. At a minimum, this list should be discussed and hopefully agreed upon by all the authors before the paper is written. Nature journals also initiated recently a system to designate someone in each of the collaborating teams to play the role of the Corresponding author of that subgroup, so that this individual can be in charge of collecting and safe keeping their original data and ensuring the integrity of the presented data.

M-4. Recommendations/Things to consider:

- Future programs for enhancing scientific integrity: We recommend the establishment of a Taiwan-wide US ORI-like unit, as well as an NTU-wide Research Integrity Office, that contains two major branches to be in charge of the handling of research misconduct and the promotion of research integrity. These can be used as a basis for an oversight mechanism similar in scope to the US Office of Research Integrity. This ORI-like unit can carry out the programs that President Yang has already initiated, including: (i) facilitate enhanced training of scientists at all levels in best practices in promoting research integrity, (ii) develop policies and procedures to allow a rigorous and standardized approach to handling allegations of research misconduct in the future, and (iii) establish a standing committee to investigate instances of possible research misconduct. These excellent programs should be fully supported.
- Criteria for assessing the relative severity of scientific misconduct: When considering what sanctions to impose on individuals found to have falsified their research or otherwise acting inappropriately, one should take into account mitigating and aggravating circumstances. The US ORI describes such factors as:
 - Whether the misconduct was committed knowingly, intentionally, or recklessly;
 - Whether the misconduct is an isolated event or a continuing pattern;
 - The impact or significance of the misconduct;
 - Whether the respondent accepted responsibility by (i) admitting the misconduct, (ii) cooperating with the investigation, (iii) demonstrating remorse, and (iv) taking steps to correct or prevent recurrence of research misconduct;
 - Whether the respondent retaliated against complainants or witnesses; and
 - Other factors to consider should include internal and external stresses such as family or personal illness, mental health issues, and excessive pressure from laboratory supervisors.
- The need for a legal framework: For the Taiwan-wide ORI to function, it requires a means of

assuring that institutions are required to follow the guidelines established by the office and report their findings.

- In the US ORI this is accomplished by requiring all institutions applying for grants from the National Institutes of Health to register with ORI, allowing ORI to potentially block further funding if institutions are not compliant with ORI's procedures.
 - The legal framework should include authority of institutional officials to secure evidence at the initiation of an investigation. Such evidence could include laboratory records, drafts of manuscripts, e-mails, digital media such as flash drives and computer hard drives, and records from core facilities (animal facility, sequencing laboratories, etc).
 - This is obviously a complex procedure which would require considerable input from multiple stakeholders such as the funding agencies, legal scholars, and institutions.
- Help needed for the innocent: Scientific misconduct can derail not only the offender's career, it can also hurt other innocent team members. Francis Collins said this about Paul Liu, a postdoc working with Hajra who faked data leading to the retraction of five papers that Liu coauthored: "In the short run it had a profoundly negative impact on other people in the lab, especially the post-doc working most closely with Hajra. He wondered for some time whether his career had just gone south. Eventually he did recover but it was an enormous challenge. It took several years of doing experiments over."
[http://www.cell.com/cell/fulltext/S0092-8674\(06\)00249-2](http://www.cell.com/cell/fulltext/S0092-8674(06)00249-2). Another consideration is that, even though many PubPeer allegations proved to be false, they can nevertheless hurt innocent researchers' reputation and career
<https://sciencereactions.wordpress.com/page/2/>. We recommend that efforts be made to restore the reputation of the innocent authors. This could include counseling to ensure that co-authors who believe they are being unfairly treated as a result of being associated with a questioned research are encouraged to seek assistance from university administrators.
 - "Moral responsibility": Our committee discussed about how to address whether Dr. Yang bears any "moral responsibility", but ran into dead-ends. This is perhaps not surprising, because "moral responsibility" is a philosophical term. For example, it is defined in Wikipedia as the following: "Moral responsibility is the status of morally deserving praise, blame, reward, or punishment for an act or omission, in accordance with one's moral obligations. **Deciding what (if anything) counts as "morally obligatory" is a principal concern of ethics.**" In this definition, each underlined word leads to another web page for explanation. A related term, "morality", is "a body of standards or principles derived from a code of conduct from a particular philosophy, religion, or culture, *or it can derive from a standard that a person believes should be universal.*" These terms are therefore notoriously difficult to define, as they can mean very different things to different people. Former ORI Deputy Director said: 'Moral responsibility' or 'ethical concerns' are very difficult to define and vary widely depending on the individual, scientific discipline, and societal norms. For these reasons, ORI never even attempted to assess 'moral responsibility' when evaluating scientific misconduct cases."

- **Misleading Reporting:** An article from Taiwan People News 民報 on 2017 年 2 月 14 日, entitled “台大案效應台灣淪「學術詐騙王國」 論文投稿得先做「誠信說明」” reported: (i) “近來國內研究人員投稿論文到《生物化學雜誌》(JBC)居然被破天荒要求提供“誠信 (integrity) 說明”, 令研究人員大感意外. (ii) “近來確實不只一位生醫界的學者反映, 投稿到國際期刊, 遭期刊主編要求提供實驗 “原始數據”, 或要求提供 “誠信原則說明”, 這些都是過去沒有發生過的事!” <http://www.peoplenews.tw/news/1b14f3e8-dcd1-413d-b8ab-61fa80c9e0f8>; see Appendix 05a.Taiwan People News article).

In reporting the recent retraction of Prof. ML Kuo’s 2008 J Biol Chem paper, a news articles (above) implied that Prof. ML Kuo’s retraction was the reason for this Journal to create new rules to target authors in Taiwan to sign a declaration form on Scientific Integrity (see Appendix 05a.People News article). However, Dr. Kaoru Sakabe, Data Integrity Manager of JBC, explained in response to our inquiry: “The JBC requires (since July 2016) that all authors, regardless of their location (Taiwan or anywhere else in the world), to indicate during submission of their manuscripts that they have read and agree to adhere to our Ethics Policy (http://www.jbc.org/site/misc/edpolicy.xhtml#ethics_policy). Additionally during submission, all authors (from all countries) are required to make all original data underlying the findings in their manuscript available upon request (http://www.jbc.org/site/misc/edpolicy.xhtml#data_availability).” (See Appendix 05b.JBC Sakabe response). Therefore, this is a new policy that the Journal initiated 5 months before Dr. ML Kuo’s retraction that occurred in December 2016. Moreover, this policy applies to scientists from every country in the world. The same article also reported that some journals newly require Taiwanese scientists to supply the original data, again implying that this is a new regulation triggered by the NTU case to target scientists in Taiwan. In fact, journals such as Nature Cell Biology has long required the submission of the original data (see, e.g., Figure S8 in Wakatsuki, et al, Nature Cell Biol 13: 1415, 2011, showing the submission of all uncropped immunoblot images used in the figures). Therefore, this is a preexisting policy for this journal, applicable to all authors from **every country in the world**, and is not at all targeted to Taiwan. Thus, to say that the recent Taida case of November 2016 led some Journals to set up new regulations targeting Taiwanese scientists, although sounded convincing, is completely misleading. Although this article appeared to have been removed (“retracted”?) from its original website, its false claims caused wide-spread confusion and concerns. We hope the Taiwan People News will do the right thing by publishing in a timely manner an article of correction and apology.

Respectfully submitted,

XXX

Chair, Ad Hoc Committee

Signed on behalf of the following members:

Dr. XXX

Dr. XXX

Dr. XXX

Dr. XXX

Dr. XXX

Appendixes:

- 01.Ad Hoc Comm Report I
- 02.Miller L letter
- 03a.Yang contribution – Yang PC
- 03b.Yang contribution - Kuo ML
- 03c.Yang response-interview
- 04a.Burden S letter
- 04b.Beer DG letter
- 05a.People News article
- 05b.JBC Sakabe response