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PETA

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS

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Kristin Bittinger, J.D.
Dean for Faculty & Research Integrity
Office for Academic and Research Integrity

Via e-mail: Kristin_Bittinger@hms.harvard.edu; ari@hms.harvard.edu

Dear Ms. Bittinger:

I'm writing on behalf of People for the Ethical Treatment of Animals (PETA) to request that the Office for Academic and Research Integrity (ARI) at Harvard Medical School investigate Dean George Q. Daley for possible research misconduct.

In recent years, several of Dean Daley's NIH-funded publications have raised concerns amongst the scientific community for their inclusion of duplicated or spliced images. The Daley laboratory has had one publication retracted[1] for errors in *ten separate figures* that could not be supported with original data. Daley's laboratory has also needed to correct several other publications[2,3,4,5] due to duplicated image panels and/or spliced images. Additionally, at least ten of his publications have raised unresolved concerns about duplicated or manipulated images,[6,7,8,9,10,11,12,13,14,15] as flagged on the online forum PubPeer.

For example, in Figure 2B from the *Blood* article, "Generation of induced pluripotent stem cells from human blood,"[12] the panels depicting two different genes' expressions look identical with enhanced contrast. Several commenters on PubPeer have also noted that for the article "LIN28 Regulates Stem Cell Metabolism and Conversion to Primed Pluripotency,"[9] published in *Cell Stem Cell*, numerous figures depict Western blot data with two histone methylation bands. A duplicated image is also used across two different cell lines in Figures 2c and 2d of the *Nature* article "Reprogramming of human somatic cells to pluripotency with defined factors."[15]

As noted by Dr. Elizabeth Bik on PubPeer, the article "The Lin28/let-7 axis regulates glucose metabolism,"[14] published in *Cell*, has multiple irregularities. Specifically, Figures 3D and 4D show Western blots that look identical across two different experimental conditions, and Figure 5A is supposed to be depicting mice of notably different sizes but shows evidence of image cropping. Additionally, Dr. Bik notes on PubPeer that in Supplemental Figure 11A of the

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PNAS article, "Signaling axis involving Hedgehog, Notch, and Scl promotes the embryonic endothelial-to-hematopoietic transition,"[10] two images, purportedly of separate embryos reported to be at different developmental stages and receiving different treatments, look concerningly similar.

Our own analysis using ImageTwin software identified several additional potentially problematic images in other Daley publications. More specifically, in the article "EZH1 repression generates mature iPSC-derived CAR T cells with enhanced antitumor activity,"[16] the images in the fourteenth panel of Figure 1C and the first panel of Figure 2F appear identical. In the article, "LIN28 cooperates with WNT signaling to drive invasive intestinal and colorectal adenocarcinoma in mice and humans",[17] there is evidence of splicing in the second western blot of Figure 1B. For the paper "Embryonic stem cell-derived hematopoietic stem cells," which has already required one published correction by the authors,[3] there are numerous Southern blot abnormalities in Figure 5 indicative of splicing that were *not* addressed in the existing corrigendum. Additionally, there are several instances of apparent splicing in the second panel of Figure 5A in the article, "Disease-Specific Induced Pluripotent Stem Cells."[18]

Dr. Daley has been a Principal Investigator on ten National Institutes of Health (NIH)–funded projects, including an NIH Director's Pioneer Award. He has received $55,344,059 in federal funds for his research. The problematic publications listed above were supported by six separate NIH projects, specifically project numbers R24DK092760, U01HL100001, R01GM107536, RC2DK120535, U01DK104218, and U01HL134812.

It is worth noting that several of the publications in question involved invasive experiments on mice, including, but not limited to breeding mice to have kidney dysfunction, feeding mice a high-fat diet to induce fatty liver disease, diabetes, and/or obesity, drilling holes into the leg bones of mice, and/or injecting cancerous cells into their bodies to create tumors. Most of the mice used in Daley's experiments are killed and dissected, often when they are very young. It is concerning that so many animals were harmed and killed for publications that are, at best, unreliable and, at worst, deliberately misleading.

We request that ARI investigate Dr. Daley to determine whether the problematic images published in the above publications resulted from research misconduct and assess whether this investigator's submitted grant applications and/or progress reports included deliberate manipulation of images and data.

Thank you for your time and consideration.

Sincerely,

Katherine V. Roe, Ph.D.
Chief Scientist
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[1] Soria-Valles C, Osorio FG, Gutiérrez-Fernández A, et al. Retraction Note: NF-κB activation impairs somatic cell reprogramming in ageing [retraction of: Nat Cell Biol. 2015 Aug;17(8):1004-13.
[2] Correction for Jing R, Falchetti M, Han T, et al. Maturation and persistence of CAR T cells derived from human pluripotent stem cells via chemical inhibition of G9a/GLP. *Cell Stem Cell*. Published online January 15, 2025.
[3] Correction for Wang et al., Embryonic stem cell-derived hematopoietic stem cells. *Proc Natl Acad Sci U S A*. 2021;118(31):e2112407118.
[4] Corrigendum to: Functional vascular smooth muscle cells derived from human induced pluripotent stem cells via mesenchymal stem cell intermediates cells via mesenchymal stem cell intermediates. *Cardiovasc Res*. 2020;116(13):2054.
[5] Yermalovich AV, Osborne JK, Sousa P, et al. Author Correction: Lin28 and let-7 regulate the timing of cessation of murine nephrogenesis. *Nat Commun*. 2020;11(1):1327. Published 2020 Mar 9.
[6] Doulatov S, Vo LT, Chou SS, et al. Induction of multipotential hematopoietic progenitors from human pluripotent stem cells via respecification of lineage-restricted precursors. *Cell Stem Cell*. 2013;13(4):459-470.
[7] Goessling W, North TE, Loewer S, et al. Genetic interaction of PGE2 and Wnt signaling regulates developmental specification of stem cells and regeneration. *Cell*. 2009;136(6):1136-1147.
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[15] Park IH, Zhao R, West JA, et al. Reprogramming of human somatic cells to pluripotency with defined factors. *Nature*. 2008;451(7175):141-146.
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[17] Tu HC, Schwitalla S, Qian Z, et al. LIN28 cooperates with WNT signaling to drive invasive intestinal and colorectal adenocarcinoma in mice and humans. *Genes Dev*. 2015;29(10):1074-1086.
[18] Park IH, Arora N, Huo H, et al. Disease-specific induced pluripotent stem cells. *Cell*. 2008;134(5):877-886.