Billing Code: 4150-31

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 Dr. Sudhakar Yakkanti (Respondent) (formerly named Sudhakar Akulapalli),[1] former staff scientist and Director of the Cell Signaling, Retinal & Tumor Angiogenesis Laboratory, Boys Town National Research Hospital (BTNRH). 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), grant R01 CA143128, National Eye Institute (NEI), NIH, grants R01 EY018179 and R01 EY16695, and National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), NIH, grants R01 DK055000, R01 DK055001, R01 DK062987, and R01 DK051711. The administrative actions, including debarment for a period of five (5) years, were implemented beginning on August 24, 2019, and are detailed below.

FOR FURTHER INFORMATION CONTACT:

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[1]The Respondent changed his name from Sudhakar Akulapalli to Sudhakar Yakkanti during the BTNRH inquiry.

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

Dr. Sudhakar Yakkanti, Boys Town National Research Hospital: Based upon the evidence and findings of an investigation report by BTNRH and additional information obtained by ORI during its oversight review of the BTNRH investigation, ORI found that Dr. Sudhakar Yakkanti, former staff scientist and Director of the Cell Signaling, Retinal & Tumor Angiogenesis Laboratory, BTNRH, engaged in research misconduct in research supported by PHS funds, specifically, NCI, NIH, grant R01 CA143128, NEI, NIH, grants R01 EY018179 and R01 EY16695, and NIDDK, NIH, grants R01 DK055000, R01 DK055001, R01 DK062987, and R01 DK051711.

ORI found by a preponderance of the evidence that Respondent intentionally, knowingly, or recklessly falsified and/or fabricated figures in the following eight (8) unfunded NIH grant applications, one (1) funded NIH grant application, seven (7) publications, and two (2) unpublished manuscripts:

- R01 CA115763-01A2 submitted to NCI, NIH (unfunded)

- R21 CA155796-01 submitted to NCI, NIH (unfunded)

- R01 CA166195-01 submitted to NCI, NIH (unfunded)

- R01 CA143128-01 submitted to NCI, NIH (unfunded)

- R01 CA143128-04 submitted to NCI, NIH (unfunded)

- R01 EY020539-01 submitted to NEI, NIH (unfunded)

- R01 EY020539-01A1 submitted to NEI, NIH (unfunded)

- R01 EY024967-01 submitted to NEI, NIH (unfunded)

- R01 CA143128-01A1 submitted to NCI, NIH (funded)

- *Biochemistry* 2000;39(42):12929-12938 (hereafter referred to as "*Biochem* 2000")

- *Proc. Natl. Acad. Sci. U.S.A.* 2003;100(8):4766-4771 (hereafter referred to as "*PNAS* 2003")

- *The Journal of Clinical Investigation* 2005;115(10):2801-2810 (hereafter referred to as "*JCI* 2005")

- *Invest. Ophthalmol. Vis. Sci*. 2009;50(10):4567-4575 (hereafter referred to as "*IOVS* 2009")

- *Pharmaceutical Research* 2008;25(12):2731-2739 (hereafter referred to as "*Pharm Research* 2008")

- *Scientific Reports* 2014;4(4136):1-9 (hereafter referred to as "*Sci Reports* 2014")

- *Current Eye Res.* 2010 Jan;35(1):44-55 (hereafter referred to as "*CER* 2010")

- Tumstatin inhibits Choroidal Neovascularization by Inhibiting MMP-2 activation *in-vitro* and *in vivo*. Submitted to *Molecular Vision* on February 7, 2011 (hereafter referred to as "*Mol Vis* Sub 2011") (unpublished)

- Inhibitory Effect of Tumstatin on Corneal Neovascularization Both *In-vitro* and *In-vivo*. Submitted to *Journal of Clinical & Experimental Ophthalmology* on January 16, 2011 (hereafter referred to as "*JCEO* Sub 2011") (unpublished)

Specifically, ORI found by a preponderance of the evidence that Respondent engaged in research misconduct by intentionally, knowingly, or recklessly:

- falsifying an image from an *in vivo* choroidal neovascularization (CNV) experiment by falsely relabeling an image representing results from an experiment with the anti-angiogenic molecule arresten (α1NC1) to represent results from a different CNV experiment with a different anti-angiogenic molecule, hexastatin (α6NC1) in Figure 9A (right panel) of grant application R01 CA166195-01
- falsifying an image from an *in vivo* CNV experiment by falsely relabeling an image representing results from an

experiment with the anti-angiogenic molecule hexastatin (α6NC1) to represent results from different CNV experiments with different anti-angiogenic molecules:

  - arresten (α1NC1) in Figure 10A (right panel) of grant application R01 EY020539-01A1

  - tumstatin (α3NC1) in Figure 6A (right panel) of *Mol Vis* Sub 2011

- falsifying and/or fabricating bar graphs in Figure 9B of grant application R01 CA166195-01, which was based on the falsified image in Figure 9A (right panel) of grant application R01 CA166195-01

- falsifying and/or fabricating bar graphs in Figure 6B of *Mol Vis* Sub 2011, which was based on the falsified image in Figure 6A (right panel) of *Mol Vis* Sub 2011

- falsifying and/or fabricating bar graphs in Figure 10B of grant application R01 EY020539-01A1, which was based on the falsified image in Figure 10A of grant application R01 EY020539-01A1

- falsifying microscope images of endothelial tube formation assays by labeling one image as two different experiments:

  - a control in an experiment performed in Human umbilical vein endothelial cells (HUVECs) in Figure 1D (first panel) of grant application R21 CA155796-01

- a control in an experiment performed in mouse choroidal endothelial cells (MCECs) in Figure 2B (first panel) of grant application R01 EY020539-01A1

- falsifying microscope images of endothelial tube formation assays by reusing and falsely labeling one image as three different experiments:

  - HUVECs treated with 0.5 μM hexastatin (α6(IV)NC1) in Figure 1D (third panel) of grant application R21 CA155796-01

  - MCECs treated with 0.5 μM arresten (α1(IV)NC1) in Figure 2B (second panel) of grant application R01 EY020539-01A1

  - MCECs treated with 1.0 μM tumstatin (α3(IV)NC1) in Figure 2C (bottom right panel) of *Mol Vis* Sub 2011

- falsifying Western blot images by reusing and falsely labeling one image as four different experiments:

  - the protein band FAK from HUVECs treated with hexastatin (α6(IV)NC1) in Figure 3A (bottom panel) of grant application R21 CA155796-01 and Figure 4A (bottom panel) of grant application R01 CA166195-01

  - the protein band FAK from MCECs treated with arresten (α1(IV)NC1) in Figure 5A (bottom panel) of grant application R01 EY020539-01A1

- the protein band Raf from HUVECs treated with rh-Endo in Figure 5A (bottom panel) of *PNAS* 2003

- the protein band FAK from mouse retinal pigmented epithelial cell (MRPECs) treated with arresten (α1(IV)NC1) in Figure 5B (bottom panel) of grant application R01 EY020539-01 and in Figure 7B (bottom panel) of *IOVS* 2009

- falsifying Western blot images by reusing and falsely labeling one image as two different experiments:

  - HUVECs treated with rh-Endo in Figure 5D (middle panel) of *PNAS* 2003

  - mouse retinal endothelial cells (MRECs) treated with arresten (α1(IV)NC1) in Figure 7C (top panel) of *IOVS* 2009

- falsifying Western blot images by reusing and falsely labeling one image as two different experiments:

  - HUVECs treated with hexastatin (α6(IV)NC1) in Figure 3C (top panel) of grant application R21 CA155796-01
  - MCECs treated with arresten (α1(IV)NC1) in Figure 5B (top panel) of grant application R01 EY020539-01A1

- falsifying Western blot images by reusing and falsely labeling one image as two different experiments:

- HUVECs treated with hexastatin (α6(IV)NC1) in Figure 3C (bottom panel) of grant application R21 CA155796-01

- MCECs treated with arresten (α1(IV)NC1) in Figure 5B (bottom panel) of grant application R01 EY020539-01A1

- falsifying Western blot images by reusing and falsely labeling one image as two different experiments:

  - HUVECs treated with hexastatin (α6(IV)NC1) in Figure 3D (top panel) of grant application R21 CA155796-01

  - MCECs treated with arresten (α1(IV)NC1) in Figure 5C (top panel) of grant application R01 EY020539-01A1

- falsifying Western blot images by reusing and falsely labeling one image as two different experiments:

  - HUVECs treated with hexastatin (α6(IV)NC1) in Figure 3D (bottom panel) of grant application R21 CA155796-01,

  - MCECs treated with arresten (α1(IV)NC1) in Figure 5C (bottom panel) of grant application R01 EY020539-01A1

- falsifying Western blot images by reusing and falsely labeling one image as three different experiments:

- the protein band FAK(P) from HUVECs treated with rh-Endo in Figure 4A (top panel) of *PNAS* 2003

- the protein band Cox-2 from HUVECs treated with arresten (α1(IV)NC1) in Figure 2B (top panel) of grant application R01 CA115763-01A2, Figure 2B (top panel) of grant application R01 CA143128-01, and Figure 2B (top panel) of grant application

  R01 CA143128-01A1

- the protein band Cox-2 from MCECs treated with arresten (α1(IV)NC1) in Figure 5C (top panel) of grant application R01 CA143128-04 and Figure 8B (top panel) of

  R01 EY024967-01

- falsifying Western blot images by reusing and falsely labeling one image as two different experiments:

  - the protein band eIF2α 51A in Figure 1A (lanes 3-5) of *Biochem* 2000

  - the protein band tumstatin (α3(IV)NC1) in Figure 2 (lanes 2-4) of *Pharm Research* 2008

- falsifying Western blot images by reusing and falsely labeling one image as two different experiments:

  - the protein band active MMP-2 in Figure 10D (top panel, lanes 1-4) of grant application R01 CA115763-01A2, Figure 10B of grant application R01 CA143128-01, Figure 10B (third panel, lanes 1-4) of grant application R01 CA143128-01A1, and Figure 7D (third panel, lanes 1-4) of grant application R01 EY020539-01A1

- the protein band arresten (α1(IV)NC1) in Figure 3C (lanes 3-6) of *Sci Reports* 2014, Figure 6D (lanes 3-6) of grant application R01 CA143128-04, and Figure 9D (lanes 3-6) of grant application R01 EY024967-01

- falsifying Western blot images by reusing and falsely labeling one image as three different experiments:

  - the protein band Raf from mouse lung endothelial cells (MLECs) at the time points 0, 5, 10, 20, and 30 minutes in Figure 5A (bottom panel, lanes 1-5) of *JCI* 2005

  - the protein band FAK(P) from MRECs at the time points 20 and 40 minutes in Figure 7A (top panel, lanes 2 and 4) of *IOVS* 2009 and Figure 5A (top panel, lanes 2 and 4) of grant application R01 EY020539-01

  - the protein band FAK from MRECs at the time points 0, 20, 20, 40, and 40 minutes in Figure 7A (bottom panel, lanes 1-5) of *IOVS* 2009 and Figure 5A (bottom panel, lanes 1-5) of grant application R01 EY020539-01

- falsifying images of corneas by reusing and falsely labeling one image as two different experiments:

  - CNV cornea treated with arresten (α1(IV)NC1) in Figure 13 (right panel) of grant application R01 EY020539-01

  - CNV cornea treated with tumstatin (α3(IV)NC1) in Figure 3A (right panel) of *JCEO* Sub 2011

- falsifying images of corneal sections by reusing and falsely labeling one image as two different experiments:

  - CNV cornea treated with arresten (α1(IV)NC1) in Figure 14 (right panel) of grant application R01 EY020539-01

  - CNV cornea treated with tumstatin (α3(IV)NC1) in Figure 4 (right panel) of *JCEO* Sub 2011

- falsifying endothelial cell migration assays by reusing and falsely labeling one image as two different experiments:

  - MRECs treated with vascular endothelial growth factor (VEGF) and arresten (α1(IV)NC1) in Figure 2A (top right panel) of *IOVS* 2009 and Figure 2 (top right panel) of grant application R01 EY020539-01

  - HUVECs treated with only VEGF in Figure 1C (middle panel) of grant application R21 CA155796-01 and Figure 2C (second panel) of grant application R01 CA166195-01

- falsifying endothelial cell migration assays by reusing and falsely labeling one image as two different experiments:

  - MRECs treated with VEGF in Figure 2A (top middle panel) of *IOVS* 2009 and Figure 2 (top middle panel) of grant application R01 EY020539-01

- MRECs treated with basic fibroblast growth factor (bFGF) in Figure 3A (second panel) of *CER* 2010

- falsifying endothelial cell migration assays by reusing and falsely labeling one image as two different experiments:

  - MRECs treated with bFGF and arresten (α1NC1) in Figure 3A (fourth panel) of *CER* 2010

  - MRECs treated with VEGF and arresten (α1NC1) in Figure 2A (bottom middle panel) of *IOVS* 2009 and Figure 2 (bottom middle panel) of grant application R01 EY020539-01

- falsifying endothelial cell migration assays by reusing and falsely labeling one image as three different experiments:

  - MRECs treated with bFGF and 10 μg/ml arresten (α1NC1) in Figure 3A (fifth panel) of *CER* 2010

  - HUVECs treated with VEGF and 0.5 μM hexastatin (α6NC1) in Figure 1C (last panel) of grant application R21 CA155796-01

  - HUVECs treated with VEGF and 0.25 μM hexastatin (α6NC1) in Figure 2C (third panel) of grant application R01 CA166195-01

The following administrative actions have been implemented, beginning on August 24, 2019:

(1) Respondent is debarred for a period of five (5) years from eligibility for any contracting or subcontracting with any agency of the United States Government and from eligibility for, or involvement in, nonprocurement programs of the United States Government referred to as "covered transactions" pursuant to HHS' Implementation (2 C.F.R. Part 376 *et seq*) of Office of Management and Budget (OMB) Guidelines to Agencies on Governmentwide Debarment and Suspension, 2 C.F.R. Part 180 (collectively the "Debarment Regulations");

(2) Respondent is prohibited from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant for a period of five (5) years; and

(3) in accordance with 42 C.F.R. 93 §§ 93.407(a)(1) and 93.411(b), HHS will send a notice of the findings and of the need for correction or retraction to the pertinent journals for each of the following:

- *Biochemistry* 2000;39(42):12929-12938
- *Proc. Natl. Acad. Sci. U.S.A.* 2003;100(8):4766-4771
- *The Journal of Clinical Investigation* 2005;115(10):2801-2810
- *Invest. Ophthalmol. Vis. Sci*. 2009;50(10):4567-4575
- *Pharmaceutical Research* 2008;25(12):2731-2739

- *Scientific Reports* 2014;4(4136):1-9
- *Current Eye Res.* 2010 Jan;35(1):44-55

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[FR Doc. 2019-24689 Filed: 11/13/2019 8:45 am; Publication Date: 11/14/2019]