



## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Office of the Secretary

### Findings of Research Misconduct

**AGENCY:** Office of the Secretary, HHS.

**ACTION:** Notice.

**SUMMARY:** Findings of research misconduct have been made against Kotha Subbaramaiah, Ph.D. (Respondent), who was a Professor of Biochemistry Research in Medicine, Department of Medicine, Weill Cornell Medical College (WCMC). Respondent engaged in research misconduct in research supported by U.S. Public Health Service (PHS) funds, specifically National Cancer Institute (NCI), National Institutes of Health (NIH), grants P01 CA077839, P01 CA106451, R01 CA108773, R01 CA154481, T32 CA009685, R25 CA105012, and N01 CN43302, National Institute on Deafness and Other Communication Disorders (NIDCD), NIH, grant T32 DC000027, and National Center for Advancing Translational Sciences (NCATS), NIH, grant UL1 TR000457. The administrative actions, including debarment for a period of seven (7) years, were implemented beginning on August 16, 2023, and are detailed below.

### FOR FURTHER INFORMATION CONTACT:

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**SUPPLEMENTARY INFORMATION:** Notice is hereby given that the Office of Research Integrity (ORI) has taken final action in the following case:

Kotha Subbaramaiah, Ph.D., Weill Cornell Medical College: Based on the report of an investigation conducted by WCMC and additional analysis conducted by ORI in its oversight review, ORI found that Kotha Subbaramaiah, Ph.D., former Weill Cornell Medical College, WCMC, engaged in research misconduct in research supported by PHS funds, specifically NCI,

NIH, grants P01 CA077839, P01 CA106451, R01 CA108773, R01 CA154481, T32 CA009685, R25 CA105012, and N01 CN43302, NIDCD, NIH, grant T32 DC000027, and NCATS, NIH, grant UL1 TR000457.

ORI found that Respondent engaged in research misconduct by intentionally, knowingly, or recklessly falsifying and/or fabricating data included in the following twelve (12) published papers:

- Increased levels of COX-2 and prostaglandin E2 contribute to elevated aromatase expression in inflamed breast tissue of obese women. *Cancer Discov.* 2012 Apr;2(4):356-65. doi: 10.1158/2159-8290.CD-11-0241 (hereafter referred to as “*Cancer Discov.* 2012”). Retraction in: *Cancer Discov.* 2021 May;11(5):1306. doi: 10.1158/2159-8290.CD-21-0224.
- EP2 and EP4 receptors regulate aromatase expression in human adipocytes and breast cancer cells. Evidence of a BRCA1 and p300 exchange. *J Biol Chem.* 2008 Feb 8;283(6):3433-44. doi: 10.1074/jbc.M705409200 (hereafter referred to as “*J Biol Chem.* 2008”). Retraction in: *J Biol Chem.* 2020 Jan 3; 295(1):295. doi: 10.1074/jbc.W119.012140.
- HDAC6 modulates Hsp90 chaperone activity and regulates activation of aryl hydrocarbon receptor signaling. *J Biol Chem.* 2009 Mar 20; 284(12):7436-45. doi: 10.1074/jbc.M808999200 (hereafter referred to as “*J Biol Chem.* 2009”). Retraction in: *J Biol Chem.* 2020 Jan 3; 295(1):297. doi: 10.1074/jbc.W119.012142.
- p53 protein regulates Hsp90 ATPase activity and thereby Wnt signaling by modulating Aha1 expression. *J Biol Chem.* 2014 Mar 7;289(10):6513-25. doi: 10.1074/jbc.M113.532523 (hereafter referred to as “*J Biol Chem.* 2014”). Retraction in: *J Biol Chem.* 2020 Jan 3; 295(1):289. doi: 10.1074/jbc.W119.012134.
- Hsp90 and PKM2 drive the expression of aromatase in Li-Fraumeni syndrome breast adipose stromal cells. *J Biol Chem.* 2016 Jul 29;291(31):16011-23. doi: 10.1074/jbc.M115.698902 (hereafter referred to as “*J Biol Chem.* 2016”). Retraction in: *J Biol Chem.* 2020 Jan 3; 295(1):290. doi: 10.1074/jbc.W119.012135.

- Heat shock protein 90 inhibitors suppress aryl hydrocarbon receptor-mediated activation of CYP1A1 and CYP1B1 transcription and DNA adduct formation. *Cancer Prev Res (Phila)*. 2008 Nov;1(6):485-93. doi: 10.1158/1940-6207.CAPR-08-0149 (hereafter referred to as “*Cancer Prev Res*. 2008”). Retraction in: *Cancer Prev Res (Phila)*. 2022 Jun 2;15(6):415. doi: 10.1158/1940-6207.CAPR-22-0200.
- Obesity is associated with inflammation and elevated aromatase expression in the mouse mammary gland. *Cancer Prev Res (Phila)*. 2011 Mar;4(3):329-46. doi: 10.1158/1940-6207.CAPR-10-0381 (hereafter referred to as “*Cancer Prev Res*. 2011”). Retraction in: *Cancer Prev Res (Phila)*. 2022 Jun 2; 15(6):413. doi: 10.1158/1940-6207.CAPR-22-0202.
- Carnosol, a constituent of Zyflamend, inhibits aryl hydrocarbon receptor-mediated activation of CYP1A1 and CYP1B1 transcription and mutagenesis. *Cancer Prev Res (Phila)*. 2012 Apr;5(4):593-602. doi: 10.1158/1940-6207.CAPR-12-0002 (hereafter referred to as “*Cancer Prev Res*. 2012a”). Retraction in: *Cancer Prev Res (Phila)*. 2022 Jun 2;15(6):412. doi: 10.1158/1940-6207.CAPR-22-0203.
- Pioglitazone, a PPAR $\gamma$  agonist, suppresses CYP19 transcription: evidence for involvement of 15-hydroxyprostaglandin dehydrogenase and BRCA1. *Cancer Prev Res (Phila)*. 2012 Oct;5(10):1183-94. doi: 10.1158/1940-6207.CAPR-12-0201 (hereafter referred to as “*Cancer Prev Res*. 2012b”). Retraction in: *Cancer Prev Res (Phila)*. 2022 Jun 2;15(6):411. doi: 10.1158/1940-6207.CAPR-22-0204.
- Caloric restriction reverses obesity-induced mammary gland inflammation in mice. *Cancer Prev Res (Phila)*. 2013 Apr;6(4):282-9. doi: 10.1158/1940-6207.CAPR-12-0467 (hereafter referred to as “*Cancer Prev Res*. 2013”). Retraction in: *Cancer Prev Res (Phila)*. 2022 Jun 2; 15(6):410. doi: 10.1158/1940-6207.CAPR-22-0205.
- p53 modulates Hsp90 ATPase activity and regulates aryl hydrocarbon receptor signaling. *Cancer Prev Res (Phila)*. 2014 Jun;7(6):596-606. doi: 10.1158/1940-6207.CAPR-14-0051

(hereafter referred to as “*Cancer Prev Res.* 2014”). Retraction in: *Cancer Prev Res* (Phila). 2022 Jun 2;15(6):408. doi: 10.1158/1940-6207.CAPR-22-0207.

- Id1 deficiency protects against tumor formation in Apc(Min/+) mice but not in a mouse model of colitis-associated colon cancer. *Cancer Prev Res* (Phila). 2015 Apr;8(4):303-11. doi: 10.1158/1940-6207.CAPR-14-0411 (hereafter referred to as “*Cancer Prev Res.* 2015”). Retraction in: *Cancer Prev Res* (Phila). 2022 Jun 2;15(6):407. doi: 10.1158/1940-6207.CAPR-22-0208.

Specifically, ORI found that Respondent reused Western blot images from the same source and falsely relabeled them to represent different proteins and/or experimental results in:

- *Cancer Discov.* 2012:
  - Figure 2B,  $\beta$ -Actin panel, representing  $\beta$ -Actin expression in inflamed breast tissue with different levels of inflammation:
    - All lanes are duplicated by reusing a same source band with manipulation
  - Figure 4C, representing the expression of progesterone receptor (PR) and  $\beta$ -Actin in inflamed breast tissue with different levels of inflammation:
    - PR panel: Lanes 1, 2, and 14-16 are duplicated by reusing a same source band with manipulation; lanes 3, 6-9, 13, and 17 are duplicated by reusing a same source band with manipulation
    - $\beta$ -Actin panel: All lanes are duplicated by reusing a same source band with manipulation
  - Figure 5H,  $\beta$ -Actin panel, representing  $\beta$ -Actin expression in macrophages with different treatments:
    - Lane 2 and lane 4 are identical
- *J Biol Chem* 2008
  - Figure 2B, lanes 1-3, aromatase panel, representing aromatase expression in adipocytes treated with PGE1 alcohol, and Figure 2E, lanes 2-4, Aromatase panel, representing

aromatase expression in adipocytes treated with PGE<sub>2</sub> with or without ONO, are duplicated by reusing the same source images with manipulation

- Figure 3B, 18S rRNA panel, representing 18S rRNA expression in adipocytes with different treatments:
  - Lanes 2 and 6 are identical
  - Lanes 3 and 7 are identical
- Figure 5A, 18S rRNA panel, representing 18S rRNA expression in adipocytes treated with different doses of PGE<sub>2</sub>:
  - Lanes 1 and 5 are identical
  - Lanes 2 and 6 are identical
- Figure 5B, β-actin panel, representing β-actin expression in adipocytes treated with different doses of PGE<sub>2</sub>:
  - Lanes 1, 3, and 4 are identical
- Figure 6D, BRCA1 and Aromatase panels, representing expression of both BRCA1 and aromatase in SKBR3 cells treated with different doses of PGE1 alcohol:
  - Lanes 3-4, BRCA1 panel and lanes 1-2, Aromatase panel are duplicated by reusing the same source images with manipulation
- Figure 5A, BRCA1 panel, representing BRCA1 expression in adipocytes treated with different doses of PGE<sub>2</sub>:
  - Lanes 3-6 are falsified and/or fabricated
- Figure 5C, 18S rRNA panel, representing 18S rRNA expression in adipocytes treated with different doses of butaprost:
  - Entire 18S rRNA panel is falsified and/or fabricated
- Figure 5E:
  - Lane 4, BRCA1 panel and lane 1, 18S rRNA panel are identical
- Figures 6C, 6D, 6E, and 6F:

- Images used in the following figures are duplicated by reusing the same source images with manipulation:
  - Figure 6C, lane 1, BRCA1 panel, representing BRCA1 expression in control sample without treatment of butaprost
  - Figure 6C, lane 3, Aromatase panel, representing aromatase expression with 0.25  $\mu\text{M}$  butaprost treatment
  - Figure 6D, lane 1, BRCA1 panel, representing BRCA1 expression in control sample without treatment of PGE1 alcohol
  - Figure 6F, lane 1, BRCA1 panel, representing BRCA1 expression in control sample without treatment of PGE<sub>2</sub> and ONO
- Images used in the following figures are duplicated by reusing the same source images with manipulation:
  - Figure 6C, lane 2, BRCA1 panel, representing BRCA1 expression in sample treated with 0.10  $\mu\text{M}$  butaprost
  - Figure 6D, lane 3, Aromatase panel, representing aromatase expression in sample treated with 0.25  $\mu\text{M}$  PGE1 alcohol
- Images used in the following figures are duplicated by reusing the same source images with manipulation:
  - Figure 6C, lane 3, BRCA1 panel, representing BRCA1 expression in sample treated with 0.25  $\mu\text{M}$  butaprost
  - Figure 6D, lane 3, BRCA1 panel, representing BRCA1 expression in sample treated with 0.25  $\mu\text{M}$  PGE1 alcohol
  - Figure 6D, lane 2, Aromatase panel, representing aromatase expression in sample treated with 0.10  $\mu\text{M}$  PGE1 alcohol
- Images used in the following figures are duplicated by reusing the same source images with manipulation:

- Figure 6C, lane 4, BRCA1 panel, representing BRCA1 expression in sample treated with 0.50  $\mu\text{M}$  butaprost
- Figure 6C, lane 1, Aromatase panel, representing aromatase expression in control sample without treatment of butaprost
- Figure 6D, lane 1, Aromatase panel, representing aromatase expression in control sample without treatment of PGE1 alcohol
- Figure 6E, lane 2, BRCA1 panel, representing BRCA1 expression in sample treated with PGE<sub>2</sub> without AH6809
- Images used in the following figures are duplicated by reusing the same source images with manipulation:
  - Figure 6C, lane 2, Aromatase panel, representing aromatase expression in sample treated with 0.10  $\mu\text{M}$  butaprost
  - Figure 6E, lane 3, BRCA1 panel, representing BRCA1 expression in sample treated with PGE<sub>2</sub> and 25  $\mu\text{M}$  AH6809
  - Figure 6F, lane 2, BRCA1 panel, representing BRCA1 expression in sample treated with PGE<sub>2</sub> but without ONO
- Images used in the following figures are duplicated by reusing the same source images with manipulation:
  - Figure 6C, lane 4, Aromatase panel, representing aromatase expression in sample treated with 0.50  $\mu\text{M}$  butaprost
  - Figure 6D, lane 2, BRCA1 panel, representing BRCA1 expression in sample treated with 0.10  $\mu\text{M}$  PGE1 alcohol
  - Figure 6E, lane 4, BRCA1 panel, representing BRCA1 expression in sample treated with PGE<sub>2</sub> and 50  $\mu\text{M}$  AH6809
  - Figure 6F, lane 3, BRCA1 panel, representing BRCA1 expression in sample treated with PGE<sub>2</sub> and 0.10  $\mu\text{M}$  ONO

- Images used in the following figures are duplicated by reusing the same source images with manipulation:
  - Figure 6D, 18S rRNA panel, representing 18S rRNA expression in samples treated with different doses of PGE<sub>1</sub> alcohol
  - Figure 6F, 18S rRNA panel, representing 18S rRNA expression in samples treated with different doses of PGE<sub>2</sub> and ONO
- *J Biol Chem.* 2009:
  - Figures 2A and 2B,  $\beta$ -actin panels, representing  $\beta$ -actin expression in KYSE450 cells and MSK-Leuk1 cells, respectively:
    - The two panels are identical
  - Figure 3B, representing protein expression at two different time points:
    - Column 4, 1-hour panel, and column 2, 3-hour panel, are duplicated by reusing the same source images with resizing
  - Figure 6H, representing expression of different proteins with different treatments:
    - Column 1, Control group and column 3, Control siRNA group are identical
  - Figure 6I, representing expression of different proteins with different treatments:
    - Lanes 2 and 5, column 1 are identical
    - Lane 3, column 1 and lane 5, column 2 are identical
  - Figure 8G, Input panel, representing input protein expression in A549 cells with different treatments:
    - Lanes 2 and 3 are identical
  - Figure 9B, Input panel, representing input protein expression in different samples:
    - Lanes 2 and 3 are identical
  - Figures 8E and 9D:
    - Images used in the following figures are duplicated by reusing a same source band with resizing:

- Figure 8E, lane 2, AhR panel, representing AhR expression in sample treated with B[a]P
- Figure 9D, lane 3,  $\beta$ -actin panel, representing  $\beta$ -actin expression in K/R sample treated with TS
- Figure 9D,  $\beta$ -actin panel, representing  $\beta$ -actin expression under different experimental conditions:
  - Lane 1 is falsified and/or fabricated
- Figure 9C, Input panel, representing input protein expression in K/A sample:
  - Lane 5 is falsified and/or fabricated
- Figure S1A, p23 panel, representing p23 expression in MSK-Leuk1 cells and A549 cells:
  - Lanes 1 and 2 are identical
- Figure S1C, XAP-2 panel, representing XAP-2 expression in control and sample treated with HDAC6 KD:
  - Lanes 1 and 2 are identical
- Figure S1B, representing expression of different proteins in MSK-Leuk1 cells with different treatments:
  - Lanes 3 and 4, Hsp90 panel are identical
  - Lanes 1 and 2, AhR panel are identical
  - Lanes 1 and 2,  $\beta$ -actin panel are identical
  - Lanes 3 and 4,  $\beta$ -actin panel are identical
- Figure S1E, representing expression of different proteins in MSK-Leuk1 cells with different treatments:
  - Lane 1, Hsp90 panel, and lanes 1 and 2, HDAC6 panel, are identical
  - Lane 3, Hsp90 panel, and lane 3, XAP-2 panel, are identical
- Figure S2, representing expression of different proteins in MSK-Leuk1 cells with different treatments:
  - Last lane, IB AcK panel, and lanes 3 and 5, IB HSP90 panel, are duplicated with resizing

- Lane 4, IB AcK panel, and lanes 1, 4, and 6, IB HSP90 panel, are duplicated with resizing
- Lane 4, IB AcK panel, is falsified and/or fabricated
- *J Biol Chem.* 2014:
  - Figure 1D, representing expression of different proteins treated with control or p53 siRNA:
    - Lane 1, p53 panel, and lanes 1 and 2,  $\beta$ -actin panel, are duplicated by reusing a same source band with manipulation
  - Figure 2B,  $\beta$ -actin panel, representing  $\beta$ -actin expression in HCT-15 cells treated with different doses of CP-31398:
    - Lane 1 and lane 5 are identical
    - Lane 2 and lane 6 are identical
  - Figure 4K, p23 panel, representing p23 expression in samples treated with different doses of CP-31398 in HCT-15 cells:
    - Lanes 2-4 are identical
  - Figures 4H, 4I, and 4L,  $\beta$ -actin panels, representing  $\beta$ -actin expression under different experimental conditions:
    - $\beta$ -actin panels in Figures 4H and 4I, and lanes 3-4,  $\beta$ -actin panel in Figure 4L are duplicated by reusing the same source images with manipulation
  - Figures 4J, 4K, and 4L, representing expression of HOP (Figure 4J) and  $\beta$ -actin (Figures 4K and 4L) under different experimental conditions:
    - Lanes 1-2, HOP panel in Figure 4J, lanes 3-4,  $\beta$ -actin panel in Figure 4K, and lanes 1-2,  $\beta$ -actin panel in Figure 4L are duplicated by reusing the same source images with manipulation
  - Figures 5A and 5B,  $\beta$ -actin panels, representing  $\beta$ -actin expression in both HCT-15 cells and EB-1 cells, are identical

- Figure 5H, c-Myc panel and Naked-1 panel, representing expression of c-Myc and Naked-1 in EB-1 cells, are duplicated with resizing
- Figures 10A and 10B, representing  $\beta$ -actin (Figure 10A) and Aha1 (Figure 10B) expression:
  - Lanes 2-3,  $\beta$ -actin panel in Figure 10A and lanes 2-3, Aha1 panel in Figure 10B are duplicated with resizing
- *J Biol Chem.* 2016:
  - Figures 1C and 7A,  $\beta$ -actin panels, representing  $\beta$ -actin expression in different cells:
    - Lanes 1-2,  $\beta$ -actin panel in Figure 1C and lanes 2-3,  $\beta$ -actin panel in Figure 7A are duplicated by reusing the same source images with manipulation
  - Figure 5B, representing expression of different proteins with different treatments:
    - Lane 6, PKM2 panel, and lane 5, Hsp90 panel, are identical
  - Figure 5A, representing expression of different proteins with different treatments:
    - Lane 2, HIF-1 $\alpha$  panel, and lane 1,  $\beta$ -actin panel, are identical
- *Cancer Prev Res.* 2008:
  - Figure 2B,  $\beta$ -actin panel, representing  $\beta$ -actin expression in different cells with different treatments:
    - Left middle  $\beta$ -actin panel and right middle  $\beta$ -actin panel are duplicated by reusing the same source images with manipulation
  - Figures 3A and 3B,  $\beta$ -actin panels, representing  $\beta$ -actin expression in different cells with different treatments:
    - Left top  $\beta$ -actin panel in Figure 3A and left top  $\beta$ -actin panel in Figure 3B are identical
    - Right top  $\beta$ -actin panel in Figure 3A and left bottom  $\beta$ -actin panel in Figure 3B are duplicated by reusing the same source images with manipulation

- Right bottom  $\beta$ -actin panel in Figure 3A and right bottom  $\beta$ -actin panel in Figure 3B are identical
- *Cancer Prev Res.* 2011:
  - Figure 3A, representing expression of different proteins with different treatments:
    - Lane 1, aP2 panel, is falsified and/or fabricated
    - Lanes 3 and 5, aP2 panel, and lanes 1-6, 18S rRNA panel, are identical
- *Cancer Prev Res.* 2012a:
  - Figure 4A, representing input expression treated with different doses of Zyflamend with or without 17-AAG:
    - Lanes 1-5 are identical
    - Lanes 6-7 are identical
  - Figure 4B, representing input expression treated with different doses of carnosol with or without 17-AAG:
    - Lanes 1-5 are identical
- *Cancer Prev Res.* 2012b:
  - Figure 2, representing expression of different proteins under different experimental conditions:
    - Lane 1, 15-PGDH panel in Figure 2B and lanes 3-4,  $\beta$ -Actin panel in Figure 2E are duplicated by reusing a same source band with manipulation
    - Lane 2,  $\beta$ -Actin panel in Figure 2B and lane 1, Snail panel in Figure 2E are duplicated by reusing a same source band with manipulation
    - Lane 3, Snail panel in Figure 2G and lane 1, 15-PGDH panel in Figure 2H are duplicated by reusing a same source band with manipulation
    - Lanes 1 and 2,  $\beta$ -Actin panel in Figure 2H are duplicated by reusing a same source band with manipulation

- Lanes 1-3,  $\beta$ -Actin panel in Figure 2J and lanes 1-2,  $\beta$ -Actin panel in Figure 2K are duplicated by reusing a same source band with manipulation
- Figure 4E,  $\beta$ -Actin panel, representing  $\beta$ -actin expression in control and pioglitazone samples:
  - Lanes 1 and 2 are identical
- *Cancer Prev Res.* 2013:
  - Figure 3, representing binding of nuclear protein from mammary glands of mice with different treatments:
    - Lanes 7-9 (first three empty lanes are counted also) and lanes 13-15 are identical
- *Cancer Prev Res.* 2014:
  - Figures 5A and 5C, representing expression of different proteins with different treatments:
    - Lanes 2-3, CYP1A1 panel, and lanes 2-3, CYP1B1 panel, in Figure 5A and lane 3, CYP1B1 panel, in Figure 5C are duplicated by reusing a same source band with manipulation
  - Figure 5B,  $\beta$ -actin panel, representing  $\beta$ -actin expression in different cells with different treatments:
    - Lanes 2-4 are identical
  - Figure 5D,  $\beta$ -actin panel, representing  $\beta$ -actin expression in different cells with different treatments:
    - Lanes 1-4 are duplicated by reusing a same source band with manipulation
- *Cancer Prev Res.* 2015:
  - Figure 3A,  $\beta$ -actin panel, representing  $\beta$ -actin expression in DLD-1 treated with different doses of PGE<sub>2</sub>:
    - Lanes 1, 3, and 5 are identical
    - Lanes 2 and 4 are identical

Respondent entered into a Voluntary Exclusion Agreement (Agreement) and voluntarily agreed to the following:

- (1) Respondent will exclude himself voluntarily for a period of seven (7) years beginning on August 16, 2023 (the “Exclusion Period”), from any contracting or subcontracting with any agency of the United States Government and from eligibility for or involvement in nonprocurement or procurement transactions referred to as “covered transactions” in 2 CFR parts 180 and 376 (collectively the “Debarment Regulations”).
- (2) During the Exclusion Period, Respondent will exclude himself voluntarily from serving in any advisory or consultant capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee.

**Dated:** September 8, 2023.

**Sheila Garrity,**

*Director, Office of Research Integrity,*

*Office of the Assistant Secretary for Health.*

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