

March 19, 2024

Axel Wolff, M.S., D.V.M. Acting Director Office of the Director Office of Laboratory Animal Welfare National Institutes of Health

Brent C. Morse, D.V.M.
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
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Via e-mail: wolffa@od.nih.gov; MorseB@mail.nih.gov

Dear Drs. Wolff and Morse:

I'm writing on behalf of People for the Ethical Treatment of Animals—PETA entities have more than 9 million members and supporters globally—to request that the Office of Laboratory Animal Welfare (OLAW) investigate possible noncompliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) in the use and treatment of animals by Augustine M.K. Choi, a Principal Investigator funded by the National Institutes of Health (NIH).

Dr. Choi is the former Stephen and Suzanne Weiss Dean of Weill Cornell Medicine (Animal Welfare Assurance ID D16-00186) and provost for medical affairs of Cornell University (Animal Welfare Assurance ID D16-00225). He has had at least ten publications retracted in the past several months for image duplication and/or manipulation. 1,2,3,4,5,6,7,8,9,10 Each of these publications was determined to have had either duplicated image panels, spliced images, and/or included images from previous publications. 11,12,13,14,15,16,17,18 Additionally, at least four of Dr. Choi's publications have required corrections, 19,20,21,22 and several other publications for which Dr. Choi is a co-author and/or corresponding author have concerns about duplicated or manipulated images 23,24,25,26,27,28 noted on the online forum PubPeer.

Dr. Choi has received more than \$71 million dollars of research funding from the NIH, and he is currently receiving funding through multiple active projects from the National Heart, Lung, and Blood Institute (NHLBI), including Projects P01-HL-114501, R33-HL-153011, and T32-HL-134629.

Several of the publications in question involve invasive procedures performed on live animals, including infecting mice with lethal doses of infectious agents, cecal ligation punctures used to induce sepsis in mice, and in some cases, procedures that induce lung fibrosis via silica administration.

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

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These research misconduct cases that involve experiments on animals indicate noncompliance with the PHS Policy.

The Health Research Extension Act of 1985 (HREA) provides the statutory mandate for the PHS Policy and asserts, "The Director of NIH shall require each applicant for a grant, contract, or cooperative agreement involving research on animals which is administered by the National Institutes of Health...a statement of the reasons for the use of animals in the research to be conducted with funds provided under such grant or contract." §495(c)(2). If Dr. Choi engaged in research misconduct in projects with animals, as indicated by the publication retractions, such misconduct also calls into question the legitimacy of any statement of reasons that he provided for the use of animals.

Additionally, the <u>U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training</u>, which are part of the PHS Policy, include the principle: "Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society." Any research misconduct by Dr. Choi in projects with animals is out of line with this principle, since any results or publications that arise from the misconduct are not reliable and thus do not have relevance to human or animal health, do not advance knowledge, and do not contribute to the good of society. Rather, research misconduct may actually cause harm to human or animal health, hinder knowledge, and contribute to fraudulent and misinformed aspects of society—all in opposition to the NIH's mission of "making important discoveries that improve health and save lives."

Furthermore, the implementation of the PHS Policy by an institution with a PHS Assurance is reliant upon honesty and transparency from and between an investigator and other staff, the Institutional Animal Care and Use Committee (IACUC), the institutional official (IO), the attending veterinarian, and the NIH. For example, under the PHS Policy, an IACUC must have procedures in place for reviewing concerns about possible non-compliance with the PHS Policy, the IO then has the responsibility to report non-compliance to OLAW, and OLAW decides on a response based on what has been reported. Any research misconduct by Dr. Choi in projects with animals undermines the NIH's obligation to uphold the PHS Policy if Dr. Choi continues to receive NIH funding.

Research misconduct undermines the integrity of the scientific process, erodes public trust in research findings, and can have serious consequences for individuals, institutions, the broader scientific community, and the public at large. And when it comes to animal experimentation, research misconduct adds insult to literal injury and death.

Moreover, the prevalence of research misconduct in animal experimentation highlights a troubling trend in which experimenters prioritize generating publications over advancing medical progress. Instead of focusing on discovering cures or treatments, their primary measure of success lies in the quantity of publications produced, rather than the impact of their research on improving health and saving lives.

We urge you to investigate the concerns summarized in this letter and to take swift and decisive action against Dr. Choi to prevent him from using any NIH funding for projects involving animals. Thank you for your time and consideration.

Sincerely,

Amanda Schemkes, J.D., M.S. Laboratory Oversight Specialist

(lub)

Laboratory Investigations Department

PETA

¹Moon JS, Nakahira K, Chung KP, et al. NOX4-dependent fatty acid oxidation promotes NLRP3 inflammasome activation in macrophages [retracted in: Nat Med. 2023 Dec;29(12):3272]. *Nat Med.* 2016;22(9):1002-1012. doi:10.1038/nm.4153

²Moon JS, Hisata S, Park MA, et al. mTORC1-Induced HK1-Dependent Glycolysis Regulates NLRP3 Inflammasome Activation [retracted in: Cell Rep. 2023 Jun 27;42(6):112639]. *Cell Rep.* 2015;12(1):102-115. doi:10.1016/j.celrep.2015.05.046

³Ryter SW, Choi AM, Kim HP. Profibrogenic phenotype in caveolin-1 deficiency via differential regulation of STAT-1/3 proteins [retracted in: Biochem Cell Biol. 2023 Aug 1;101(4):380]. *Biochem Cell Biol.* 2014;92(5):370-378. doi:10.1139/bcb-2014-0075

⁴Siempos II, Ntaidou TK, Filippidis FT, Choi AM. RETRACTED: Effect of early versus late or no tracheostomy on mortality of critically ill patients receiving mechanical ventilation: a systematic review and meta-analysis [retracted in: Lancet Respir Med. 2015 Feb;3(2):102]. *Lancet Respir Med.* Published online June 26, 2014. doi:10.1016/S2213-2600(14)70125-0

⁵Slebos DJ, Ryter SW, van der Toorn M, et al. Mitochondrial localization and function of heme oxygenase-1 in cigarette smoke-induced cell death [retracted in: Am J Respir Cell Mol Biol. 2023 Apr;68(4):463]. *Am J Respir Cell Mol Biol*. 2007;36(4):409-417. doi:10.1165/rcmb.2006-0214OC

⁶Song R, Mahidhara RS, Liu F, Ning W, Otterbein LE, Choi AM. Carbon monoxide inhibits human airway smooth muscle cell proliferation via mitogen-activated protein kinase pathway [retracted in: Am J Respir Cell Mol Biol. 2023 Jul;69(1):118]. *Am J Respir Cell Mol Biol*. 2002;27(5):603-610. doi:10.1165/rcmb.4851

⁷Wang X, Wang Y, Lee SJ, Kim HP, Choi AM, Ryter SW. Carbon monoxide inhibits Fas activating antibody-induced apoptosis in endothelial cells [retracted in: Med Gas Res. 2023 Oct-Dec;13(4):180]. *Med Gas Res*. 2011;1(1):8. Published 2011 May 18. doi:10.1186/2045-9912-1-8

⁸Moon JS, Lee S, Park MA, et al. UCP2-induced fatty acid synthase promotes NLRP3 inflammasome activation during sepsis. *J Clin Invest*. 2015;125(2):665-680. doi:10.1172/JCI78253

⁹Song R, Ning W, Liu F, et al. Regulation of IL-1beta -induced GM-CSF production in human airway smooth muscle cells by carbon monoxide [retracted in: Am J Physiol Lung Cell Mol Physiol. 2020 Dec 1;319(6):L1062]. *Am J Physiol Lung Cell Mol Physiol*. 2003;284(1):L50-L56. doi:10.1152/ajplung.00212.2002 ¹⁰ Wang X, Wang Y, Kim HP, Nakahira K, Ryter SW, Choi AM. Carbon monoxide protects against hyperoxia-induced endothelial cell apoptosis by inhibiting reactive oxygen species formation [published correction appears in J Biol Chem. 2024 Feb 19;300(3):105758]. *J Biol Chem*. 2007;282(3):1718-1726. doi:10.1074/jbc.M607610200 ¹¹Moon JS, Nakahira K, Chung KP, et al. Retraction Note: NOX4-dependent fatty acid oxidation promotes NLRP3 inflammasome activation in macrophages [retraction of: Nat Med. 2016 Sep;22(9):1002-12]. *Nat Med*. 2023;29(12):3272. doi:10.1038/s41591-023-02723-8

¹²Moon JS, Hisata S, Park MA, et al. Retraction Notice to: mTORC1-Induced HK1-Dependent Glycolysis Regulates NLRP3 Inflammasome Activation [retraction of: Cell Rep. 2015 Jul 7;12(1):102-115]. *Cell Rep.* 2023;42(6):112639. doi:10.1016/j.celrep.2023.112639

¹³Retraction: Profibrogenic phenotype in caveolin-1 deficiency via differential regulation of STAT-1/3 proteins [retraction of: Biochem Cell Biol. 2014 Oct;92(5):370-8]. *Biochem Cell Biol*. 2023;101(4):380. doi:10.1139/bcb-2023-0089

¹⁴The Editors Of The Lancet Respiratory Medicine. Retraction and republication-Effect of early versus late or no tracheostomy on mortality of critically ill patients receiving mechanical ventilation: a systematic review and meta-analysis [retraction of: Lancet Respir Med. 2014 Jun 26;. pii: S2213-2600(14)70125-0. doi: 10.1016/S2213-2600(14)70125-0]. *Lancet Respir Med.* 2015;3(2):102. doi:10.1016/S2213-2600(15)00005-3

¹⁵Retraction: Mitochondrial Localization and Function of Heme Oxygenase-1 in Cigarette Smoke-induced Cell Death [retraction of: Am J Respir Cell Mol Biol. 2007 Apr;36(4):409-17]. *Am J Respir Cell Mol Biol*. 2023;68(4):463. doi:10.1165/rcmb.6804Retraction

¹⁶Retraction: Carbon Monoxide Inhibits Human Airway Smooth Muscle Cell Proliferation via Mitogen-activated Protein Kinase Pathway [retraction of: Am J Respir Cell Mol Biol. 2002 Nov;27(5):603-10]. *Am J Respir Cell Mol Biol.* 2023;69(1):118. doi:10.1165/rcmb.691Retraction

¹⁷Retraction [retraction of: Am J Physiol Lung Cell Mol Physiol. 2003 Jan;284(1):L50-6]. *Am J Physiol Lung Cell Mol Physiol.* 2020;319(6):L1062. doi:10.1152/ajplung.00212.2002_RET

¹⁸Retraction: Carbon monoxide inhibits Fas activating antibody-induced apoptosis in endothelial cells [retraction of: Med Gas Res. 2011 May 18;1(1):8]. *Med Gas Res.* 2023;13(4):180. doi:10.4103/2045-9912.374045

¹⁹Lee CM, He CH, Park JW, et al. Correction: Chitinase 1 regulates pulmonary fibrosis by modulating TGF-β/SMAD7 pathway via TGFBRAP1 and FOXO3. *Life Sci Alliance*. 2023;6(5):e202302065. Published 2023 Apr 10. doi:10.26508/lsa.202302065

²⁰Zhang X, Shan P, Otterbein LE, et al. Correction: Carbon monoxide inhibition of apoptosis during ischemia-reperfusion lung injury is dependent on the p38 mitogen-activated protein kinase pathway and involves caspase 3. *J Biol Chem.* 2023;299(10):105304. doi:10.1016/j.jbc.2023.105304

²¹Li W, Liu H, Zhou JS, et al. Correction: Caveolin-1 inhibits expression of antioxidant enzymes through direct interaction with nuclear erythroid 2 p45-related factor-2 (Nrf2). *J Biol Chem*. 2020;295(28):9766. doi:10.1074/jbc.AAC120.014808

²²Lam HC, Cloonan SM, Bhashyam AR, et al. Histone deacetylase 6-mediated selective autophagy regulates COPD-associated cilia dysfunction. *J Clin Invest*. 2020;130(11):6189. doi:10.1172/JCI143863

²³Lee SJ, Zhang J, Choi AM, Kim HP. Mitochondrial dysfunction induces formation of lipid droplets as a generalized response to stress. *Oxid Med Cell Longev*. 2013;2013:327167. doi:10.1155/2013/327167

²⁴Li CJ, Ning W, Matthay MA, Feghali-Bostwick CA, Choi AM. MAPK pathway mediates EGR-1-HSP70-dependent cigarette smoke-induced chemokine production. *Am J Physiol Lung Cell Mol Physiol*. 2007;292(5):L1297-L1303. doi:10.1152/ajplung.00194.2006

²⁵Kim HP, Wang X, Chen ZH, et al. Autophagic proteins regulate cigarette smoke-induced apoptosis: protective role of heme oxygenase-1. *Autophagy*. 2008;4(7):887-895. doi:10.4161/auto.6767

²⁶Wang X, Wang Y, Zhang J, Kim HP, Ryter SW, Choi AM. FLIP protects against hypoxia/reoxygenation-induced endothelial cell apoptosis by inhibiting Bax activation. *Mol Cell Biol*. 2005;25(11):4742-4751. doi:10.1128/MCB.25.11.4742-4751.2005

²⁷Romero F, Hong X, Shah D, et al. Lipid Synthesis Is Required to Resolve Endoplasmic Reticulum Stress and Limit Fibrotic Responses in the Lung. *Am J Respir Cell Mol Biol*. 2018;59(2):225-236. doi:10.1165/rcmb.2017-0340OC

²⁸Yasuoka H, Zhou Z, Pilewski JM, Oury TD, Choi AM, Feghali-Bostwick CA. Insulin-like growth factor-binding protein-5 induces pulmonary fibrosis and triggers mononuclear cellular infiltration. *Am J Pathol*. 2006;169(5):1633-1642. doi:10.2353/ajpath.2006.060501.