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RESEARCH ARTICLE

Prejudice, against GMO crops and Golden Rice, in US Academia drove unethical behaviour, with global and detrimental consequences for vitamin A deficiency alleviation.

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Abstract

In 2015, Tang et al 2012 was retracted. The paper concerned human research, relevant to public health, conducted in China in 2008. Retraction represents the most severe criticism of a scientific article. This article recounts events over a four-year period and challenges the justification for retraction based on the Committee on Publication Ethics principles.

This research focuses on analysing contemporary (2012–2015) documentary evidence, organised by key narrative participants: Greenpeace, the Chinese Government, Tufts University, the American Society for Nutrition, the US National Institutes of Health, and the US Office for Human Research Protections.

The analysis indicates that technological bias within a university and a learned society, which is also a publisher, led to unethical behaviour and the subsequent retraction. In the USA, oversight of an Institutional Review Board falls under the Office for Human Research Protections. Despite being the principal funder, the NIH's reliance on this office for the retracted paper's research to be publicly available, suggests ineffective oversight.

The retracted paper detailed a crucial nutritional study relevant to combating vitamin A deficiency, a significant cause of child mortality and blindness in Low- and Middle-Income countries. The retraction likely heightened suspicion around this vital public health intervention.

Recommendations are made which are designed to partially ameliorate the injustices perpetrated.

Keywords

Tufts University, ASN, AJCN, China, VAD.

Introduction

In 2015 a unique research paper, published in 2012, was retracted. The paper's title was "β-Carotene in Golden Rice is as good as β-carotene in oil at providing vitamin A to children". These results, when available in the published literature, would encourage countries to adopt Golden Rice, as an additional approach to combating vitamin A deficiency (VAD), especially as Golden Rice costs no more than white rice. VAD has been and remains a very significant public health problem, killing millions of children in the past three decades, (Wu, et al, 2021) especially in Bangladesh and India, in Asia and Africa. The stated reasons for retraction diverge from the Committee on Publication Ethics recommendations, prompting a thorough examination of contemporaneous documentation. This analysis seeks to unveil the motivations behind the retraction decision and the refusal to accept opposing data which preceded it. The analysis is followed by recommendations to partially ameliorate what the documentation suggests was unjust treatment of clinical researcher authors and unwarranted retraction.

Methodology

Correspondence within the 2012-2015 timeframe, involving individuals and institutions, underwent systematic analysis. Employing the scientific method, the author logically scrutinized implications in the presented documentation and associated data to comprehend individual and institutional motivations. Critical documentation (Online Resources 1-28) is universally accessible via a weblink to an immutable independent data repository,

resistant to deletion. Given the unique nature of this dataset, alternative scientific methods are unavailable.

Chronology

On August 29, 2012, just twenty-eight days after Tang et al.'s 2012 online publication and four years post the completion of field work in China, 'Greenpeace' issued a highly critical press release (Online Resource 1), sparking hysteria in China (Figure 1).



Figure 1: Chinese hysteria followed Greenpeace's 2012 Press Release. (The Chinese headline translates to 'GMO Rice Trials'. Source, Chinese News Agency Xinhua, 2012)

The Chinese Government released a report on the research and its conduct on December 6, 2012, (Online Resource 2).

On June 28, 2013, Tufts University reported a compliance review to the US Government's OHRP¹ for Research Protocol #8458, outlining corrective actions for Principal Investigator² Dr. Tang and Tufts Institutional Review Board³ and for Tufts University⁴ (Online Resource 3).

On September 6, 2013, a letter reached the Editor of the American Journal of Clinical Nutrition⁵ from Tufts, allegedly from the four

American based co-authors of Tang et al 2012, but sent by Dr. Tang under extreme duress. The other three 'signatories' had not seen it, and their signatures were copied digitally, and *not* by Dr Tang (Online Resource 4). By September 17, 2013, Tufts issued a statement (Online Resource 5) on the results of their IRB's investigations into the criticized research. On December 5, 2013, the Vice-President of Publications, American Society for Nutrition⁶, proposed to the PI retraction of Tang et al 2012, to "maintain the ethical standards of

¹ Division of Compliance Oversight, Office for Human Research Protections (henceforward: OHRP), Department of Health and Human Services (henceforward: HHS) of the US Government.

² Henceforward: PI

³ Henceforward: IRB

⁴ Henceforward: Tufts

⁵ Henceforward: AJCN

⁶ Henceforward: ASN

AJCN and to ensure the integrity of the scientific record". (Online Resource 6). Despite the ASN threat to unilaterally retract the paper if the authors did not comply, Dr. Tang and her co-authors did not agree.

On December 11, 2013, Dr. Tang disavowed the September 6, 2013, communication in a three-page letter with 90 pages of additional documentation proving that the research was ethically conducted. (Online Resource 7).

However, on July 29, 2015, three years post-publication and seven years after the Chinese field research, Tang et al. 2012 was retracted by its publisher ASN (Online Resource 8).

Henry Miller⁷, has written that the retracted article "*might have been the most important contribution to public health worldwide since Jonas Salk's announcement of the successful trials of polio vaccine. The operative phrase is might have been, because intimidation, politics and especially the dishonest, anti-science efforts of NGOs like Greenpeace to discredit the research have delayed the translation of its findings to life-saving interventions for millions of children.*" (Miller, 2015, and Personal Communication: November 4 2023)

Analysis of ASN Retraction Decision

How does the ASN justification for retraction compare with the four reasons for retraction recommended by The Committee on Publication Ethics?

ASN retracted the Tang et al 2012 paper on July 29th, 2015, citing the following reasons (Online Resource 8, and Tang et al, 2015):

1. The authors are unable to provide sufficient evidence that the study had been reviewed and approved by a local ethics committee in China in a manner fully consistent with NIH⁸ guidelines. Furthermore, the engaged institutions in China did not have US Federal Wide Assurances and had not registered their Institutional Review Board (or Ethics Review Committee).

2. The authors are unable to substantiate through documentary evidence that all parents or children involved in the study were provided with the full consent form for the study.

3. Specific eligibility issues were identified in regard to 2 subjects in the study.

The Committee on Publication Ethics⁹ provides guidelines, (COPE Council 2019) stating that journal editors should consider retracting a publication if:

1. *Findings are Unreliable*: Due to misconduct or honest error.

2. *Redundant Publication*: The findings have been published elsewhere without proper cross-referencing, permission, or justification.

3. *Plagiarism*: The publication constitutes plagiarism.

4. *Unethical Research*: The publication reports unethical research.

It is evident from the Tufts University statement on September 17th, 2013 (Online Resource 5), that COPE's items 1, 2, and 3 do not apply to the case of Tang et al 2012. Thus, ASN retracted the paper for reason 4: unethical research.

⁷ Physician and molecular biologist, and the founding director of the US, Food and Drug Administration's Office of Biotechnology, and in 2015, the Robert Wesson Fellow in Scientific Philosophy and Public Policy at Stanford University's Hoover Institution.

⁸ NIH is the abbreviation for the US National Institutes of Health

⁹ Henceforward: COPE

Now, the question arises: How can ASN justify that the research reported by Tang et al 2012 was deemed 'unethical research'?

1. ASN's first point.

ASN contends that there was evidence suggesting that a local ethics committee (IRB) in China had approved the study, but the approval might not have been "in a manner fully consistent with NIH guidelines"

A February 2002 grant application to the US NIH, for the project titled "Retinol Equivalents of Plant Carotenoids in Chinese Children" was designed to ascertain the vitamin A value of dietary provitamin A carotenes from spinach, Golden Rice, and pure β -carotene (β -c) in oil. The research would involve children (ages 6-8) with/without sufficient vitamin A nutrition. Despite the initial plan in 2002, challenges in producing an ample supply of the required deuterium-labelled Golden Rice in the USA persisted until shortly before March 2008, delaying the subsequent human research in China (Dubock, 2014).

On February 10, 2004, Tufts University IRB approved research Protocol "version 3 dated 28 March 2003" for "Retinol Equivalents of Plant Carotenoids in Chinese Children," noting the presence of Zhejiang Academy of Medical Sciences approval. In China, all research documents originally in English underwent translation into Chinese and were notarized as accurate translations of the approved text by Tufts IRB. The Ethics Review Committee (=IRB) of Zhejiang Academy of

Medical Sciences had reviewed and documented agreement to the same research Protocol on November 27th, 2003 (Online Resource 9).

Tufts IRB reapproved the study in 2008, and the Zhejiang Academy of Medical Sciences Ethical Review Committee confirmed the ongoing validity of its 2003 approval, also in 2008. (Online Resource 11). All approvals in both countries referenced the same NIH Grant 1R01 DK060021-01 for the research.

ASN highlighted incomplete evidence of Chinese approval being "in a manner fully consistent with NIH guidelines," acknowledging this as a procedural point open to interpretation.

Chinese laws govern research in China, not the US NIH nor Tufts, and Chinese regulations¹⁰ emphasize adherence to national laws, ethical principles, and an independent, objective, fair, and transparent review process.

Research in other countries must respect local laws, as emphasized on the US's NIH website (Gostin, 2019).

ASN noted the absence of US Federal Wide Assurances and unregistered Chinese institutions. However, the requirement to register foreign IRBs was established in 2009 (Online Resource 12, page 3), after all of the initial planning in 2002, IRB clearance in 2003, pilot trial in 2005, and fieldwork in China in June 2008. Tufts IRB in 2008 did not mandate Chinese IRB registration.

¹⁰ 第四条 伦理审查应当遵守国家法律、法规和规章的规定以及公认的生命伦理原则。伦理审查过程应当独立、客观、公正和透明。(Translation: Number 4.

Ethical review should comply with national laws, regulations and rules as well as generally accepted regulations and rules as well as accepted life ethics principles, ethical review process should be independent, objective, fair and transparent.)

Dr. Tang, in a letter to OHRP dated October 30, 2013, asserted, with US OHRP source references: "The US recognizes the Chinese 2007 Ministry of Health policy on ethics review documents. Consequently, the ZAMS ERC¹¹ did qualify as a recognized institution for human subject research." (Online Resource 12).

ASN has not substantiated the claim that the research reported by Tang et al. in 2012 was "unethical research."

2. ASN's second point.

ASN's second concern revolves around the authors' inability to substantiate, through documentary evidence, the provision of the full consent form to all parents or children involved in the study.

The research Protocol, approved by both Chinese and US IRBs, delineates the roles of the research team. Dr. Shi'an Yin, Director of the Department of Maternal and Child Nutrition at the Institute of Nutrition and Food Hygiene, Chinese Academy of Preventative Medicine, Beijing, China, is responsible for recruiting children volunteers, implementing the study protocol, and overseeing various aspects of the project. The Informed Consent Form, in Chinese, specifies that Dr. Yin will securely store the code of a child's identity in his office for seven years. Dr. Tang handles sample analysis in her US laboratory, ensuring confidentiality through coding.

A November 17, 2003, letter from Drs. Russell & Tang to Professors Yin & Wang emphasized the latter's role in conducting field investigations for the NIH research Grant. Tufts University expressed concern about handwritten signatures and dates on Informed

Consent Forms and their completeness, although the official record was maintained by Dr. Yin.

ASN's claim that "the authors are unable to substantiate" is based solely on information supplied by Tufts. Tufts investigators did not verify facts with Dr. Yin or other Chinese researchers. Communication between Tufts and Chinese investigators did not occur during Tufts investigation, and Tufts restricted Dr. Tang from contacting her co-investigators. Chinese officials visiting Tufts in October 2012 did not meet Dr. Tang.

Verbal transmission of information before obtaining informed consent is customary, particularly in studies involving large subject groups. In a November 12, 2013, letter with attachments (Online Resource 7), Dr. Tang included photos (Online Resource 13) of the May 22, 2008 meeting with parents and children, where verbal communication took place. These photos and their significance were disregarded by ASN and AJCN.

ASN has not provided justification for categorizing the research reported by Tang et al. in 2012 as "unethical research."

3. ASN's third point.

ASN raises concerns about specific eligibility issues for two subjects in the study, as reported by Tufts University. These concerns stem from the deviation of two children from the age range specified by the research team and approved by both IRBs. The chosen age range aimed to avoid hormonal effects on results while ensuring participants' comprehension and sufficient blood for sampling.

¹¹ = IRB

While only one meal, on a single day, covered the prepared spinach, beta-carotene in oil, or Golden Rice, the Protocol required recording food intake for all three meals a day, five school days a week for three weeks. The class teacher, supervising these meals, lacked time to prepare her family's evening meal and requested her child to partake in the provided meals.

On June 27, 2005, the Zhejiang Academy of Medical Sciences issued a statement permitting investigators to make practical adjustments to the Protocol, provided such adjustments do not increase risk to subjects. (Online Resource 10). In line with this allowance, the investigators accommodated the teacher's request. Tufts' 2012 investigation reported "no concerns related to the safety of the research subjects" (Online Resource 5). The teacher-parent signed the Informed Consent Form, and her child consumed the spinach meal on the designated day.

The second child, within the correct age group and formally consented to the study, later revoked consent for the separate agreement on using pre-screen blood sample data, resulting in the absence of baseline data for this subject. Data from these two children were excluded from the analysis.

ASN has not provided justification for labelling the research reported by Tang et al. in 2012 as "unethical research."

Analysis Of Other Organisations

The retraction of Tang et al. 2012, ostensibly based on allegations of 'unethical research,'

lacks substantiated proof for each of the three criticisms presented by ASN. The justification for retraction becomes a subject of scrutiny, prompting an exploration of contemporaneous documents from the 2012-2015 period. These previously undisclosed materials, accessible as 'Online Resources' through embedded links, encompass contributions from Tufts, ASN, AJCN, OHRP, and various Chinese sources. Additionally, Greenpeace's press releases and other now-unavailable web content offer valuable context. Information from the NIH¹² is part of this broader examination which aims to shed light on the circumstances surrounding the retraction of Tang et al 2012, in the absence of conclusive evidence supporting the claims of 'unethical research' by ASN.

Greenpeace

Greenpeace has maintained a longstanding opposition to GMO-crops since 1997, aligning with similar views held by many organizations in 2015. Golden Rice, designed for public benefit and not for profit, challenges the activists' primary accusation that GMO-crops prioritize multinational profits, disadvantaging the poor. Benedict Herlin, lead for Greenpeace's anti-GMO-crop campaign, proposed exempting Golden Rice due to its humanitarian profile in the early 2000s, a suggestion rejected by Greenpeace's leaders shortly thereafter. In 2005, Greenpeace claimed in a press release that Golden Rice would "exacerbate malnutrition and undermine food security, because it encourages a diet based on a single industrial staple food". (Editorial, 2005).

¹² "On June 26, 2018 a response was received to a Freedom of Information Act request (FOIA Case Number: XX-FOI-XXXXX-NIDKMK; Case Number:

XXXXX) . . . including 839 pages responsive to your request."

Jens Katzek, the lead anti-GMO campaigner for Friends of the Earth, reported in 2013 that his colleagues were vehemently opposed to Golden Rice, stating, "If we lose the Golden Rice battle, we lose the GMO war." Such attitudes led to accusations of "ideological bigotry" against "Greenpeace, Friends of the Earth, and their political allies in European governments and nongovernmental organisations". (Editorial, 2005).

On August 18 2012, eleven days before Greenpeace's 2012 press release, one Chinese journalist reported: (Online Resource 14) "Critics had claimed that [Golden Rice] is impractical. According to calculations by Greenpeace, people would need to eat . . . 18 kilograms of cooked rice a day . . . Guangwen Tang of Tufts University and colleagues have demonstrated that just 100 to 150 grams of the rice – about half the children's daily intake - provided 60 per cent of the recommended daily intake of vitamin A." This study "demolishes the criticism". (The 2001 Greenpeace press release referred to is Online Resource 15).

Greenpeace, driven by their anti-GMO-crop campaign in China and their global fundraising efforts, was highly motivated to discredit Tang et al. 2012. In their August 29, 2012 press release, Greenpeace falsely asserted that the Chinese Ministry of Agriculture confirmed the non-importation of Golden Rice and a supposed Chinese government decision to abort the trial. However, documents produced by Greenpeace, dated July 2008, were irrelevant, as Tang et al.'s research in China had concluded in June 2008, a month earlier. (Online Resource 16).

Greenpeace criticized exposing Chinese children to genetically modified rice untested on animals, overlooking the necessity of studying beta-carotene bioconversion in humans. Importation of precisely weighed samples of Golden Rice and Spinach into China adhered to regulations, as they were in frozen form, (Online Resource17) and did not violate any GMO-crop laws designed to control importation of living GMO-crop organisms.

The Chinese Government

Before the publication of Tang et al. 2012, GMO-crops, as a politically charged issue in the Chinese Communist Party elections, became heightened by Greenpeace's press release, which triggered anti-GMO crop hysteria in China. The involvement of "American Principal Investigator, Dr. Tang" carried a xenophobic undertone (Figure 1), despite Dr. Tang being a female born in China.

Greenpeace's press release alleged a violation of Chinese law, leading to intimidation of Chinese co-investigators by the police. Some were visited at home for six consecutive nights, seeking an admission regarding the Golden Rice used in the study. The Chinese clinical researchers faced intense investigations by Chinese public health authorities, causing mental distress. Fearing for their safety and jobs, the Chinese co-investigators initially distanced themselves from the study under Greenpeace's criticism.

The Chinese authorities arranged a visit to the U.S. through their embassy, with two senior officials from the Chinese Center for Disease Control and Prevention arriving in Boston during the first week of October 2012. Due to the controversy, Tufts had already, in early September, initiated efforts to establish an

investigatory committee, possibly external, with expertise in human subject research, children as subjects, and GMOs¹³ (Online Resource 18). The Chinese officials could have interacted with this committee during their visit.

Tufts' investigation of Dr. Tang's actions did not commence until February 2013, (Online Resource 21, page 2, second point) four months after the Chinese officials' visit. During their visit to Tufts, there was no meeting between the Chinese officials and Dr. Tang, the Chinese-born Principal Investigator of Tang et al. 2012.

As the Chinese-born scientist and Principal Investigator of Tang et al. 2012, Dr. Tang was uniquely positioned to address inquiries from the visitors, particularly in the Chinese language. Confirming her presence at Tufts during the first week of October 2012, it becomes evident that, apart from adherence to US regulations governing human subject research and individual perspectives within Tufts or external committee members, discussions with Chinese visitors were limited in scope.

The Chinese officials left Boston for Washington D.C. on October 5, 2012, to meet with NIH the following week.

During the internal discussions both before and after meeting the Chinese delegation, NIH staff frequently cited Dr. Tang and Tufts IRB as the primary sources of relevant information, emphasizing that ethical

considerations fall under the purview of OHRP in HHS, not NIH, with authority delegated to local IRBs.

Preceding their meeting with the Chinese officials, NIH corresponded with the retired grant manager (KN) seeking information on the NIH funded study which resulted in Tang et al 2012. KN recalled a previous Health and Safety concern raised by an external NGO entity, noting satisfactory responses to NIH from Tufts officials and Dr. Tang. He recalled that the study obtained necessary approvals from both Tufts and Chinese officials before commencement.

On October 9, 2012, the Chinese visitors met with representatives from US Government Departments NIH, HHS, USDA¹⁴, and FDA¹⁵. They were informed that requests for US Government documents must follow standard Freedom of Information Act processes, a procedure taking at least a week even with expedited handling.

Seeking information for a meeting with other Chinese health officials on October 11, 2012, the Chinese guests faced time constraints due to the expedited nature of their US visit.

Only after they returned from the US trip (Hvistendahl & Enserink, 2012) was the Chinese December 6 2012 (Online Resource 2) report written¹⁶. The report amalgamates Greenpeace's allegations, refers to US processes for research with human subjects, and

¹³ No person, anywhere, had experience of all three of these topics, except for Dr Tang's team of investigators. Any others in the US with experience of children subject research in China would have no professional knowledge of "GMO's". For Dr Tang's team, the only important thing about Golden Rice was that it was a source of beta-carotene, potentially useful in combatting vitamin A deficiency. To

investigate that potential, was the only purpose of the research.

¹⁴ U.S. Department of Agriculture

¹⁵ U.S. Food and Drug Administration

¹⁶ "China CDC reportedly prepared the statement after dispatching an official to the United States to consult representatives of both Tufts and NIH;" quote from Hvistendahl & Enserink, 2012

Chinese explanations of what had occurred in 2008 and prior to the research conducted in China following Chinese law and processes. The report confirms that ethical clearance, by the appropriate Chinese IRB, was in place for the 2008 research. (Online Resource 2).

The report also raised as an issue for the first time (Greenpeace did not raise it): that the genetic modification of Golden Rice not being clearly stated as part of the informed consent information, was ethically significant. It can be strongly implied, from the FOIA records, that the source of this criticism was the Tufts 'external advisory committee' whose membership has never been publicly announced, or Dr DLS of Tufts. The external advisory committee criticised Tufts IRB for agreeing in the Protocol governing the research not to use any terms relating to "genetic modification" (Online Resource 3).

The Chinese Center for Disease Control, Zhejiang Academy of Medical Sciences and Hunan Provincial Center for Disease Control and Prevention also undertook, in their Report, "to further strengthen the supervision of scientific research projects, improve internal rules and regulations, strengthen laws and regulations, Research integrity, professional ethics and medical ethics education". (Online Resource 2)

Despite tacitly admitting that the Greenpeace criticism was not due to their conduct, the December 6, 2012 Chinese report announced the punishment of co-investigators Yin Shi'an, Wang Yin, and Hu Yuming by the Chinese authorities.

Tufts University

On June 21, 2012, an Associate Editor at AJCN informed Dr. Tang that her paper, later published as Tang et al. 2012, had been accepted. Following her previous publication on Golden Rice (Tang et al. 2009), which generated minimal interest, an anti-GMO-crop group in the UK raised concerns about the 2008 Chinese children research protocol available on NIH's website. NIH responded positively to the complaint, acknowledging the research's validity and NIH's applied controls (Online Resource 19).

The day after AJCN's acceptance, on June 22, 2012, Dr. Tang informed Tufts' public relations department¹⁷. On July 18, 2012, five weeks before Greenpeace's press release, Tufts PR sought an advance copy of the paper due to anticipated external interest in Golden Rice research.

JK, introduced as Tufts' new deputy director of PR in June 2012, likely had no knowledge of the Tang et al. 2009 criticism in July 2012. There is speculation about whether Tufts PR, in July 2012, anticipated potential criticism upon the 2008 research's publication and if so why, and if this anticipation originated from AJCN, ASN, or Tufts.

In September 2013, JK authored the Tufts Statement (Online Resource 5), criticized within NIH for being overly defensive¹⁸. On September 7, 2012, Tufts' Vice Provost (PN) sought OHRP's assistance, noting Greenpeace's impact in China and engaging a law firm (Hogan Lovells) for investigation¹⁹, (Online Resource 18) The law firm's

¹⁷ PR

¹⁸ especially with respect to the "We regret..." of the final paragraph.

¹⁹ "... Greenpeace China. . . have set off a firestorm in China We have engaged a law firm in China to help us Initial review suggests that the researcher

engagement in China was not further documented, suggesting the fulfilment of Chinese laws by the Tang et al 2012 research there in 2008.

Around September 9, 2012, NIH prepared responses to press inquiries from China, aware of AJCN reports of Chinese scientists complaining about Tang 2012. Dr. DLS, appointed Tufts Vice Provost for Research in 2012, later exerted significant influence.

Nine months later, on June 28, 2013, Dr. DLS reported Tufts' fact-finding review to OHRP, (Online Resource 3) listing non-compliance issues by Dr. Tang and Tufts University IRB in Tang et al. 2012. A severe 'Corrective Action Plan' was proposed for both, impacting Dr. Tang's career (Online Resource 21), and no-one-else's career at Tufts.

Dr. DLS's Corrective Action Plan required Dr. Tang to write to AJCN's Editor-in-Chief. Dr Tang wrote the required letter, but Dr DLS found it inadequate. Discussion between Dr Tang and Dr DLS about a revision was very protracted (for more than a month, from August 2 2013 to September 6 2013) because Dr Tang disagreed with the text Dr DLS was proposing. Dr DLS, involved the law firm Ropes and Gray in drafting her revised text – which was meant to be a letter from Dr Tang. Dr DLS threatened Dr Tang, that unless Dr DLS's version was accepted, Tufts University would also write to the AJCN Editor.

Dr. DLS's subsequent letters to NIH, USDA, and China CDC in July 2013 (Online Resource 20) did not mention Greenpeace, despite its

central role in Tufts' investigation. Each letter listed alleged non-compliance by Dr. Tang, emphasizing inadequacies in the informed consent process regarding the genetically-altered nature of one of the three source of beta-carotene investigated. This was all of scientifically irrelevant, consistent with US Government guidance and accordingly agreed by Tufts IRB as part of the Research Protocol. Only after Dr Tang requested copies of the letters via Tufts Legal department did Dr. DLS provide them, despite each being personally critical of her as the PI (Online Resource 20).

Tufts University's September 17, 2013, statement summarizing the investigation, also omitted any reference to Greenpeace (Online Resource 5)

Dr Tang's letter, in the form insisted upon by Dr DLS, was eventually signed, only under extreme duress, by Dr Tang, and was sent to the AJCN Editor-In-Chief on September 6 2013. (Online Resource 4). The letter purported to be from all four of the US resident co-authors of Tang et al 2012. However, Dr Tang was the only author to have seen Dr DLS's final version before it was sent. Dr DLS had digitally 'copy pasted' the other three signatures to it from other documents. The letter, was addressed to the Editor-in-Chief of AJCN, Dr DMB, and was copied to KMK, the Vice President of Publications, ASN, as owners of AJCN, and to Dr DLS (Online Resource 4).

Despite the detailed corrective action plan, (Online resource 3) Tufts also imposed income and employment sanctions on Dr. Tang. In

did obtain appropriate IRB approval in China. . . . many of the more serious allegations . . . would require information from China, where people seem to be too frightened to tell the truth about this study. I am

hoping that you might be able to give me some suggestions for how we might best investigate . . . , I have asked our IRB chair to review the study documents and the review that was done at Tufts."

July 2013, the Dean's office strongly recommended her to defer her promotion application. Despite her 27-year tenure and global recognition in carotenoid research, subsequently her laboratory was closed in March 2014, leading to termination of her employment in September 2014. Dr Tang endured these actions while retaining her professional courtesy in sending season's greetings to Dr. DLS (Online Resource 21).

The American Society for Nutrition

On September 9, 2012, just eleven days subsequent to Greenpeace's critical press release, NIH disclosed that the "Journal of Clinical Nutrition²⁰" had received numerous letters from Chinese scientists citing ethical and legal concerns, including a flawed Institutional Review Board (IRB) process. AJCN told NIH that AJCN would investigate the allegation. Later, NIH confirmed that AJCN had provided no follow up information.

On September 6, 2013, Dr. Tang's letter (Online Resource 4) reached Dr. DMB, Editor-in-Chief of AJCN, with a copy sent to KMK, Vice-President of Publications, ASN, and Dr DLS (Online Resource 4).

On December 05, 2013, KMK responded, expressing gratitude for Dr. Tang's letter and stating, "Thank you for your letter of September 6, 2013after careful review of the information provided in it and the findings of the Tufts Institutional Review Board . . . " retraction of Tang et al 2012 "is appropriate and necessary" to "maintain the ethical

standards of AJCN and to ensure the integrity of the scientific record". (Online Resource 6). KMK encouraged the authors to initiate retraction, accompanied by a threat to proceed even if the authors did not concur, along with a sample retraction notice (Online Resource 6). The letter was copied to all six of her co-authors and was not copied to Dr DMB the Editor-in-Chief of AJCN or anyone else.

In a December 10, 2013, email, IR a former head of Dr. Tang's laboratory, in strong terms, advised Dr Tang's team to reject the request and hinted at potential public denouncement, emphasizing the study's significance²¹.

On December 11, 2013, Dr. Tang responded to KMK at ASN, asserting that the September 5, 2013 letter was written by Dr. DLS, Tufts Vice-Provost for Research, that she, the PI, did not agree with it (Online Resource 7), and attaching 90 pages of evidence, including positive ethical reviews from 2003 and 2008 and photographs from the 2008 consent meeting (Online Resources 9, 11, 13).

Referencing the attachments, Dr. Tang defended the validity of the study's statements, challenging the inadequacy found by ASN "*The study recruitment processes and protocol were approved by the Institutional Review Board-Tufts Medical Center in the United States and by the Ethics Review Committee of Zhejiang Academy of Medical Sciences in China. Both parents and pupils consented to participate in the study.*" (Online Resource 7). Dr. Tang requested ASN

²⁰ Actually, AJCN

²¹ ". . . I suggest that you and co-authors reject, however, this outrageously passive-aggressive request . . . I and others at Tufts and beyond are prepared to write a letter to the editor for publication in AJCN denouncing their action on multiple grounds, not

least, the effect of their action on the Battle against Vit A deficiency, the victory for Greenpeace in re GMO's in nutrition, and the chilling effect on GMO research. This study deserves, I think, to be in the citable peer-reviewed literature especially with wide access to developing countries."

to consider the facts and defer the threatened retraction.

On December 12, 2013, a four-page letter was sent by e-mail to KMK by the author. (Online Resource 22). One of the 4 pdf attachments sent with the letter, contained the 2009 NIH defence of Dr Tangs 2008 research, (Online Resource 19).

Around 20 months later, on July 29, 2015, ASN unilaterally retracted Tang et al 2012 (Online Resource 23). Contrary to COPE recommendations²², Dr. DMB the AJCN Editor-In-Chief confirmed on August 25, 2015, that the legal retraction was by the society, not his personal editorial decision (DMB Statement, Online Resource 24).

The US Government's OHRP & NIH

Internal discussions at NIH affirmed the Office for Human Research Protections (OHRP) as the designated institution to investigate accusations of unethical behaviour in U.S.-based human research. The NIH identified the Tufts Institutional Review Board (IRB) and Principal Investigator (PI), Dr. Tang, as pertinent sources of information.

On October 30, 2013, Dr. Tang corresponded with Dr. KCB, Director of the Division of Compliance Oversight at OHRP presenting 11 points to rebut Dr. DLS's account of non-compliance (Online Resource 3). Dr. Tang explicitly stated "This is not true" for two points and provided substantial evidence contradicting the statements in Dr. DLS's June

28, 2013 letter for the other nine points (Online Resource 12).

Despite communications from Dr. DLS, Dr. Tang, and the author on the same subject, OHRP responded uniformly, stating, 'I will file the correspondence.' (for example third highlight in Online Resource 25).

On February 28, 2014, an email was sent by the author to Dr. KCB, OHRP, copied to NIH and USDA funding agencies and the President of Tufts University, Dr. AM, seeking clarification on OHRP's authority to dispute an IRB's conclusions and hold it accountable for managing an investigation's findings. The email also questioned whether OHRP had jurisdictional authority to intervene when a PI is accused of adhering strictly to the agreed-upon protocol (Online Resource 25).

Dr. KCB responded nearly a month later, on March 21, 2014, stating that if an institution provided demonstrably false statements to OHRP in reporting noncompliance, they would be interested in such information. Dr. KCB suggested that OHRP would refer evidence of fraud or false statements to the HHS Office of the Inspector General, acknowledging a lack of awareness of another office or agency capable of addressing these concerns (Online Resource 25).

A CATS Report, dated October 10, 2017, with Dr. KCB, OHRP, named as Coordinator, noted that the case was received on September 7, 2012, and the activity report was opened and closed on July 23, 2013 (Online Resource 26).

²² "Who should issue the retraction? Articles may be retracted by their author(s) or by the journal editor. In some cases, retractions are issued jointly or on behalf of the journal's owner (eg, a learned society or publisher). However, since responsibility for the journal's content rests with the editor s/he should

always have the final decision about retracting material. Journal editors may retract publications (or issue expressions of concern) even if all or some of the authors refuse to retract the publication themselves." COPE Council, 2019 [emphasis added]

The report referenced only Dr. DLS's June 28, 2013 letter (Online Resource 3), incorporating language from PN's emails of September 7, 2012 (Online Resource 18). Notably, both the NIH's 2009 defence of the research (Online Resource 19) and Dr. Tang's October 30, 2013 letter to Dr. KCB, OHRP (Online Resource 12), appeared to be disregarded, despite the latter containing evidence of at least two false statements.

Discussion

Dr. Tang's tenure at the Carotenoids and Health Laboratory spanned 27 years, until her employment was terminated in 2013, during which she became an internationally recognized expert in carotenoid research. Her extensive experience, leadership in international consultations, and a dozen-member laboratory, marked by 75 scientific publications, reflected her prominence. Notably, 62% of her 21 human research publications were in ASN-owned journals, 52% involved China, and 33% centred on children, with 24% specifically concerning Chinese children. The controversial Tang et al 2012 study, involving Golden Rice and Chinese children, was uniquely criticized, and by an anti-GMO crop activist group. By the retraction in 2015, the study had been downloaded 53,256 times and cited three times (Online Resource 27).

Despite AJCN's acknowledgment of investigating Greenpeace's allegations, NIH's October 05, 2012 e-mail revealed that AJCN had not submitted any "evidence" for review. Before KMK's retraction demand on December 6, 2013 (Online Resource 6), ASN had minimal information, relying on the

Greenpeace press release (Online Resource 1), the confusing Chinese report (Hvistendahl and Enserink, 2012 and Online Resource 2) the purported September 2013 letter from four US co-authors which was actually written by Dr. DLS with 3 forged signatures (Online Resource 4), and Tufts' September 17, 2013 statement (Online Resource 5).

In a departure from COPE's guidance, KMK of ASN issued an "outrageously passive-aggressive"²¹ retraction demand without discussion with the PI, Dr. Tang, on December 5, 2013 (Online Resource 6). The Editor-in-Chief's potential recusal due to a co-author's institutional affiliation was not explicitly addressed, (Online Resource 24) and the ASN decision to prioritize Greenpeace's allegations over robust challenges to the evidence was ethically questionable.

The subsequent implications were severe for Dr. Tang and her Chinese co-investigators (Online Resource 2, 3, 21). ASN chose – and it is clear that they had choice - to prioritize Greenpeace's press release, the Chinese report, and the letter purportedly from the US co-authors (Online Resource 6), despite thorough challenges to the evidence (Online Resources 7, 19, 22, and the statement from NIH grant manager KN).

Tufts' initial response, as reflected in emails between Vice Provost PN and Dr. KCB of OHRP, was measured and understanding of the political context, recognizing Greenpeace's involvement (Online Resource 18). However, the subsequent retraction by ASN on July 29, 2015 (Online Resource 8), irrespective of whose decision it was, was ethically questionable given the well-challenged evidence, the scientific authority

of the research team (Online Resource 27), and the source of the criticism.

The oversight responsibility for human research ethics, delegated to IRBs by OHRP, demands experience, expertise, and diversity in decision-making (Online Document, Institutional Review Board). Despite Dr. DLS's micromanagement, her qualifications in computer science and mathematics raise questions about her adequacy in judging the ethical aspects of carotenoid research in China.

The Vice Provost Research at Tufts, plays a crucial role in overseeing the ethical and legal conduct of research and grants for the University, supported by both legal and Institutional Review Board (IRB) resources. Dr DLS's approach faced criticism from scientists not directly engaged in the scrutinized research²³.

Dr DLS's approach continuously emphasised the genetically modified nature of Golden Rice²⁴, one of the three test subjects, despite this being scientifically irrelevant, and that this was not disclosed in documents approved by the involved IRB's (including Tufts IRB) Protocols consistent with US Government policy concerning the use of language in human research documentation. Dr DLS persistently ignored that the criticism of the Tang et al 2012 research was initiated by a Greenpeace press release. The absence of visits to China and communication with Chinese co-investigators during the Tufts

investigative processes was notable, given that the criticized research occurred in China (Online resource 18, paragraph 5, line 8).

Dr. DLS's influence on ASN's retraction decision and her disproportionate "Corrective Action Plan for Dr. Tang" (Online Resource 21) is evident. ASN's choice to prioritize Greenpeace's allegations without thorough consideration of the evidence was ethically unsound, causing severe consequences for Dr. Tang and her Chinese co-investigators. OHRP's handling of detailed evidence challenging Dr. DLS's report raised concerns about due diligence and adherence to COPE guidance.

The behaviour which led to the retraction of Tang et al 2012 was by individuals in senior management positions in academia who were able to ignore scientific merit both of the research and the dedicated scientists, instead basing their decisions on ideology.

Such behaviour is part of what has stimulated 167 Nobel Laureates (Roberts, et al, 2016) to call on:

"... GREENPEACE to cease and desist in its campaign against Golden Rice specifically, and crops and foods improved through biotechnology in general;

"... GOVERNMENTS OF THE WORLD to reject Greenpeace's campaign against Golden Rice specifically, and crops and foods improved through biotechnology in general; and to do everything in their power to oppose

²³ To quote an e-mail from (JB) the Director of the Antioxidants Research Laboratory and Professor in the Friedman School of Nutrition Science and Policy "...I am in strong agreement with almost all your points. I have raised many of these same issues at Tufts in defence of Guang and her research on Golden Rice. I have literally stood by Guang's side in confronting Dr [DLS]".

²⁴ Testing of the 'genetically modified nature' was not the specific purpose, or any purpose, of the research which is clearly stated with the heading 'Objective' on the first page of the retracted paper: "The objective was to compare the vitamin A value of b-carotene in GR and in spinach with that of pure b-carotene in oil when consumed by children."

Greenpeace's actions and accelerate the access of farmers to all the tools of modern biology, especially seeds improved through biotechnology. Opposition based on emotion and dogma contradicted by data must be stopped.”

The aftermath to the controversy prompted changes in regulations by both Tufts University (Online Resource 3) and Chinese authorities²⁵ overseeing human subjects research, suggesting a recognition that investigators were not culpable for alleged ethical transgressions in 2008. Dr. DLS's role as Vice Provost Research only from 2012 to 2016 adds context to her actions during this period (Online document, 2023).

Conclusion

The retraction of Tang et al 2012 rests heavily on a September 2013 Tufts letter, employing threatening and deceptive tactics, detailing an analysis conducted solely in the US on events from mid-2008 in China. The decision to retract disregarded both Chinese and US laws and regulations, often inaccurately or pedantically interpreted. Despite the availability of substantial contextual information provided by the Principal Investigator and others to both Tufts and the ASN, this pertinent data was disregarded.

Crucial figures in the research review, such as the Chair of the Tufts IRB and the Editor-in-

Chief of the AJCN, played negligible roles in the retraction decision. It seems that two influential individuals, one at Tufts University and the other at the American Society for Nutrition, were fixated on the GMO-crop aspect of Golden Rice emphasized by Greenpeace, overlooking the scientific and nutritional merit, as well as the context and evidence presented.

Both individuals used threats against the PI Dr. Tang to underscore their perspectives, despite their roles representing institutions focused on human nutrition. Rather than being inspired by the potential of Tang et al 2012's excellent results in combating vitamin A deficiency through Golden Rice, they, acting on behalf of their institutions, dismantled a leading collaborative nutritional research center that had operated successfully for over a decade and a half since 1999.

The OHRP failed in ensuring that its delegated authority to a local IRB was correctly discharged. Tufts University and the American Society for Nutrition did a disservice to nutritional science and the Principal Investigator and Co-investigators, all of Chinese origin.

Presently, it is estimated that over half of preschool-aged children and two-thirds of non-pregnant women of reproductive age globally suffer from micronutrient deficiencies (Stevens et al., 2022).

²⁵ “In July [2013] China's National Health and Family Planning Commission released new draft guidelines for studies involving humans, which the state news agency Xinhua says were triggered by the golden rice incident.

Among the changes is that trials must be registered with the sponsoring institution before they begin, to allow proper oversight.” . . . “Cao

Xuetao, president of the Chinese Academy of Medical Sciences, says the issue is a reminder that Chinese regulatory authorities haven't kept up with the nation's burgeoning research enterprise. "Chinese science has expanded so fast in the past few years," he says, and "now there are so many clinical trials." (Enserink, 2013)

The biased retraction of Tang et al (2012) has eroded confidence in adopting Golden Rice as a new crop, organically biofortified with beta-carotene, and at no extra cost compared to white rice, as a source of vitamin A to combat the sight and life-threatening vitamin A deficiency affecting millions of children worldwide. Nevertheless, it is being actively adopted by the Government of the Philippines since 2022, to assist in reducing vitamin A deficiency (VAD) there, which is considered to affect 15.5% of Philippine children, a small proportion of 125 million VAD affected children globally.

Recommendations

1. The retraction of Tang et al 2012 should be rescinded by ASN for the same reasons given by KMK Vice President for Publications, ASN when she threatened Dr Tang and her co-authors on December 5 2013 (Online Resource 6): "to maintain the ethical standards of *AJCN* and to ensure the integrity of the scientific record."
2. Tufts University should repay Dr Tang the salary not paid in 2014, should properly consider her application for promotion to Professor withheld in 2013 and back date her pay due between then and now, and compensate her for unfair dismissal associated with this case.
3. The Chinese Center for Disease Control and Prevention should reinstate the professional status of Yin Shi'an and repay lost income, and compensate for unfair treatment.
4. The Zhejiang Academy of Medical Sciences should reinstate the professional status of Wang Yin and repay lost income, and compensate for unfair treatment.

5. The Hunan Provincial Center for Disease Control and Prevention should reinstate the professional status of Hu Yuming and repay lost income, and compensate for unfair treatment.

6. To prevent further miscarriages of justice, Human Health Services of the US National Institutes of Health, should review their Office for Human Research Protections processes used to review supportable challenges to Institutional Review Board decisions.

Conflict of Interest:

None

Funding:

None

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Given my extensive involvement since 2000 in the Golden Rice project (www.goldenrice.org), I engaged in frequent discussions with Dr. Tang about her research until 2015. Dr. Tang, a globally recognized expert (Online Resource 27; Grune et al., 2010, Tang, 2013), contributed to sophisticated science on beta-carotene as a source of circulating vitamin A, crucial in combating vitamin A deficiency, a leading cause of childhood blindness and under-5 child deaths worldwide. Her detailed explanations and documentation of the 'Chinese children' trials were invaluable.

Special thanks to Professor Drew L. Kershen for filing a Freedom of Information Act request to NIH on my behalf, yielding a substantial response of 839 pages on June 26, 2018.

Index of Online Resources 1-28 available at <https://doi.org/10.5281/zenodo.10639988>

1 August 29 2012 Greenpeace press release.

- 2 December 6 2012 Chinese Report on the investigation of Tang et al 2012
- 3 June 28 2013 DLS Tufts 10-page letter to KCB OHRP
- 4 September 6 2013 Tufts Letter to Editor-in-Chief AJCN with 3 copied signatures
- 5 September 17 2013 Tufts University Statement
- 6 December 05 2013 KMK ASN VP to Tang must retract
- 7 December 11 2013 3-page letter Tang to ASN and AJCN (with 2 highlights) with multiple attachments
- 8 July 29 2015 retraction notice ajcn093229 715.715
- 9 November 27 2003 Ethical Review_2003 Zhejiang Academy of Medical Sciences
- 10 June 27 2005 Academy of Zhejiang Medical Sciences Discretionary Protocol adjustments
- 11 March 30 2008 Ethical Review Zhejiang Academy of Medical Sciences
- 12 Oct 30 2013 Tang to KCB OHRP (with 2 highlights)
- 13 December 11 2013 Dr Tang's reply to KMK ASN included May 22 2008 Meeting photos
- 14 August 18 2012 Chinese Media 'This study demolishes the Greenpeace Criticism'
- 15 February 12 2001 Greenpeace Golden Rice Press release
- 16 July 2008 Greenpeace 'proof' that research stopped by Chinese authorities
- 17 60-gram samples of labelled & cooked Golden Rice to be carried to China frozen
- 18 E mail exchange September 7 to 11 2012 PN Tufts and KCB, CHRP
- 19 April 30 2009 NIH public defence of Tang's 2008 research with Chinese children
- 20 DLS Tufts to NIH, USDA July 26 2013, & China CDC 29 July 2013 with highlights
- 21 Career & financial punishment for Dr Tang 4 pages with highlight
- 22 A December 12 2013 Dr ACD 2-page e-mail to KMK, ASN, with highlight
- 23 July 29 2015 Retraction notice ajcn093229 715.715
- 24 August 24 & 25 2015 e-mail exchange Sir RR FRS & Dr DMB AJCN Editor-in-Chief.
- 25 E mail exchange February & March 2014 Dr ACD & Dr KCB, with three highlights
- 26 October 17 2017 3-page OHRP CATS Record by KCB.
- 27 1999-2013 Dr Tang's research publications including human subjects & 2013 cv.
- 28 Pages 2 & 4 June 28 2013 from Online Resource 3 written by Dr DLS, with highlights.

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